

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

Date: 03/20/2006

MEMORANDUM

SUBJECT: Occupational and Residential Exposure Assessment for Proposed Section 3 Registration of Cyphenothrin on Domestic Pets. DP Barcode: 317077

FROM: Wade Britton, MPH, Industrial Hygienist Reregistration Branch 3 Health Effects Division (7509C)

THROUGH: Richard Loranger, Branch Senior Scientist Registration Action Branch 2 Health Effects Division (7509C)

TO: George LaRocca Insecticide Branch Registration Division (7505C)

DP Barcode	PC Code	Trade Name	EPA Reg #	Class
D317077	129013	Sergeant's Cyphenothrin Squeeze-On for Dogs	2517 - XXXX	Insecticide
		Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs		
		Sergeant's Cyphenothrin + Methoprene Squeeze-on for Dogs		

Sergeant's Pet Care Products, Inc. has requested a registration of the active ingredient (ai) cyphenothrin on domestic pets (dog and puppies). This document contains an occupational and residential exposure/risk assessment for the requested uses. In addition, the previously registered products containing cyphenothrin will be assessed since exposures were not previously evaluated.

## **Executive Summary**

Cyphenothrin (Cyclopropanecarboxylic Acid, 2,2-Dimethyl-3-(2-Methyl-1-Propenyl)-, Cyano(3-Phenoxyphenyl) Methyl Ester) is a pyrethroid type insecticide. Pyrethroids act upon both the peripheral and central nervous system of the insect to stimulate the nerve cells to produce repetitive discharges and eventually cause paralysis. Cyphenothrin is proposed for use on domestic pets (dogs and puppies) and is currently registered for use on horses and also in residential premises. It is formulated as a squeeze-on product, fogger, and aerosol spray. Cyphenothrin can be used by homeowners and by commercial applicators.

## **Use Patterns**

Cyphenothrin is formulated as a liquid, squeeze-on product for the control of fleas, ticks and other insects on dogs and horses, as a fogger for the control of insects in indoor residential settings and storage facilities, and as an aerosol spray for control of insects in indoor and outdoor residential areas (crack and crevice and spot treatments).

## **Hazard Identification**

Exposures to occupational handlers are expected to be short- and intermediate-term in duration via the dermal and inhalation routes. Residential postapplication exposures are expected to be short-term in duration via the dermal and oral routes (children only). For all exposure routes, the HED/RAB2 toxicology team selected the same endpoint from a 90-day subchronic dog study (MRID 42717503) with a NOAEL of 10 mg/kg/day based upon clinical signs of toxicity (emesis, tremors, and reddish/pale mucosa) observed at the LOAEL of 30 mg/kg/day. Since dermal and inhalation endpoints were based on oral studies, a dermal absorption factor (DAF) of 20% and a default inhalation absorption factor of 100% were applied. There were no appropriate dermal absorption or toxicity studies available to allow an estimation of the dermal absorption by a route-to-route comparison for cyphenothrin. Therefore, the DAF of 20% was estimated using DAF values from chemicals with structural similarities (i.e., C-permethrin, C-cypermethrin, C-pyrethrin, cypermethrin, and sumithrin). The acute toxicity data indicate that cyphenothrin is moderately toxic (Category II) via the oral route of exposure, slightly toxic (Category III) via the inhalation route of exposure, and has low toxicity (Category IV) via the dermal route of exposure. Cyphenothrin is non-irritating to the eye (Category IV) and is neither a dermal irritant nor a skin sensitizer.

## **Occupational Handler Exposure/Risks**

HED determined there is a potential for short- (1 to 30 days) and intermediate-term (1 to 6 months) exposure in occupational settings during the application of products containing cyphenothrin. Proposed domestic pet spot-on use of cyphenothrin could be performed by professional animal care workers; however, exposure/risk from application to dogs and horses was not assessed because handler contact is expected to be negligible. The spot-on

product is designed to be self-contained as it is applied directly from the tube to the pet with the tip of the applicator used to part the pet's hair.

Cyphenothrin is currently registered for use in domestic dwellings in indoor spaces, and on indoor and outdoor surfaces (crack and crevice and spot treatments). Commercial use of cyphenothrin by pesticide control operators (PCOs) is likely and could result in exposure/risk. Cyphenothrin occupational handler exposure/risk was assessed for the aerosol spray (crack and crevice and spot treatment) use only. The short- and intermediate-term combined dermal and inhalation occupational handler risk assessment indicates that with only baseline clothing (i.e., long sleeve shirt, long pants, shoes plus socks, and no gloves), the combined (dermal + inhalation) risk estimate for the PCO handler scenario results in a margin of exposure (MOE) greater than 100, and therefore is not of concern.

### **Occupational Postapplication Exposure/Risks**

To develop a postapplication assessment, HED considers the types of tasks and activities that individuals are likely to be doing in areas recently treated with a pesticide. For cyphenothrin, postapplication activities are either not expected to occur or are expected to be significantly less than residential postapplication risks. Even if the spot-on pet treatment is administered by a professional animal care worker, minimal involvement with the animal is assumed to occur after such treatment occurs. Furthermore, PCO postapplication exposure/risk to areas treated with cyphenothrin aerosol sprays and indoor foggers was not assessed. EPA believes that the residential postapplication exposure and risk assessment (Section 4.2) is a reasonable worst-case surrogate for occupational exposures.

### **Residential Handler Exposure/Risks**

HED determined that exposure to pesticide handlers is likely during the residential use of cyphenothrin on dogs and horses and in indoor/outdoor spaces as a crack and crevice, spot or air treatment. Cyphenothrin is proposed for residential use in the control of insects on domestic pets. Exposure/risk from cyphenothrin application to domestic pets was not assessed because handler contact is expected to be negligible.

Cyphenothrin is currently registered for use in domestic dwellings, including indoor/outdoor surfaces and indoor spaces (crack and crevice and spot treatments). An exposure assessment was conducted for users applying indoor broadcast and crack and crevice sprays using aerosol products. Those exposures are likely to be greater than the exposures anticipated during the brief period required to start a total release fogger and the time in which the applicator left the treatment area.

Based on the types of equipment and techniques that can potentially be used to make cyphenothrin applications, it was determined that exposure/risk was likely during aerosol spray (crack and crevice and spot treatment) applications. However, exposure/risk for this scenario was not assessed due to factors from PHED version 1.1, which indicate that the

number of aerosol cans applied is expected to be 1 for residential handlers versus 2 for occupational handlers. Therefore, the exposure/risk estimated for occupational handlers of aerosol cans (Section 3.1.2) was used as a reasonable worst-case surrogate. The estimated risk to occupational handlers does not exceed HED's LOC with baseline attire and, therefore, it is assumed that residential handler risks also do not exceed the LOC.

### **Residential Postapplication Exposure/risks**

HED has determined that exposure to cyphenothrin is likely following residential use on animals as well as indoor and outdoor premise treatments. A wide array of individuals of varying ages can potentially be exposed when they have contact with treated companion animals or when they perform activities in areas that have been previously treated (fogger, sprays). It is assumed that most residential uses of cyphenothrin will result in short-term (1 to 30 days) postapplication dermal and oral exposures. Furthermore, it is assumed that toddler exposures result in the worst case risks and, therefore, only toddler postapplication exposures to treated companion animals, from playing on floors after fogger treatment, and following space spray applications were assessed.

The resulting MOEs were combined (dermal + oral) to estimate the body burden expected from exposure to multiple routes of exposure for the appropriate scenarios. Combined MOEs estimated for exposures to children (proposed uses) from hugging treated companion dogs are less than 100 (day zero and when assessed at a 31-day average residue level) and, therefore, are of concern. Combined MOEs estimated for exposures to children (currently registered uses) from dermal activity on treated indoor hard surfaces and carpet are greater than 100 and, therefore, are not of concern.

## 1.0 Hazard and Toxicity Profile

**Dermal, Inhalation, and Oral Routes (non-cancer):** For short- and intermediate-term dermal, inhalation, and oral exposures an endpoint was selected from a subchronic (90 day) oral dog study (MRID 42717503). A NOAEL of 10 mg/kg/day and a LOAEL of 30 mg/kg/day were selected, based upon clinical signs of toxicity (emesis, tremors, and reddish/pale mucosa). Since dermal and inhalation endpoints were based on oral studies, a dermal absorption factor (DAF) of 20% and a default inhalation absorption factor of 100% were applied. There were no appropriate dermal absorption or toxicity studies available to allow an estimation of the dermal absorption by a route-to-route comparison for cyphenothrin. Therefore, the DAF of 20% was estimated using DAF values from chemicals with structural similarities (i.e., C-permethrin, C-cypermethrin, C-pyrethrin, cypermethrin, and sumithrin).

**Non-Cancer Level of Concern (LOC):** HEDs level-of concern (LOC) for cyphenothrin dermal, inhalation, and oral exposures is 100 (i.e., a margin of exposure (MOE) less than 100 exceeds HED's level of concern) for occupational and residential scenarios. The level of concern is based on 10X to account for interspecies extrapolation (differences between humans and animals) to humans from the animal test species, and 10X to account for intraspecies sensitivity (differences among humans).

**Acute Toxicity:** The acute toxicity data indicate that cyphenothrin is moderately toxic (Category II) via the oral route of exposure, slightly toxic (Category III) via the inhalation route of exposure, and has low toxicity (Category IV) via the dermal route of exposure. Cyphenothrin is non-irritating to the eye (Category IV) and is neither a dermal irritant nor a skin sensitizer. The acute toxicity and endpoint selection for cyphenothrin is presented in Tables 1.0 and 1.1, respectively.

**Body Weight:** The adverse effects for the short- and intermediate-term inhalation endpoints are based on studies where the effects were observed in males and females, therefore, the body weight of an average adult (i.e. 70 kg) was used to estimate occupational and residential exposures. The body weight of the average 3 year old toddler (15 kg) was used to estimate residential postapplication exposure.

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral-rat	00155346	LD <sub>50</sub> = 318 (219-463) mg/kg- males 419 (281-624) mg/kg females	II
870.1200	Acute dermal-rabbit	00155347	LD <sub>50</sub> = >5000 mg/kg (both sexes)	IV

870.1300	Acute inhalation-rat	00155348	LC <sub>50</sub> = 1.850 mg/l (MMAD = 1.0µm)	III
870.2400	Acute eye irritation-rabbit	00155350	One hour after instilling the doses, two rabbits with unrinsed eyes had injected conjunctival vessels and discharge with moistening of the lids and hairs just adjacent to the lids	IV
870.2500	Acute dermal irritation - rabbit	00155350	Non-irritant	IV
870.2600	Skin sensitization-guinea pig	00155351	Not a sensitizer	N/A

**Table 1.1 Summary of Toxicological Doses and Endpoints for Cyphenothrin**

Exposure Scenario	Dose Used in Risk Assessment, UF	Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term (1 to 30 days) Incidental Oral  Intermediate-Term (1 to 6 months) Incidental Oral	NOAEL (oral study) = 10 mg/kg/day	Occupational and Residential LOC for MOE = 100*	Subchronic (90-day) Dog (MRID 42717503 )  LOAEL (mg/kg/day): 30 based on clinical signs of toxicity (emesis, tremors, and reddish/pale mucosa)
Short-Term (1 to 30 days) Dermal  Intermediate-Term (1 to 6 months) Dermal	NOAEL (oral study) = 10 mg/kg/day (Dermal absorption factor = 20%)	Occupational and Residential LOC for MOE = 100*	Subchronic (90-day) Dog (MRID 42717503 )  LOAEL (mg/kg/day): 30 based on clinical signs of toxicity (emesis, tremors, and reddish/pale mucosa)
Short-Term (1 to 30 days) Inhalation  Intermediate-Term (1 to 6 months) Inhalation	NOAEL (oral study) = 10 mg/kg/day (Inhalation absorption factor = 100%)	Occupational and Residential LOC for MOE = 100*	Subchronic (90-day) Dog (MRID 42717503 )  LOAEL (mg/kg/day): 30 based on clinical signs of toxicity (emesis, tremors, and reddish/pale mucosa)

\* LOC of 100 = 10X (intraspecies) x 10X (interspecies)

UF = uncertainty factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, MOE = margin of exposure, LOC = level of concern, N/A = Not Applicable

## 2.0 Use Profile

Cyphenothrin is a synthetic pyrethroid which has been proposed for the control of fleas, ticks and other insects on dogs and puppies. Three end-use products are proposed: Sergeant's Cyphenothrin Squeeze-On for Dogs, a 40% ai RTU product formulated in a

squeeze-tube applicator for use on dogs and puppies; Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs, a 40% ai RTU product formulated in a squeeze-tube applicator for use on dogs and puppies, and; Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs, a 40% ai RTU product formulated in a squeeze-tube applicator for use on dogs and puppies. Currently registered uses of cyphenothrin are formulated as a squeeze-on product for horses, a fogger for the control of insects in indoor residential settings and storage facilities, and as an aerosol spray for control of insects in indoor and outdoor residential areas (crack and crevice and spot treatments). The registered uses were not assessed in the past and were, therefore, assessed in conjunction with the proposed end-use products. The proposed and currently registered cyphenothrin products are further described in Table 2.0.



**Table 2.0 Summary of Registered and Proposed End-Use Products Containing Cyphenothrin**

Product	EPA Reg #	Use Sites	Max. Application Rate	Instructions
Spot-on Treatments				
Sergeant's Cyphenothrin + IGR Squeeze-on for Dogs (40% ai)	2517 - XXX (proposed)	Dogs and Puppies	<ul style="list-style-type: none"> <li>* Dogs ≤ 15 lbs: 430 mg ai/ treatment</li> <li>* Dogs 15 - 33 lbs: 645 mg ai/ treatment</li> <li>* Dogs 33 - 66 lbs: 1290 mg ai/ treatment</li> <li>* Dogs &gt; 66 lbs: 1935 mg ai/ treatment</li> </ul>	<ul style="list-style-type: none"> <li>* Using the tip of the applicator, part dogs hair and squeeze tube firmly to apply as a spot or stripe to the dog's back between the shoulder blades (dogs weighing 33 lbs and under) or a continuous stripe on the dog's back starting between the shoulder blades and ending directly in front of the base of the tail (dogs weighing 33 lbs and over).</li> <li>* Do not apply more often than every 4 weeks.</li> <li>* Do not use on puppies under 12 weeks of age.</li> <li>* For external use on dogs only.</li> <li>* Do not use on cats.</li> </ul>
Sergeant's Cyphenothrin Squeeze-on for Dogs (40% ai)	2517 - XXX (proposed)			
Sergeant's Cyphenothrin + Methoprene Squeeze-on for Dogs (40% ai)	2517 - XXX (proposed)			
Sergeant's Equine Squeeze-On (40% ai)	2517 - 84	Horses	* Horses: 3870 mg ai/ treatment	<ul style="list-style-type: none"> <li>* Applicator tube squeezed to apply product onto the horse, with applications made to the poll, each side of the withers, each side of the hindquarters, on the front of each leg below the knee, and on the back of each hind leg below each hock on the gaskin muscle.</li> <li>* Reapply every 3 weeks as needed to maintain pest control.</li> <li>* Do not apply to foals less than 3 months of age.</li> <li>* For external use on horses only.</li> </ul>
Aerosol Spray				
Multicide Multi-purpose spray 27373 (0.25% ai)	1021 - 1765	Indoor/outdoor crack and crevice and spot treatments.	0.00016 lb ai/ 1000 ft <sup>2</sup>	<ul style="list-style-type: none"> <li>* Repeat every 5 weeks as needed.</li> <li>* Indoor/ outdoor use sites include furniture, rugs, carpets, baseboards, walls, floors, window frames, animal quarters, shelves, dark corners of patios, center of rooms into air.</li> </ul>

**Table 2.0 Summary of Registered and Proposed End-Use Products Containing Cyphenothrin**

Product	EPA Reg #	Use Sites	Max. Application Rate	Instructions
Total Release Fogger				
Multicide Total Release Aerosol 27382 (0.40% ai)	1021 - 1681	Homes, Apartments, Cabins, Campers, Boat Cabins, Storage Facilities	0.00025 lb ai/ 1000 ft <sup>2</sup>	* One unit treats 6000 cubic feet (30 x 25 x 8 ft) of unobstructed space (do not use in room smaller than 5 by 5 ft). * Leave building during treatment. Ventilate 30 minutes before reoccupying treated area
Multicide Total Release Aerosol 27371 (0.25 % ai)	1021 - 1684	Homes, Apartments, Cabins, Campers, Boat Cabins, Storage Facilities	0.00016 lb ai/ 1000 ft <sup>2</sup>	* One unit treats 6000 cubic feet (30 x 25 x 8 ft) of unobstructed space (do not use in room smaller than 5 by 5 ft). * Leave building during treatment. Ventilate 30 minutes before reoccupying treated area
Multicide Total Release Aerosol 27372 (0.25 % ai)	1021 - 1685	Homes, Apartments, Cabins, Campers, Boat Cabins, Storage Facilities	0.00016 lb ai/ 1000 ft <sup>2</sup>	* One unit treats 6000 cubic feet (30 x 25 x 8 ft) of unobstructed space (do not use in room smaller than 5 by 5 ft). * Leave building during treatment. Ventilate 30 minutes before reoccupying treated area.
Multicide Total Release Aerosol 27381 (0.40 % ai)	1021 - 1686	Homes, Apartments, Cabins, Campers, Boat Cabins, Storage Facilities	0.00025 lb ai/ 1000 ft <sup>2</sup>	* One unit treats 6000 cubic feet (30 x 25 x 8 ft) of unobstructed space (do not use in room smaller than 5 by 5 ft). * Leave building during treatment. Ventilate 30 minutes before reoccupying treated area.
Raid Fumigator G (6.48% ai)	4822 - 383	Homes - Indoor	0.00047 lb ai/ 1000 ft <sup>2</sup>	* One unit treats approximately 3000 cubic feet (16' x 20' x 8'). * Before re-entering open all doors and windows and air for 30 minutes.
Red Earth G-8-F Fumigator Fumigating Fogger (7.2% ai)	10308 - 18	Homes - Indoor	0.00037 lb ai/ 1000 ft <sup>2</sup>	* One unit treats a room of 3000 cubic feet. * Before re-entering open all doors and windows and air for 30 minutes.

### **3.0 Occupational Exposure/Risk**

HED determined there is a potential for short- (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation exposure in occupational settings during the application of products containing cyphenothrin. No occupational postapplication exposure is expected from cyphenothrin use.

#### **3.1 Occupational Handler**

The Agency uses the term "handlers" to describe those individuals who are involved in the pesticide application process. The anticipated use patterns and current labeling indicate a several occupational exposure scenarios based on the types of equipment and techniques that can potentially be used for cyphenothrin applications.

Cyphenothrin is proposed for use as spot-on application to domestic pets with occupational use likely occurring in a veterinary or professional pet groom setting; however, exposure/risk from application to domestic pets was not assessed because handler contact is expected to be negligible. The spot-on product is designed to be self-contained as it is applied directly from the tube to the pet with the tip of the applicator used to part the pet's hair.

Cyphenothrin is currently registered for use in domestic dwellings in indoor spaces, and on indoor and outdoor surfaces (crack and crevice and spot treatments). Commercial use of cyphenothrin by pesticide control operators (PCOs) is likely and could result in short- (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation exposures. Cyphenothrin occupational handler dermal exposure/risk was assessed for the aerosol spray (crack and crevice and spot treatment) use only. The indoor fogger use was not assessed since it is assumed, and the product labels state, that the rooms to be treated must be evacuated during treatment.

##### **3.1.1 Data and Assumptions for Occupational Handler Exposure Scenario**

The term "handler" applies to individuals who mix, load, and apply the pesticide product. The anticipated use patterns and current labeling indicate several occupational handler exposure scenarios based on the types of equipment and techniques that can potentially be used to make cyphenothrin PCO applications; however, as explained above, only one exposure scenario was assessed. The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenario:

###### Pesticide Control Operator Scenario

- (1) Liquid ready-to-use: applying with aerosol can

No chemical-specific handler exposure data were submitted in support of this proposed Section 3 registration. It is the policy of the HED to use data from the PHED Version 1.1, as presented in PHED Surrogate Exposure Guide (8/98) to assess handler exposures

for regulatory actions when chemical-specific monitoring data are not available ( HED Science Advisory Council for Exposure Draft Policy # 7, dated 1/28/99). HED believes the use of the Surrogate Exposure Guide provides a more reliable exposure estimate than individual subsets because of the larger number of replicates in the pooled data. Therefore, HED performed its analysis of occupational handlers using the PHED surrogate table for unit exposure values. Also used were HED standard values for aerosol cans used per day, body weight, and the level of personal protective equipment to assess handler exposures (if necessary). The unit exposure values from PHED are considered to be central tendency. The application rates, treatment variables, etc. used in this assessment are upper percentile values. Therefore, the potential dose is characterized as central to high-end.

The assumptions and factors used in the risk calculations include:

- the adverse effects for the short- and intermediate-term inhalation endpoints are based on a study where the effects were observed in males and females, therefore the average body weight of an adult handler (i.e., 70 kg) is used to complete the non-cancer risk assessment;
- short- and intermediate-term assessments were completed based on the toxicity endpoints that were identified;
- the amount handled by a pest control operator for crack and crevice treatment of indoor and outdoor surfaces is assumed to be two 16 oz aerosol cans per day;
- for risk assessments, HED always considers the maximum application rates allowed by labels in its risk assessments in order to be able to consider what is legally possible based on the label;
- The average occupational workday is assumed to be 8 hours.

### **3.1.2 Occupational Handler Exposure and Risk Estimates**

With only baseline clothing (i.e., long sleeve shirt, long pants, shoes plus socks, and no gloves), the combined (dermal + inhalation) risk estimate for the PCO handler scenario resulted in a margin of exposure (MOE) greater than 100 and, therefore, is not of concern. A summary of estimated exposure and risks are presented in Table 3.1.2.

Scenario	Application Rate <sup>1</sup>	Route of Exposure	Unit Exposure <sup>2</sup>	Dose <sup>3</sup>	MOE <sup>4</sup>	Combined MOE (dermal + inhalation) <sup>5</sup>
Liquid ready-to-use: applying with aerosol can	0.0026 lb ai/ aerosol can (2 16 oz. cans per day)	Dermal	190 mg/ lb ai handled	0.0028	3500	3400
		Inhalation	1300 µg/ lb ai handled	0.000097	100000	

1. Application rate derived from Multicide Multi-purpose spray 27373 (Table 2.0) considering 16 applications (1000 ft<sup>2</sup>/ oz spray) per 16 oz can of spray
2. Unit Exposure from PHED Version 1.1
3. Dose = (Application Rate x Unit Exposure x DA (0.2) x 2 cans)/ BW (70 kg)
4. MOE = NOAEL (10 mg/kg/day) ÷ Dose
5. Combined MOE = 1/ [(1/ Dermal MOE) + (1/ Inhalation MOE)]

### 3.2 Occupational Postapplication

Occupational postapplication exposure to treated animals is not expected. Domestic pets are expected to be treated and immediately returned to their owners such that postapplication contact will be negligible. Furthermore, occupational postapplication exposure to areas treated with cyphenothrin aerosol sprays and indoor foggers was not assessed. EPA believes that the residential postapplication exposure/risk assessment (Section 4.2) is a reasonable surrogate for occupational postapplication exposures.

### 4.0 Residential (Non-Occupational) Exposure/Risk

HED determined there is a potential for short-term (1 to 30 days) dermal and inhalation exposure in residential settings during the application process for homeowners who use products containing cyphenothrin. There is also a potential for dermal, inhalation, and incidental ingestion exposures from entering cyphenothrin-treated areas.

#### 4.1 Residential Handler Exposure/Risk

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 as was described above for occupational handlers. Residential handlers are addressed somewhat differently by the Agency as homeowners are assumed to complete all elements of an application with little use of any protective equipment.

Cyphenothrin is formulated for residential use for the control of insects on domestic pets. Exposure/risk from cyphenothrin application to domestic pets was not assessed because

handler contact is expected to be negligible. The spot-on product is designed to be self-contained as it is applied directly from the tube to the pet with the tip of the applicator used to part the pet's hair.

Cyphenothrin is currently registered for use in domestic dwellings, including indoor/outdoor surfaces and indoor spaces (crack and crevice and spot treatments). Applicator exposure/risk for homeowners applying cyphenothrin via indoor foggers was not assessed since it is assumed, and the product labels state, that the rooms must be evacuated during treatment.

HED has determined that short-term dermal and inhalation exposure to residential handlers is likely during the use of cyphenothrin for handlers applying indoor broadcast and crack and crevice sprays using aerosol products; however, exposure/risk for this scenario was not assessed. This is due to factors from PHED version 1.1, which indicate that the number of aerosol cans (16 oz) applied is expected to be 1 for residential handlers versus 2 for occupational handlers. Therefore, the exposure/risk estimated for occupational handlers of aerosol cans (Section 3.1.2) was used as a reasonable worst-case surrogate. The estimated risk to occupational handlers does not exceed HED's LOC and, therefore, it is assumed that residential handler risks also do not exceed the LOC.

#### **4.2 Residential Postapplication Exposure/Risk**

Cyphenothrin uses are varied and include companion animals as well as indoor and outdoor premise treatments. As a result, a wide array of individuals of varying ages can potentially be exposed when they perform activities in areas that have been previously treated (fogger, aerosol sprays) or have contact with treated companion animals.

Proposed cyphenothrin residential uses include spot-on treatments for companion animals (dogs and puppies). In addition, currently registered cyphenothrin residential uses include indoor/outdoor surfaces and indoor spaces (crack and crevice and spot treatments). Potential routes of exposure include dermal, inhalation, and incidental ingestion. It is assumed that toddler exposures result in the worst-case risks and, therefore, only toddler postapplication exposures from playing on floors after fogger treatment, following space spray applications, and contact with treated companion animals were assessed.

Of the three use scenarios previously mentioned, the total release fogger represents the worst case scenario for postapplication inhalation exposure. However, postapplication inhalation exposure from indoor fogger use was not assessed since it is assumed, and the product labels state, that the rooms to be treated must be evacuated during treatment (no one is to enter and occupy room for half an hour following application) and the room is to be ventilated by opening windows. Furthermore, since no chemical specific data were submitted, HED has assumed that due to cyphenothrin's relatively low vapor pressure ( $5.6 \times 10^{-9}$  mmHg), and the dispersion characteristics of foggers, aerosolized particles of cyphenothrin have dissipated over the half hour re-entry period as specified on label. Therefore, risk of inhalation exposure will be reduced to negligible amounts.

While airborne particles from foggers may be present in the treated room, it is believed that, a large percentage of particles will be on surfaces rather than in the air. Therefore, it is expected that the dermal and hand-to-mouth components of indoor exposure will result in the most significant potential exposure from this use, while the inhalation component from this use is anticipated to be negligible.

The quantitative exposure/risk assessment developed for residential postapplication is based on the following scenarios:

- (1) Dermal exposure to children from treated companion animal (hug)
- (2) Hand-to-mouth exposure to children from treated companion animal
- (3) Dermal exposure to children from activity on treated indoor hard surfaces and carpet
- (4) Hand-to-mouth exposure to children from activity on treated indoor hard surfaces and carpet

#### **4.2.1 Data and Assumptions for Residential Postapplication Exposure Scenarios**

The default factors used for the residential postapplication assessment are taken from the HED Exposure Science Advisory Committee SOPs including the following interim changes: *SOP12: Recommended Revisions to the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (2/22/2001)* and *SOP13: Postapplication Exposure Assessment For Children From Pet Treatments (1/2002)*. SOP 12 provides the values necessary to assess postapplication dermal and hand-to-mouth exposure to indoor broadcast and crack and crevice treatments. SOP 13 provides the values necessary to assess postapplication exposures from pet treatment products, including exposures resulting from treated companion animal hug and hand-to-mouth scenarios.

General assumptions and factors used in the risk calculations include:

- only toddlers are considered because they are thought to be the highest exposed population (i.e., they are considered the sentinel population by HED);
- 3 year old toddlers are expected to weigh 15 kilograms (representing an average weight from years one to six);
- for risk assessments, HED always considers the maximum application rates allowed by labels in its risk assessments in order to be able to consider what is legally possible based on the label;
- the dermal absorption factor is 20% as determined by HED;
- short-term hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm<sup>2</sup> representing 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;
- Exposure is assessed on day of application (i.e., day zero)

Assumptions and factors used in the risk calculations of companion animal hug and hand-to-mouth scenarios include:

- 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; however, for the purposes of this assessment, the application rate applicable to a medium-sized dog (i.e., 15 – 30 lb dog at 645 mg ai/ treatment) was used because estimated risks are based on an even loading of residues across the entire surface of a 30 lb dog (chosen as a representative animal), with the animal surface area calculated using  $(12.3 * \text{Body Weight (g)}^{0.65})$  from HED's 1993 Wildlife Exposure Factors Handbook (i.e., dog surface area of 5986 cm<sup>2</sup>);
- HED default for the surface area of a child hug is 1875 cm<sup>2</sup>;
- exposure durations are expected to be 2 hours (hand-to-mouth scenario only);

A 31-day average residue level for toddler exposure/risk to cyphenothrin from pet spot-on treatments was assessed as well as the HED general assumption of day of application (day zero) residues. The dermal and oral doses (a NOAEL of 10 mg/kg/day) identified by HED were selected from a subchronic (90 day) oral dog study and, therefore, HED recognizes that extrapolating this endpoint for the estimation of day zero (acute) exposure is conservative. HED assumes that if a short-term (acute) study was available, that the dose could potentially be greater than a NOAEL of 10 mg/kg/day, thus resulting in larger estimated margins of exposure (MOEs) and, likewise, reduced estimated risk. This approach presents a range of anticipated exposure/risk to the toddler throughout the month, beginning at application until re-treatment on day 31, assuming a residue dissipation rate of 5% per day.

In addition, it should be noted that the value to be used in this assessment for the percent of the application rate initially available to transfer from pet to human is 5%, and not the 20% standard value from HED's Residential Exposure SOPs 1,2,3. The rationale for using the 5% value includes the following:

- the 20% transferrability factor in the SOPs is a bounding value, determined from a study that employed a vigorous rubbing of the treated area for an extended period of time;
- the 20% value was derived from a study on a shampoo product, which is presumed to have more readily available surface residues for transfer to humans



than the proposed spot-on treatments which are applied to the animals skin, and thought to migrate more along the skin of the animal (i.e., not the fur);

- the results from a study on the dislodgeability of tetrachlorovinphos from animals treated by a pump-spray treatment product (MRID 45485501) were used as a surrogate for the cyphenothrin spot-on product. The dataset for this study includes estimates for the percent of applied dose transferred to the hand (~ 2%) and percent available on the fur that is transferred to the hand (5%);
- while HED has used the 5% value in this assessment, the concept that the proposed cyphenothrin pet spot-on products are similar to the tetrachlorovinphos product is assumed;
- a dislodgeability study, "Amended Final Report II: Operator Exposure Assessment and Dislodgeability of Etofenprox from the Haircoat of Cats Treated with a Spot-on Formulation," was submitted by the registrant which sought to measure applicator exposure to Etofenprox – which has chemical class and use similarities to Cyphenothrin product - during treatment of cats and thereafter the dislodgeability of the test substance from the haircoats of cats treated with a spot-on formulation. This study was reviewed by HED (DP Barcode: 327770) and was determined to not be fit for quantitative risk assessment purposes. In addition, the registrant used latex gloves for the above dislodgeability study, instead of the more typically used cotton gloves. A comparison study, "Validation Study Comparing Dose Residue Recoverability of Etofenprox from Cotton and Latex Gloves Analysis of Data and Conclusions." of the two gloves was submitted by the registrant in support of this decision. This study was reviewed by HED (DP Barcode: 298228) and results determined that information gaps associated with the study severely limited the confidence that could be placed in its results and, therefore, precluded the use of the study for risk assessment purposes.

Assumptions and factors used in the risk calculations of dermal and hand-to-mouth exposure to indoor broadcast and crack and crevice treatments include:

- a maximum application rate of 0.00016 lbs ai/ 1000 ft<sup>2</sup> ( $1.6 \times 10^{-7}$  lb ai/ sq ft) for indoor crack and crevice treatments and 0.0047 lbs ai/1000 ft<sup>2</sup> ( $4.7 \times 10^{-7}$  lb ai/ sq ft) for indoor foggers;
- for spray treatments to carpets, 5 percent of the application rate has been used to calculate the day-zero transferable residue levels for assessing risks from dermal and hand-to-mouth exposures, since cyphenothrin-specific transferable residue study data are not available;
- for spray treatments to hard flooring, 10 percent of the application rate has been used to calculate the day-zero transferable residue levels for assessing risks from dermal and hand-to-mouth exposures, since cyphenothrin-specific transferable residue study data are not available;

- exposure durations for hard flooring scenarios are estimated to be 4 hours based on information in HED's *Exposure Factors Handbook* and;
- exposure durations for carpet scenarios are estimated to be 8 hours based on information in HED's *Exposure Factors Handbook*.

Data provided by the Non-Dietary Exposure Task Force (NDETF) were used in the estimation of postapplication exposure/risk resulting from the use of foggers and aerosols in indoor settings for several exposure scenarios. NDETF data are based upon studies conducted with formulations of pyrethrin/piperonyl butoxide and permethrin/pyrethrins. While not specific to cyphenothrin, a synthetic pyrethrin, these data are considered a better surrogate than default values based upon non-pyrethrin studies.

The NDETF conducted studies to examine the deposition of residues from total release foggers. The studies were submitted to EPA in January 2004. The studies simulated the use of a fogger and aerosol products indoors to provide data on air dispersion and deposition on surfaces (walls, floor). Carpet and vinyl were selected as the flooring surfaces of interest because of their different physical and chemical properties and because they represent a significant amount of the floor coverings used in homes in North America.

Since cyphenothrin was not one of the active ingredients considered in the study, mean values from all of the applicable studies were used in this assessment. Hand transfer data used in this assessment comes from the bare wetted hand scenarios that were performed in some of the NDETF studies. Transfer of cyphenothrin to bare hands from fogger treated carpet was assumed to be 9.1 percent of deposition based on data from Project ID 98-031-PY01 (Volume 5) and Project ID 01-017-PY01 (Volume 25) of the NDETF studies. Transfer of cyphenothrin to bare hands from fogger treated vinyl flooring was assumed to be 5.8 percent of deposition based on data from Project ID 98-031-PY01 (Volume 5) and Project ID 01-017-PY01 (Volume 25) of the NDETF studies. These data were used to assess the toddler incidental oral ingestion from indoor surfaces scenario.

Roller and drag sled transfer data were averaged together for use in this assessment as there was little difference between the data sets. Transfer of cyphenothrin to rollers from fogger treated carpet was assumed to be 4.5 percent of deposition based on data from Project ID 98-031-PY01 (Volume 5) and Project ID 01-017-PY01 (Volume 25) of the NDETF studies. Transfer of cyphenothrin to rollers/drag sleds from fogger treated vinyl flooring was assumed to be 2.3 percent of deposition based on data from Project ID 98-031-PY01 (Volume 5) and Project ID 01-017-PY01 (Volume 25) of the NDETF studies. These data were used to assess the toddler dermal exposure from indoor surfaces scenarios.

The assumptions and factors used in the risk calculations of dermal and hand-to-mouth exposure to indoor broadcast and crack and crevice treatments (based upon NDETF data) include:

- for fogger treatments to indoor carpeted areas, 4.5 percent (for dermal exposures) and 9.1 percent (for hand-to-mouth exposures) of the application rate (using data from NDETF) have been used to calculate the day-zero transferrable residue levels for assessing postapplication risks, since cyphenothrin-specific transferable residue study data are not available;
- for fogger treatments to indoor hard surface areas, 2.3 percent (for dermal exposures) and 5.8 percent (for hand-to-mouth exposures) of the application rate (using data from NDETF) have been used to calculate the day-zero transferrable residue levels for assessing postapplication risks, since cyphenothrin-specific transferable residue study data are not available;

#### 4.2.2 Residential Handler Exposure and Risk Estimates

The MOEs calculated for the estimation of postapplication dermal and incidental oral hand-to-mouth exposures to children (proposed uses) from hugging treated companion dogs (30 lbs), and dermal and incidental oral hand-to-mouth exposures to children (currently registered uses) from dermal activity on treated indoor hard surfaces and carpet are presented in Table 4.2.2. The resulting MOEs were combined (dermal + oral) to estimate the body burden expected from exposure to multiple routes of exposure for the scenarios. Combined MOEs estimated for exposures to children (proposed uses) from hugging treated companion dogs are less than 100 (day zero and 31-day average residue level) and, therefore, are of concern. Combined MOEs estimated for exposures to children (currently registered uses) from dermal activity on treated indoor hard surfaces and carpet are greater than 100 and, therefore, are not of concern.

The algorithms used for indoor/outdoor surface (fogger, aerosol can) and pet exposure scenarios are presented below, with summaries of the estimated exposures and risks presented in Table 4.2.2.

#### Toddler exposure from dermal activity on treated indoor hard surfaces and carpet:

The following demonstrates the method used to calculate exposures that are attributable to a child touching treated carpet or a hard surface (SOP 12 and NDETF):

Where:

$$D_t \text{ (mg/kg/day)} = \frac{[(AR \text{ (lb ai/1000 ft}^2) \times F \times (1 - DR)^t \times CF_2 \times CF_3] \times CF_1 \times T_c \times ET}{BW \text{ (kg)}}$$

$D_t$	=	potential dose rate on day "t" (mg/day)
AR	=	application rate or amount dispersed from aerosol/ fogger can (lb ai/ ft <sup>2</sup> )
F	=	fraction of the residue retained on hard surface or carpet (refer to Section 4.2.1)
DR	=	fractional dissipation rate per day (0.05 per day)
t	=	postapplication day on which exposure is being assessed (day 0)

CF <sub>1</sub>	=	weight unit conversion factor to convert lbs ai in the application rate to μg for the carpet/ hard surface residue value (4.54E8 μg/ lb)
CF <sub>2</sub>	=	area unit conversion factor to convert the surface area units (ft <sup>2</sup> ) in the application rate to cm <sup>2</sup> for the carpet value (1.08E-03 ft <sup>2</sup> / cm <sup>2</sup> )
CF <sub>3</sub>	=	conversion factor to convert μg units in the carpet/ hard surface residue value to mg for the daily exposure (0.001 mg/μg)
Tc	=	transfer coefficient (6000 cm <sup>2</sup> / hr)
ET	=	exposure time (4 hr/ day for hard surfaces, 8 hr/ day for carpet )
BW	=	toddler body weight (15 kg)

### Toddler oral exposure from hand-to-mouth activity on treated indoor hard surfaces and carpet:

The following demonstrates the method used to calculate exposures that are attributable to a child touching treated carpet or a hard surface and then putting their hands in their mouth (SOP 12 and NDETF):

Where:

$$D \text{ (mg/kg/day)} = \frac{AR \text{ (lb ai/1000 ft}^2\text{)} \times CF_1 \times CF_2 \times CF_3 \times F \times SA \text{ (cm}^2\text{)} \times EXT \times FO \text{ (events/hr)} \times ET \text{ (hrs/day)}}{BW \text{ (kg)}}$$

D	=	oral dose on day of application (mg/kg/day)
AR	=	application rate or amount dispersed from aerosol/ fogger can (lb ai/ ft <sup>2</sup> )
CF <sub>1</sub>	=	conversion factor to convert μg units in the carpet/ hard surface residue value to mg for the daily exposure (0.001 mg/μg)
CF <sub>2</sub>	=	weight unit conversion factor to convert lbs ai in the application rate to μg for the carpet/ hard surface residue value (4.54E8 μg/ lb)
CF <sub>3</sub>	=	area unit conversion factor to convert the surface area units (ft <sup>2</sup> ) in the application rate to cm <sup>2</sup> for the carpet value (1.08E-03 ft <sup>2</sup> / cm <sup>2</sup> )
F	=	fraction of residue dislodgeable from wet hands (refer to Section 4.2.1)
SA	=	surface area of 1 to 3 fingers (20 cm <sup>2</sup> )
EXT	=	extraction rate by saliva (0.5)
FQ	=	frequency of hand-to-mouth events (20 events/hour)
ET	=	exposure duration (4 hr/ day for hard surfaces, 8 hr/ day for carpet)
BW	=	toddler body weight (15kg)

### Toddler exposure from dermal activity (hug) to treated companion animal:

The following demonstrates the method used to calculate dermal exposures that are attributable to a child touching a treated companion pet (SOP 13).

Where:

$$D \text{ (mg/kg/day)} = \frac{[AR \text{ (mg ai/ treatment)} \times F] / (SA_{pet}) \times (1 - DR)^t \times (SA_{hug}) \times (AB)}{BW \text{ (kg)}}$$

D	=	daily dose from dermal pet contact (mg/day)
AR	=	application rate or amount applied to animal (mg ai/ treatment)

F	=	fraction of the application rate available as transferable residue (0.05)
SA <sub>pet</sub>	=	surface area of a treated dog (5986 cm <sup>2</sup> / animal)
SA <sub>hug</sub>	=	surface area of a child hug (1875 cm <sup>2</sup> / animal)
t	=	time after application (day zero)
DR	=	fractional dissipation rate per day (0.05 per day)
AB	=	absorption factor (20%)
BW	=	toddler body weight (15 kg)

**Toddler 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 (SOP 13).

Where:

$$D \text{ (mg/kg/day)} = \frac{[(AR * F_{AR}) / SA_{pet}] * (1 - DR)^t * (SAL) * SA_{hands} * Freq * Hr]}{BW \text{ (kg)}}$$

D	=	daily nondietary ingestion dose from treated pets (mg/day)
AR	=	application rate or amount applied to animal (mg ai/ treatment)
F	=	fraction of the application rate available as transferable residue (0.05)
SA <sub>pet</sub>	=	surface area of a treated dog (5986 cm <sup>2</sup> / animal)
SA <sub>hands</sub>	=	surface area of a child's hands (20 cm <sup>2</sup> )
SAL	=	saliva extraction factor (50%)
Freq	=	frequency of hand-to-mouth events (20 events/ hour)
Hr	=	exposure duration (2 hours)
t	=	time after application (day 0)
DR	=	fractional dissipation rate per day (0.05 per day)
BW	=	toddler body weight (15 kg)

<b>Table 4.2.2 Toddler Residential Risk Estimates for Postapplication Exposure to Cyphenothrin</b>						
<b>Exposure Scenario</b>	<b>Application Rate</b>	<b>Route of Exposure</b>	<b>Surface</b>	<b>F<sub>AR</sub> (Transferrable Fraction)</b>	<b>Dose (mg/kg/day)</b>	<b>MOE at Day Zero</b>
<b>Indoor Surfaces (Registered Use)</b>						
Indoor Surfaces – High Contact Activities (Spray)	1.6 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Dermal	Carpet	5 %	0.0025	4000
			Hard Flooring	10 %	0.0025	4000
Indoor Surfaces – High Contact Activities (Fogger)	4.7 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Dermal	Carpet	4.5 %	0.0066	1500
			Hard Flooring	2.3 %	0.0017	5900
Hand-to-Mouth Activity on Indoor Surfaces (Spray)	1.6 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Oral	Carpet	5 %	0.00042	24000
			Hard Flooring	10 %	0.00042	24000
Hand-to-Mouth Activity on Indoor Surfaces (Fogger)	4.7 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Oral	Carpet	9.1 %	0.0022	4500
			Hard Flooring	5.8 %	0.00071	14000
<b>Companion Animal (Proposed Use)</b>						
Pet Contact	645 mg ai/ treatment (15 to 33 lb dog)	Dermal	Treated Pet	5%	0.13	74
Hand-to-Mouth Activity Following Pet Contact	645 mg ai/ treatment (15 to 33 lb dog)	Oral	Treated Pet	5%	0.14	70
<b>Companion Animal (Proposed Use) Assessed with 31-day Average Residue Level</b>						
Pet Contact	645 mg ai/ treatment (15 to 33 lb dog)	Dermal	Treated Pet	5%	0.07	140
Hand-to-Mouth Activity Following Pet Contact	645 mg ai/ treatment (15 to 33 lb dog)	Oral	Treated Pet	5%	0.075	130

<b>Table 4.2.3 Toddler Residential Combined Risk from Exposure to Cyphenothrin</b>				
<b>Exposure Scenario</b>	<b>Application Rate</b>	<b>Routes of Exposure</b>	<b>Surface</b>	<b>Total MOE</b>
<b>Indoor Surfaces (Registered Uses)</b>				
Indoor Surfaces – High Contact and Hand-to-Mouth Activities (Spray)	1.6 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Dermal + Oral	Carpet	3400
			Hard Flooring	3400
Indoor Surfaces – High Contact and Hand-to-Mouth Activities (Fogger)	4.7 x 10 <sup>-7</sup> lb ai/ ft <sup>2</sup>	Dermal + Oral	Carpet	1100
			Hard Flooring	4200
<b>Companion Animal (Proposed Use)</b>				
Companion Animal – Contact and Hand-to-Mouth Activities	645 mg ai/ treatment (15 to 33 lb dog)	Dermal + Oral	Treated Pet	36
<b>Companion Animal (Proposed Use) Assessed with 31-day Average Residue Level</b>				
Companion Animal – Contact and Hand-to-Mouth Activities	645 mg ai/ treatment (15 to 33 lb dog)	Dermal + Oral	Treated Pet	67

13544

R119195

**Chemical:** Clomazone

**PC Code:**  
125401

**HED File Code:** 14000 Risk Reviews

**Memo Date:** 3/23/1994

**File ID:**

**Accession #:** 412-06-0012

**HED Records Reference Center**  
2/2/2006