

US EPA ARCHIVE DOCUMENT

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.

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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 LD₅₀ = 325 mg/kg
- (Tech) Female LD₅₀ = 290 mg/kg
- (Tech) Female LD₅₀ = 310 mg/kg
- (Tech) Female LD₅₀ = 245 mg/kg
- (Tech) Male LD₅₀ = 215 mg/kg
- (Tech) Male LD₅₀ = 190 mg/kg
- (Tech) Male LD₅₀ = 250 mg/kg
- (Tech) Male LD₅₀ = 150 mg/kg
- (Tech) Male LD₅₀ = 220-310 mg/kg
- (Tech) Male LD₅₀ = 215 mg/kg
- (Tech) Female LD₅₀ = 615 mg/kg
- (Tech) Male LD₅₀ = 175-250 mg/kg
- (Pure) Female LD₅₀ = 275 mg/kg
- (Pure) Male LD₅₀ = 300 mg/kg
- (Pure) Male LD₅₀ = 470 mg/kg
- (Tech) LD₅₀ = 310 mg/kg
- (47.5% Spray) LD₅₀ = 100 mg/kg
of active ingredient
- (25% Powder) LD₅₀ = 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)

- : (Tech) Male LD₅₀ = 500 mg/kg
 (Tech) Female LD₅₀ = 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) : LC₅₀ = 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.

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- 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 poison-
ing 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 ChE inhibition. 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.

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- 6-Day Cattle Feeding : Levels of 2.5 - 10 mg/kg produced no toxicity.
- Potential 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 : P₂S 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

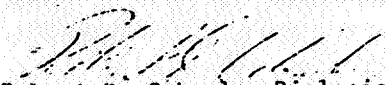
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on several different formulations sufficient to form a solid understanding of the chemical. The inert ingredient used in this formulation is cleared as an inert and is not expected to alter the basic toxicological aspects of Fenthion.

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


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