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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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

MEMORANDUM

Date: **February 16, 2010**

SUBJECT: **Propoxur.** Section 18 Emergency Exemption for Propoxur Use on Bed Bugs

PC Code: 047802
Decision No.: 423746
Petition No.: NA
Risk Assessment Type: NA
TXR No.: NA
MRID No.: None

DP Barcode: D371752
Registration No.: 655-546, 9444-186, 499-501
Regulatory Action: New Use
Case No.: NA
CAS No.: 114-26-1
40 CFR: NA

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2/16/10

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In a memorandum dated October 21, 2009, the Ohio Department of Agriculture submitted a request for the use of three formulations of propoxur for the control of bed bugs in residential single or multiple unit dwellings, apartments, hotels, motels, office buildings, modes of transportation, and commercial industrial buildings in Ohio. The formulations may be used as crack and crevice or spot treatments applied around baseboards, floorboards, floor molding, bed frames, wall hangings, mirrors, pictures, headboards, undersides of box springs, electrical switch plates, furniture, door frames, closests, bookcases, window frames or other places where bed bugs are found or known to forage. Propoxur may also be used to treat furniture; however, applications may not be made to seating areas, arms or areas where direct skin contact can occur. In addition, the label specifically states that the formulation is prohibited from treating mattresses. Based on the submitted labels, propoxur may be applied every 14 days during the course of the infestation. The Registration Division has requested a risk assessment for this use.

Rcvd in RD 2/19/2010

The three submitted labels for the proposed use on bed bugs (499-501, 655-446, and 9444-186) have been previously registered for use in and around various commercial, institutional, and food handling establishments to target a variety of pests. Based on the voluntary cancellation of all indoor residential spray formulations of propoxur in 2007, all three labels currently restrict the use of these products on residential use sites, including schools, day care facilities, motels, hotels, and other indoor locations where children may be present.

Hazard Characterization

Propoxur is in the class of carbamate insecticides which function by inhibiting the acetylcholinesterase (AChE) by carbamylation of the serine hydroxyl group located in the active site of the enzyme. The *N*-Methyl Carbamate Cumulative Risk Assessment (September 24, 2007) (http://www.epa.gov/oppsrrd1/REDs/nmc_revised_cra.pdf) can be referenced for the most current toxicological data in regards to propoxur. Points of Departure (PoDs) required to assess the residential and occupational exposure/risk include short- and intermediate-term incidental oral (child) and short- and intermediate-term inhalation (adult and child) endpoints. A risk assessment for dermal exposure of any duration is not required as no adverse effects were observed at the highest dose tested (1000 mg/kg/day). Since peak inhibition of cholinesterase occurs rapidly with recovery occurring within hours, the daily exposure to propoxur is the main duration of concern. Therefore, toxicological dose and endpoints selected for short- and intermediate-terms routes of exposure are the same. Table 1 includes the points of departure for propoxur.

While propoxur is classified as a Group B2: Probable human carcinogen by the U.S. EPA with a linear low-dose approach for quantification of risk using the oral slope factor (Q_1*) of 3.7×10^{-3} (mg/kg/day), this linear low-dose approach was based on concentrations of exposure that were orders of magnitudes greater than what is currently allowable. Therefore, a cancer assessment was not conducted.

The 10x intraspecies and 10x interspecies factors are applicable. In addition, the Agency does not have a comparative cholinesterase study that evaluates the sensitivity of young animals compared to the adult animals; therefore, the Agency retained the 10X FQPA factor for propoxur. A margin of exposure (MOE) of 1000 defines HED's level of concern (LOC) for non-occupational exposures and an MOE of 100 for occupational exposures.

Table 1. Summary of Toxicological Doses and Endpoints for Propoxur Human Health Risk Assessment

Exposure Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (all population)	$BMDL_{10}$= 0.28 mg/kg/day	UF_A= 10X UF_H= 10X FQPA SF= 10X Total UF= 1000X	aPAD= Acute RfD / FQPA SF aPAD= 0.00028 mg/kg/day	Padilla *et al.*, 2007. BMD_{10} = 1.54 mg/kg/day $BMDL_{10}$ = 0.28 mg/kg/day based on RBC ChE inhibition in adult male rats

Table 1: Summary of Toxicological Doses and Endpoints for Propoxur Human Health Risk Assessment

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Incidental oral (Short and intermediate-term)	$BMDL_{10}$= 0.28 mg/kg/day	UF_A= 10X UF_H= 10X FQPA SF= 10X Total UF= 1000X	Residential LOC= 1000	Padilla *et al.*, 2007. BMD_{10} = 1.54 mg/kg/day $BMDL_{10}$ = 0.28 mg/kg/day based on RBC ChE inhibition in adult male rats
Inhalation (Short and intermediate-term)	$BMDL_{10}$ F= 0.0076 mg/L	UF_A = 10X UF_H = 10X FQPA SF= 10X	Residential LOC= 1000 Occupational LOC= 100	Chronic inhalation study - Rats (MRID 42648001; 40836402) BMD_{10} F= 0.0095 mg/L **$BMDL_{10}$ F**= 0.0076 mg/L based on ChE in the brain BMD_{10} M= 0.016 mg/L **$BMDL_{10}$ M**= 0.011 mg/L based on ChE in the brain
Dermal	A risk assessment for dermal exposure of any duration is not required as no adverse effects were observed at the highest dose tested (1000 mg/kg/day) (MRID 41066001).			
Cancer (oral & dermal)	Classification: Group B2; " Probable Human Carcinogenic " based on dose- related and highly significant increased incidence of urinary bladder papillomas and carcinomas in both sexes, and a borderline statistically significant increased incidence of uterine carcinomas in high- dose females (MRID 00142725). The Q_1* is 3.69×10^{-3} (mg/kg/day).			

Residential Exposures

For the proposed bed bug crack and crevice use, residential handler exposures are not expected since, according to the proposed label, use is restricted to certified applicators or persons under their direct supervision. There is potential for residential postapplication exposure from the bed bug crack and crevice and spot treatment use. For the bed bug use, dermal postapplication exposure was not assessed because a dermal endpoint was not determined at the highest dose tested (1000 mg/kg/day). Inhalation exposures were assessed for both adults and children and were found to be of concern (MOEs < 1000). In addition, for the crack and crevice use, incidental oral (children only) exposures are of concern (i.e., MOEs < 1000).

Postapplication inhalation and incidental oral exposures were assessed using the HED Draft Standard Operating Procedures (SOP's) for Residential Exposure Assessments (12/18/97), and the Revisions to the Standard Operating Procedures (SOP's) for Residential Exposure Assessment (Science Advisory Council for Exposure Policy 12, Revised February 22, 2001). The inhalation scenario assumes that pesticidal residues are available for inhalation after spraying activities have completed in the residential setting. The incidental oral scenario assumes pesticide residues are transferred to the skin of children during postapplication contact with treated indoor areas and are subsequently ingested as a result of hand-to-mouth transfer.

The following assumptions and factors were used to estimate postapplication exposure:

- Deposited residue: based on default residue value of 12 ug/cm^2 for a 0.5% spray. For the current product, applications are to be made with a 1% spray. Therefore, the residue value for propoxur from the crack and crevice use is 24 ug/cm^2 for the 1% spray.
- Fraction of ai available for transfer: 0.05 for carpet and 0.1 for hard surfaces.
- The median surface area of both hands for children: 20 cm^2.
- The mean rate of hand-to-mouth activity: 20 events per hour for short-term exposure scenarios and 9.5 events per hour for intermediate-term exposure scenarios.
- Duration of hand-to-mouth exposure indoors for children on hard surfaces and carpets: 4 and 8 hours per day, respectively.
- Duration of inhalation exposure indoors for children and adults: 16 hours per day.
- The saliva extraction factor: 50%.
- Toddlers are assumed to weigh 15 kg.
- Adults are assumed to weigh 70 kg.
- Inhalation rates for a child and adult are 0.36 and 0.55 m^3/hour, respectively.

For propoxur, the non-occupational postapplication exposure scenarios are of concern as the MOE for the proposed uses exceed the Agency's LOC (MOE < 1000). The resulting doses and MOEs are presented in Tables 2 and 3.

Table 2: Postapplication Incidental Oral (Hand-to-Mouth) Exposure for Children for Crack and Crevice Use

Type of Surface	Percent spray applied	Fraction transferred	Surface area of the hand (cm^2)	Exposure Frequency (events/hr)		Saliva Extraction Factor	Exposure Time (hrs/day)	Surface Residue (ug/cm^2)[a]	Oral Dose (mg/kg/day)[b]		Incidental Oral MOE[c]	
				S-T	I-T				S-T	I-T	S-T	I-T
Carpet	1% spray	0.05	20	20	9.5	50%	8	24	0.128	0.06	2	5
Hard surfaces	1% spray	0.10					4		0.128	0.06	2	5

a. Surface residue = (12 ug/cm^2 * 1% spray) / (0.5% spray) = 24 ug/cm^2
b. Dose (mg/kg/day) = Surface residue (ug/cm^2) * Surface area of hands (cm^2/event) * Exposure frequency (events/hr) * Exposure time (hr/day) x Saliva extraction factor x Conversion factor (0.001 mg/ug) / Body Weight (15 kg for toddlers).
c. MOE = NOAEL (mg/kg/day) / Dose (mg/kg/day), where short-term (S-T) and intermediate-term (I-T) incidental oral NOAEL = 0.28 mg/kg/day

Table 3: Postapplication Inhalation Exposure for Adults and Children for Crack and Crevice Use

Application Type	Population	Percent spray applied	Saturation Concentration (mg/m^3)[a]	Inhalation Rates (m^3/hr)[b]	Exposure Time (hrs/day)[c]	Inhalation Dose (mg/kg/day)[d]	Inhalation MOE[e]
Crack and Crevice	Adults	1% spray	0.0736	0.55	16	0.0093	220
	Children	1% spray	0.0736	0.36	16	0.028	71

a. Saturation Concentration: Csat = (Vapor Pressure*(atm/760mmHg)*Molecular Weight *(10^3 mg/g)*(10^3 L/m^3))/0.0821*296K
b. From ExpoSAC Policy 12

c. Exposure Time = time spent indoors (hrs/day) based on mean time spent in a residence from the U.S EPA Exposure Factors Handbook (1997)

d. Dose (mg/kg/day) = Saturation Concentration (mg/m^3)* Inhalation Rate (m^3/hr)* Exposure Time (Hrs/day)/ Body Weight (15 kg for toddlers or 70 kg for adults).

e. MOE = NOAEL (mg/kg/day) / Dose (mg/kg/day), where short-term (S-T) and intermediate-term (I-T) inhalation NOAEL = 0.0076 mg/L converted to 2 mg/kg/day)

Occupational Handler and Postapplication Exposure and Risk

Occupational handler exposure is expected for certified applicators applying propoxur to treat bed bugs. Handler risks were assessed using surrogate unit exposures from the Pesticide Handlers Exposure Database (PHED). Values for amount handled per day are based on ExpoSAC Policy 3.0. The occupational handler scenario resulted in MOEs that do not exceed HED's level of concern (i.e., MOEs > 100) with baseline attire (i.e., single layer of clothing, no gloves).

Chemical-specific data were not submitted to the Agency in support of this Section 18 application; however propoxur specific-studies were utilized in the 1997 RED for indoor residential uses exposure estimates. Dose and risk estimates were not quantitatively calculated at that time. It is HED policy to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures when chemical specific data is not submitted. According to the propoxur labels, the products may be applied via injector tip or air compressed sprayers. Therefore, the relevant exposure scenarios for occupational handlers are (1) application via ready-to-use formulations with aerosol cans, (2) application via a low-pressure handwand, and (3) applying ready-to-use formulations via pour-on (using PHED mix/load liquid). The unit exposure values provided in PHED for the aerosol cans scenario include propoxur-specific exposure information. The applying ready-to-use formulations via pour-on scenario was included to assess occupational handlers that load the ready-to-use product into pest control equipment prior to application.

The average adult weight of 70 kg was used for estimating inhalation exposure. It is anticipated that occupational propoxur exposures will generally occur in short- (1-30 days) and intermediate- (1-6 months) term durations. Since no dermal endpoint or absorption data are available, toxicity by the dermal route was not quantitatively assessed. Inhalation exposure with the use of an aerosol can and/or low pressure handwand was assessed for occupational handlers and is not of concern (MOEs > 100) with baseline protection. The resulting doses and MOEs are presented in Table 4.

Based on the uses associated with the proposed Section 18 labels, HED believes the presence of commercial handlers in treated residential areas is minimal after application. Therefore, a postapplication quantitative assessment for the commercial handlers for these products was not conducted.

Table 4. Short- and Intermediate-Term Occupational Handler Exposure and Risk for Crack and Crevice Use

Application Rate (lb ai/can)[a]	Amount Handled (cans/ day)[b]	Unit Exposures (mg/lb ai)[c]	Dose (mg/kg/day)[e]	MOE[f]
		Baseline Inhalation[d]	Baseline Inhalation[d]	Baseline Inhalation[d]
Short- and Intermediate-term				
Applying Ready to Use Formulations with Aerosol Cans (PHED)				
0.01	8	1.3	0.0015	1300
0.04	8		0.0059	340
Applying Ready to Use Formulations via Pour-on (using PHED mix/load liquid)				
0.01	8	0.0012	1.4×10^{-6}	1.5×10^{6}
0.04	8		5.5×10^{-6}	3.6×10^{5}
Mixing/Loading/Applying Liquids with Low Pressure Handwand (PHED)				
0.04[g]	4[h]	0.03	6.9×10^{-5}	29,000

a. Application Rates: 0.01 and 0.04 lb ai/can based on proposed use on label for propoxur (Reg No. 499-501, 9444-186, and 655-546)
b. 1 can per household treated from Policy 12 and assuming 8 households treated in one day by one PCO.
c. Unit Exposures based on PHED Version 1.1.
d. Baseline Inhalation: no respirator.
e. Inhalation Dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/can) x amount handled (cans/day) / body weight (70 kg).
f. Inhalation MOE = NOAEL (short- and intermediate-term = 2 mg/kg/day) / inhalation daily dose (mg/kg/day). Level of concern = 100; where short-term (S-T) and intermediate-term (I-T) inhalation NOAEL = 0.0076 mg/L converted to 2 mg/kg/day)
g. 0.04 lb ai/0.5 gallon: based on 0.5 gallon used to treat one home
h. 4 gallons/day: 8 homes treated in one day by a certified applicator with 0.5 gallons per home

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Chemical Name: Propoxur

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