ENVIRONMENTAL PROTECTION AGENCY

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DATE June 13, 1974

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Mr. Lee Terbush, Acting Chief
Coordination Branch
Registration Division (WH-567)

Registration Number: 11556-34

Registrant: Chemagro

Action Requested: Registration with Petition

Related Petitions: 7F0531, 6I1859, 9F0774, 9F0811, 1F1019, 4F1472

Formulation: Tiguvon Animal Insecticide Pour-On

3% Fenthion (o,o-dimethyl o-[4-methylthio-m-tolyl] phosphorothioate

[redacted]*

* cleared as an inert under 40 CFR 180.1001(e)

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Physical State: Liquid

Use: Control of grubs and lice on cattle and lice on swine

Application Rate: 0.5 fluid ounce (15cc) per 100 lbs.

Application Method: Pour directly on animal

Restrictions: Do not treat lactating dairy cattle, calves less than 3 months old, sick, convalescent, or stressed livestock.

Do not treat non-lactating dairy cattle within 28 days of freshening. If freshening should occur within 28 days after treatment, do not use milk as human food for the balance of the 28-day interval.

Do not treat cattle for 10 days before or after shipping, weaning, dehorning or after exposure to contagious or infectious diseases.

DO NOT SLAUGHTER CATTLE WITHIN 35 DAYS FOLLOWING A SINGLE TREATMENT. IF A SECOND APPLICATION IS MADE FOR LOUSE CONTROL, DO NOT SLAUGHTER WITHIN 45 DAYS OF THE SECOND TREATMENT. 00155

TIGUVON (Brand of fenthion) is a cholinesterase inhibitor. Do not use this product on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides or chemicals.

Do not slaughter swine within 14 days of treatment.

Toxicity Data

No new toxicity data were submitted with this application. Reference was made to the toxicity data submitted in Pesticide Petition No. 7F0531. A summary of these plus other data are as follows:

Acute Toxicity

Rat Oral :

(Tech) Male and Female LD_{50} = 325 mg/kg
(Tech) Female LD_{50} = 290 mg/kg
(Tech) Female LD_{50} = 310 mg/kg
(Tech) Female LD_{50} = 245 mg/kg
(Tech) Male LD_{50} = 215 mg/kg
(Tech) Male LD_{50} = 190 mg/kg
(Tech) Male LD_{50} = 250 mg/kg
(Tech) Male LD_{50} = 150 mg/kg
(Tech) Male LD_{50} = 220-310 mg/kg
(Tech) Male LD_{50} = 215 mg/kg
(Tech) Female LD_{50} = 615 mg/kg
(Tech) Male LD_{50} = 175-250 mg/kg
(Pure) Female LD_{50} = 275 mg/kg
(Pure) Male LD_{50} = 300 mg/kg
(Pure) Male LD_{50} = 470 mg/kg
(Tech) LD_{50} = 310 mg/kg
(47.5% Spray) LD_{50} = 100 mg/kg of active ingredient
(25% Powder) LD_{50} = 150 mg/kg of active ingredient

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Guinea Pig Oral (Tech)	:	Male LD_{50} = >1,000 mg/kg Male LD_{50} = 260 mg/kg
Mouse Oral (Tech)	:	Male LD_{50} = 150 mg/kg Female LD_{50} = 190 mg/kg
Chicken Oral (Tech)	:	LD_{50} = 30-40 mg/kg * Symptoms noted at 15 and 25 mg/kg
Cattle Oral (Tech)	:	No symptoms at 10-25 mg/kg
Rabbit Oral (Tech)	:	Male LD_{50} = 150-175 mg/kg
Rat IP (Tech)	:	Male LD_{50} = 260 mg/kg Female LD_{50} = 325 mg/kg (Tech) Male LD_{50} = 100-175 mg/kg (Tech) Male LD_{50} = 90 mg/kg (Pure) Female LD_{50} = 295 mg/kg (Pure) Male LD_{50} - 125-220 mg/kg (4 lb/gal) Female LD_{50} = 90 mg/kg (25% W.P.) Female LD_{50} = 110 mg/kg
Mouse IP	:	(Tech) Male LD_{50} = 125 mg/kg (Tech) Female LD_{50} = 150 mg/kg
Guinea Pig IP (Tech)	:	(Male LD_{50} = 310 mg/kg
Calf IM (Tech)	:	Levels of 40 mg/kg and higher caused death and/or symptoms.
Rat Dermal	:	(Tech) Female LD_{50} = 500 mg/kg (Tech) Male LD_{50} = 330 mg/kg (Tech) Female LD_{50} = 330 mg/kg (Tech) Male LD_{50} = 650 mg/kg (4 lb/gal) Female LD_{50} = 250 mg/kg (25% W.P.) Female LD_{50} = >250 mg/kg (Tech) Male LD_{50} = >1,000 mg/kg (2 hrs) (Pure) Male LD_{50} = >1,250 mg/kg (4 hrs)

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: (Tech) Male LD_{50} = 500 mg/kg
(Tech) Female LD_{50} = 500 mg/kg
~~(Tech) 400 mg/kg caused total mortality~~

Rabbit Ear (Tech) : Exposure for 24 hours caused death. Four hour exposure caused irritation.

Calf Dermal (Tech) : 120 mg/kg produced cholinergic symptoms.

Rat Inhalation (Tech) : LC_{50} = 2.4 mg/L
(Tech) (2 hours) 10.0 mg/L caused total mortality (2/2). The 1.0 mg/L caused 50% mortality (1/2).

Guinea Pig Inhalation (Tech) (2 hours) : 10.0 mg/L caused total mortality (1/1). The 1.0 mg/L caused restlessness but no toxicity symptoms.

Rabbit Inhalation (Tech) : 10 mg/L caused some symptoms. The 1.0 mg/L caused no symptoms.

Subacute Toxicity

5-Day Rabbit Inhalation (Tech) : 1.0 mg/L caused death.

16-Week Rat Feeding : Levels tested were 2, 3, 5, 25, and 100 ppm. Females at 5 ppm and higher and males at 25 ppm and higher showed CHI.

28-Day Rat Feeding : Levels tested were 5, 10, 25, and 250 ppm. Slight effect at 5 ppm after four weeks of treatment. Higher level showed significant CHI of the brain. No-effect level at three weeks is 5 ppm; at four weeks it is less than 5 ppm.

30-Day Rat Inhalation : (Tech) No mortality at 0.163 mg/L. Total mortality at 0.415 mg/L and higher.

(Tech) 0.038 mg/L showed CHI
0.163 mg/L showed CHI

(Tech) (5 days) No mortality at 1 mg/L.

Mice Inhalation	:	(Tech) 0.163 mg/L results not reported. 0.415 mg/L showed 100% mortality by day 9. (Tech) (5 days) 1 mg/L caused 50% mortality (2/4) five days post treatment.
Rat Cholinesterase Study	:	Recovery of significant plasma and erythrocyte cholinesterase inhibition required about two weeks, where recovery in the brain required four weeks.
5-Day Guinea Pig Inhalation (Tech)	:	1.0 mg/L caused no mortality.
28-Day Rat Oral	:	5.0 mg/kg/day produced ChE inhibition by day 3-4 and 80% by day 15. Recovery required 25 days.
63-Day Rat Oral	:	Dosing level - 25 mg/kg/day. Produced significant ChE inhibition by day 3 and 15/50 deaths.
5-Day Rat Oral	:	Levels tested were 10, 25, 50, and 100 mg/kg/day. The 50 mg/kg/day gave 75% mortality (3/4). The 100 mg/kg/day gave 100% mortality.
60-Day Rat Intraperitoneal	:	Levels tested were 10, 20, 40, 50, 100 mg/kg/day. 20 mg/kg gave 80% mortality by 18 days. Higher levels gave 100% mortality.
12-Day Rat Dermal (2.9%)	:	Levels tested were 100, 250, or 500 mg/kg of formulation or 2.9, 7.25 and 14.5 mg/kg of active ingredient. Significant ChE inhibition noted at 3 days for all levels.
5-Day Rat Dermal	:	ALD_{50} = 73 mg/kg/day. The level of 60 mg/kg was tolerated.
Metabolite Toxicity	:	Sulfoxide showed no signs of poisoning at 800 mg/kg or lower. Sulfone showed some signs of poisoning at 400 mg/kg and total mortality at 1600 mg/kg.

4-Day Rabbit Dermal	:	Slight to moderate plasma ChE inhibition was noted at all levels, i.e., 1.5, 2.5 and 5 mg/kg. No RBC ChE inhibition at 1.5 mg/kg.
60-Day Rat Dermal (2.9% Formulation)	:	No mortality at 500 mg/kg (14.5 mg/kg of active material).
(5.0% Formulation)	:	Forty percent mortality at 500 mg/kg (25 mg/kg of active material).
84-Day Dog Feeding	:	Levels tested were 2, 5, and 50 ppm. The 50 ppm level caused serum and RBC CHI. The 5.0 ppm caused serum ChE inhibition only. No-effect level is >2 and <5 ppm.
1-Year Rat Feeding	:	Summary states no effect at 2.0 or 3.0 ppm. Slight ChE inhibition at 5.0 ppm. ChE inhibition and decreased life span of males at 25 ppm ChE inhibition, decreased life span and increased hemosiderosis at 100 ppm.
1-Year Dog Feeding	:	Levels tested were 2, 5, and 50 ppm. All levels caused slight to moderate spleen enlargement. ChE inhibition at 5 and 50 ppm. No ChE inhibition at 2 ppm.
Wild Fowl	:	Not reviewed
Acute Dog Intramuscular		
Study No. 1	:	50% mortality at 40 mg/kg. Total mortality (4/4) at 60 mg/kg. Autopsy showed hemorrhagic cystitis, enteritis and colitis.
Study No. 2	:	50% mortality (1/2) at 30 mg/kg. Total mortality (2/2) at 35 mg/kg.
Acute Horse Intramuscular	:	Levels tested i.e. 50, 60, 70 mg/kg caused no symptoms of toxicity.

6-Day Cattle Feeding	:	Levels of 2.5 - 10 mg/kg produced no toxicity.
Potentiation Study	:	Malathion, Delnav, and Co-Ral caused potentiation of acute toxicity.
Antidote Study		
Study No. 1	:	Separately or combined, 2-PAM and TMB showed no antidotal effects.
Study No. 2	:	Atropine had a slight effect.
Study No. 3	:	P_2S and Atropine are effective when given on a repeat basis.
Study No. 4	:	2-PAM on a repeat basis is somewhat effective.
Mechanism of Action	:	Write up of study is not clear.
30-Day Rat Inhalation	:	No symptoms noted using vapor chamber at about 0.1 mg/L. No ChE inhibition determinations were made.
Human Experience Data	:	No outstanding effects.
Human Accidental Case	:	No adverse effects.
Nigeria Report	:	Practically all the people in the treated village show plasma ChE inhibition.
P.C.O. Report	:	No physical or property damage.
Controlled Human Exposure	:	No effects.

Conclusion

No specific toxicological data have been submitted by the registrant on the formulation being considered for registration. However, the reviewer considers the vast amount of toxicity data on the technical material and

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on several different formulations sufficient to form a solid understanding of the chemical. The inert ingredient used in this formulation is cleared as an inert and is not expected to alter the basic toxicological aspects of Fenthion.

The labeling precaution appear adequate. TB has no objection to the registration of this formulation for the described use.

Robert D. Coberly, Biologist
Toxicology Branch
Registration Division (HM-567)

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Div. File
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RDCoberly/ccw 6/18/74