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WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

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Memorandum

SUBJECT: Response to "Evaluation of the Potential Exposure of Workers to Propanil During Mixing/Loading and Aerial Application to Rice Fields Using Simultaneous Dermal Dosimetry and Biological Monitoring Techniques" and "Propanil Exposures and Risk Assessment Based on Data from an Aerial Application Study in Rice with Liquid Formulations"

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Attached is the Health Effects Division's (HED) response to both "Evaluation of the Potential Exposure of Workers to Propanil During Mixing/Loading and Aerial Application to Rice Fields Using Simultaneous Dermal Dosimetry and Biological Monitoring Techniques" and "Propanil Exposure and Risk Assessment Based on Data from an Aerial Application Study in Rice with Liquid Formulations" submitted by The Propanil Task Force II to EPA on August 15, 2003 and December 5, 2003, respectively.

06/04

The Propanil Task Force II submitted to EPA September 13, 2003, a study titled *Evaluation of the Potential Exposure of Workers to Propanil During Mixing/Loading and Aerial Application to Rice Fields Using Simultaneous Dermal Dosimetry and Biological Monitoring Techniques* (MRID #46075501). The purpose of this study was to quantify inhalation and dermal exposure of handlers during mixing/loading and aerial application of propanil to rice fields. Thirty individuals participated in the study at eleven test sites (15 mixer/loaders, 14 pilots, and 1 combined mixer/loader/pilot). The sites for this study were located in Texas, Louisiana, and Arkansas and there were multiple sites in each state.

The study produced propanil-specific biomonitoring and passive dosimetry data. The study author indicates that the study design employs a "commonly used technique of simultaneous dosimetry and biological monitoring." The technique involves the use of an outer dosimeter (long-sleeve shirt and long pants) worn over an inner dosimeter (tee shirt and briefs). The author states that this dosimetry design "allows for penetration of the propanil residues through the clothing as would occur under normal field agricultural practices, and does not block the penetration of propanil through the skin as would occur if a long underwear whole body dosimeter were worn under the long-sleeve shirt and long pants."

Total Handler Exposure

Total handler exposure was calculated in the study through combining inhalation exposures (measured using personal air samplers) with dermal exposures (measured through passive dosimetry techniques). The dermal passive dosimetry techniques included hand washes, hat patches, and by the use of an "outer" dosimeter for the torso, arms, and legs and an "inner" dosimeter for the torso. The study author compared the residues on the inner dosimeter to the torso residues on the outer dosimeter and derived a "protection factor" attributable to the outer dosimeter. Dermal exposure to the torso, arms, and legs was then estimated by applying the protection factor to the outer dosimeter residues. Total dermal exposure was calculated by adding the adjusted torso, arms, and legs exposure to the hand exposure values and head/face/neck exposure values.

Total handler exposure was also calculated in the study using biomonitoring techniques – through analysis of the handlers' urine for 3,4-dichloroaniline (3,4-DCA), which the study author cites as the major metabolite of propanil. The study protocol required that handlers participating in the study would not be exposed to propanil for at least 3 days prior to and at least 3 days following the day of the study. In the study itself, however, only two handlers out of the 30 participants were known to have had no exposure in the 3 days before and 3 days following the study. Six other handlers may not have had exposures in the 3 days before and 3 days following the study, but there was some uncertainty. The remaining 22 participants were known to have had exposures in one or more of the 3 days before and 3 days following the study. The urine data collected for eight handlers who were presumed to have had no propanil exposures for three days before or three days after the study were input into a model to determine the half-life of the excretion of detectable urine residues. The half-life of the excretion of propanil metabolites was found to be 23.9 hours. Using a model to adjust for propanil residues that handlers may have received other than during the study, the study author calculated an approximate dose of propanil for each handler on day 0. The study author calculated unit exposures of 54.7 ± 120 μg/kg ai/day for mixer/loaders and 35.5 μg/kg ai/day for pilots. For both mixer/loaders and pilots, the unit exposure values obtained from biomonitoring are much higher than those obtained from whole body dosimetry.

Use of the Passive Dosimetry Study Data

HED has numerous concerns about the data produced by the study, including:

- The study protocol states that "mixer/loaders will wear new or freshly laundered long-sleeved shirts, new or freshly laundered long pants, new or freshly laundered t-shirt and brief, new chemical-resistant gloves, new shoes, new socks, and protective eyewear as required by the label." However, mixers/loaders in the study wore either a chemical-resistant apron or a Tyvek coverall over the "outer" dosimeter (cotton coverall) and also wore chemical-resistant footwear. In calculating potential dermal exposures to mixers/loaders, the study author does not factor in this additional personal protective equipment, which exceeds the requirements of the product labeling.

- The study states that most mixers/loaders used a siphoning device to transfer the propanil from the drum into the mix tank and then used a dry-lock system (an engineering control) to pump the dilute mixture into the airplane spray tank. This would result in artificially low mixer/loader exposures due to the use of the engineering control in part of the mix/load process.

- The study protocol states that "all workers will perform their work tasks for a typical amount of time that represents an entire workday. One replicate will be an entire workday for each test subject. . . . The air sampling pump will operate for the entire monitoring replicate (estimated to be 6-12 hours)." However, the average duration of actual handling for each replicate in the study was only 2.2 hours for mixers/loaders and only 1.7 hours for pilots.

- The study protocol states: "applications of the test substance to rice fields will be made at a rate of 6 lbs ai/acre." However, the average application rate used in the study was approximately 2.8 pounds active ingredient per acre – ranging from 1.9 to 4.5 lb ai/acre.

- Overall, there were thirteen amendments and forty deviations to the study protocol.

Triple Layers for Mixers/Loaders: In the study protocol, where the use of a protection factor was presented as an approach to calculating exposure to the torso, arms, and legs, the study authors stated that mixers/loaders would wear new or freshly laundered long-sleeve shirt and long pants over a tee-shirt and briefs. EPA agreed that such attire would permit the calculation of a penetration factor for estimating risks to the torso, arms, and legs. However, in the actual study, all mixers/loaders wore either a chemical-resistant apron or a Tyvek coverall as an additional layer over cotton coveralls. The study did not use the residues on the apron or Tyvek coveralls, but measured residues on the cotton coverall as the "outer dosimeter" and on the tee shirt and briefs as the "inner dosimeter." However, the apron provided a chemical-resistant barrier over the coverall in the torso section and presumably reduced penetration to the coverall itself to a significant degree. Since an apron would not provide similar exposure to the legs and arms, applying a penetration factor calculated on the torso exposures to the residues measured on the arms and legs would result in a calculated penetration factor that would be artificially low. Similarly, the Tyvek coverall reduced exposure to the cotton coverall to a significant degree. Therefore, any calculated penetration factor also would be artificially low. HED considered calculating a penetration factor using the Tyvek coverall as the outer dosimeter and the cotton coverall as the inner dosimeter. However, only four mixer/loader replicates were performed with Tyvek coveralls, which would not provide a statistically significant number. In addition, nonwoven fabric, such as Tyvek, is known to allow significantly less penetration than a cotton coverall, therefore a calculated penetration factor would not be representative of the penetration through cotton coveralls. Due to many practical considerations, including cost and heat stress concerns, EPA does not require routine use by mixers/loaders or applicators of coveralls made from Tyvek or other nonwoven fabrics.

Reduced Likelihood of Penetration of Coverall: Penetration of a chemical through a matrix is dependent on three factors:

1. composition of the matrix,
2. concentration of the residue on the matrix surface, and
3. time of residue contact with the matrix surface.

This study used application rates lower than the maximum 6 pounds active ingredient listed in the protocol and on the product labeling (STAM M4), with an average application rate in the study slightly less than 3 pounds active ingredient per acre. In addition, this study involved much lower handling times than were listed in the protocol. The average actual handling time for mixers/loaders was only 2.2 hours and for pilots was only 1.7 hours and the average dermal monitoring time was less than 4.5 hours for both handling tasks. The application-rate factor would be expected to result in less residue being deposited on the outer dosimeter and the handling time factor would be expected to result in less time for the residue to penetrate the outer dosimeter.

Dermal Exposures to Mixers/Loaders and Pilots: HED used the propanil passive dosimetry data to calculate dermal exposure to the torso, arms, and legs for the pilot scenarios only. HED did not calculate dermal exposure to the torso, arms, and legs for the mixer/loader or for the mixer/loader/applicator scenarios, since an appropriate protection factor could not be calculated from the data as presented in the study. HED calculated the dermal-body exposure to pilots using the same method as the study author. First, a penetration factor was derived by dividing the amount of residue on the inner dosimeter (tee shirt and briefs) by the residue on the torso section of the outer dosimeter. Then outer dosimeter residues for arms, legs, and torso were multiplied by the penetration factor. For the pilot study, dermal unit exposures averaged 1.05E-04 mg/lb ai for the arms, 4.82E-05 mg/lb ai for the legs, and 7.46E-05 mg/lb ai for the torso.

HED then calculated **total** dermal unit exposure for pilots by summing the dermal unit exposures to hands (from hand washes), to face, head, and neck (from head patches), and to the arms, legs, and torso (as described above). Total dermal unit exposure estimates averaged 1.27E-03 mg/lb ai handled for the pilots. Total dermal unit exposure to mixers/loaders and to the mixer/loader/ applicator were not calculated by HED, since an appropriate protection factor could not be calculated from the data as presented in the study for dermal exposure to the torso, arms, and legs for these two scenarios.

Use of the Biomonitoring Study Data

HED has the same concerns – excess PPE, short handling periods, and low amount of active ingredient handled – about the biomonitoring study data as for the passive dosimetry study data. In addition, HED has concerns that 22 of 30 study participants were known to have had propanil exposures in one or more of the 3 days before and 3 days following the study.

The report that the Propanil Task Force II submitted to EPA on December 5, 2003, titled "Propanil Exposure and Risk Assessment Based on Data from an Aerial Application Study in Rice with Liquid Formulations" states:

> Analysis of DCA in urine was conducted only as a marker metabolite to afford a qualitative indication of exposure to propanil. DCA is not a major metabolite, but the short term dosing study in rats shows that approximately 47% of parent metabolizes into dicarboxylic acids in rats that, when hydrolyzed with hydrochloric acid, are converted to the DCA moiety. Only rat metabolism data is available for propanil. Because no human metabolism data exist, urine analysis for DCA is <u>not</u> valid as a tool for quantification of exposure to propanil, but is valid as a qualitative tool to indicate exposure to propanil. (Dow AgroSciences LLC, Study ID: GH-C 5691, page 14-15)

Therefore, the Propanil Task Force II did not attempt to use the biomonitoring data to perform a quantitative assessment of mixers/loaders and pilots exposures to propanil.

Revised Exposure and Risk Assessment to Pilots Applying Propanil to Rice

HED assessed the exposure and risks to pilots applying propanil to rice using data from version 1.1 of the Pesticide Handlers Exposure Database (which contains 24 to 48 replicates for pilots using enclosed cockpits) and using passive dosimetry and biomonitoring data from the study (MRID #46075501) titled *Evaluation of the Potential Exposure of Workers to Propanil During Mixing/Loading and Aerial Application to Rice Fields Using Simultaneous Dermal Dosimetry and Biological Monitoring Techniques* (which contains 14 replicates for pilots using enclosed cockpits). HED believes the propanil-specific passive dosimetry study data represents artificially low exposure values, due to the limited amount of active ingredient handled by pilots and the limited period of time the pilots wore the dosimeters. In a normal work day, HED believes it is unlikely that pilots would change out of their work clothes until the end of an 8 to10-hour workday.

The results of the revised exposure and risk assessment indicate that:

- **risks are not a concern using the propanil-specific *passive dosimetry* data** when applying propanil at the 3 or 6 pounds active ingredient per acre application rate at up to 3200 acres per day. (Note: HED believes the passive dosimetry data represents artificially low exposure values.)

- **risks remain a concern using the propanil-specific *biomonitoring* data** when applying propanil at the 3 or 6 pounds active ingredient per acre application rate at 350 to 3200 acres per day.

- **risks remain a concern using PHED data**
  > at the 6 pounds active ingredient per acre application rate for scenarios, even when only 350 acres are treated per day and
  > at the 3 pounds active ingredient per acre application rate and 1200 or 3200 acres per day.

- **risks are not a concern using PHED data** when applying propanil at the 3 pounds active ingredient per acre application rate to 350 or 500 acres per day.

These risks calculated from the study passive dosimetry data are essentially the same as those calculated in the report titled "Propanil Exposure and Risk Assessment Based on Data from an Aerial Application Study in Rice with Liquid Formulations" that was submitted to EPA on December 5, 2003, by the Propanil Task Force II.

See table below – Summary of Risks to Pilots in Enclosed Cockpits Using PHED and Propanil-Specific Data.

Summary of Risks to Pilots in Enclosed Cockpits Using PHED and Propanil-Specific Data

Exposure Scenario	Data Source[a]	Application Rate (lb ai/A)	Area Treated Daily[b] (acres)	Engineering Controls (Enclosed Cockpits)					
				Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Biomonitoring Unit Exposure (mg/lb ai)	Dermal MOE	Inhalation MOE	Dermal + Inhalation MOE
				Geometric Mean			Target MOE = 300		
Applying Sprays to Rice with Enclosed Cockpit Aerial Equipment	PHED	6	3200	0.005	0.068	N/A	33	480	**31**
	Propanil Dosimetry			0.00027	0.00093	N/A	610	35,000	600
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**2.1**
	PHED data		1200	0.005	0.068	N/A	88	1300	**82**
	Propanil Dosimetry			0.00027	0.00093	N/A	1600	94,000	1600
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**5.5**
	PHED data		500	0.005	0.068	N/A	210	3100	**200**
	Propanil Dosimetry			0.00027	0.00093	N/A	3900	230,000	3800
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**13**
	PHED data		350	0.005	0.068	N/A	300	4400	**280**
	Propanil Dosimetry			0.00027	0.00093	N/A	5600	320,000	5500
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**19**
	PHED data	3	3200	0.005	0.068	N/A	66	970	**62**
	Propanil Dosimetry			0.00027	0.00093	N/A	1200	71,000	1200
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**4.1**
	PHED data		1200	0.005	0.068	N/A	180	2600	**170**
	Propanil Dosimetry			0.00027	0.00093	N/A	3200	190,000	3100
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**11**
	PHED data		500	0.005	0.068	N/A	420	6200	390
	Propanil Dosimetry			0.00027	0.00093	N/A	7800	450,000	**7700**
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	**26**
	PHED data		350	0.005	0.068	N/A	600	8800	560
	Propanil Dosimetry			0.00027	0.00093	N/A	11,000	650,000	11,000

Exposure Scenario	Data Source[a]	Application Rate (lb ai/A)	Area Treated Daily[b] (acres)	Engineering Controls (Enclosed Cockpits)					
				Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Biomonitoring Unit Exposure (mg/lb ai)	Dermal MOE	Inhalation MOE	Dermal + Inhalation MOE
				Geometric Mean			Target MOE = 300		
	Propanil Biomonitoring			N/A	N/A	0.016	N/A	N/A	38

Footnotes:

a PHED data is from version 1.1 of the Pesticide Handlers Exposure Database; Propanil Data is from the Propanil Study *Evaluation of the Potential Exposure of Workers to Propanil During Mixing/Loading and Aerial Application to Rice Fields Using Simultaneous Dermal Dosimetry and Biological Monitoring Techniques* dated September, 13, 2003.

b Acres treated daily: 3200 acres was the high end estimate for rice provided by the Propanil Task Force at the SMART Meeting that occurred on March 23, 2001, 1200 acres per day is the default acres treated for rice under Policy 9 of the Science Advisory Council for Exposure (06/23/2000) titled "Standard Values for Daily Acres Treated in Agriculture," and 500 acres and 300 acres are presented for rangefinder purposes.

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