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

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 16 October 2001

SUBJECT: **CHLORFENAPYR** - Exposure/Risk Assessment for Pesticide Handlers and Residents from Post-Construction Termiticide or Crack and Crevice Use.
PC Code: 129093 DP Code: 238777, 255715, 255758, 277150

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INTRODUCTION

The BASF Corporation has requested registration of the compound chlorfenapyr (4-bromo-2-(chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1*H*-pyrrole-3-carbonitrile) for use as a post-construction soil applied termiticide and as a "spot or crack and crevice spray for residential pest control." The proposed product is "PHANTOM® termiticide-insecticide" which is a 2.0 lb active ingredient per gallon liquid. This memorandum is the Health Effects Division's (HED) assessment of exposure and risk to pesticide handlers applying the material and to residents following application.

SUMMARY OF PROPOSED USE PATTERN

As a termiticide it is "For sale to, use and storage by individuals/firms licensed or registered by the state to apply termiticide and general pest control products." Under the label heading of Use Directions For General Pest Control the label indicates the product "is intended for use by Pest Management Professionals as a spot or crack and crevice spray...."

See Table 1.0 for a summary of the proposed new use pattern.

Table 1.0 Summary of Proposed New Use of Chlorfenapyr for Termite, Cockroach and Nuisance Ant Control	
Formulation	2.0 lb a.i./gal emulsifiable concentrate
Use Site	structural soil termiticide - post construction crack & crevice - cockroaches, ants
Method of Application	rodding/trenching for termites low pressure hand wand spray
Pest	termites, cockroaches, ants
Maximum Application Rate	termites - 0.25% (1.5 fl oz/gal) cockroaches/ants - 0.50% (3.0 fl oz/gal)
Frequency/Timing	cockroach/ant = "repeat as necessary to maintain control" Annual retreatment for termites is NOT permitted.
REI	sprays have dried
Manufacturer	BASF Corporation

For the proposed use as a termiticide, chlorfenapyr will be applied using methods typical for post-construction soil termiticides i.e., rodding and trenching with surface sprays for "Inaccessible Crawl Spaces". For cockroaches and ants, treatment will be crack and crevice with limited "spot" treatments. "Limited spot treatments of PHANTOM dilution can be made to surfaces **beneath** cabinets, spaces between equipment or expansion joints, surfaces behind sinks, lockers, water pipes, cabinets, or other areas where cockroaches may hide" (emphasis added). The label does not direct any application to flooring or counter tops or other openly exposed surface areas.

The proposed labeling for PHANTOM termiticide-insecticide under the heading "USE DIRECTIONS FOR GENERAL PEST CONTROL" indicates the product may be used "In and around houses, apartments or other residential structures, and the **food/feed** and non-food/feed handling areas...." The label further states: "**Food/feed product areas are defined as....**" And finally the label also indicates that crack and crevice and limited spot applications can be made in **food handling areas in operation....**" Emphases added.

Based on the proposed labeling, HED expects commercial pesticide applicators to be exposed during short-term (1-30 days) and possibly during intermediate-term exposures (1-6 months). Application is limited to professional, commercial applicators. Residents could receive post-application exposures. HED expects that for residents, only inhalation exposure might occur

following termiticide soil application. The crack and crevice application directions preclude dermal post-application contact by residents by directing that the material be placed in a manner that would not make dermal contact possible under normal conditions (e.g. beneath cabinets. Therefore only inhalation exposure might occur. HED herein assesses dermal and inhalation exposure to pesticide handlers and post-application inhalation exposure to residents.

PESTICIDE HANDLER EXPOSURE

The HED Hazard Identification Assessment Review Committee (HIARC) evaluated the adequacy of the toxicological database relative to the compound chlorfenapyr (Memo, M. Copley, HED Doc. No. 013857, 18 November 1999; Memo, M. Copley, HED Doc. No. 013499, TES, 17 NOV 1997; Memo, G. Reddy, HED Doc. No. 013500, 27 JAN 1997). Toxicological endpoints were identified for short- and intermediate-term dermal exposures. The No Observable Adverse Effect Level (NOAEL) identified was 100 mg a.i./kg bw/day from a 28 day rabbit dermal toxicity study. Short- and Intermediate-term inhalation endpoints were identified as 4.2 mg a.i./kg bw/day based on a sub-chronic oral study in the dog. The 19 October 1999 HIARC document cites a 25 September 1996 Cancer Peer Review document which describes chlorfenapyr as a "cannot be determined, suggestive" carcinogen. A Q_1^* was not established. Since the dermal and inhalation toxicological effects are different and are derived from different studies, the risks (MOEs) are not combined (see Table 2.0).

No chemical specific data were available with which to assess potential human exposures from handling for exposure due to re-entry into a treated area. As such, the estimates of exposure are based upon the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, August 1998). Assumptions include the use of maximum label rates of application and the use of a single layer of clothing (long sleeved shirt, long pants, shoes plus socks) and chemical resistant gloves. However HED policy dictates that whenever possible, estimates of exposure also be presented for a handler NOT wearing gloves. See Table 2.0 for a summary of exposure and risk to commercial pesticide handlers applying chlorfenapyr as a termiticide and as a crack and crevice application.

Table 2.0 Estimated Exposures and Risks to Pesticide Handlers Applying Chlorfenapyr as a Soil Termiticide and as Crack and Crevice Spray

Unit Exposure[1] mg a.i./lb handled	Application Rate[2]	Units Treated[3]	Avg. Daily Dose[4]	NOAEL[5]	MOE[6] Short & Intermediate Term
Mixer/Loader/Applicator -Liquid Open Pour - Termiticide Injection					
DSLNG no data avail DSLWG 2.5 LC Inhalat 0.120 LC	1.5 fl oz product/gal	125 gal/house	no data 0.11 0.005	no data 100 4.2	no data D = 910 I = 840
Mixer/Loader/Applicator - Liquid Open Pour-Low Pressure Handwand					
DSLNG 100 LC DSLWG 0.43 LC Inhalat. 0.030 MC	3.0 fl oz product/gal	2 gal/day	0.13 0.0057 0.00004	100 100 4.2	D = 770 D = >175K I = 105K

1. Unit Exposure = mg a.i./lb a.i. handled; taken from the Pesticide Handler's Exposure Database PHED Surrogate Exposure Guide version 1.1; August 1998; DSLNG = Dermal exposure from single layer clothing NO gloves; DSLWG = Dermal exposure from single layer clothing WITH gloves; Inhalat. = Inhalation exposure (assumes 100% absorption); Dermal exposure not adjusted for % dermal absorption as endpoints are derived from 28 day dermal study; LC = Low Confidence data; MC = Medium Confidence data.
2. Application Rate from proposed PHANTOM® label. Termiticide 1.5 fl oz (2.0 lb ai/gal product)/gallon * 125 gal/house; for crack and crevice 3.0 fl oz (2.0 lb ai/gal product)/gal * 2 gal/day. 2.0 lb a.i./gal ÷ 128 fl oz/gal = 0.016 lb a.i./fl oz
3. Units Treated are from Memo. D. Smegal and T. Leighton 20 June 2000, DP Code 266562 indicates an average of 124 gallons per residence for termiticide treatments. The HED Standard Operating Procedures for Residential Exposure Assessments 18 December 1997 indicate 2.0 gallons/day used by pco for crack and crevice treatment.
4. Average Daily Dose (ADD) = Unit Exposure * Application Rate * Units Treated ÷ 70 kg body weight.
5. NOAEL = No Adverse Effect Level (mg a.i./kg bw/day); Short- and Intermediate-term Dermal NOAEL = 100 mg a.i./kg bw/day from 28 day dermal toxicity study in the rabbit; Short- and Intermediate-term Inhalation NOAEL = 4.2 mg a.i./kg bw/day from a subchronic oral study in the dog.
6. Margin of Exposure (MOE) = NOAEL ÷ ADD. **D = Dermal; I = Inhalation;** K = 1000

HED's level of concern is for MOEs <100. For commercial pesticide handlers in this case, MOEs exceed 100 and are therefore not of concern to HED.

POST-APPLICATION RESIDENTIAL EXPOSURE

Due to the proposed use patterns, HED does not expect post-application dermal exposures to adults or children as residents of dwellings treated either for termites or for cockroaches or ants. Since the vapor pressure of chlorfenapyr is **<1.0 x 10^{-7} mm Hg** at 25C°, and once the material is applied, aerosols are not expected therefore HED does not expect significant post-application inhalation exposure. There are no chemical specific data with which to assess possible post-application inhalation exposure to residents. As a worst case, screening level assessment, the Ideal Gas Law* is utilized which estimates exposure at **saturation** of a material in the air. For purposes of the expression here, Volume is assumed to be 1.0 liter. Breathing rates are assumed to be 13.3 m^3/day, 8.7m^3/day and 4.5 m^3/day for adults, child 1-12 and child < 1 year respectively. The Ideal Gas Law is expressed as:

PV = nRT where:

P = Pressure $\frac{1.0 \times 10^{-7} \text{ mm Hg}}{760 \text{ mm Hg/atmos}} = 1.3 \times 10^{-10}$ atmos
V = Volume liter (assumed to be 1.0 liter)
n = Number of moles
R = Constant 0.0821 liter atmos/mole K°
T = Temperature 298 K° (= 25 C° = 77 F°)

Therefore $n = \frac{PV}{RT} \quad \frac{1.3 \times 10^{-10} \text{atmos} * 1.0 \text{ liter}}{0.0821 \text{ liter atmos/mol K}^\circ * 298 \text{ K}^\circ} = 5.3 \times 10^{-12}$ mols in 1.0 liter

Molecular weight of chlorfenapyr = 407.6 g/mol

g/mol * mol/liter = g/liter = 407.6 g/mol * 5.3×10^{-12} mol/liter = 2.2×10^{-9} g/liter

= 2.2×10^{-3} ug/liter = 2.2×10^{-3} mg/m^3 = 2.2ug/m^3

The Average Daily Dose (ADD) may be calculated as:

2.2 ug/m^3 * 13.3 m^3/day ÷ 70 kg bw = 4.18×10^{-4} mg a.i./kg bw/day

*From Personal Communication - D. Jaquith/HED/OPP 29 August 2001.

The HIARC (Memo, M. Copley, HED Doc. No. 013857, 18 Nov 1999) also identified a long-term inhalation toxicological endpoint (2.6 mg a.i./kg bw/day from a 1 year neurotoxicity study in the rat and chronic/carcinogenicity study in the mouse). Calculations of residential post-application inhalation Margins of Exposure utilize Short- and Intermediate-term inhalation NOAEL (4.2 mg a.i./kg bw/day) and Long-term NOAEL (2.6 mg a.i./kg bw/day). HED believes it is highly unlikely that Long-term inhalation exposures will exist from either use pattern. First, there is very little material used in a crack and crevice application, second the soil applied material is expected to be bound and more significantly, the vapor pressure of the active ingredient is quite low (<1.0 x 10^{-7} mm Hg). MOEs are:

Adult

Short- and Intermediate-term $\frac{4.2 \text{ mg a.i./kg bw/day}}{0.00042 \text{ mg a.i./kg bw/day}}$ **= 10,000**

Long-term $\frac{2.6 \text{ mg a.i./kg bw/day}}{0.00042 \text{ mg a.i./kg bw/day}}$ **= 6,200**

For child 1 -12 years:

2.2 ug/m^3 * 8.7 m^3/day ÷ 39 kg bw (12 yr old) = 0.00049 mg a.i./kg bw/day

Short- and Intermediate-term $\frac{4.2 \text{ mg a.i./kg bw/day}}{0.00049 \text{ mg a.i./kg bw/day}}$ **= 8,600**

Long-term $\frac{2.6 \text{ mg a.i./kg bw/day}}{0.00049 \text{ mg a.i./kg bw/day}}$ **= 5,300**

For toddler < 1 year:

2.2 ug/m^3 * 4.5 m^3/day ÷ 15 kg bw (toddler) = 0.00066 mg a.i./kg bw/day

Short - and Intermediate-term $\frac{4.2 \text{ mg a.i./kg bw/day}}{0.00066 \text{ mg a.i./kg bw/day}}$ **= 6,400**

Long-term $\frac{2.6 \text{ mg a.i./kg bw/day}}{0.00066 \text{ mg a.i./kg bw/day}}$ **= 3,900**

In reality HED expects MOEs to **greatly exceed** those presented primarily because structures are not air-tight thus the theoretical **saturation** concentration could not be achieved. HED's concern is for MOEs < 100. Since highly conservative (i.e., worst case) assumptions result in MOEs that are >100, these exposures do not exceed HEDs level of concern.

The preceding estimates of exposure and risk do not exceed HED's levels of concern for dermal or inhalation exposure as may be applicable. **However,** this assessment does not address possible oral/dietary exposure that might occur **from proposed use in food handling areas** as was noted earlier. Therefore, this assessment **does not support** the proposed use patterns in food/feed handling or processing areas. HED suggests that those label claims be held in abeyance until adequate data are analyzed to support those claims.

cc: M.Dow(RAB1)
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APPENDIX

Summary of Toxicological Endpoints for Chlorfenapyr

EXPOSURE SCENARIO	DOSE	ENDPOINT	STUDY
Acute Dietary	HIARC did not address the Acute RfD for Chlorfenopyr at this time.		
Chronic Dietary (non-cancer)	HIARC did not address the Chronic RfD for Chlorfenopyr at this time.		
Short-Term (dermal)	NOAEL=100 mg/kg/day (dermal study)	LOAEL=400 mg/kg/day (increased cholesterol, relative liver weights and cytoplasmic vacuolation of the liver in male and females	28-day dermal toxicity study - rabbits
Intermediate-Term (dermal)	NOAEL: 100 mg/kg/day (dermal study)	LOAEL=400 mg/kg/day (increased cholesterol, relative liver weights and cytoplasmic vacuolation of the liver in male and females	28-day dermal toxicity study - rabbits
Long-Term (dermal)	NOAEL=2.6 mg/kg/day[1] (oral study)	LOAEL = 13.6 mg/kg/day (decreased body weight gains brain lesions (vacuolation) and/or scabbing of the skin in a 1 year neurotoxicity study in rats and a chronic/carcinogenicity study in mice) Acceptable MOE = 100	1 yr neurotox. study - rats (oral), chr/ onco - mice
Short-Term (inhalation)	NOAEL=4.2 mg/kg/day[2] (oral study)	LOAEL = 6.1 mg/kg/day (reduced body weight gain and feed efficiency and emaciation)	Subchronic oral study-dog
Intermediate- Term (inhalation)	NOAEL=4.2 mg/kg/day[2] (oral study)	LOAEL = 6.1 mg/kg/day (reduced body weight gain and feed efficiency and emaciation)	Subchronic oral study-dog
Long-Term (inhalation)	NOAEL=2.6 mg/kg/day[2] (oral study)	LOAEL = 13.6 mg/kg/day (decreased body weight gains, brain lesions (vacuolation) and/or scabbing of the skin in a 1 year neurotoxicity study in rats and a chronic/ carcinogenicity study in mice)	1 yr neurotox. study - rats (oral), chr/ .onco - mice
Cancer		Classified as "cannot be determined, suggestive". Use the RfD for chronic exposures.	Dietary/ Dermal/ Inhalation

[1] Use the appropriate dermal absorption factor (5 %) since the NOAEL is from an oral study.
[2] Use the appropriate inhalation absorption factor (100 %) since the NOAEL is from an oral study.

Taken from: HIARC Report, Memo M. Copley, 18 Nov 1999, HED Doc. No. 013857

The Health Effects Division has revised the definitions used in its human health risk assessments to describe occupational and residential exposure durations (Memo, M.

Stasikowski, June 4, 2001, "Changes in the Definition of Exposure Durations for Occupational/Residential Risk Assessments Performed in the Health Effects Division"). The 28-day rabbit dermal toxicity study originally selected for both short- (1-7 days) and intermediate-term (7 days-3 months) exposure is deemed applicable (by J. Kidwell, HED RAB1) for the new short-term exposure duration of 1-30 days. This study is also applicable for the new intermediate exposure duration of 1-6 months since it is a route-specific study and there are no developmental or reproductive concerns. In addition, the 28-day rabbit dermal study can be used for exposure up to six months, despite the shorter dosing duration, based on the defined segments of animal-lifetime to human-lifetime as referred to in the memo. For example, one month in the rabbit lifetime corresponds to about 1 year in the human lifetime. The subchronic oral toxicity study in the dog that was originally selected for both short (1-7 days) and intermediate-term (7 days-3 months) inhalation exposures is also applicable for the new short- (1-30 days) and intermediate-term (1-6 months) inhalation exposure durations.

ACUTE TOXICITY ENDPOINTS:
Acute Toxicity of Pirate

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral	42770207/ 42884201	LD_{50} (95% C.I.) = 441 (195 - 832) mg/kg, males LD_{50} (95% C.I.) = 1152 mg/kg, females LD_{50} (95% C.I.) = 626 (274 - 1085) mg/kg, combined	II
81-2	Acute Dermal	42770208	LD_{50} > 2000 mg/kg (Limit Dose)	III
81-3	Acute Inhalation	42770209	LC_{50} (95% C.I.) = 0.83 (0.48 - 1.4) mg/l, (males) LC_{50} (95% C.I.) = > 2.7 mg/l, females] LC_{50} (95% C.I.) = 1.9 (1.1 - 3.3) mg/l, combined	III
81-4	Primary Eye Irritation	42770210	Corneal opacity (4/6), iritis (2/6) and conjunctivitis (6/6) present at 48 hours. At 72 hours iritis was resolved. All rabbits were normal by Day-7.	III
81-5	Primary Skin Irritation	42770211	Non-irritating	IV
81-6	Dermal Sensitization	42770212	Not a skin sensitizer	N/A
81-8	Acute Neurotoxicity	43492829	The LOEL is 90 mg/kg, based on lethargy of the rats on the day of treatment. The NOEL is 45 mg/kg.	Supplementary

Taken from HED Doc. No. 013499; Memo. M. Copley 17 Nov 1997, Toxicology Endpoint Selection Document, Second Revision