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Bernadette Juarez
United States Department of Agriculture
Animal and Plant Health Inspection Service
Biotechnology Regulatory Services
4700 River Road Unit 147
Riverdale, MD 20737-1236

Re: Request for a Regulatory Status Review of Glufosinate, Dicamba, 2,4-Dichlorophenoxyacetic Acid and Mesotrione Tolerant Soybean MON 94313

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July 22, 2022

Jessica Fernandez
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Bernadette Juarez:

Bayer CropScience LP is submitting this request to USDA-APHIS for an initial Regulatory Status Review (RSR) of the enclosed information in regards to a determination of nonregulated status for the new genetically engineered (GE) soybean product, MON 94313, any progeny derived from crosses between MON 94313 and conventional soybean, and any progeny derived from crosses between MON 94313 and other GE soybean not subject to 7 CFR Part 340 regulations.

Bayer has developed herbicide tolerant MON 94313 soybean, which is tolerant to the herbicides glufosinate (2-amino-4-(hydroxymethylphosphinyl)butanoic acid), dicamba (3,6-dichloro-2-methoxybenzoic acid), 2,4-D (2,4-dichlorophenoxyacetate), and mesotrione (2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione). MON 94313 soybean will be combined, through traditional breeding methods, with other deregulated soybean events (e.g., glyphosate-tolerant trait) and will offer North American growers multiple choices for effective weed management including tough-to-control and herbicide-resistant broadleaf and grass weeds. MON 94313 soybean combined with glyphosate-tolerant soybean systems will provide additional weed management tools and flexibility to enhance weed management and maintain or improve soybean yield and quality. This enhanced system will help meet the growing needs of food, feed, and industrial markets, provide broader grower choice, improve production efficiency, increase pest control durability, and promote sustainable agriculture practices.

The enclosed information is being submitted in accordance with the Guidance for Requesting a Regulatory Status Review under 7 CFR part 340 (USDA-APHIS Document ID BRS-GD-2020-003).

We would be pleased to meet with you and other USDA officials and scientists to respond to any questions you may have, or to provide you with additional information that you may request. Should you have any questions on this letter, the enclosed information or wish to set up a meeting to further discuss MON 94313 please contact James Nyangulu, Federal Engagement Lead, at (202) 304-6594, or Gregory Tilton at (412) 676-9691.

Yours sincerely,

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Request for a Regulatory Status Review for Glufosinate, Dicamba, 2,4-Dichlorophenoxyacetic Acid and Mesotrione Tolerant Soybean MON 94313

OECD Unique Identifier: MON-94313-8

The undersigned submits this Regulatory Status Review (RSR) request under 7 CFR § 340.4 to request that the Administrator make a determination that the article should not be regulated under 7 CFR Part 340

July 22, 2022

DocuSigned by:
Jessica Fernandez
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RELEASE OF INFORMATION

Bayer CropScience LP (hereafter Bayer) is submitting this request for a Regulatory Status Review (RSR) by the USDA. Bayer understands that the USDA complies with the provisions of the Freedom of Information Act (FOIA). In the event the USDA receives a FOIA request, pursuant to 5 U.S.C., § 552, and 7 CFR Part 1, covering all or some of the information in this request, Bayer expects that, in advance of the release of the document(s), USDA will provide Bayer with a copy of the material proposed to be released and the opportunity to object to the release of any information based on appropriate legal grounds, e.g., responsiveness, confidentiality, and/or competitive concerns. Bayer understands that a CBI-deleted copy of this information may be made available to the public in a reading room and made available via the internet as part of a public comment period. Bayer also understands that if the review proceeds to the plant pest risk assessment (PPRA) step and the RSR request has been deemed complete, a copy of the RSR request may be posted to the USDA-APHIS BRS website or other U.S. government websites (e.g., www.regulations.gov). Except in accordance with the foregoing and required under applicable law, Bayer does not authorize the release, publication or other distribution of this information without Bayer's prior notice and consent.

ABBREVIATIONS AND DEFINITIONS

APHIS	Animal and Plant Health Inspection Service
CTP	Chloroplast transit peptide
DNA	Deoxyribonucleic Acid
DMO	Dicamba mono-oxygenase
DCSA	Dichlorosalicylic acid
FT_T.1	Modified FOPs and 2,4-D dioxygenase protein
GE	Genetically Engineered
ILSI-CERA	International Life Sciences Institute – Center for Environmental Risk Assessment
mRNA	Messenger Ribonucleic Acid
OECD	Organization for Economic Co-operation and Development
PAT	Phosphinothricin N-acetyltransferase
RdpA	R-2,4-dichlorophenoxypropionate dioxygenase
RSR	Regulatory Status Review
T-DNA	Transfer Deoxyribonucleic Acid
TDO	Triketone dioxygenase
USDA	United States Department of Agriculture
WHO	World Health Organization

I REQUESTOR

The submitter of this initial Regulatory Status Review request for soybean MON 94313 is:

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Communications with regard to this submission should be directed to Jessica Fernandez, B.S., Global Regulatory Manager, at the Bayer address listed above, or by email at jessica.fernandez@bayer.com.

II RATIONALE FOR THE DEVELOPMENT OF MON 94313

The Animal and Plant Health Inspection Service (APHIS) of the United States (U.S.) Department of Agriculture (USDA) has responsibility, under the Plant Protection Act (Title IV Pub. L. 106-224, 114 Stat. 438, 7 U.S.C. § 7701-7772) to prevent the introduction and dissemination of plant pests into the U.S. APHIS regulations at 7 CFR § 340.4, that are in effect on the date this Regulatory Status Review (RSR) request was filed, provide that an applicant may request a RSR of a plant developed using genetic engineering to evaluate whether the combination of the plant, introduced trait, and the trait's mechanism of action (MOA) pose an increased plant pest risk relative to the comparator plant.

II.A Basis for the Request

Bayer is submitting this request for an initial RSR to APHIS for the agency to evaluate whether the genetically engineered (GE) soybean product, MON 94313, any progeny derived from crosses between MON 94313 and conventional soybean, and any progeny derived from crosses between MON 94313 and other GE soybean not subject to 7 CFR Part 340 regulations should continue to be regulated by APHIS.

II.B Rationale for the Development of Herbicide Tolerant Soybean

Bayer CropScience LP has developed herbicide tolerant MON 94313 soybean, which is tolerant to the herbicides glufosinate (2-amino-4-(hydroxymethylphosphinyl)butanoic acid), dicamba (3,6-dichloro-2-methoxybenzoic acid), 2,4-D (2,4-dichlorophenoxyacetate), and mesotrione (2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione). MON 94313 contains the phosphinothricin N-acetyltransferase (*pat*) gene from *Streptomyces viridochromogenes* that expresses the PAT protein to confer tolerance to glufosinate herbicide, a demethylase gene from *Stenotrophomonas maltophilia* that expresses a dicamba mono-oxygenase (DMO) protein to confer tolerance to dicamba herbicide, the *ft_t.1* gene, a modified version of the R-2,4-dichlorophenoxypropionate dioxygenase *(RdpA*) gene from *Sphingobium herbicidovorans* that expresses a modified FOPs and 2,4-D dioxygenase protein (FT_T.1) to confer tolerance to 2,4-D herbicide, and the *TDO* gene from *Oryza sativa* that expresses the triketone dioxygenase (TDO) protein to confer tolerance to mesotrione herbicide.

MON 94313 soybean will offer growers multiple choices for effective weed management including tough-to-control and herbicide-resistant broadleaf and grass weeds. The flexibility to use combinations of any of these four herbicides representing multiple modes-of-action provides an effective and more durable weed management system for soybean production. The best management practices for minimizing the development of herbicide resistant weeds involve implementing diversified weed management programs, which includes using multiple herbicides with different modes of action either in mixtures, sequences or in rotation and other recommended integrated weed management principles.

MON 94313 soybean will be combined, through traditional breeding methods, with other deregulated soybean events (e.g., glyphosate-tolerant trait). MON 94313 soybean combined with glyphosate-tolerant soybean systems will provide: 1) an opportunity for an efficient, effective weed management system for hard-to-control and herbicide-resistant weeds; 2) a flexible system with multiple herbicide modes-of-action for in-crop application in current soybean production systems; 3) an opportunity to delay selection for further resistance to glyphosate and other herbicides that are important in crop production; 4) excellent crop tolerance to dicamba, glufosinate, 2,4-D, mesotrione and glyphosate; and 5) additional weed management tools to enhance weed management systems necessary to maintain or improve soybean yield and quality to meet the growing needs of the food, feed, and industrial markets.

III DESCRIPTION OF COMPARATOR PLANT

Soybean (*Glycine max* L. Merrill) variety A3555 is the parental line of MON 94313 and was used as the conventional soybean comparator in the safety assessment of MON 94313. MON 94313 and A3555 have similar genetic backgrounds with the exception of the *dmo, pat, ft t.1* and *TDO* expression cassettes, thus the effect of the *dmo, pat, ft t.1* and *TDO* cassesttes could be assessed in an unbiased manner in the comparative safety assessment. Variety A3555 was developed via conventional breeding and is characterized by indeterminant growth habit and maturity group 3.5, making it best adapted to the central portion of the U.S. soybean growing region.

IV GENOTYPE OF THE MODIFIED PLANT FOR MON 94313

This section describes information to understand the genetic differences between the modified plant and the comparator plant, including nucleotide sequence and annotation of the genetic material that has been inserted into and remains in the genome of the modified plant, as described in the "Guidance for Requesting a Regulatory Status Review under 7 CFR part 340" (USDA-APHIS Document ID BRS-GD-2020-003).

IV.A Sequence, Identity and Sources of the Genetic Material Inserted into MON 94313

MON 94313 was created through an *Agrobacterium*-mediated transformation in A3555 soybean meristem explants with the PV-GMHT529103 binary vector DNA (~24.5 kb) based on the methods described by (Ye et al., 2008). After co-culturing with *Agrobacterium* AB30 strain carrying the plasmid vector, meristem explants were placed on selection medium to favor selection of transgenic events and inhibit the overgrowth of *Agrobacterium*.

PV-GMHT529103 contains two separate T-DNAs, each delineated by Left and Right Border regions and the vector backbone sequences. The first T-DNA, designated as T-DNA I, contains the *dmo, pat, ft_t.1*, and *TDO* expression cassettes. The second T-DNA, designated as T-DNA II, contains the selectable marker genes *splA* and *aadA* expression cassettes. During transformation, both T-DNAs were inserted into the soybean genome. Subsequently, segregation, selection and screening were used to isolate those plants that contained the *dmo, pat, ft_t.1*, and *TDO* expression cassettes (T-DNA I) and did not contain the *splA* and *aadA* expression cassettes (T-DNA II) or the backbone sequences from the transformation vector. MON 94313 was selected as the lead event based on superior agronomic, phenotypic and molecular characteristics. The nucleotide sequence of the inserted genetic material in MON 94313 is provided in 0, and an annotation of the different genetic elements is provided in Table IV-1.

Table IV-1. Annotation of the Inserted Genetic Material in MON 94313

Genetic Element	Location in Sequence	Function (Reference)
B[1]-Right Border Region[r1]	1-71	DNA region from *Agrobacterium tumefaciens* containing the right border sequence used for transfer of the T–DNA (Depicker et al., 1982, Zambryski et al., 1982) **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	72-110	"Synthetic[2] sequence" used in DNA cloning
P[3]-*ubq3-At1*	111-1118	Promoter, leader and intron from *Arabidopsis thaliana* of the polyubiquitin gene *ubq3* (Norris et al., 1993), which directs transcription in plant cells **(Note: GenBank accession number not yet available)[8]**
TS[4]-*apg6-At1*	1119-1322	Targeting sequence of the *APG6* gene from *Arabidopsis thaliana* encoding a HSP101 (heat shock protein) homologue and acts as a transit peptide that directs transport of the protein to the chloroplast (Myouga et al., 2006) **(Note: GenBank accession number not yet available)[8]**
CS[5]-*dmo*	1323-2345	Codon optimized coding sequence for the dicamba mono-oxygenase (DMO) protein of *Stenotrophomonas maltophilia* that confers dicamba tolerance (Herman et al., 2005); (Wang et al., 1997) **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	2346-2364	"Synthetic" sequence used in DNA cloning
T[6]-*sali3-2-Mt1*	2365-2864	3′ UTR sequence from *Medicago truncatula* (barrel medic) of an aluminum-induced Sali3-2 protein that directs polyadenylation of the mRNA (Hunt, 1994) **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	2865-2942	"Synthetic" sequence used in DNA cloning
P-*GSP579*	2943-3442	A promoter and 5′ UTR that has been developed from multiple promoter and 5′ UTR sequences from *Arabidopsis thaliana* (To et al., 2021) that directs transcription in plant cells. **(Note: GenBank accession number not yet available)[8]**
I[7]-*GSI102*	3443-3752	An intron that has been developed from multiple intron sequences from *Arabidopsis thaliana* (To et al., 2021) that is involved in regulating gene expression **(Note: GenBank accession number not yet available)[8]**

Table IV-1. Annotation of the Inserted Genetic Material in MON 94313 (Contiued)

Intervening sequence	3753-3758	"Synthetic" sequence used in DNA cloning
CS-*pat*	3759-4310	Codon optimized coding sequence for the phosphinothricin N–acetyltransferase (PAT) protein of *Streptomyces viridochromogenes* that confers tolerance to glufosinate (Wehrmann et al., 1996); (Wohlleben et al., 1988) **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	4311-4318	"Synthetic" sequence used in DNA cloning
T-*Hsp20-Mt1*	4319-4818	3′ UTR sequence from *Medicago truncatula* (barrel medic) of a putative *Hsp20* gene encoding a heat shock protein that directs polyadenylation of the mRNA (Hunt, 1994) **(GenBank accession: OK149196)**
Intervening sequence	4819-4901	"Synthetic" sequence used in DNA cloning
P-*ubq10-At1*	4902-6103	Promoter, leader and intron from *Arabidopsis thaliana* of the polyubiquitin gene *ubq10* (Norris et al., 1993), which directs transcription in plant cells **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	6104-6109	"Synthetic" sequence used in DNA cloning
CS-*ft_t.1*	6110-6997	Modified version of R-2,4 dichlorophenoxypropionate dioxygenase (*rdpA*) gene of *Sphingobium herbicidovorans* that expresses a modified FOPs and 2,4-D dioxygenase protein (FT_T.1) that confers tolerance to 2,4-D herbicide in soybean (Larue et al., 2019). **(GenBank accession: MH043115)**
Intervening sequence	6998-7005	"Synthetic" sequence used in DNA cloning
T-*guf-Mt2*	7006-7505	3′ UTR from an expressed gene of *Medicago truncatula* of unknown function that directs polyadenylation of mRNA (Hunt, 1994) **(GenBank accession: OK149195)**
Intervening sequence	7506-7643	"Synthetic" sequence used in DNA cloning
P-*GSP576*	7644-8143	A promoter and 5′ UTR that has been developed from multiple promoter and 5′ UTR sequences from *Arabidopsis thaliana* (To et al., 2021) that directs transcription in plant cells. **(Note: GenBank accession number not yet available)[8]**
I-*GSI17*	8144-8443	An intron that has been developed from multiple intron sequences from *Arabidopsis thaliana* (To et al., 2021) that is involved in regulating gene expression **(Note: Genbank accession number not yet available)[8]**

Table IV-1. Annotation of the Inserted Genetic Material in MON 94313 (Contiued)

Intervening sequence	8444-8478	"Synthetic" sequence used in DNA cloning
CS-*TDO*	8479-9534	Codon optimized coding sequence for the triketone dioxygenase (TDO) protein of *Oryza sativa* that confers tolerance to mesotrione (Maeda et al., 2019) **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	9535-9564	"Synthetic" sequence used in DNA cloning
T-*GST7*	9565-9864	A 3′ UTR that has been developed from multiple 3′ UTR sequences from *Zea mays* (maize) (To et al., 2021) that directs polyadenylation of the mRNA. **(Note: GenBank accession number not yet available)[8]**
Intervening sequence	9865-9964	"Synthetic" sequence used in DNA cloning
B-Left Border Region[r1]	9965-10196	DNA region from *Agrobacterium tumefaciens* containing the left border sequence used for transfer of the T–DNA (Barker et al., 1983) **(GenBank accession: OK586894 positions 1 through 232)**

[1] B, Border

[r1] Superscript in the Left and Right Border Regions indicates that the sequence in MON 94313 was truncated compared to the sequences in PV-GMHT529103.

[2] The term "synthetic" used in this table is defined and described in the USDA/APHIS-BRS Guidance Document BRS-GD-2020-0003. In the context of this table, the word synthetic does not indicate that the sequence was manufactured but rather that the sequence is not purposefully obtained from a known source and does not have an assigned function, although some homology may exist to known DNA sequences.

[3] P, Promoter

[4] TS, Targeting sequence

[5] CS, Coding sequence

[6] T, Transcription termination sequence

[7] I, Intron

[8] GenBank accession numbers not available as of July 13, 2022

V DESCRIPTION OF THE NEW TRAIT FOR MON 94313

This section describes the intended MON 94313 trait, intended phenotype associated with the trait, and mechanism of action by which the intended phenotype will be conferred, as described in the Guidance for Requesting a Regulatory Status Review under 7 CFR part 340 (USDA-APHIS Document ID BRS-GD-2020-003).

V.A Description of the Intended MON 94313 Trait

MON 94313 is intended to provide herbicide tolerance.

V.B Intended Phenotype of MON 94313

Herbicide tolerant soybean MON 94313 is intended to provide tolerance to dicamba, glufosinate, 2,4-D, and mesotrione herbicides and will offer growers multiple choices for effective weed management including tough-to-control and herbicide-resistant broadleaf and grass weeds.

V.C Description of the Mechanism of Action for MON 94313

DMO Protein

MON 94313 soybean contains a demethylase gene from *Stenotrophomonas maltophilia* that expresses a dicamba mono-oxygenase (DMO) protein. As a mono-oxygenase protein, the DMO protein is part of the larger oxygenase family of enzymes that incorporate one or two oxygen atoms into substrates and are widely distributed in many universal metabolic pathways (Harayama et al., 1992). The DMO protein enzymatically catalyzes the demethylation of the broadleaf herbicide dicamba to the non-herbicidal compound 3,6-dichlorosalicylic acid (DCSA) and formaldehyde, thus conferring dicamba tolerance (Chakraborty et al., 2005). Expression of the DMO protein in MON 94313 is targeted to the chloroplast by a chloroplast transit peptide (CTP), which facilitates its co-localization with the endogenous reductase and ferredoxin enzymes required to supply electrons for the DMO demethylation reaction (Behrens et al., 2007).

The DMO protein expressed in MON 94313 is identical to one of the DMO variants in MON 87429 maize (Petition Number 19-316-01p), submitted to APHIS in 2019 for determination of nonregulated status. Designated as DMO+0 in Petition 19-316-01p, the DMO protein in MON 94313 contains 340 amino acids and an apparent molecular weight ~35.6 kDa.

The MON 94313 DMO protein shares a high level of sequence identity with other DMO proteins previously assessed and present in biotechnology-derived crops that were deregulated by USDA-APHIS (MON 87708 soybean, USDA-APHIS Petition #10-188-01p, MON 88701 cotton, USDA-APHIS Petition #12-185-01p and MON 87419 maize, USDA-APHIS Petition #15-113-01p). The minor amino acid substitutions between the wild-type DMO protein from the DI-6 strain of *S. maltophilia*, the MON 94313 DMO protein and the DMO proteins expressed in these other biotechnology-derived crops are localized to the N-terminus of the proteins and at positions 2 and 112 of the amino acid sequences (Herman et al., 2005); (Figure V-1). Additionally, based upon the crystal structure of the wild-type DMO proteins, these amino acid substitutions are structurally distant from the active site and are not expected to impact catalytic site coordination,

functional activity, immunoreactivity or specificity (D'Ordine et al., 2009, Dumitru et al., 2009, Wang et al., 2016). Thus, prior evaluations of the DMO protein expressed in other biotechnology-derived crops are directly applicable to the DMO protein expressed in MON 94313.

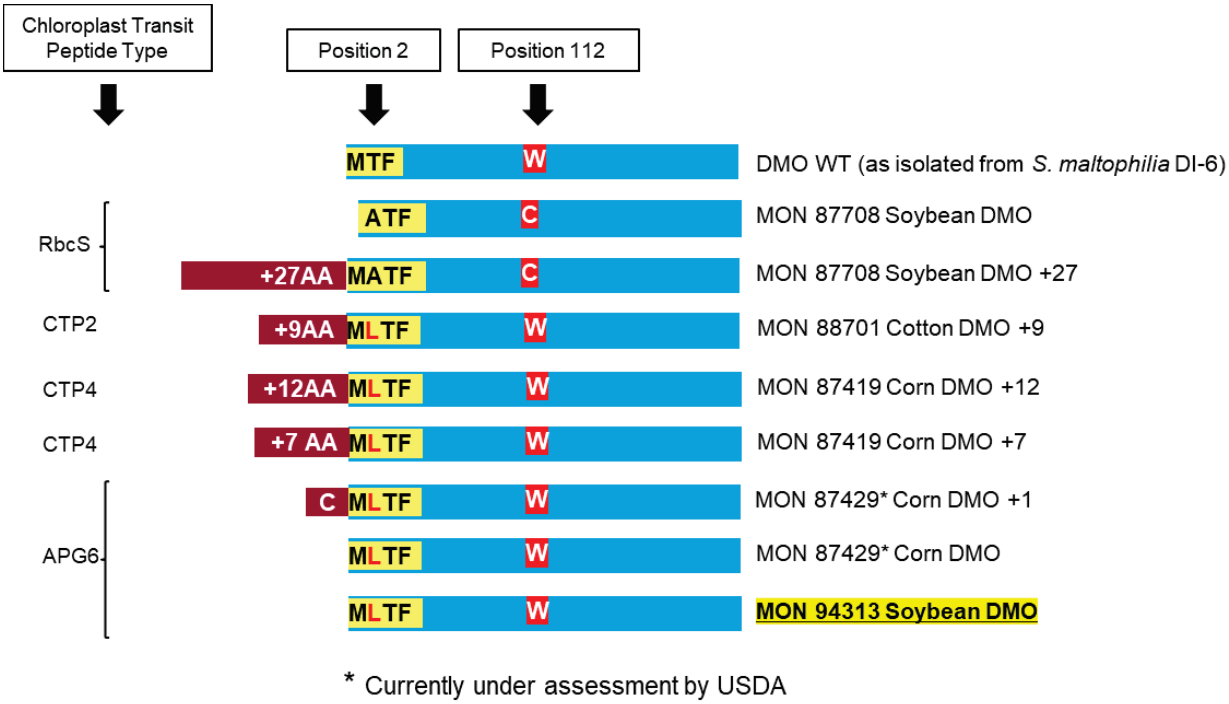

Figure V-1. Variants of DMO Protein and Their Relation to the Wild-Type DMO Protein
The diagram represents the wild-type DMO from *S. maltophilia* relative to various DMO variants discussed in this section. Position refers to amino acid residues as wild-type DMO and the N-terminal maroon region indicate residues from chloroplast transit peptides (CTPs). The blue regions indicate regions of 100% amino acid identity. The MON 94313 DMO protein is identical to one of the MON 87429 DMO variants and to wild-type DMO, except for the insertion of a leucine at position 2. The MON 94313 DMO protein is also identical to DMO isoforms from other crop products with the exception of some minor differences at either position 2 or position 112. Other DMO variants also have additional N-terminal amino acids remaining from the processing of the CTP. The MON 87708 DMO (fully processed) protein additionally lacks a lead methionine residue.

The DMO protein is specific for the oxidative demethylation of dicamba, forming DCSA. Dicamba interacts with amino acids in the catalytic site of DMO through both the carboxylate moiety and the chlorine atoms of dicamba, which are primarily involved in orienting the substrate in the catalytic site. These chlorine atoms are required for catalysis (D'Ordine et al., 2009, Dumitru et al., 2009). Given the limited existence of chlorinated compounds with structures similar to dicamba in plants and other eukaryotes (Wishart et al., 2009, Wishart, 2010), it is unlikely that MON 94313 DMO will catalyze the metabolism of endogenous compounds. An assessment of MON 94313 DMO which evaluated the potential for DMO to catabolize dicamba and *o*-anisic acid confirmed the specificity of the DMO protein expressed by MON 94313. *O*-anisic acid was the natural plant metabolite chosen for this confirmatory assessment since it is the plant metabolite most structurally similar to dicamba (identical to dicamba, except for absence of chlorine atoms) (Dumitru et al., 2009). Similar results were

obtained for other DMO variants, such as MON 87419 DMO (USDA-APHIS Petition #15-113-01p). The assessment demonstrates that the minor differences in amino acid sequences present in the MON 94313 DMO protein relative to other DMO proteins expressed in previous biotechnology-derived crops do not impact the activity or selectivity for dicamba herbicide as compared to potential endogenous substrates.

The data and information summarized in this section confirm that the molecular mechanism of the MON 94313 DMO protein that confers dicamba tolerance is well understood, that the MON 94313 DMO protein is specific for dicamba, and that aside from dicamba tolerance, no changes to metabolism, physiology or development of the soybean plant are expected. Furthermore, the MON 94313 DMO protein is structurally and functionally homologous to the DMO proteins present in biotechnology-derived crops that have been deregulated by USDA-APHIS.

PAT Protein

MON 94313 soybean contains an acetyltransferase gene from *Streptomyces viridochromogenes* that expresses phosphinothricin N-acetyltransferase (PAT) protein. The molecular mechanism of the PAT protein, which acetylates glufosinate in the presence of acetyl CoA to form N-acetyl glufosinate, is well understood (Thompson et al., 1987). Glufosinate is a racemic mixture of the D- and L-forms of the amino acid phosphinothricin. The herbicidal activity of glufosinate results from the binding of L-phosphinothricin to glutamine synthetase (OECD, 1999, 2002). Expression of the PAT protein in MON 94313 soybean results in the ability to convert L-phosphinothricin to the non-herbicidal N-acetyl-L-phosphinothricin, thus conferring glufosinate tolerance to the crop.

Phosphinothricin N-acetyltransferase (PAT) proteins have been isolated from two separate species of *Streptomyces*, *S. hygroscopicus* (Thompson et al., 1987) and *S. viridochromogenes* (Wohlleben et al., 1988). The PAT protein isolated from *S. hygroscopicus* is encoded by the *bar* gene, and the PAT protein isolated from *S. viridochromogenes* is encoded by the *pat* gene. These PAT proteins are made up of 183 amino acids with 85% identity to each other at the amino acid level (Wohlleben et al., 1988). Based on previous studies (Wehrmann et al., 1996) that have extensively characterized PAT proteins produced from *bar* and *pat* genes, OECD recognizes both proteins to be equivalent with regard to function and safety (OECD, 1999). Expression of the *pat* gene in MON 94313 results in a single polypeptide of 182 amino acids with an apparent molecular weight of ~25 kDa. Data from N-terminal sequencing analysis of the MON 94313-produced PAT protein indicate that it is identical to the wild type PAT protein encoded by *S. viridochromogenes* and to the PAT proteins produced in several glufosinate tolerant crops previously deregulated by USDA-APHIS, (USDA-APHIS Petitions #94-357-01p, #00-136-01p, #03-353-01p and #15-113-01p maize; #98-278-01p and #01-206-01p canola; #96-068-01p, #98-014-1p #12-215-01p, #11-234-01p and #09-349-01p soybean; #97-336-01p sugarbeet, #98-329-01p rice; and #12-185-01p, #13-262-01p and #08-340-01p cotton) (Hérouet et al., 2005, ILSI-CERA, 2011), except for the first methionine that is removed due to cotranslational processing in MON 94313. N-terminal methionine cleavage is common and naturally occurs in the vast majority of proteins (Meinnel and Giglione, 2008).

PAT proteins have been extensively assessed by regulatory agencies in at least 15 different countries for more than 30 biotechnology-derived events in several different crop species (e.g., maize, soybean, cotton, canola and sugar beet). Prior assessments of the PAT proteins expressed in these other biotechnology-derived crops are directly applicable to the MON 94313 PAT protein because the amino acid sequence of the MON 94313 PAT protein is identical to the PAT proteins in these biotechnology-derived crops that are derived from the *pat* gene. Furthermore, PAT proteins produced from the *bar* and *pat* genes are equivalent in terms of function and safety.

The PAT protein expressed in MON 94313 is highly specific for glufosinate. Enzyme assays indicated that the PAT protein does not acetylate other common L-amino acids that are structurally similar to L-phosphinothricin, and substrate competition assays showed no inhibition of glufosinate acetylation in the presence of high concentrations of L-amino acids that are structurally similar to L-phosphinothricin (including the glufosinate analog L-glutamate) (Wehrmann et al., 1996). Recent metabolic profiling reported some non-specific PAT (bar) mediated acetylation of two amino acids (aminoadipate and tryptophan) in senescent leaf extracts from *A. thaliana* and also in PAT (pat)-expressing soybean (Christ et al., 2017). However, the activity level for these two amino acids was very low relative to the activity for L- phosphinothricin, indicating that PAT (pat) has a very high level of specificity for the herbicidal molecule.

The data and information summarized in this section confirm that the molecular mechanism of the MON 94313 PAT protein that confers glufosinate tolerance is well understood, that the MON 94313 PAT protein is identical to the PAT proteins present in several biotechnology-derived crops that have been deregulated by USDA-APHIS, and is highly specific for glufosinate. Aside from glufosinate tolerance, no changes to metabolism, physiology or development of the soybean plant are expected. Thus, prior evaluations for the PAT protein are directly applicable to the MON 94313 PAT protein.

FT_T.1 Protein

The FT_T.1 protein produced in MON 94313 soybean is encoded by the *ft_t.1* gene that provides tolerance to 2,4-D. The *ft_t.1* gene in MON 94313 is a modified version of the R-2,4- dichlorophenoxypropionate dioxygenase (*Rdpa*) gene from the soil bacteria *Sphingobium herbicidovorans*. The amino acid sequence of the FT_T.1 protein shares ~ 89% sequence identity with wild type RdpA and >98% identity with the FT_T protein from MON 87429 maize. FT_T.1 maintains high activity at the elevated temperatures experienced during the summer months in typical soybean growing areas, which was a characteristic introduced into the FT_T protein. Three additional amino acid changes provide FT_T.1 with enhanced enzymatic activity for the 2,4-D molecule relative to FT_T (Larue et al., 2019). This modification is important as soybean is highly sensitive to 2,4-D.

RdpA protein is an alpha-ketoglutarate-dependent non-heme iron dioxygenase (Müller et al., 2006), and given their structural similarity, the FT_T.1 protein is also an alpha-ketoglutarate-dependent non-heme iron dioxygenase. Alpha-ketoglutarate-dependent non-heme iron dioxygenases belong to a diverse superfamily of Fe(II)/alpha-ketoglutarate dependent hydroxylases that catalyze a range of oxygenation reactions in synthesis and decomposition

reactions that include hydroxylation reactions, desaturations, demethylations, ring expansions, ring formations and other oxidative reactions (Hausinger, 2004). This protein superfamily is broadly distributed across the plant, animal and bacterial kingdoms, therefore environmental exposure to Fe(II)/alpha-ketoglutarate dependent hydroxylases is ubiquitous. Members of this superfamily share a common structural fold comprised of eight β-strands forming two, four-stranded sides, with three metal-binding ligands found in a His1-X-Asp/Glu-Xn-His2 motif (Hausinger, 2004). In oxygenation reactions, alpha-ketoglutarate (αKG) chelates Fe(II) using its C1 carboxylate and C2-ketone. Decarboxylation of αKG results in the formation of succinate and carbon dioxide, which leads to the generation of an Fe(IV)-oxo or other activated oxygen species that subsequently hydroxylate the primary substrate, e.g., 2,4-D (Carolis and Luca, 1994, Bugg, 2003, Hausinger, 2004). Thus, the FT_T.1 protein catalyzes the dioxygenase reaction that degrades 2,4-dichlorophenoxyacetic acid (2,4-D), a synthetic auxin herbicide, into herbicidally-inactive 2,4-dichlorophenol (2,4-DCP) and glyoxylic acid in the presence of αKG and oxygen. Succinate and carbon dioxide are released as products of this reaction.

FT_T.1 has been optimized for 2,4-D activity by three amino acid changes to the FT_T sequence, but these modifications do not impact the specificity of FT_T.1 relative to FT_T. Both proteins are still active on the same substrate molecules, with FT_T.1 displaying higher enzymatic activity for 2,4-D (see Table 1 in Larue et al., 2019 (Note: FT_T.1 is referred to as FT_Tv7 in this article) (Larue et al., 2019).

In order to confirm that the FT_T.1 enzyme is specific for herbicide substrates and not endogenous metabolites, an *in vitro* assessment of potential substrates was conducted. Information submitted previously for MON 87429 maize examined the substrate specificity of FT_T protein by measuring the functional response of purified FT_T protein to potential endogenous plant specific compounds. These compounds, which included soybean metabolites, were selected through an *in silico* screen of a plant metabolite database that gauged their 2-D and 3-D similarity to a known FT_T substrate (dichlorprop) and the potential of the compound to fit correctly into the active site. Available candidate compounds were tested *in vitro* to examine if any were substrates for the FT_T protein. Given the high level of similarity between the expected structure, active site, and function of FT_T.1 and FT_T, the same list of potential plant metabolites were assayed to examine the specificity of FT_T.1. The results were nearly identical to the those of FT_T from MON 87429 maize (USDA-APHIS Petition #19-316-01p, page 82) where FT_T.1 showed activity against the same herbicidal positive controls but did not demonstrate activity on any of the plant specific molecules, showing that FT_T.1 is specific towards the herbicidal substrates and not endogenous plant metabolites.

The data and information summarized in this section confirm that the molecular mechanism of the MON 94313 FT_T.1 protein that confers 2,4-D tolerance is well understood, that the MON 94313 FT_T.1 protein is highly specific for its herbicide substrates and that aside from the intended herbicide tolerance, no changes to metabolism, physiology or development of the soybean plant are expected.

TDO Protein

MON 94313 soybean expresses triketone dioxygenase (TDO) protein encoded by the *TDO* gene that provides tolerance to mesotrione. *TDO* itself is a codon-optimzed version of the *HPPD INHBITOR SENSITIVE 1* (*HIS1*) gene from rice that has the same amino acid sequence as the HIS1 protein. Mesotrione, a β-triketone herbicide, is an inhibitor of 4-hydroxyphenylpyruvate dioxygenase (HPPD; EC: 1.13.11.27) which catalyzes the first committed step of tyrosine catabolism in plants. Inhibition of HPPD in plants leads to a depletion of key downstream metabolites, most notably tocopherols and plastoquinone. Plastoquinone is critical for the functioning of photosystem II and carotenoid biosynthesis (Mitchell et al., 2001). Carotenoids and tocopherols are, in turn, key molecules in protecting the photosynthetic machinery from oxidative damage. As a result of the reduction in levels of these protective molecules after application of mesotrione to susceptible plants, characteristic bleaching occurs, ultimately leading to plant death. Natural tolerance to β-triketone herbicides in certain *Oryza sativa* (rice) cultivars was determined to be a result of the presence of the HIS1 protein, which includes motifs conserved in Fe(II)/alpha-ketoglutarate-dependent dioxygenases and was shown to oxidize the mesotrione herbicide molecule (Maeda et al., 2019). Expression of the codon-optimized *TDO* gene in MON 94313 soybean results in soybean plants that are capable of tolerating in-crop applications of mesotrione through oxidation of the mesotrione molecule.

Like other Fe(II)/alpha-ketoglutarate-dependent dioxygenases, such as FT_T.1 described above, TDO uses iron and alpha-ketoglutarate as cofactors in the oxidation of its substrate, producing succinate and the oxidized product. *In vitro* studies of recombinant TDO shows that the initial oxidation of mesotrione takes place at the 5C, yielding hydroxy-mesotrione. The second oxidation at the same carbon creates oxy-mesotrione, which non-enzymatically cyclizes to produce hydroxy-xanthone (Figure V-2). *In vitro* assays demonstrated that hydroxy-mesotrione is less inhibitory to HPPD than mesotrione, and oxy-mesotrione had virtually no impact on the activity of HPPD. Thus, the oxidative capabilities of TDO provide a mechanism by which mesotrione is metabolized to a non-herbicidal molecule(s) and prevented from inhibiting the native soybean HPPD activity.

In vivo studies of soybean expressing the TDO protein show that the plants can tolerate in-crop applications of mesotrione (Dai et al., 2022). Metabolic analysis of soybean leaves in soybean expressing TDO demonstrated that tolerance is accomplished through quick conversion of mesotrione to products such as hydroxy-mesotrione, hydroxy-xanthone, and downstream glucosyl and malonyl conjugates (oxy-mesotrione is not detected in TDO-expressing soybean, likely due to non-enzymatic cyclization to hydroxy-xanthone). In addition, mesotrione is not translocated from the treated tissues in TDO-expressing soybean, thus preventing inhibition of HPPD in newly developing apex or root tissues. In contrast, apical and root tissues of treated conventional soybean accumulate mesotrione, resulting in the inhibition of HPPD and the bleaching phenotype typical of β-triketone treatments of susceptible plants (Dai et al., 2022).

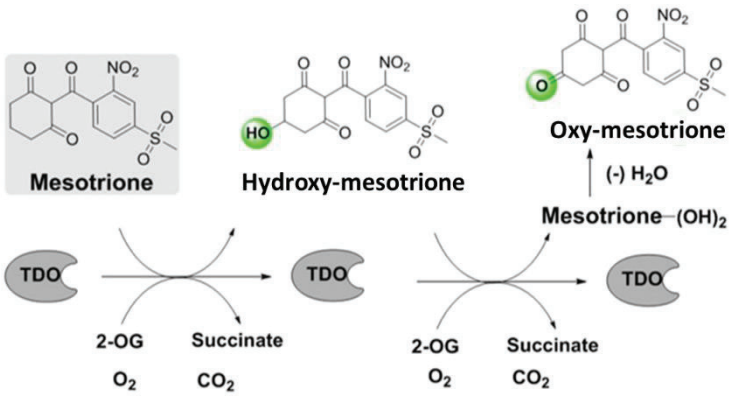

Figure V-2. TDO Biochemical Mechanism of Action
TDO oxidizes mesotrione sequentially, yielding hydroxy-mesotrione in the first round of oxidation, followed by oxy-mesotrione after the second oxidative step and the loss of a water molecule. Hydroxy- and oxy-mesotrione are progressively less inhibitory to HPPD than the parent mesotrione molecule, providing MON 94313 soybean with tolerance to in-crop applications. Oxy-mesotrione is likely quickly and non-enzymatically converted to hydroxy-xanthone, which is further metabolized to glucosyl and malonyl conjugates (Dai et al., 2022) (2-OG = alpha-ketoglutarate).

In vitro assays of TDO demonstrate that it is specific for β-triketone type HPPD inhibitors (ex. mesotrione, tembotrione, sulcotrione) but not other HPPD inhibitor class herbicide molecules (ex. isoxaflutole and topramezone). To more fully characterize the specificity of TDO, an *in silico* approach was used to identify potential plant substrates.

Similar to the *in silico* screen described above for the FT_T.1 protein, a screen was conducted to identify potential soybean endogenous molecules that could be substrates for TDO. The results showed that TDO had no activity with any of the putative plant substrates, and was specific to the β-triketone class of herbicide compounds (ex. mesotrione, tembotrione, and sulcotrione).

The data and information summarized in this section confirm that the molecular mechanism of the MON 94313 TDO protein that confers mesotrione tolerance is well understood, and is not expected to have any impact on metabolism, physiology, and/or the development of the soybean plant.

Finally, based on the unique mechanisms of action and the specificity exhibited by each of the four proteins expressed in MON 94313, there is no plausible hypothesies suggesting likelihood of potential interaction between the proteins.

Conclusion

This request for Regulatory Status Review (RSR) of MON 94313, provides details on our next generation herbicide tolerant genetically engineered soybean product following the guidance outlined in the Agency's document titled "Guidance for Requesting a Regulatory Status Review (RSR) under 7 CFR part 340", Document ID BRS-GD-2020-003. Molecular characteristics as well as mechanism of action for the expressed proteins are provided herein and support the

conclusion that MON 94313 soybean does not include any expected changes in metabolism, physiology, and/or the development of the soybean plant due to the trait/genetic modification.

REFERENCES

Barker, R. F., K. B. Idler, D. V. Thompson and J. D. Kemp. 1983. Nucleotide sequence of the T-DNA region from the *Agrobacterium tumefaciens* octopine Ti plasmid pTi15955. Plant Molecular Biology 2(6):335-350

Behrens, M. R., N. Mutlu, S. Chakraborty, R. Dumitru, W. Z. Jiang, B. J. LaVallee, P. L. Herman, T. E. Clemente and D. P. Weeks. 2007. Dicamba resistance: Enlarging and preserving biotechnology-based weed management strategies. Science 316:1185-1188

Bugg, T. D. H. 2003. Dioxygenase enzymes: Catalytic mechanisms and chemical models. Tetrahedron 59(36):7075-7101

Carolis, E. d. and V. d. Luca. 1994. 2-Oxoglutarate-dependent dioxygenase and related enzymes: Biochemical characterization. Phytochemistry 36(5):1093-1107

Chakraborty, S., M. Behrens, P. L. Herman, A. F. Arendsen, W. R. Hagen, D. L. Carlson, X.-Z. Wang and D. P. Weeks. 2005. A three-component dicamba *O*-demethylase from *Pseudomonas maltophilia*, strain DI-6: Purification and characterization. Archives of Biochemistry and Biophysics 437(1):20-28

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

D'Ordine, R. L., T. J. Rydel, M. J. Storek, E. J. Sturman, F. Moshiri, R. K. Bartlett, G. R. Brown, R. J. Eilers, C. Dart, Y. Qi, S. Flasinski and S. J. Franklin. 2009. Dicamba monooxygenase: Structural insights into a dynamic Rieske oxygenase that catalyzes an exocyclic monooxygenation. Journal of Molecular Biology 392:481-497

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

Depicker, A., S. Stachel, P. Dhaese, P. Zambryski and H. M. Goodman. 1982. Nopaline synthase: Transcript mapping and DNA sequence. Journal of Molecular and Applied Genetics 1(6):561-573

Dumitru, R., W. Z. Jiang, D. P. Weeks and M. A. Wilson. 2009. Crystal structure of dicamba monooxygenase: A Rieske nonheme oxygenase that catalyzes oxidative demethylation. Journal of Molecular Biology 392:498-510

Harayama, S., M. Kok and E. L. Neidle. 1992. Functional and evolutionary relationships among diverse oxygenases. Annual Review of Microbiology 46:565-601

Hausinger, R. P. 2004. Fe(II)/α-Ketoglutarate-dependent hydroxylases and related enzymes. Critical Reviews in Biochemistry and Molecular Biology 39(1):21-68

Herman, P. L., M. Behrens, S. Chakraborty, B. M. Chrastil, J. Barycki and D. P. Weeks. 2005. A three-component dicamba *O*-demethylase from *Pseudomonas maltophilia*, strain DI-6: Gene isolation, characterization, and heterologous expression. Journal of Biological Chemistry 280(26):24759-24767

Hérouet, C., D. J. Esdaile, B. A. Mallyon, E. Debruyne, A. Schulz, T. Currier, K. Hendrickx, R.-J. van der Klis and D. Rouan. 2005. Safety evaluation of the phosphinothricin acetyltransferase proteins encoded by the *pat* and *bar* sequences that confer tolerance to glufosinate-ammonium herbicide in transgenic plants. Regulatory Toxicology and Pharmacology 41(2):134-149

Hunt, A. G. 1994. Messenger RNA 3' end formation in plants. Annual Review of Plant Physiology and Plant Molecular Biology 45:47-60

ILSI-CERA. 2011. A review of the environmental safety of the PAT protein. International Life Sciences Institute, Center for Environmental Risk Assessment, Washington, D.C. http://cera-gmc.org/docs/cera_publications/pub_05_2011.pdf

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

Maeda, H., K. Murata, N. Sakuma, S. Takei, A. Yamazaki, M. R. Karim, M. Kawata, S. Hirose, M. Kawagishi-Kobayashi, Y. Taniguchi, S. Suzuki, K. Sekino, M. Ohshima, H. Kato, H. Yoshida and Y. Tozawa. 2019. A rice gene that confers broad-spectrum resistance to β-triketone herbicides. Science (Washington) 365(6451):393-396

Meinnel, T. and C. Giglione. 2008. Tools for analyzing and predicting N-terminal protein modifications. Proteomics 8(4):626-649

Mitchell, G., D. W. Bartlett, T. E. M. Fraser, T. R. Hawkes, D. C. Holt, J. K. Townson and R. A. Wichert. 2001. Mesotrione: a new selective herbicide for use in maize, Chichester, UK, John Wiley & Sons.

Müller, T. A., M. I. Zavodszky, M. Feig, L. A. Kuhn and R. P. Hausinger. 2006. Structural basis for the enantiospecificities of R- and S-specific phenoxypropionate/α-ketoglutarate dioxygenases. Protein Science 15(6):1356-1368

Myouga, F., R. Motohashi, T. Kuromori, N. Nagata and K. Shinozaki. 2006. An Arabidopsis chloroplast-targeted Hsp101 homologue, APG6, has an essential role in chloroplast development as well as heat-stress response. Plant Journal 48(2):249-260

Norris, S. R., S. E. Meyer and J. Callis. 1993. The intron of *Arabidopsis thaliana* polyubiquitin genes is conserved in location and is a quantitative determinant of chimeric gene expression. Plant Molecular Biology 21:895-906

OECD. 1999. Consensus document on general information concerning the genes and their enzymes that confer tolerance to phosphinothricin herbicide. ENV/JM/MONO(99)13. Series on Harmonization of Regulatory Oversight in Biotechnology No.11. Organisation for Economic Co-operation and Development, Paris, France.

OECD. 2002. Module II: Herbicide biochemistry, herbicide metabolism and the residues in glufosinate-ammonium (Phosphinothricin)-tolentant transgenic plants. ENV/JM/MONO(2002)14. Series on Harmonization of Regulatory Oversight in Biotechnology No. 25. Organisation for Economic Co-operation and Development, Paris, France.

Thompson, C. J., N. R. Movva, R. Tizard, R. Crameri, J. E. Davies, M. Lauwereys and J. Botterman. 1987. Characterization of the herbicide-resistance gene *bar* from *Streptomyces hygroscopicus*. EMBO Journal 6(9):2519-2523

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. Frontiers in Plant Science 12:712179

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. Regulatory Toxicology and Pharmacology 81:171-182

Wang, X.-Z., B. Li, P. L. Herman and D. P. Weeks. 1997. A three-component enzyme system catalyzes the O demethylation of the herbicide dicamba in *Pseudomonas maltophilia* DI-6. Applied and Environmental Microbiology 63(4):1623-1626

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

Wishart, D. S. 2010. Human metabolome database. www.hmdb.ca [Accessed June 2, 2010].

Wishart, D. S., C. Knox, A. C. Guo, R. Eisner, N. Young, B. Gautam, D. D. Hau, N. Psychogios, E. Dong, S. Bouatra, R. Mandal, I. Sinelnikov, J. Xia, L. Jia, J. A. Cruz, E. Lim, C. A. Sobsey, S. Shrivastava, P. Huang, P. Liu, L. Fang, J. Peng, R. Fradette, D. Cheng, D. Tzur, M. Clements, A. Lewis, A. De Souza, A. Zuniga, M. Dawe, Y. Xiong, D. Clive, R. Greiner, A. Nazyrova, R. Shaykhutdinov, L. Li, H. J. Vogel and I. Forsythe. 2009. HMDB: A knowledgebase for the human metabolome. Nucleic Acids Research 37(Database):D603-D610

Wohlleben, W., W. Arnold, I. Broer, D. Hillemann, E. Strauch and A. Pühler. 1988. Nucleotide sequence of the phosphinothricin *N*-acetyltransferase gene from *Streptomyces viridochromogenes* Tü494 and its expression in *Nicotiana tabacum*. Gene 70(1):25-37

Ye, X., E. Williams, J. Shen, J. Esser, A. Nichols, M. Petersen and L. Gilbertson. 2008. Plant development inhibitory genes in binary vector backbone improve quality event efficiency in soybean transformation. Transgenic Research 17(5):827-838

Zambryski, P., A. Depicker, K. Kruger and H. M. Goodman. 1982. Tumor induction by *Agrobacterium tumefaciens*: Analysis of the boundaries of T-DNA. Journal of Molecular and Applied Genetics 1(4):361-370

APPENDICES

Appendix A: Sequence of the Insertion for MON 94313

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Jessica Fernandez jessica.fernandez@bayer.com Security Level: Email, Account Authentication (Required)	Jessica Fernandez Signature Adoption: Pre-selected Style Signature ID: EB89DC73-F310-4C55-9DD5-BD840F5D7FBB Using IP Address: 161.69.123.10 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document	Sent: 7/22/2022 11:59:00 AM Viewed: 7/22/2022 12:28:51 PM Signed: 7/22/2022 12:30:04 PM
Electronic Record and Signature Disclosure: Accepted: 7/22/2022 12:28:51 PM ID: d9d77b64-e72a-4aa6-8984-58e5458f4fbf		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	7/22/2022 11:59:00 AM
Certified Delivered	Security Checked	7/22/2022 12:28:51 PM
Signing Complete	Security Checked	7/22/2022 12:30:04 PM
Completed	Security Checked	7/22/2022 12:30:04 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

Electronic Signatures – Consent and Privacy statement

Herewith, signers agree that the electronic signatures are intended to be the legally binding equivalent of traditional handwritten signatures according to CFR – Code of Federal Regulations Title 21, Part 11 Electronic Records; Electronic Signatures, Subpart C – Electronic Signatures.

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