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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 26-APR-2001

SUBJECT: PP# 8F04954. Mesotrione: Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting of 4/10/01. Chemical No. 122990. DP Barcode D274111. Case No. 063670. Submission No. S541375.

FROM: Sarah J. Levy, Chemist *Sarah J. Levy*
David Nixon, D.V.M., Toxicologist *David Nixon*
Registration Action Branch 1 (RAB1)/HED (7509C)

THRU: G. Jeffrey Herndon, Branch Senior Scientist *G. Jeffrey Herndon*
RAB1/HED (7509C)

and

Christine Olinger, Chair *Christine Olinger*
HED MARC (7509C)

TO: Yan Donovan, Executive Secretary
HED MARC (7509C)

Attendance

1. MARC Members
Yan Donovan, Leung Cheng, Alberto Protzel, William Wassell, Abdallah Khasawinah, Chris Olinger, Rick Loranger, John Doherty, Norman Birchfield
2. MARC Members in Absentia
Kit Farwell, Sheila Piper
3. Scientists (non-MARC members)
Sarah Levy, David Nixon, Jeff Herndon, George Kramer, Alex Clem

Summary of Deliberations

The HED MARC reviewed and discussed the field corn, livestock, rotational crop, and drinking water studies for the herbicide mesotrione (2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione) (see Attachment 1 for structures). Sarah Levy, David Nixon, and Alex Clem (of the Environmental Fate and Effects Division (EFED)) were responsible for data review and preparation of the briefing document (D273597, 03-APR-2001). The MARC used the following considerations in supporting their conclusions:

- Similarly to the parent, metabolites MNBA (4-(methylsulfonyl)-2-nitrobenzoic acid) and AMBA (2-amino-4-(methylsulfonyl)benzoic acid) are not mutagenic in a bacterial system.
- Based on the weight of evidence, the MARC was not specifically concerned about neurotoxicity of metabolites MNBA and AMBA. Although a non-guideline 28-day study in rats dosed with MNBA showed an increase in motor activity in females, no other neurological effects were observed.
- Metabolites MNBA and AMBA are very polar, acidic compounds; therefore, these metabolites are rapidly excreted and are found at low residue levels in the tissues.
- Low levels of the metabolites MNBA and AMBA are expected in plants, livestock and drinking water.
- Metabolites MNBA and AMBA were both detected at low levels in both the rat and mouse metabolism studies.
- Metabolites MNBA and AMBA did not likely contribute to the toxicological doses/endpoints selected for the parent. Compared to the parent, MNBA and AMBA are not of toxicological concern and are weak inhibitors of the enzyme p-hydroxyphenylpyruvate dioxygenase (HPPD).
- The ruminant metabolism studies were conducted at 540x-700x the maximum theoretical dietary burden (MTDB). Based on the residue identification/characterization performed in the metabolism study and the MTDB, it was concluded that there was no reasonable expectation of finite residues in livestock commodities (Category 180.6(a)(3)).
- The poultry metabolism study was conducted at 1100x the MTDB. Based on the residue identification/characterization performed in the metabolism study and the MTDB, it was concluded that there was no reasonable expectation of finite residues in poultry commodities (Category 180.6(a)(3)).

- Data provided by the EFED indicates these compounds are relatively short-lived under aerobic conditions.

MARC Decisions

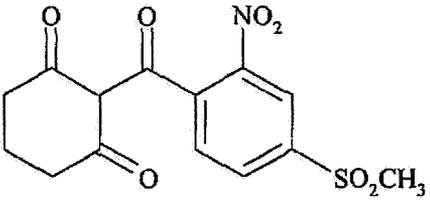
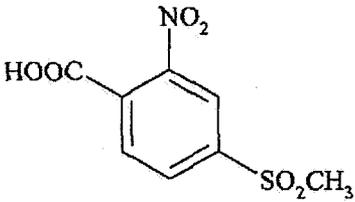
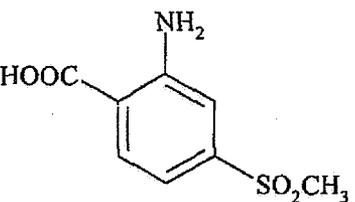
- Field Corn:* The MARC concluded that for the tolerance expression and risk assessment purposes, the residue of concern in/on field corn is mesotrione *per se*.
- Livestock:* The MARC concluded that for the tolerance expression and risk assessment purposes, the residue of concern in/on livestock commodities is mesotrione *per se*.
- Rotational Crop:* The MARC concluded that for the tolerance expression and risk assessment purposes, the residue of concern in/on rotational crops is mesotrione *per se*.
- Drinking Water:* The MARC concluded that for risk assessment purposes, the residue of concern in/on drinking water is mesotrione *per se*.

Attachments

Attachment 1. Chemical Names/Codes and Structures of Mesotrione Residues Mentioned in this Memorandum.

cc with Attachment 1: S. Levy (RAB1), D. Nixon (RAB1), J. Stone/J. Tompkins (RD), A. Clem (EFED), F. Griffith (BEAD-7503C)
RDI: G.J. Herndon (4/26/01), G. Kramer (4/11/01), RAB1 Chemistry Team (4/17/01), Chem SAC (4/4/01)
S.J. Levy:806T:CM#2:(703)305-0783:7509C:RAB1

**Attachment 1. Chemical Names/Codes and Structures of Mesotrione Residues
Mentioned in this Memorandum.**

Common Name/Code Chemical Name	Chemical Structure	Matrices
<p>Mesotrione ZA1296</p> <p>2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione</p>		<p>Field corn forage</p> <p>Cow liver and kidney</p> <p>Hen egg yolk, subcutaneous fat, liver</p> <p>Rotated soybean forage and hay, and wheat forage, hay, and straw</p>
<p>MNBA</p> <p>4-(methylsulfonyl)-2-nitrobenzoic acid</p>		<p>Field corn forage and stover</p> <p>Rotated endive, radish roots and tops, soybean forage, hay, and soybeans, and wheat forage, hay, straw, and grain</p>
<p>AMBA^a</p> <p>2-amino-4-(methylsulfonyl)benzoic acid</p>		<p>Field corn grain, forage, and stover</p> <p>Cow kidney and perirenal fat^b</p> <p>Rotated endive, soybean forage, hay, and soybeans, and wheat forage, hay, and straw</p>

^a Includes conjugates.

^b Identification in kidney from [¹⁴C]mesotrione and [¹⁴C]AMBA metabolism studies; identification in perirenal fat from [¹⁴C]AMBA metabolism study only.