

Mesotrione

Summary of Analytical Chemistry and Residue Data

DP# 364044



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

**OFFICE OF PREVENTION, PESTICIDES,
AND TOXIC SUBSTANCES**
 OPP OFFICIAL RECORD
 HEALTH EFFECTS DIVISION
 SCIENTIFIC DATA REVIEWS
 EPA SERIES 361

MEMORANDUM**Date:** 13-JAN-2010**SUBJECT:** Mesotrione. Request for New End-use Product on Corn.**PC Code:** 122990**DP Barcode:** D364044**Decision No.:** 406567**Registration No.:** 100-RGUO-MESOTRIONE 50WG**Petition No.:** NA**Regulatory Action:** Section 3**Risk Assessment Type:** NA**Case No.:** NA**TXR No.:** NA**CAS No.:** 104206-82-8**MRID No.:** 47687903**40 CFR:** §180.571

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1/26/2010
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Executive Summary

Mesotrione [2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione] is a triketone herbicide which inhibits the enzyme *p*-hydroxyphenyl-pyruvate dioxygenase (HPPD), disrupting carotenoid biosynthesis. Mesotrione is intended for preemergence and postemergence use for the selective control of annual broadleaf weeds. Mesotrione is the active ingredient (a.i.) in a number of other registered formulations, in both liquid and granular formulations. Mesotrione is currently registered for use on a variety of commodities. Permanent tolerances for mesotrione are established under 40 CFR 180.571(a) for a variety of crops, including the following corn tolerances:

Corn, field, forage	0.01 ppm
Corn, field, grain	0.01 ppm
Corn, field, stover	0.01 ppm
Corn, pop, grain	0.01 ppm

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Corn, pop, stover	0.01 ppm
Corn, sweet, forage	0.5 ppm
Corn, sweet, kernel plus cob with husks removed	0.01 ppm
Corn, sweet, stover	1.5 ppm

Syngenta Crop Protection has submitted an application for a new end-use product, Mesotrione 50WG (wetable granule). This new end-use product is proposed for preemergence and early season post-emergence use to control annual broadleaf weeds in corn. Mesotrione 50WG contains the active ingredient, mesotrione, which currently is registered for use on corn, as well as other crops, under the product Callisto[®], a soluble-concentrate (SC) formulation (EPA Reg. No. 100-1131). The directions for use on corn (rates, application timing, instructions, etc.) are identical to the currently-registered directions for use of Callisto[®]. The proposed Mesotrione 50WG label (dated 26-FEB-2009) is adequate to allow evaluation of the additional proposed use on corn.

The submitted field trial data are adequate and reflect the use of two broadcast applications of mesotrione (4SC (soluble concentrate) and 50WG formulations) at a nominal rate of 0.094 lb ai/A/application. Side-by-side treatment plots were established at three trials, with one treatment plot for 4SC applications and one treatment plot for 50WG applications. Following two broadcast applications of the 4 lb/gal SC formulation, maximum residues of mesotrione were 0.169 ppm and 0.0942 ppm in sweet corn forage and stover, respectively. Maximum residues of metabolite 4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA) were 0.0131 ppm and 0.0132 ppm in sweet corn forage and stover, respectively. Residues of mesotrione and MNBA were below the limit of quantitation (limit of quantitation (LOQ) = 0.01 ppm) in/on all ear samples. Following two broadcast applications of the 50% WG formulation, maximum residues of mesotrione were 0.073 ppm in sweet corn forage and 0.094 ppm in sweet corn stover; residues were below the LOQ in sweet corn ears. Residues of MNBA were <LOQ in all sweet corn matrices. In general, residues following application of the 50% WG formulation were equal to or less than residues resulting from application of the 4 lb/gal SC formulation.

Samples were analyzed for residues of mesotrione and MNBA using Syngenta Method RAM 366/01, a high-performance liquid chromatography method with tandem mass-spectrometry detection (HPLC/MS/MS), with minor modifications. Based on the lowest level of method validation (LLMV), the LOQ was 0.01 ppm for each analyte. The method was adequate for data collection based on acceptable concurrent method recoveries.

Available storage stability data submitted with a previous petition for field corn support the storage conditions and intervals of samples from the sweet corn field trials.

The petitioner has not requested a change to the existing corn tolerances (40 CFR: §180.571). The currently-established corn tolerances are adequate to cover any residues in/on corn commodities from the new formulation use.

Regulatory Recommendations and Residue Chemistry Deficiencies

There are no residue chemistry issues that would preclude granting a registration for the new end-use product, Mesotrione 50WG. Because there is not a change in the currently-established corn tolerance levels, a human-health risk assessment is not needed for this action.

Note to RD: The established tolerances listed under 40 CFR §180.571(b) for sweet corn commodities (expiration date 30-JUN-2004) and cranberry (expiration dated 31-DEC-2010) have expired and/or are no longer needed and should be removed.

Background

The chemical structure and nomenclature of mesotrione are presented in Table 1, and the physicochemical properties of the technical grade of mesotrione are presented in Table 2.

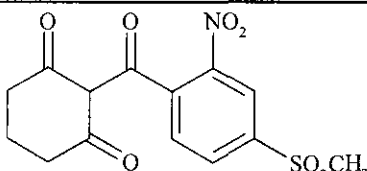
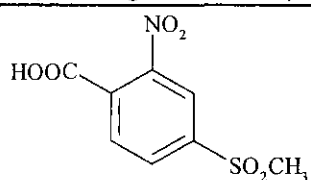
Table 1. Test Compound Nomenclature.	
Chemical structure	
Common name	Mesotrione
Company experimental name	ZA1296
IUPAC name	2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione
CAS name	2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione
CAS registry number	104206-82-8
End-use product (EP)	4 lb/gal SC (Callisto® Herbicide; EPA Reg. No. 100-1131)
Compound	
Common name	MNBA
Chemical name	4-(methylsulfonyl)-2-nitrobenzoic acid

Table 2. Physicochemical Properties of the Technical Grade Test Compound Mesotrione.		
Parameter	Value	Reference
Melting range	148.7-152.5°C	RD Memo, H. Podall, 2/24/2000; DP#: 263245.
pH	3.4 (1% dispersion in water; 25°C)	
Density	1.46 g/mL, 20°C	
Water solubility	20°C 160 ppm, unbuffered water 0.22 g/100 mL, pH 4.8 1.5 g/100mL, pH 6.9 2.2 g/100 mL, pH 9	

Parameter	Value	Reference
Solvent solubility	20°C 0.37 g/100 mL, methanol 1.7 g/100 mL, ethyl acetate 0.27 g/100 mL, toluene 10.4 g/100 mL, acetonitrile <0.03 g/100 mL, heptane 8.1 g/100 mL, acetone	
Vapor pressure	4.3 x 10 ⁻⁸ torr, 20°C	
Dissociation constant, pK _a	3.12, 20°C	
Octanol/water partition coefficient, Log(K _{ow})	20°C log P _{ow} = 0.11 in unbuffered water log P _{ow} = 0.90 in pH 5 buffer log P _{ow} <-1 at pH 7 and 9 buffered water	
UV/visible absorption spectrum	Absorption maximum in methanol at 256 mu, with a molar extinction coefficient of 2.24 x 10 ⁴ M cm.	

860.1200 Directions for Use

The petitioner has submitted a draft specimen label (dated 26-FEB-2009) for the 50.0% WG formulation of mesotrione (EPA Reg. No. 100-xxxx). With regards to corn, HED notes that the draft label is nearly identical to the registered label for the 4 lb/gal SC formulation (Callisto[®]; EPA Reg. No. 100-1131). A summary of the proposed use pattern is presented in Table 3.

Applic. Timing, Type, and Equip. ¹ (Spray Volume)	Application Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations ¹
Corn ²					
Early Post-emergence; Broadcast; Ground (10-30 gal/A)	0.094 (maximum single postemergence rate); 0.19 (maximum two postemergence rate)	2	0.24	45	Special adjuvant restrictions must be followed for postemergence applications in yellow popcorn or sweet corn. Retreatment interval (RTI) = 14 days. Corn may be treated up to 30 inches tall or up to the 8-leaf stage of growth. Do not feed or harvest forage, grain, or stover within 45 days of application.
Preemergence; Broadcast; Ground (10-30 gal/A; up to 80 gal if applied with liquid fertilizers)	0.19-0.24 (used alone)				

¹ See label specifications for tank-mixed applications.

² Do not apply to white popcorn or ornamental (Indian) corn.

Mesotrione 50WG may be used preemergence or postemergence on field corn, production seed field corn, field corn grown for silage, yellow popcorn and sweet corn. The draft label states that aerial application and application through any type of irrigation system is prohibited.

The proposed label for the 50%WG formulation states that crop yield loss may occur: (i) if postemergence application of mesotrione is made to corn treated with Counter[®] or Lorsban[®]; (ii) if mesotrione is tank-mixed with any organophosphate or carbamate insecticide as a foliar postemergence application; or (iii) if any organophosphate or carbamate insecticide is applied foliar postemergence within 7 days before or after application of mesotrione to corn. If Mesotrione 50WG is applied postemergence to ground that received a preemergence application of an HPPD-inhibiting herbicide, atrazine must be tank mixed with Mesotrione 50WG, or a herbicide with an alternate mode of action that is active on the target species should be used in areas where the use of triazines is not appropriate. If atrazine is mixed with Mesotrione 50WG, do not apply to corn that is more than 12 inches in height.

The following rotational crop restrictions are specified on the draft label: corn (all types), asparagus, cranberry, flax, millet (pearl), grasses grown for seed, oats, rhubarb, sorghum (grain and sweet), and sugarcane may be replanted immediately. Small grains may be planted 120 days after application. Alfalfa, blueberry, canola, cotton, ligonberry, peanuts, potatoes, soybeans, sunflowers, sweet potatoes, and tobacco can be planted back the following season, but not less than 10 months after the last Mesotrione 50WG application. If Mesotrione 50WG is applied postemergence following a mesotrione containing preemergence herbicide, only corn (all types) or grain sorghum may be replanted the year following application or severe crop injury will occur. Sugar beets, peas, dry beans, snap beans, cucurbits, red clover, and all other rotational crops may be replanted 18 months after application.

Conclusions: The proposed Mesotrione 50WG label (dated 26-FEB-2009) is adequate to allow evaluation of the additional proposed use on corn. The residue data support the new use on the label.

860.1340 Residue Analytical Methods

Memo, W. Cutchin, 12-JAN-2005; DP#: 283827

Samples were analyzed for residues of mesotrione and MNBA using Syngenta Method RAM 366/01 "Residue Analytical Method for the Determinations of Residues of Mesotrione and 4-(Methylsulfonyl)-2-Nitrobenzoic Acid (MNBA) in Crop Samples," with minor modifications. This method was previously reviewed and forwarded to the U.S. Food and Drug Administration (FDA) for inclusion in the Pesticide Analytical Manual (PAM) Volume II as a confirmatory enforcement method for plant commodities (Memo, W. Cutchin, 12-JAN-2005; DP# 283827).

Briefly, residues of mesotrione and MNBA were extracted with acetonitrile:water (50:50 v/v) after addition of sodium chloride. Aliquots of the extracts were diluted with ultra-pure water followed by solid-phase extraction (SPE). Residues were eluted from the SPE cartridge using methanol and evaporated to dryness. Residues were then dissolved in ultra-pure water:methanol (90:10 v/v) with ultra-sonication. Samples were analyzed using HPLC/MS/MS. Based on the LLMV, the LOQ was 0.01 ppm for both analytes; the method limit of detection (LOD) was not reported.

Conclusions: An acceptable method was used for the quantitation of residues of mesotrione and MNBA.

860.1380 Storage Stability

Memo, S. Levy, 6-JUN-2001; DP#: 245477.

Samples were stored frozen at $<-10^{\circ}\text{C}$ at the field sites and analytical laboratory, except for brief periods during preparation or sub-sample for analysis. The maximum storage interval from collection to extraction was 69 days (2.2 months) for sweet corn forage samples, 70 days (2.3 months) for ear samples, and 49 days (1.6 months) for corn stover samples. All sample extracts were analyzed within 2 days of extraction. The storage durations and conditions of samples from the crop field trials associated with this action are presented in Table 4.

Storage stability data submitted with a previous petition for field corn uses demonstrate that mesotrione and MNBA are stable in corn matrices stored frozen for up to 42 months (Memo, S. Levy, 06-JUN-2001; DP#: 245477).

Matrix	Storage Temperature (°C)	Actual Storage Duration ¹	Interval of Demonstrated Storage Stability ²
Sweet corn, forage (without ear)	$<-10^{\circ}\text{C}$	59-69 days (1.9-2.2 months)	Residues of mesotrione are relatively stable in/on fortified corn matrices (forage, stover, and grain) stored frozen for up to 42 months.
Sweet corn, ear		60-70 days (1.9-2.3 months)	
Sweet corn, stover		33-49 days (1.1-1.6 months)	

¹ Duration from harvest to extraction. Samples were prepared between 4 and 36 days after collection and extracted between 28 and 54 days after preparation. All samples were analyzed within 2 days of extraction.

² Memo, S. Levy, 06-JUN-2001; DP# 245477.

Conclusions: The available corn storage stability data will support the storage conditions and intervals of samples from the sweet corn field trials.

860.1500 Crop Field Trials

DER Reference: 47687903.de1.doc

Syngenta Crop Protection, Inc. has submitted crop trial data for mesotrione and its metabolite, MNBA, on sweet corn matrices using two different formulations. The objective of the study was to determine whether residues in/on sweet corn were similar between the two formulations using side-by-side plots. Three outdoor crop trials were conducted in the North American Free Trade Agreement (NAFTA) Growing Zones 2 (1 trial in NC), 7 (1 trial in ND), and 10 (1 trial in CA) during the 2008 growing season. Each trial site included one control plot and two treated plots. The treated plots each received two broadcast applications of either a 4 lb/gal SC formulation of mesotrione or a 50% (w/w) WG formulation of mesotrione, after crop emergence. Applications were made at a nominal rate of 0.094 lb ai/A, for a total seasonal rate of 0.19 lb ai/A. The re-treatment interval (RTI) was 11-15 days. All applications were made using a tractor or backpack sprayer in 15–26 gal/A; an adjuvant (non-ionic surfactant) was added to the spray mixtures at a nominal rate of 0.25% v/v. Samples of sweet corn forage, ear, and stover were harvested from treated and untreated plots at pre-harvest intervals (PHIs) ranging from 28 to 69 days.

The results of the residue field trials are summarized in Table 5. Following two broadcast applications of the 4SC formulation, maximum residues of mesotrione were 0.169 ppm and

0.0942 ppm in sweet corn forage and stover, respectively. Maximum residues of MNBA were 0.0131 ppm and 0.0132 ppm in sweet corn forage and stover, respectively. Residues of mesotrione and MNBA were below the LOQ in/on all ear samples. Following two broadcast applications of the 50WG formulation, maximum residues of mesotrione were 0.073 ppm in sweet corn forage and 0.094 ppm in sweet corn stover; residues of mesotrione were below the LOQ in sweet corn ears. Residues of MNBA were <LOQ in all sweet corn matrices. Residue levels were similar between the two formulation types.

Table 5. Summary of Residue Data from Crop Field Trials with Mesotrione.									
Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels ¹ (ppm)						
			n	Min.	Max.	HAFT ²	Median	Mean	Std. Dev.
4 lb/gal SC									
Mesotrione									
Sweet corn, forage	0.188 to 0.190	28 to 45	6	<0.01	0.169	0.121	0.010	0.047	0.065
Sweet corn, ears	0.188 to 0.190	28 to 45	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn, stover	0.188 to 0.190	53 to 69	6	<0.01	0.0942	0.0764	0.010	0.032	0.036
MNBA									
Sweet corn, forage	0.188 to 0.190	28 to 45	6	<0.01	0.0131	0.0116	0.010	0.011	0.001
Sweet corn, ears	0.188 to 0.190	28 to 45	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn, stover	0.188 to 0.190	53 to 69	6	<0.01	0.0132	0.0116	0.010	0.011	0.001
50% WG									
Mesotrione									
Sweet corn, forage	0.188 to 0.190	28 to 45	6	<0.01	0.073	0.065	0.010	0.028	0.029
Sweet corn, ears	0.188 to 0.190	28 to 45	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn, stover	0.188 to 0.190	53 to 69	6	<0.01	0.0942	0.0831	0.010	0.034	0.038
MNBA									
Sweet corn, forage	0.188 to 0.190	28 to 45	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn, ears	0.188 to 0.190	28 to 45	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn, stover	0.188 to 0.190	53 to 69	6	<0.01	<0.01	<0.01	<0.01	<0.01	0.0

¹ For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ.

² HAFT = highest-average field trial.

Conclusions: The submitted field trial data are adequate and reflect the use of two broadcast applications of mesotrione (4SC and 50WG formulations) at a nominal rate of 0.094 lb ai/A/application. Side-by-side treatment plots were established at three trials, with one treatment plot for 4SC applications and one treatment plot for 50WG applications. An acceptable method was used for the quantitation of residues of mesotrione and MNBA, and adequate data are available to support sample storage intervals and conditions used in the study.

Following two broadcast applications of the 4 lb/gal SC formulation, maximum residues of mesotrione were 0.169 ppm and 0.0942 ppm in sweet corn forage and stover, respectively. Maximum residues of MNBA were 0.0131 ppm and 0.0132 ppm in sweet corn forage and stover, respectively. Residues of mesotrione and MNBA were below the LOQ in all ear samples. Following two broadcast applications of the 50% WG formulation, maximum residues of mesotrione were 0.073 ppm in sweet corn forage and 0.094 ppm in sweet corn stover; residues were below the LOQ in sweet corn ears. Residues of MNBA were <LOQ in all sweet corn matrices. In general, residues following application of the 50% WG formulation were equal to or less than residues resulting from application of the 4 lb/gal SC formulation.

860.1520 Processed Food and Feed

Adequate field corn processing data were submitted under a previous petition (PP#8F04954; Memo, S. Levy, 06-JUN-2001; DP#: 245477) for field corn uses which indicated that tolerances for mesotrione residues were not required for field corn processed commodities.

860.1650 Submittal of Analytical Reference Standards

Analytical standards for mesotrione (expiration 31-JAN-2011) and the metabolite MNBA (01-JUN-2011) are currently available in the EPA National Pesticide Standards Repository (personal communication with Dallas Wright, ACB, 21-APR-2009).

860.1550 Proposed Tolerances

The petitioner has not requested a change to the existing corn tolerances (40 CFR: §180.571). The currently-established corn tolerances are adequate to cover any residues in/on corn commodities from the new formulation use.

References

DP#: 260570
 Subject: PP#8F04954. Mesotrione (Proposed Name). Multiresidue Method Testing of ZA1296. Chemical #: 122990. Case #: 289589. Submission #: S541377
 From: S. Levy
 To: F. Griffith
 Date: 16-NOV-1999
 MRID#: 44505224

DP#: 263245
 Subject: Product Chemistry Review of Mesotrione (ZA 1296 Technical (dry)).
 From: H. Podall
 To: J. Tompkins/J. Stone
 Date: 24-FEB-2000
 MRID#s: 44373503-44373505, 44505003, 44505004, and 44901701

Mesotrione

Summary of Analytical Chemistry and Residue Data

DP# 364044

DP#: 274111
Subject: PP# 8F04954. Mesotrione: Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting of 4/10/01. Chemical No. 122990. Case No. 063670. Submission No. S541375.
From: S. Levy
To: Y. Donovan
Date: 26-APR-2001
MRID#: None

DP#s: 245477 and 260267
Subject: PP#: 8F04954. Mesotrione in/on Field Corn. Evaluation of Residue Data and Analytical Methods. PC Code: 122990. Case #: 289589. Submission #s: S541377 and S569871.
From: S. Levy
To: J. Stone /J. Tompkins
Date: 06-JUN-2001
MRID#s: 44505118, 44505212-23, 44537109-12, 44901719, and 44942401-03

DP#: None
Subject: Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Commodity Definitions [40 CFR §180.1(h)] and Crop Group/Subgroups [40 CFR §180.41].
From: B. Schneider
To: H. Jamerson
Date: 14-JUN-2002
MRID#: None

DP#: 283827
Subject: Mesotrione. Summary of Analytical Chemistry and Residue Data for Sweet Corn, PP#2F06443, and Response to Data Deficiencies of a Previous HED Review (PP#8F04954, DP Barcodes: D245477 and D260267, 6/6/01, S. Levy).
From: W. Cutchin
To: J. Stone/J. Miller
Date: 12-JAN-2005
MRID#s: 45651801-45651803, 45651813, 45651814, 45651816, 45651817, and 45665901

DP#s: 326898 and 332812
Subject: Mesotrione. Section 3 Request for Use on Berry Group 13, Cranberry, Flax, and Millet (PP#6F7023) and Section 18 Request for Emergency Exemption Use on Grain Sorghum (Reg#: 06KS01). Summary of Analytical Chemistry and Residue Data.
From: S. Levy
To: J. Miller and A. Ertman
Dated: 2-MAR-2007
MRID#s: 46726301-46726307

Mesotrione

Summary of Analytical Chemistry and Residue Data

DP# 364044

DP#: 338109
Subject: PP#6F7162. Mesotrione. Section 3 Registration Request for Uses on Asparagus, Grass Grown for Seed, Oats, Okra, Rhubarb, Sugarcane, Grain Sorghum, and Sweet Sorghum. Summary of Analytical Chemistry and Residue Data.
From: S. Levy
To: J. Miller and J. Stone
Dated: 05-DEC-2007
MRID#s: 46726301-46726307

cc: S. Levy (RAB1)
RDI: RAB1 Chemists (13-JAN-2010); G.F. Kramer (11-JAN-2010)
S. Levy:S10953:PY-S:(703)305-0783:7509P:RAB1

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