10-25-78

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

(Circle 11

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003233

DATE: October 25, 1978

SUBJECT: Amendment to existing registration for reduction fo the concentration of the active ingredient from 24.5% (Dermaton Dip) to 12.25% (Dermaton II) and the substitution of an aliphatic petroleum solvent for a aromatic petroleum solvent in the existing formulation.

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TO: Tim Gardner PM 15
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Registration No. 59-136

Registrant: Burroughs Wellcome Company

Recommendations: With reference to 40 CFR 162.10 (j) (2) the paragraph titled Restricted Use Classification requires the statement "For retail sale to and application only by certified application or persons under their direct supervision" to appear on the front panel of a restricted use pesticide. The use limitation proposed with this amendment "This product is for use by or under the direction of a licensed verterinarian" is misleading with the requested classification for general use and should be deleted.

The antidote paragraph should be divided into two separate paragraphs Practical treatment:

If swallowed- Consult a physician immediately. Do not induce vomiting XXX

Note to Physician: 2-chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate is a cholinesterase inbibitor XXX

Discussion:

Dermaton Dip containing chlorfenvinphos (Supona) was originally accepted for registration on October 3, 1963 with the following active ingredient statement:

2-chloro-1-(2,4-dichorophenyl)vinyl diethylphosphate	24.5%
Aromatic petroleum solvent	58.5%

FIFRA as amended October 1972 provided for the classification of pesticide uses which promulgated the regulations 40 CFR 162, July 3, 1975 titled Registration, Reregistration and Classification Procedures. This was followed by 40 CFR 162.3, September 1, 1977 titled Optional Procedures for Classification of Pesticide Uses by Regulation. Then in a draft document dated November 9, 1977 all uses of Dematon Dip were proposed for restricted use classification. The registrant was subsequently informed in a letter dated October 14, 1977 of our proposal to classify Dermaton Dip for restricted use based on the acute oral and dermal toxicity of the 24.5% formulation.

EPA FORM 1320-6 (REV. 3-76)

This amendment is a significant change in the existing registration, by reducing the concentration of chlorfenvinphos by half and substituting the heavy aromatic petroleum solvent with an aliphatic petroleum solvent toxicity category has changed from one to two. The registrant has also proposed to market their four ounce container intended for domestic use in a container with a child-resistant cap.
A category two product with directions for domestic use is a candidate for restricted use classification (162.11 (c) (2)). The special packaging proposed for this formulation can reasonably be expected to eliminate the route of exposure. With special packaging the restricted domestic uses of this product maybe classified for general use classification.

Physical and Chemical Properties of Dermaton II a 12.25% formulation

1. Miscible in acetone, methanol, ethanol, xylene heavy aromatic naphtha and kerosene.
2. Specific gravity 0.9 at 25°C
3. Flash point 115°F-130°F
4. Weight of active ingredient- 0.92 lbs/gal of 97% technical
5. Color yellow to brown

Formulation (amended) of Dermaton II

2-chloro-1-2(2,4-dichlorophenyl)vinyl diethylphosphate	12.25% ✓
[redacted]	

* Substituted for [redacted] in the orginal formulation (Dermaton Dip).

Packaging

4 ounce glass bottle with child-resistant cap
1 gallon metal drum

Use: As 0.1% active ingredient emulson with water to bathe or dip dogs for the control of fleas and ticks.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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Summary of the acute toxicity of Dermaton II
A 12.25% formulation without [redacted]

Study	Species	Sex	Results	Toxicity Category
Oral	Rat	Male	LD 50 111 mg.kg ± 15.6	II
		Female	LD 50 67 mg/kg ± 15.2	II
Dermal	Rat	Male	LD 50 924 (635-1346) mg/kg	II
		Female	LD 50 1079 (741-1572) mg/kg	II
		Combined M and F	LD 50 998 (773-1289) mg/kg	II
Dermal	Rabbit	Male	LD 50 1732 mg/kg ± 382.9	II
		Female	LD 50 1758 mg/kg ± 771.2	II
		Combined M and F	LD 50 1726 ± 404.4	II
Eye Irritation	Rabbit		Slight irritation reversible at 72 hour (unwashed)	III
Eye Irritation	Rabbit		Slight to moderate irritation reversible by the 4th day (unwashed and washed)	III
Dermal Irritation	Rabbit		Moderate irritation score 4.6	III
Inhalation	Rat		Male Data not suitable for calculation	
			Female LC 50 2.48 (1.61-3.82) mg/l	III
			Combined M and F LC 50 2.16 (1.61-2.82) mg/l	III

Acute rat oral LD 50

Material: 12.25% formulation without [redacted]

Method : Single oral doses were administered to 6 male and 6 female Charles River (CD) rats per level of 50, 75, 100, 125 and 150 mg/kg. All animals were fasted for 18 hours and weighted 200-300 grams prior to dosing. Following administration of the test material all rats were observed daily for clinical signs for 14 days.

Results:

Observations: Profuse salivation, tremors, decreased motor activity brownish-red lacrimation, dyspnea and death usually within 4 hours after dosing. Additional signs included piloerection, exophthalmos extension of the tail and facial edema prior to death.

LD 50 values: Males 111 mg/kg ± 15.6 (S.D.)
Females 67 mg/kg ± 15.2 (S.D.)

Toxicity Category II

Data evaluation: Core Minimum data

Deficiency of this study: (1) Acute oral LD 50 on the other active ingredient (petroleum distillate) is not available for review.

(2) Acute oral LD 50 on the use dilution is not available for review.

(3) Results of gross necropsy not available

Acute rat dermal LD 50 INERT INGREDIENT INFORMATION IS NOT INCLUDED

Material: 12.25% formulation without [redacted]

Method: The test material was applied to the shaven intact backs of 5 males and 5 females per dosage level of 215, 464, 1000, 2150, 4640 and 20,000 mg/kg. The application sites were wrapped with gauze then overwrapped with saran wrap and restrained in stock for 24 hour exposure Observations were made at 4 hours after dosing and at 24 hours, then daily for 14 days.

Results:

Observations: Lacrimation, hypoactivity, ataxia decreased limb tone, impaired righting reflex and ataxia occuring within 1 to 4 hours at all levels. Death reported at the 1000 mg/kg level and above within one hour following application of the test material.

LD 50 values: Males 924 (635-1345) mg/kg
Females 1079 (741-1572) mg/kg

Combined male and female 998 (773-1289) mg/kg

slope 1.0

Toxicity Category II

Data evaluation: Supplementary Study

Deficiency of this study: (1) Animals were not abraded

(2) Acute dermal LD 50 on the other active ingredient (petroleum distillate) is not available for review.

Acute rabbit dermal LD 50 INERT INGREDIENT INFORMATION IS NOT INCLUDED

Material: 12.25% formulation without [redacted]

Method: The test material was applied to the shaven backs of 4 male and 4 females per dosage level of 1500, 2000, 2500, 3000 and 3500 mg/kg. The application sites covered with gauze then overwrapped with saran wrap and the animals were placed in restraining cages for 24 hours. Observations were made at 24 hours and daily for 14 days.

Results:

Observations: No definite difference in lethality was evident between intact or abraded animals. The majority of deaths occurred within the first 24 hours after dosing. Clinical signs include lacrimation; micosis, mydriasis, ataxia, decreased activity, anorexia, moist rales, dyspnea, salivation and death. Skin appeared dry and wrinkled with little or no hair replacement by 6th day.

LD 50 values: Males 1732 mg/kg $\pm$ 382.9 (S.O)
Females 1758 mg/kg $\pm$ 771.2 (S.D.)

Combined male and female 1726 mg/kg $\pm$ 404.4 (S.D.)

Toxicity Category II

Data evaluation: Core Minimum

Deficiency of the this study: (1) Acute dermal LD 50 on the active ingredient not available

(2) Results of gross necropsy not available.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Eye Irritation

Material: 12.25% formulation without [redacted]

Method: Both eyes of six male New Zealand White rabbits were examined with 2% ophthalmic solution of sodium fluorescein prior to dosing. An aliquot 0.1 ml of the test material was instilled into the conjunctival sac of the right eye and held closed for one second. Signs of eye irritation were made prior to dosing then at 24, 48, 72 hours and on 7 days post-instillation. Irritation was graded and scored according to the system of J.H. Draize. Fluorescein was instilled after the gross eye examination at 7 days to confirm any possible corneal damage.

Results: Slight irritation of the conjunctival observed at 24 hours was reversable at 72 hours. Slight chemosis observed at 24 hours was reversed at 48 hours. No corneal damage was observed from the instillation of the test material.

Toxicity category III

Data evaluation: Minimum data

Deficiency of the study: (1) Three additional rabbits need to be treated and the eyes flushed for one minute.

Eye Irritation

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Material: 12.25% formulation without [redacted]

Method: Both eyes of four male and five female New Zealand White Rabbits were examined with 2% ophthalmic solution of sodium fluorescein prior to dosing. An aliquot of 0.1 ml of the test material was instilled into the conjunctival sac of the right eye of each rabbit. The eye was held closed for one second. The eyes of six animals were not washed. Three eyes washed 30 seconds following instillation for a period of one minute. All treated eyes were examined at 1, 24, 48, 72 hours and on 7 days following instillation. At 72 hours and 7 days all eyes were examined with sodium flurescein for corneal injury. Irritation was graded and scored according to the system of J.H. Draize.

Results: Slight to moderate irritation of the conjunctiva was observed at 24 hours and clearing by the fourth day for the nonwashed group. Slight chemosis and discharge reported at one hour with clearing by the fourth day. Slight corneal opacity was observed in one rabbit at the 24 hour observations with clearing for the fourth day. The company considers the occurrence of corneal opacity in one animal to be spontaneous in nature and not related to the test material. This reviewer concurs with this evaluation that this false positive should not influence the category of toxicity of this formulation. Eye of the washed group showed

slight to moderate irritation at one hour with clearing by the fourth day. Slight chemosis and discharge was observed at one hour with clearing by 72 hours. No corneal involvement observed with the washed eyes.

Toxicity Category III

Data Evaluation: Core guidelines

Dermal Irritation

Material: 12.25% formulation without [redacted]

Method: The hair removed from 28-30% of the body surface of three male and three female New Zealand White rabbits. A volume of 0.5 ml of the test material was applied under gauze patches to two intact and two abraded sites per animal. The application sites were overwrapped with saran wrap and secured with elastoplast tape. Observations for irritation were made when the bandages were removed at 24 hours then at 7, 14 and 21 days. Irritation was scored according to the technique of J.H. Draize.

Results: Primary Irritation Score 4.6 at 72 hours.

Slight to moderate fissuring, slight to moderate disquamation and exfotiations was reported only at the 7 day observations. These signs were not present at the 14 and 21 day observation. Only slight irritation presisted through days 14 and 21.

Toxicity Category III

Data Evaluation: Core guidelines

Acute Rat Inhalation LC 50

Material: 12.25% formulation without [redacted]

Method: Groups of five males and five female Charles River CD rats were exposed to five dosage levels of 1.02, 2.05, 4.05, 7.91 and 20.16 mg/l metered concentration of the formulation. The animals were housed individually during the 4 hour exposure. Observations were made during the 4 hour exposure and twice daily thereafter for 14 days.

Results:

Observations at the 2.05 mg/l exposure were rapid respiration and dyspnea after 90 minutes of exposure. Additional signs were noted at 150 minutes exposure include ataxia, salivation and nasal discharge. Tremors and death was reported at the conclusion of the four hour exposure. Slight to marked dyspnea and fast breathing was reported for the one to seven days post-exposure.

necropsy of animals which succumbed during the exposure revealed dark red patches in the lungs and air filled stomachs. No compound related gross lesions observed in the animals which survived the 14 day observation period.

LD 50 values: Male rat: Data not suitable for calculation
slope 1.127

Female rats: 2.48 (1.6.-3.82) mg/l
slope 1.127

Combined male and female: 2.16 (1.66-2.82) mg/l
slope 1.127

Toxicity Category III

Data evaluation: Core Minimum Data

Deficiency of this study: (1) Actual chamber concentrations were not determined.

(2) No particle size determinations

11/3/82