



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

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

**MEMORANDUM**

DATE: 17-MAY-2001

SUBJECT: PP #: 8F04954. **Mesotrione: Chronic Dietary Exposure Analysis for Use on Field Corn.** Chemical #: 122990. DP Barcode: D274113. Case #: 063670. Submission #: S541375.

FROM/TO: Sarah Levy, Chemist *Sarah Levy*  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

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

and

Jose Morales, Chemist *Jose Morales*  
Mohsen Sahafeyan, Chemist *Mohsen Sahafeyan*  
Dietary Exposure Science Advisory Council (DE SAC)

**Action Requested**

As a result of a Section 3 request (PP# 8F04954) for use of a new active ingredient, mesotrione, on field corn, it was requested that an estimate be provided of the dietary exposure and associated risk resulting from the proposed tolerance levels. This is the first food use request for mesotrione. The proposed and HED-recommended tolerance levels for field corn raw agricultural commodities (RACs) are 0.01 ppm (Memo, S. Levy, DRAFT, D245477).

## Executive Summary

No acute doses or endpoints were selected; therefore, an acute dietary exposure analysis was not performed. The chronic dietary exposure analysis for mesotrione was performed using the Dietary Exposure Evaluation Model (DEEM™ version 7.72). For the chronic dietary analysis, HED-recommended tolerance level residues, DEEM™ default processing factors, and 100% CT information were used for all commodities (Tier 1). All chronic dietary risk estimates are below HED's level of concern for the general U.S. population and all population subgroups (including infants and children). Specifically, the highest chronic dietary risk estimate was 4.3% cPAD for the "all infants (< 1 year old)" population subgroup. Mesotrione has been classified as "not likely" to be carcinogenic to humans via relevant routes of exposure; therefore, a cancer dietary exposure risk analysis was not performed.

## Toxicological Information

### *Hazard Identification Assessment Review Committee (HIARC)*

The HED HIARC met on March 13, 2001 and selected doses and endpoints for dietary and non-dietary exposure risk assessments (Memo, D. Nixon, 12-APR-2001, HED Doc. 014536; see Table 1).

### *FQPA Recommendation*

The FQPA Safety Factor Committee met on April 16, 2001 (Memo, B. Tarplee, 30-APR-2001, HED Doc. No. 014552) to evaluate the hazard and exposure data for mesotrione and recommended that the FQPA safety factor (as required by FQPA of August 3, 1996) be retained (10x) in assessing the risk posed by this chemical.

A Population Adjusted Dose (PAD) is a modification of the acute or chronic RfD to accommodate the FQPA safety factor. The PAD is equal to the acute or chronic RfD divided by the applicable FQPA safety factor. Therefore, the cPAD for the general U.S. population and other subgroups (including infants and children) is 0.0007 mg/kg/day ( $0.007 \text{ mg/kg/day} \div 10 = 0.0007 \text{ mg/kg/day}$ ).

### *Cancer*

The HIARC classified mesotrione as "not likely" to be carcinogenic to humans via relevant routes of exposure. Therefore, a carcinogenicity dietary analysis was not performed.

**Table 1. Summary of Doses and Toxicological Endpoints for Mesotrione.**

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary <u>all populations</u>	Not Applicable	Not Applicable	No appropriate study available
Chronic Dietary <u>all populations</u>	LOAEL= 2.1 mg/kg/day UF =3 Chronic RfD = 0.007 mg/kg/day	FQPA SF = 10X  cPAD = $\frac{\text{chronic RfD}}{\text{FQPA SF}}$ = 0.0007 mg/kg/day	Reproduction Study - mouse Offspring LOAEL = 2.1 mg/kg/day based upon tyrosinemia in F <sub>1</sub> and F <sub>2a</sub> offspring and ocular discharge in F <sub>1</sub> pups.
Cancer (oral, dermal, inhalation)	“not likely”	Not Applicable	Acceptable oral rat and mouse carcinogenicity studies; no evidence of carcinogenic or mutagenic potential.

### Residue Information

For the chronic dietary analysis, HED-recommended tolerance level residues, DEEM™ default processing factors, and 100% CT information were used for all commodities (Tier 1). The residue information used in the chronic analysis is attached (Attachment 1).

### Consumption Data

Chronic dietary exposure analyses were conducted using the Dietary Exposure Evaluation Model (DEEM™, ver 7.72) and consumption data from the USDA 1989-92 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII). For chronic dietary risk assessments, the three-day average consumption for each sub-population is combined with residues in commodities to determine average exposure in mg/kg/day.

### Results/Discussion

#### *Acute Dietary Exposure Analysis*

No acute doses or endpoints were selected for mesotrione; therefore, an acute dietary exposure analysis was not performed.

#### *Chronic Dietary Exposure Analysis*

A conservative analysis was performed using the HED-recommended tolerance level residues, DEEM™ default processing factors, and 100% CT information for all commodities. For

chronic dietary risk, HED's level of concern is >100% cPAD. Dietary exposure estimates for the U.S. population and other representative subgroups are presented in Table 2. A full listing of chronic dietary exposure estimates is attached (Attachment 2).

**Table 2. Summary of Results from Chronic DEEM™ Analysis.**

Subgroups <sup>1</sup>	Exposure (mg/kg/day)	% cPAD
U.S. Population	0.000013	1.8
All infants (< 1 year old)	0.000030	4.3
Children (1-6 years old)	0.000029	4.2
Children (7-12 years old)	0.000023	3.2
Females (13-50 years old)	0.000009	1.3
Males (13-19 years old)	0.000016	2.3
Males (20+ years old)	0.000009	1.3
Seniors (55+ years old)	0.000007	1.0

<sup>1</sup> HED notes that there is a degree of uncertainty in extrapolating exposures for certain population subgroups which may not be sufficiently represented in the consumption surveys, (e.g., non-nursing infants, etc.). Therefore, risks estimated for these subpopulations were included in representative populations having sufficient numbers of survey respondents (e.g., all infants, females, 13-50 years, etc.).

The results of the chronic analysis indicate that the estimated chronic dietary risk associated with the recommended uses of mesotrione are below HED's level of concern.

*Cancer Dietary Exposure Analysis*

Mesotrione has been classified as "not likely" to be carcinogenic to humans via relevant routes of exposure. Therefore, a cancer dietary exposure risk analysis was not performed.

**List of Attachments**

- Attachment 1: Chronic Residue Information
- Attachment 2: Chronic DEEM™ Analysis

cc with Attachments: J. Stone/J. Tompkins (RD), M. Sahafeyan (CEB1/HED)  
 RDI: G. Jeffrey Herndon 5/17/01: DE SAC [J. Morales (5/17/01), M. Sahafeyan (5/16/01)]  
 S. Levy:RAB1:806T:CM#2:(703)305-0783:7509C

## Attachment 1: Chronic Residue Information

U.S. Environmental Protection Agency Ver. 7.72  
 DEEM Chronic analysis for MESOTRIONE 1989-92 data  
 Residue file: C:\deem\Mesotrione\chronic.RS7 Adjust. #2 used  
 Analysis Date 05-17-2001 Residue file dated: 05-17-2001/14:49:30/8  
 Reference dose (RfD) = 0.0007 mg/kg bw/day  
 Comment: Chronic endpoint only.

Food Crop			RESIDUE	Adj. Factors	
Comment					
Code	Grp	Food Name	(ppm)	#1	#2
266	15	Corn grain-endosperm	0.010000	1.000	1.000
267	15	Corn grain-bran	0.010000	1.000	1.000
268	15	Corn grain/sugar/hfcs	0.010000	1.500	1.000
289	15	Corn grain-oil	0.010000	1.000	1.000
388	15	Corn grain/sugar-molasses	0.010000	1.500	1.000

## Attachment 2: Chronic DEEM™ Analysis

U.S. Environmental Protection Agency

Ver. 7.72

DEEM Chronic analysis for MESOTRIONE

(1989-92 data)

Residue file name: C:\deem\Mesotrione\chronic.RS7 Adjustment factor #2 used.

Analysis Date 05-17-2001/14:50:19 Residue file dated: 05-17-2001/14:49:30/8

Reference dose (RfD, Chronic) = .0007 mg/kg bw/day

COMMENT 1: Chronic endpoint only.

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### Total exposure by population subgroup

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Population Subgroup	mg/kg body wt/day	Total Exposure Percent of PAD
U.S. Population (total)	0.000013	1.8%
U.S. Population (spring season)	0.000012	1.8%
U.S. Population (summer season)	0.000013	1.8%
U.S. Population (autumn season)	0.000013	1.9%
U.S. Population (winter season)	0.000012	1.7%
Northeast region	0.000011	1.6%
Midwest region	0.000013	1.9%
Southern region	0.000013	1.9%
Western region	0.000012	1.7%
Hispanics	0.000013	1.9%
Non-hispanic whites	0.000012	1.7%
Non-hispanic blacks	0.000015	2.1%
Non-hisp/non-white/non-black	0.000011	1.6%
All infants (< 1 year) (.0007*)	0.000030	4.3%
Nursing infants (.0007*)	0.000008	1.1%
Non-nursing infants (.0007*)	0.000040	5.7%
Children 1-6 yrs (.0007*)	0.000029	4.2%
Children 7-12 yrs (.0007*)	0.000023	3.2%
Females 13-19 (not preg or nursing) (.0007*)	0.000013	1.8%
Females 20+ (not preg or nursing) (.0007*)	0.000008	1.1%
Females 13-50 yrs (.0007*)	0.000009	1.3%
Females 13+ (preg/not nursing) (.0007*)	0.000009	1.3%
Females 13+ (nursing) (.0007*)	0.000009	1.3%
Males 13-19 yrs (.0007*)	0.000016	2.3%
Males 20+ yrs (.0007*)	0.000009	1.3%
Seniors 55+ (.0007*)	0.000007	1.0%
Pacific Region	0.000011	1.6%

\*PAD in mg/kg-bw-day

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