



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: 6-JUNE-2001

SUBJECT: **Occupational and Residential Exposure and Risk Assessment/Characterization for the Proposed use of Mesotrione on Field Corn. PC Code:122990. DP Barcode: D269077.**

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Summary

The proposed use of the herbicide Callisto™, a suspension concentrate (SC) formulation containing 40% of the active ingredient (a.i.), mesotrione, is for pre- and postemergence control of broadleaf weeds in field corn. Mesotrione may be applied either by ground sprayers or by aerial application up to corn height of 30 inches tall. A maximum of two applications per season and 0.43 lbs a.i./A/season are proposed. For preemergence application, Callisto™ is proposed for use at 0.188-0.24 lbs ai/A by groundboom. In a single postemergence application, 0.094 lbs a.i./A should not be exceeded.

In the case of mesotrione, the short-term dermal endpoint [rat developmental endpoint (LOAEL = 100 mg/kg/day)] is appropriate for the 0 to 30 day exposure period since it provides protection for developmental effects seen below maternally toxic doses. For the proposed use of mesotrione, no longer than 30 days of exposure is expected for both private and commercial

handlers.

Based on the proposed use patterns, short-term dermal and inhalation exposures are expected for private applicators (farmers treating their own crops) and commercial applicators. Since no chemical-specific data are available to assess potential exposure to workers, the exposure and risk assessment presented in this document are based on the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, August 1998). The maximum application rate listed on the label was used for all calculations. The standard values for acreage were taken from HED Exposure Science Advisory Committee (Expo SAC) Policy #09, effective 5-JUL-2000. Both the low and high number of acres treated per day were used to demonstrate a range of potential exposure. When wearing the label required personal protective equipment (PPE) (single layer of clothing and gloves), all Margins of Exposure (MOEs) are below HED's level of concern.

Workers having potential re-entry exposure to mesotrione from the proposed use include scouts and workers re-entering treated fields to perform irrigation tasks. Since mesotrione will be applied at the early stages of crop growth (pre- or post-emergent), low potential for post-application exposure is expected. In order to demonstrate that minimal exposure and risk are expected, a post-application exposure assessment was done for scouts. The estimated MOE for scouting activities related to the proposed use of mesotrione on field corn do not exceed HED's level of concern.

Use Patterns and Formulations

Syngenta has proposed the registration of the herbicide Callisto™, a SC formulation containing 40% of the (a.i.) mesotrione. The proposed use is for pre- and post-emergence selective contact and residual control of broadleaf weeds in field corn, (including production seed corn, and silage corn; use is prohibited on sweet corn, popcorn, and ornamental (Indian) corn). According to the label, this product is absorbed through the soil or by the foliage of emerged weeds, and should be applied to actively growing weeds. Mesotrione may be applied either by ground sprayers or by aerial application up to corn height of 30 inches (or up to the V8 leaf corn growth stage for field corn). Application using irrigation equipment is prohibited. A maximum of two applications per season totaling 0.43 a.i./A/season is proposed. For preemergence application, Callisto™ is proposed for use at 0.188-0.24 lbs a.i./A by groundboom. In a single postemergence application, 0.094 lbs a.i./A should not be exceeded. The petitioner did not propose a PHI, however, the residue chemistry data support a PHI of 45 days (Memo, S. Levy, 6-JUN-2001, D245477). Table 1.0 summarizes the use pattern of mesotrione for the proposed use. Currently, there are no registered or proposed residential uses of mesotrione.

Table 1.0 Use Pattern Summary of Mesotrione on Field Corn.

Crop	field corn
Formulation	liquid SC
Pests	broadleaf weeds
Application methods	groundboom sprayer and aerial application
Maximum application rate (AR)	0.24 lbs a.i./Acre
Maximum seasonal AR	0.43 lbs a.i./A/season
Number of applications per season	2
Manufacturer	Syngenta

Toxicological Profile

The exposure estimates are based on toxicological endpoints identified in HED's HIARC document dated 4/21/2001. The acute toxicity of mesotrione and the doses and toxicological endpoints selected for various occupational exposure scenarios are summarized in Table 1.1 and 1.2.

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral	44373512	LD ₅₀ > 5000 mg/kg	IV
81-2	Acute Dermal	44373514	LD ₅₀ > 2000 mg/kg	III
81-3	Acute Inhalation	44373516	LC ₅₀ > 4.75 mg/L	IV
81-4	Primary Eye Irritation	44373518	Mild eye irritant	IV
81-5	Primary Skin Irritation	44373520	Not a dermal irritant	IV
81-6	Dermal Sensitization	44373522	Not a dermal sensitifer	N/A

Table 1.2 Summary of Dose and Toxicological Endpoints for Mesotrione

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Dermal, Short-Term ¹	NOAEL = 33 mg/kg/day MOE = 100	Delays in skeletal ossification and changes in <i>manus/pes</i> ossification assessments	Developmental Toxicity - Rat
Dermal, Intermediate-/ Long-Term ¹	NOAEL = 0.7 mg/kg/day MOE = 100	Tyrosinemia in F ₁ adults and F _{2a} pups and ocular discharge in F ₁ pups	Multi-generational Reproduction Study - Mouse
Inhalation, Short-Term ²	NOAEL = 33 mg/kg/day MOE = 100	Delays in skeletal ossification and changes in <i>manus/pes</i> ossification assessments	Developmental Toxicity - Rat
Inhalation, Intermediate-/ Long-Term ²	NOAEL = 0.7 mg/kg/day MOE = 100	Tyrosinemia in F ₁ adults and F _{2a} pups and ocular discharge in F ₁ pups	Multi-generational Reproduction Study - Mouse

- 1 Since an oral endpoint was selected, a dermal absorption factor of 25% should be used in route-to-route extrapolation.
- 2 Since an oral endpoint was selected, an inhalation factor of 100% should be used in route-to-route extrapolation.

Occupational Exposure Assessment

Mixer/Loader/Applicator Exposure Assessment

In the case of mesotrione, the short-term dermal endpoint [rat developmental endpoint (LOAEL = 100 mg/kg/day)] is appropriate for the 0 to 30 day exposure period since it provides protection for developmental effects seen below maternally toxic doses (Personal Communication, S. Makris to D. Nixon, 9-MAY-2001). For the proposed use of mesotrione, no longer than 30 days of exposure is expected for both private and commercial handlers.

Based on the proposed use patterns, short-term dermal and inhalation exposures are expected for private applicators (farmers treating their own crops) and commercial applicators. Since mesotrione may be applied only twice per year, long-term exposures are not expected from the proposed uses.

Since no chemical-specific data are available to assess potential exposure to workers, the exposure and risk assessment presented in this document are based on the PHED Version 1.1 (Surrogate Exposure Guide, August 1998). PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association (ACPA). PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates).

Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The

subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., wettable powders, granulars), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing).

Once the data for a given exposure scenario have been selected, the data are normalized (i.e., divided) by the amount of pesticide handled resulting in standard unit exposures (milligrams of exposure per pound of active ingredient handled). Following normalization, the data are statistically summarized. The distribution of exposure values for each body part (e.g., chest upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments (Exposure SAC, Policy #007).

PHED does not contain exposure scenarios for the SC formulation. However, HED believes that the data for mixer/loaders and applicators using "liquid" formulations are adequate to confidently estimate exposures for these job functions. Table 1.4 provides exposure estimates for workers wearing a single layer of clothing, with or without gloves. It should be noted that the label requires a single layer of clothing and chemical resistant gloves as the necessary personal protective equipment (PPE). All data are rated medium to high confidence (see Attachment 1).

Currently, HED recommends that the exposure and risk estimates for mixer/loaders and applicators of tractor drawn equipment remain separate unless specific chemical and/or crop information exists to warrant the combining of the two estimates (HED Exposure SAC, Draft Policy, 29-MAR-2000). Therefore, scenarios applicable to mixing/loading SCs and applying by groundboom were not included in the handler exposure assessment for the proposed uses of mesotrione.

The maximum application rate listed on the label was used for all calculations. The standard values for acreage were taken from the HED Exposure SAC Policy #09, effective 5-JUL-2000. Both the low and high number of acres treated per day were used to demonstrate a range of potential exposure. Table 1.4 lists what is considered to be typical to high-end worker exposure and risk assessment for handlers of mesotrione.

Table 1.3 Assumptions Used in Mesotrione Occupational Handler Exposure Calculations.

Exposure Scenario	Application Rate ¹ (lb ai/acre)	Surrogate Unit Exposures ² (mg/lb ai)				Amount Treated ³ (acres/day)
		Baseline		With Gloves		
		Dermal	Inhalation	Dermal	Inhalation	
Mixer/Loader						
Open Mixing/ Loading Liquids for Aerial Application	0.24	2.9	0.0012	0.023	0.0012	350
						1200
Open Mixing/ Loading Liquids for Groundboom Application	0.24	2.9	0.0012	0.023	0.0012	80
						200
Flagger						
Flagging	0.24	0.011	0.00035	-NA ⁴	-NA ⁴	350
Applicator						
Aerial Application (Enclosed Cockpit)	0.24	0.005	0.000068	-NA ⁴	-NA ⁴	350
						1200
Groundboom Application (Open Cab)	0.24	0.014	0.00074	0.014	0.00074	80
						200

¹ Maximum application rates which are based on the proposed Callisto™ label.

² Surrogate unit exposures are from the PHED as presented in the PHED Surrogate Exposure Guide (AUG-1998). mitigation levels: **baseline** (long pants, a long-sleeved shirt, no chemical-resistant gloves, and no respirator), **plus gloves** (baseline clothing, and chemical-resistant gloves).

³ The number of acres treated per day were based on Exposure SAC Policy #09 (dated 5-JUL-2000).

⁴ Only engineering controls are available.

Table 1.4 Mesotrione Exposure and Risk Estimates for Handler Exposure to Mesotrione.

Exposure Scenario	Acres/Day	Baseline ¹		With Gloves ²	
		Total ADD ³ (mg/kg/d)	Combined Short-term MOE ⁴	Total ADD ³ (mg/kg/d)	Combined Short-term MOE ⁴
Mixer/Loader					
Mixing/Loading Liquids for Aerial application	low	1.0	100	0.010	10000
	high	3.5	30	0.29	3000
Mixing/Loading for Groundboom application	low	0.23	420	0.0022	45000
	high	0.58	170	0.0056	18000
Flagger					
Flagging		0.0044	23000		
Applicator					
Aerial application	low	0.0019	54000		
	high	0.0063	16000		
Groundboom application	low	0.0013	72000	0.0013	72000
	high	0.0034	29000	0.0034	29000

¹ Baseline = long pants, a long-sleeved shirt, no chemical-resistant gloves, and no respirator.

² Plus Gloves = Baseline clothing plus chemical-resistant gloves.

³ Total Average Daily Dose (mg/kg/day) = Average Dermal Daily Dose (mg/kg/day) + Average Inhalation Daily Dose (mg/kg/day)

where: Average Daily Dose (ADD) (mg/kg/day) = Unit Exposure (mg/lb ai) x (lb ai/acre) x (acres/day) x Absorption Factor (25% and 100% used to convert dermal and inhalation, respectively to an oral equivalent dose) / Body Weight (60 kg)

⁴ Combined MOE = LOAEL/Total ADD, LOAEL = 100 mg/kg/day for short-term.

level of concern is for MOEs below 300.

With the addition of gloves, all MOEs are greater than 300. Since the label required PPE is a single layer of clothing and gloves, the MOEs for all scenarios do not exceed HED's level of concern.

Post-Application Exposure Assessment

Most cultural practices related to field corn are mechanized, having low potential for dermal contact. According to information from the *USDA OPMP & PIAP Crop Profiles* website (http://pestdata.ncsu.edu/cropprofiles/Detail.CFM?FactSheets_RecordID=62), field corn is planted mechanically with a row crop planter or grain drill. Corn may be grown using till or non-till methods. Tillage is mainly accomplished by use of a rotary hoe and harvest is done by combine. Scouting and irrigation may be performed throughout the season.

Workers having potential exposure to mesotrione from the proposed use include scouts and workers re-entering treated fields to perform irrigation tasks. Since mesotrione will be applied at the early stages of crop growth (or up to the V8 leaf corn growth stage) and up to corn height of 30 inches, limited potential for post-application exposure is expected. Therefore, short-term post-application exposures are assessed for scouting activities occurring around the time of application. This assessment is considered to be screening level, demonstrating that there are minimal potential risks to workers re-entering fields treated with mesotrione.

There are no chemical-specific data available to determine the potential risks from post-application activities associated with the proposed use of mesotrione. To provide an screening level estimate of the potential risks and exposures, a risk assessment was conducted using the following assumptions:

- ▶ Maximum application rate of 0.24 lb a.i./A
- ▶ HED standard transfer coefficients (TC) of 400 cm²/hour for scouting
- ▶ 20% of the application rate available as dislodgeable residues
- ▶ Work day of 8 hours
- ▶ Reentry on day 0
- ▶ 25% dermal absorption (considered an upper bound assumption)

The TC used in this assessment are from an interim TC policy developed by HED's Exposure SAC for using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (Policy # 3.1). It is the intention of HED's Exposure SAC that this policy will be periodically updated to incorporate additional information about agricultural practices in crops and new data on TC. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Exposure estimates for scouting activities are listed in Table 1.5 and are expected to represent high-end estimates of potential post-application exposure resulting from the proposed uses of mesotrione.

Table 1.5 Post-application Exposure Assessment for Mesotrione.

Post-application Activity	TC ¹ cm ² /hr	DFR ² ug/cm ² DAT = 0	ADD ³ mg/kg/day	Short-term MOE ⁴
Early season scouting of field corn	400	0.54	0.0072	14000

¹TC(Standard TC for Agricultural Activities, field corn scouting (minimum foliage), HED Exposure SAC, 3-AUG-2000, taken from ARTF009 for sweet corn)

²Surrogate DFR₀ = application rate X 20% available as dislodgeable residue X 4.54E8 ug/lb X 2.47E-8 A/cm²

³ADD = DFR X TC X Duration X 0.001 mg/ug /BW (60 kg) X 25%DA

⁴MOE = LOAEL/ADD; Short-term dermal LOAEL = 100 mg/kg/day
level of concern is for MOEs below 300.

HED's level of concern for mesotrione is for MOEs below 300. The calculated MOE is 14,000 for scouting activities related to the proposed use of mesotrione on field corn. This screening level assessment demonstrates that potential post-application exposures for workers contacting mesotrione treated surfaces are not expected to exceed HED's level of concern.

REI

Mesotrione is in toxicity category III for the dermal route of exposure. Based on the Worker Protection Standard (WPS), an interim REI of 12 hours is sufficient to protect workers performing re-entry activities for the proposed use of mesotrione.

Incident Reports

Since mesotrione is a new ai, no incidence data are available.

cc (with attachment): chemical file, D. Vogel (RAB1), G. Kramer (RAB1).
RDI: ORE (15-MAY-2001), Exposure SAC (17-MAY-2001), Team (17-MAY-2001), Branch (23-MAY-2001), G. Herndon (6-JUN-2001); D.Vogel:809B:CM#2:(703)305-0874:7509C:RAB1

Attachment 1: PHED Data Quality

Exposure Scenario	Data Source	Data Confidence
Mixer/Loader Descriptors		
Mixing/Loading Liquid Formulations	PHED V1.1	<p>Baseline: Hands, dermal, and inhalation = AB grades. Hands = 53 replicates; Dermal = 72 to 122 replicates; and Inhalation = 85 replicates. High confidence in hands/dermal, and inhalation data. No protection factor was needed to define the unit exposure value.</p> <p>PPE: The same dermal data are used as for baseline, coupled with a 50% protection factor to account for an additional layer of clothing, with gloved hand data. A 10-fold PF (i.e., 90% PF) was applied to the baseline inhalation data. Hands = AB grades. Hands = 59 replicates. High confidence in hands data.</p> <p>Engineering Controls: Hands, dermal, and inhalation = AB grades. Hands = 31 replicates; Dermal = 16 to 22; and Inhalation = 27 replicates. High confidence in hands/dermal, and inhalation data. No protection factor was needed to define the unit exposure value. Engineering controls based on closed mixing/loading.</p>
Applicator Descriptors		
Applying Sprays with Aerial Equipment	PHED V1.1	<p>Baseline: Not feasible for this scenario.</p> <p>PPE: Not feasible for this scenario.</p> <p>Engineering Controls: Hands = AB grade, dermal and inhalation = ABC grade. Hands = 34 replicates, dermal = 24 to 48 replicates, and inhalation = 23 replicates. Medium confidence in hands, dermal, and inhalation data. No protection factor was needed to define the unit exposure value.</p>
Applying Sprays with a Groundboom Sprayer	PHED V1.1	<p>Baseline: Hands, dermal, and inhalation = AB grades. Hands = 29 replicates, dermal = 23 to 42 replicates, and inhalation = 22 replicates. High confidence in hands, dermal, and inhalation data. No protection factor was needed to define the unit exposure value.</p> <p>PPE: The same dermal data are used as for baseline, coupled with a 50% protection factor to account for an additional layer of clothing, with gloved hand data. Hands = ABC grade, 21 replicates, and medium confidence. A 10-fold (i.e., 90% PF) was applied to the baseline inhalation data to account for the use of an organic vapor removing respirator.</p>
Flagger Descriptors		
Flagging Aerial Spray Applications	PHED V1.1	<p>Baseline: Hands, dermal, and inhalation = AB grades. Dermal = 18 to 28 replicates; Hands = 30 replicates; and Inhalation = 28 replicates. High confidence in dermal, hands, and inhalation data.</p> <p>PPE: The same dermal data are used as for baseline coupled with a 50% protection factor to account for an additional layer of clothing. Hands = AB grades. Hands = 6 replicates. Low confidence in hands data. A 10-fold PF (i.e., 90% PF) was applied to the baseline inhalation data to account for the use of an organic vapor removing respirator.</p>