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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: July 12, 2010

SUBJECT: Issues for Consideration Related To **Propoxur:** Occupational and Residential Exposure and Risk Assessment for Propoxur Formulated Pet Collars (D371250, April 7, 2010, S. Shelat)

PC Code: 047802
Decision No.: 436679
Petition No.: N/A
Risk Assessment Type: N/A
TXR No.: N/A
MRID No.: N/A

DP Barcode: D379902
Registration No.: N/A
Regulatory Action: Transmittal Memo
Case No.: 2555
CAS No.: 114-26-1
40 CFR: N/A

FROM: Shalu Shelat
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THROUGH: Felecia Fort, Branch Chief
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TO: Monica Wait
Chemical Review Manager
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On April 7, 2010, an occupational and residential exposure risk assessment was completed for the propoxur formulated pet collars.[1] Since D371250 was issued, the registrants (Sergeant's Pet Care Products, Inc and Wellmark International) have provided additional interim data which could be used to refine the risk calculations. The Agency is in the process of reviewing this information and will incorporate it in a future revised risk assessment, as appropriate. The submitted data are considered interim and may help define the active lifetime of emissions from a collar and the amounts of active ingredient being released by a collar over time. As indicated, these data are under review but it does appear that this information will allow risk estimates to be reduced. Further information provided by the registrants included a correction in the amount of active ingredient levels in the propoxur formulated collars (i.e., an error correction) resulting in

[1] D371250, S. Shelat (4/7/10).

revised risk estimates which are provided in Table 1 below. These corrections do not alter the risk conclusions as described in D371250.

The Agency is also anticipating additional data from the registrants which will provide chemical and formulation specific information on pet fur residue transferability. These data are a more direct and appropriate measurement of the residues coming off pet fur than provided in the interim data. It is possible that these data will also reduce risk estimates given the trends observed in the interim data, but it is not appropriate to predict a quantitative effect at this time.

The Agency has accounted for the error correction based on the amount of active ingredient present in each type of collar. Though the Agency believes that risks may be of less concern than indicated by the calculated margins of exposure below, revised risk estimates will not be quantitatively calculated until all anticipated data have been received and reviewed.

Table 1. Revised Risk Estimates Based on Error Correction.

Summary of Post-application Child Hand-to-Mouth Exposure/Risk from Contacting Pets Wearing Propoxur Collars with 20% Available for Transfer Over 15 Days							
Scenario	**Net Amount[1]**	**Days**	**SA_{PET}[2] (cm^2)**	**Dose (mg/kg/day)**	**NOAEL (mg/kg/day)**	**LOC**	**MOE[3]**
Wellmark International							
Dog Collar	34 g (1.2 oz)	15	5986	0.0051	0.28	1000	55
Cat Collar	10.5 g (0.37oz)		2737	0.0034			82
Sergeant's Pet Care Products, Inc							
Dog Collar	30 g (1.1 oz)	15	5986	0.0043	0.28	1000	70
Cat Collar	14 g (0.5 oz)		2737	0.0041			68

1. The net amount reported is the maximum amount based on product packaging submitted by Wellmark International (EPA Reg No. 2724-493 and 2724-491) and Sergeant's Pet Care Products, Inc (EPA Reg No. 2517-61 and 2517-78). Maximum amount of propoxur indicated in D371250 for Wellmark International and Sergeant's Pet Care Products, Inc was 1.5 oz and 1.2 oz, respectively.

2. Surface area of the treated pet is calculated using the body weight to surface conversion algorithm: SA = 12.3*(lbs of pet*454)^(0.65). A medium sized dog and cat were assumed to be 30 and 9 lbs, respectively.

.3. Risk estimates in D371250 indicated MOEs of 44 and 20 for Wellmark International dog and cat collars, respectively, and 62 and 28 for Sergeant's Pet Care Products, Inc dog and cat collars, respectively.

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: April 7, 2010

SUBJECT: **Propoxur:** Occupational and Residential Exposure and Risk Assessment for Propoxur Formulated Pet Collars.

PC Code: 047802
MRID No.: 41066001; 42648001; 40836402; 00142725
Petition No.: NA
Assessment Type: NA
TXR No.: NA

DP Barcode: D371250
Registration No.: NA

Regulatory Action: Risk Assessment
Reregistration Case No.: NA
CAS No.: 114-26-1

FROM: Shalu Shelat, Industrial Hygienist
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THROUGH: Felecia Fort, Branch Chief
Risk Assessment Branch VI
Health Effects Division (7509P)

TO: Monica Wait, Chemical Review Manager
Reregistration Branch 3
Pesticide Re-evaluation Division (PRD) (7508P)

The purpose of this document is to provide an exposure and risk assessment for the insecticide active ingredient, propoxur, as it is formulated in pet collar products. This assessment has been conducted as a response to a petition submitted by the Natural Resources Defense Council (NRDC). The exposure estimates for propoxur use in pet collars had been previously assessed in the 1997 Reregistration Eligibility Decision (RED) Document and risk estimates were assessed as part of the *N*-Methyl Carbamate Cumulative Risk Assessment.

Executive Summary

Propoxur [o-isopropoxyphenyl methylcarbamate] is a carbamate insecticide registered under 37 currently active labels for use by pest control operators to control ants, roaches, hornets, and other pests in and around commercial, industrial, and institutional buildings as well as in food handling establishments and outside residences. Propoxur may also be used by homeowners in granular, paste, and impregnated formulations (i.e., pet collars and bait strips) of the insecticide. It was first registered in 1963. Exposures to propoxur can be expected to occur via the dietary as well as through the occupational and residential handler and post-application routes of exposure.

Propoxur is in the toxicity category II by oral routes, category III by dermal, inhalation, and eye irritation. The most sensitive indication of toxicity is inhibition of red blood cell (RBC) ChE. A $BMDL_{10}$ analysis was also conducted based on ChEI in the brain. 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 for propoxur. Therefore, a cancer occupational and residential assessment for adults and children was not conducted.

Risk estimates for handling of propoxur pet collar products in the residential setting as well as occupational settings were not assessed as part of this risk assessment because no endpoints have been identified for dermal exposure which is the only viable route of exposure for the handling of the pet collar formulation of propoxur. The vapor pressure for propoxur is 6.5×10^{-6} mmHg and, given the formulation of propoxur in pet collars, inhalation is not considered to be a viable route of exposure. Therefore, no inhalation exposure or risk estimate is reported as part of this assessment. Incidental oral ingestion (hand-to-mouth) exposure is not anticipated for residential handler or occupational exposure with the pet collar because applicators are assumed to be adults and hand-to-mouth exposure is only assessed for children less than six years of age.

Residential post-application risk from exposure to the propoxur pet collar was assessed using the Agency's Standard Operating Procedures (SOPs) for Residential Exposure Assessments (1997) and appropriate default values. Results indicate that child residential post-application incidental oral ingestion (hand-to-mouth) exposure is of concern to the Agency (i.e., an MOE < 1000). While post-application dermal exposure to the propoxur collar is anticipated for children and adults, this route of exposure has not been assessed due the lack of a dermal endpoint (i.e., no adverse effects were measured at the limit dose, 1000 mg/kg/day). The vapor pressure for propoxur is 6.5×10^{-6} mmHg and, given the formulation of propoxur in pet collars, inhalation is not considered to be a viable route of exposure. Therefore, no inhalation exposure or risk estimate is reported as part of this assessment.

Post-application exposure from occupational application of pet collars is anticipated to be negligible since minimal involvement with the animal is anticipated to occur post-treatment. Furthermore, if contact with the animal did occur, it is assumed that a greater potential for exposure exists from the direct occupational application of the pet collar product.

1.0 Use Profile

Propoxur [o-isopropoxyphenyl methylcarbamate] is a carbamate insecticide registered under 37 currently active labels for use by pest control operators to control ants, roaches, hornets, and other pests in and around commercial, industrial, and institutional buildings as well as in food handling establishments and outside residences. Propoxur may also be used by homeowners in granular, paste, and impregnated formulations (i.e., pet collars and bait strips) of the insecticide. It was first registered in 1963. Exposures to propoxur can be expected to occur via the dietary as well as through the occupational and residential handler and post-application routes of exposure.

The propoxur pet collar product was first registered in 1975. Pet collar labels are currently registered under both Wellmark International and Sergeant's Pet Care Products. These pet collar products contain the active ingredient propoxur with percent active ingredient of 9% (Sergeant's Pet Care Products) and 10% (Wellmark International). The collar is a ready to use (RTU) product formulated for residential use to control fleas and ticks on both dogs and cats. The amount of active ingredient per collar ranges from 0.0012 to 0.0094 lbs a.i./unit depending on the net weight of the collar, as it is marketed in different sizes based upon pet weight ranges.

2.0 Hazard Concerns

Propoxur is an *N*-methyl carbamate (NMC) insecticide in which the mode of action is carbamylation of acetylcholinesterase. The *N*-Methyl Carbamate Cumulative Risk Assessment (NMC CRA) can be referenced for the most current toxicological data in regard to propoxur. Points of Departure (PoDs) required to assess the residential exposure/risk including short- and intermediate-term incidental oral (child) endpoints.

Incidental Oral: Since the 1996 completion of the HED Chapter of the RED for Propoxur (TXR# 012005), a revised NMC CRA was conducted (September, 24, 2007). The points of departure for this assessment were taken from the revised *N*- Methyl Carbamate Cumulative Risk Assessment document as the latest toxicity information was utilized; therefore, EPA used the same benchmark dose (BMD) modeling approach that was developed for the OP cumulative risk assessment to assess the N-methyl carbamates. Analyses were conducted to estimate BMD_{10}s and $BMDL_{10}$s for brain and RBC AChE inhibition. The BMD_{10} is the estimated dose resulting in 10% ChE inhibition. The $BMDL_{10}$ is the lower 95% confidence limit on the BMD_{10}. Consistent with EPA policy, the BMDL is used as the point of departure for propoxur as with other NMCs. At the present time, the only RBC and whole brain ChE data via the oral route for propoxur are the EPA's NHEERL dose- response and time course studies in male rats (Padilla *et al*., 2007). The appropriate acute oral time-course and recovery data for propoxur were provided by the NHEERL or ORD (Padilla *et al*., 2007). Refer to Table 1 for the points of departure for propoxur.

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 a 10X FQPA factor for propoxur. A margin of exposure (MOE) of 1000 defines HED's level of concern (LOC).

Dermal: In the 90-day dermal toxicity study in rabbits (MRID 41066001), ChE inhibition was not observed at various time points following 6 hours of exposure. No dermal or systemic toxicity was observed at 1000 mg/kg/day (limit dose) and, therefore, a dermal endpoint was not established for propoxur. In addition, dermal absorption data are not available for propoxur.

Inhalation: A chronic inhalation study (MRID 42648001; 40836402) is available that measured ChE activity within the appropriate time for peak effect after the last exposure. Inhalation is not considered to be a viable route of exposure for the formulated pet collar use; therefore, no inhalation exposure or risk estimate is reported as part of this assessment.

FQPA Considerations: As with other NMCs, propoxur inhibits acetylcholinesterase (AChE) by carbamylation of the serine hydroxyl group located in the active site of the enzyme. Toxicological characteristics of propoxur like the other NMCs involves maximal ChE inhibition (typically within 15 minutes to an hour) followed by rapid reactivation of the enzyme and then recovery (minutes to hours). As such, the critical duration of exposure for propoxur is acute ChE inhibition of brain and RBC AChE measured at the peak time of effect. Although the Agency has an acute and subchronic neurotoxicity study, these studies did not appropriately measure ChE activity for propoxur. The Agency does not have a comparative cholinesterase study that evaluates the sensitivity of young animals compared to the adult animals to address the FQPA factor in risk assessment. Therefore, the Agency retained a 10X FQPA factor for propoxur.

Cancer: Propoxur was classified as a Group B; "Probable Human Carcinogenic" and was assessed for carcinogenic risk from exposure using a linear, low dose extrapolation approach with a Q_1* is 3.69 x 10^{-3} (mg/kg/day). Classification was 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). However, this linear low-dose approach was based on concentrations of exposure that were orders of magnitudes greater than what is currently allowable for propoxur. In addition, based on the current knowledge of the mode of action for propoxur (i.e., rapid reactivation of recovery) and the other *N*-methyl carbamates, a cancer assessment is not appropriate.

A hazard summary detailing the updates based on the *N*-Methyl Carbamate Cumulative Risk Assessment and benchmark dose analysis are summarized above and are outlined in Table 1, below.

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 B; " 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).			

Point of Departure (POD) = A data point or an estimated point derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). LOC = level of concern. MOE = margin of exposure. $BMDL_{10}$ = lower 95% confidence limit of the 10% benchmark response, in this case the estimated dose resulting in 10% ChE inhibition.

3.0 Occupational Handler and Post-application Exposure/ Risks

HED determined there is potential for short-term exposure in occupational settings during the application of the pet collar product. No assessment of exposure/risk from pet collar application (handling) in occupational settings was performed in the 1997 Reregistration Eligibility Document (1997 RED) nor as part of the NMC Cumulative Risk Assessment. Risk estimates for occupational handling of propoxur pet collar were not assessed as part of this risk assessment because no endpoints have been identified for dermal exposure which is the only viable route of exposure for the handling of the pet collar formulation of propoxur. The vapor pressure for propoxur is 6.5×10^{-6} mmHg and, given the formulation of propoxur in pet collars, inhalation is not considered to be a viable route of exposure. Therefore, no inhalation exposure or risk estimate is reported as part of this assessment. Hand-to-mouth exposure is not anticipated for occupational exposure with the pet collar because applicators are assumed to be adults and hand-to-mouth exposure is only assessed for children less than six years of age.

Post-application exposure from occupational application of pet collars is anticipated to be negligible since minimal involvement with the animal is anticipated to occur post-treatment. Furthermore, if contact with the animal did occur, it is assumed that a greater potential for exposure exists from the direct occupational application of the pet collar product.

4.0 Residential Handler and Post-application Exposure/Risks

It has been determined that there is a potential for exposure in residential settings during the application process for homeowners who purchase and use the propoxur pet collar. There is also potential for post-application exposure from contacting a companion animal previously treated with the pet collar.

Residential risks are typically calculated for short- and intermediate-term exposures because repeated exposures are likely. Since peak inhibition of cholinesterase occurs rapidly with recovery occurring within hours, the daily exposure to propoxur is the main duration of concern. Therefore, endpoints selected for short- and intermediate-terms routes of exposure are the same and intermediate-term (30 days to several months) exposure was not assessed for the propoxur pet collar.

4.1 Residential Handler Exposure/Risks

The Agency uses the term "handlers" to describe those individuals who are involved in the pesticide application process. The Agency believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. The amount of chemical to be used in an application, the kinds of equipment used and the target being treated can cause exposure levels to differ in a manner specific to each application event.

HED has determined that there is potential for short-term exposure through the dermal route of exposure in residential settings during the application of the pet collar product. However, given that there is no dermal endpoint for propoxur, an exposure and risk estimate and assessment has not been performed. The vapor pressure for propoxur is 6.5×10^{-6} mmHg and, given the formulation of propoxur in pet collars, inhalation is not considered to be a viable route of exposure. Therefore, no inhalation exposure or risk estimate is reported as part of this assessment. Hand-to-mouth exposure is also not anticipated for the application of a pet collar because applicators are assumed to be adults and hand-to-mouth exposure is only assessed for children less than six years old.

4.2 Residential Post-application Exposure/Risks

The Agency uses the term "post-application" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. Propoxur can be used in limited areas that can be frequented by the general population including outside of residential areas or within commercial and industrial areas. As a result, individuals can be exposed by entering these areas if they have been previously treated. The use of a propoxur pet collar can result in exposure through contact with a previously treated animal and is, therefore, subject to post-application assessment.

A quantitative assessment of residential post-application exposure of a propoxur pet collar was conducted in the 1997 RED using surrogate data based on propoxur pest strips and dog aerosol spray treatment data. An inhalation exposure of 6.3×10^{-6} mg/kg/day was calculated. In addition, residential post-application risk was assessed in the 2007 NMC CRA for propoxur pet collars. Based on inputs, assumptions, and algorithms that were specific to the cumulative risk assessment, the propoxur pet collar dermal and incidental oral ingestion risk estimates were not of concern at that time. The current assessment is based on the anticipated exposure from the single chemical and risk and chemical specific toxicological information as described above.

HED has determined that exposure to propoxur is likely following residential pet collars use. Adults and children are likely to contact a previously treated pet, however, since no dermal endpoint was selected, only child incidental oral ingestion (hand-to-mouth) exposure was assessed. The incidental oral ingestion exposure scenario using default inputs and a 15 day average result in MOEs ≤ 62, this scenario exceeds the Agency's level of concern (MOE <1000).

4.2.1 Residential Post-application Noncancer Exposure/Risk Estimates

Adults and children in residential settings are likely to contact a pet previously treated with a propoxur pet collar and, therefore, risk estimates were calculated as appropriate for each. Adult exposures are limited to dermal post-application exposure for which no toxicological endpoint exists; therefore, exposure/risk was not estimated. Children can be exposed to the propoxur collar through dermal and incidental oral ingestion routes of exposure. Again, due to the lack of a dermal toxicological endpoint this route of exposure was not assessed; however, the incidental oral ingestion route of exposure was assessed for children.

The Agency combines or aggregates risks resulting from exposures to individual chemicals when it is likely they can occur simultaneously based on the use pattern and the behavior associated with the exposed population. Children can be exposed to a previously treated dog through either dermal or incidental oral ingestion routes of exposure. These routes of exposure are typically aggregated; however, in the case of propoxur, dermal risk estimates were not calculated.

Data and Assumptions

A series of assumptions and factors served as the basis for completing the residential post-application risk assessment of adult and child exposure to propoxur pet collars. The assumptions and factors used in this risk assessment are consistent with current Agency policy for completing residential exposure assessments (i.e., *Draft HED SOPs for Residential Exposure Assessment (1997)* and 1999 Draft Policy 13, *Post-application Exposure Assessment for Children from Treated Pets*).

The assumptions and factors used in the risk calculations are as follows:

- The Agency always considers the maximum application rates allowed by labels in its risk assessments to consider what is legally possible based on the label;

- Pet collar products are intended to emit pesticide residues over extended periods of time to ensure a level of protection for the treated pet for that active product lifetime (i.e., 4 to 7 months is specified on current propoxur pet collar labels). The mechanisms involved in such emissions are not thoroughly understood but it is clear that pet collar products must provide some level of efficacy over time, indicating that actual time-release emissions occur from the propoxur collars. Because little is known about the mechanisms of emission, it is possible that once a pet collar is placed on a pet they could be relatively constant over time or it is also plausible that higher concentrations may be emitted in the first days or weeks after initial placement on a pet. In order to address these types of uncertainties and still account for the time-released nature of pet collars, a steady emission profile over the course of a 15 day period was used to develop this assessment. [Note: The results of this assessment are not sensitive to other plausible averaging times in lieu of data. For example, if other values such as 30 or 60 days are considered, which still likely result in conservative estimates of exposure, they do not impact the overall results of the assessment.]

- In the absence of chemical-specific data, it may be assumed that on the day of application 20 percent (0.20) of the maximum application rate is available on the pet's body and transferred to the adult/child as a transferable residue. This value is based on the professional judgment and experience of the OPP/HED staff from the review of data and is believed to be an upper-percentile assumption (US EPA, 1999 SAP).

- A 3 year old child is expected to weigh 15 kilograms (representing an average weight from years one to six).

- The approach used to address the hand-to-mouth exposure pathway has been modified since 1999 Draft Policy 13, *Post-application Exposure Assessment for Children from Treated Pets*. In the draft policy, contact with dogs is based on 40 events per day (20 mouthing events/day for 2 hours). For each event, the palmar surface of the hands (i.e., $20cm^2$/event) is placed in the mouth of the child contributing to incidental oral ingestion exposure. In the revised approach, the frequency term has been modified to an equilibrium approach analogous to the dermal exposure component (i.e., the frequency = 1 event/day). The approach was revised since the data from which the transferable residue concentrations were determined rely on a continuous contact (grooming) technique that would lead to concentrations on the hands which are anticipated to be significantly higher than would result from petting/hugging.

- Hand surface area per event is 20 cm^2, which represents the palmar surfaces of three fingers;

- Saliva extraction efficiency is 50 percent meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed;

- HED's default for the surface area of an adult hug is 5625 cm^2, a child hug is 1875 cm^2 (US EPA, 1999 SAP).

- HED's default for the surface area of a treated pet is 5986 cm^2 (30 lb dog) and 2737 cm^2 (9 lb cat) (calculated by an algorithm provided in US EPA, Wildlife Exposure Factors Handbook, 1993)

Post-application Exposure Assessment Algorithms

The algorithms used for the assessment of residential post-application incidental oral ingestion (hand-to-mouth) pet exposure scenarios are as follows:

Child exposure from hand-to-mouth activity to treated companion animal:

The following demonstrates the method used to calculate hand-to-mouth exposures that are attributable to a child touching a treated companion pet and then placing their hands in their mouth.

$$D\ (mg/kg/day) = \frac{TR * SAL * SA_{hands} * Freq}{BW\ (kg)}$$

Where:

D	=	daily nondietary ingestion dose from treated pets (mg/kg/day)
TR	=	amount of residue anticipated to transfer from treated animal to the exposed individual (mg/cm^2)
SA_{hands}	=	surface area of a child's hands (20 cm^2)
SAL	=	saliva extraction factor (50%)
Freq	=	frequency of hand-to-mouth events (1 event/day)
BW	=	child body weight (15 kg)

$$TR\ (mg/cm^2) = \frac{AR * F_{AR}}{SA_{pet}}$$

Where:

AR	=	application rate of the pet collar formulation (mg a.i./event)
F_{AR}	=	fraction of the maximum application rate is available on the pet's body and transferred to the adult/child as a dislodgeable residue (unitless)
SA_{PET}	=	default surface area of a treated pet (5986 cm^2 dog and 2737 cm^2 cat)

$$MOE = \frac{NOAEL}{D}$$

Where:

NOAEL	=	No Observed Adverse Effect Level (mg/kg/day)
D	=	daily dose from hand-to-mouth pet contact (mg/kg/day)

Risk Summary

Child incidental oral ingestion (hand-to-mouth) exposure from contacting a treated pet is of concern to the Agency (i.e., an MOE < 1000). An estimate of dermal exposure/risk was not assessed.

Table 2 presents child hand-to-mouth exposure and risk estimates for 20% transferability of residues over 15 day time period. This adjusted scenario results in risks that **are of concern to the Agency (MOEs < 1000)**.

Table 2. Summary of Post-application Child Hand-to-Mouth Exposure/Risk from Contacting Pets Wearing Propoxur Collars with 20% Available for Transfer Over 15 Days

Scenario	Net Amount[1] (oz)	Days	SA_{PET}[2] (cm^2)	Dose (mg/kg/day)	NOAEL (mg/kg/day)	LOC	MOE
Wellmark International[3]							
Dog Collar	1.5	15	5986	0.0063	0.28	1000	44
Cat Collar			2737	0.0138			20
Sergeant's Pet Care Products, Inc[4]							
Dog Collar	1.2	15	5986	0.0045	0.28	1000	62
Cat Collar			2737	0.0099			28

1. The net amount reported is the maximum amount report for the labels.
2. Surface area of the treated pet is calculated using the body weight to surface conversion algorithm: SA = 12.3*(lbs of pet*454)^(0.65). A medium sized dog and cat were assumed to be 30 and 9 lbs, respectively.
3. Net weight information for Wellmark International pet collar products was provided by professional communication with the OPP Registration Division (RD).
4. Net weight information for Sergeant's Pet Care Products, Inc pet collar products was provided by professional communication with the OPP Pesticide Re-evaluation Division (PRD).

4.3 Residential Post-application Cancer Exposure/Risk Estimates

Propoxur was classified as a Group B2; " Probable Human Carcinogenic " and was assessed for carcinogenic risk from exposure using a linear, low dose extrapolation approach with a Q_1* is 3.69×10^{-3} (mg/kg/day). However, this linear low-dose approach was based on concentrations of exposure that were orders of magnitudes greater than what is currently allowable for propoxur. In addition, based on the current knowledge of the mode of action for propoxur (i.e., rapid reactivation of recovery), like other *N*-methyl carbamates, a cancer exposure and risk assessment is not appropriate.

5.0 Public Health and Pesticide Epidemiology Data

An updated review of propoxur incident reports was recently prepared by HED (M. Hawkins, 2009). The Office of Pesticide Programs Incident Data System (IDS) was consulted for reports of propoxur poisoning incidents occurring in the United States from 2002 to the present. The IDS includes reports of incidents from registrant reporting, other government agencies, and individual consumers. Of the 48 incidents reported, 8 reported incidents are reported after the use of Zodiac dog and cat pet collars. Symptoms include diarrhea, nausea, rashes, swelling, pruritus, abdominal pain, and breathing issues. Evaluation of the incident data is equivocal. It

was not possible to relate them to exposure, and there is no clear evidence of a trend or exposure pattern. Therefore, at this time, the Agency can not discern any suggestion of a trend or pattern regarding the health effects due to the alleged exposure to the pesticide propoxur.