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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: J. Ellenberger
Registration Division (TS-769)

THRU: William Butler, Section Head
Review Section #3
Toxicology Branch/HED (TS-769)

4/18/82

SUBJECT: EPA Reg. No. 2724-262, Starbar GX-118.
Request for Amended Pesticide Product Registration;
consideration of additional data. CASWELL No. 543

Action Requested:

To amend label to include addition of the product's use on swine only as a spray application with a 1:100 dilution rate and with a 1 day pre-slaughter interval.

New Data Reviewed and Accepted:

	Category	Core
Acute oral LD_{50}, rat	II	Guideline
Acute dermal LD_{50}, rabbit	III	Guideline
Primary skin irritation, rabbit	III	Guideline
Primary eye irritation, rabbit	I	Guideline
1:2 dilution	I	Guideline
1:49 dilution	IV	Guideline
Swine irritation study		Supplementary
Suckling and weanling Pig irritation studies		Supplementary

INERT INGREDIENT INFORMATION IS NOT INCLUDED 001759

Conclusion:

The label amendment should not be approved until adequate response is made to the following remarks.

1. The inert [redacted] is not cleared for direct use on animals.

2. The acute inhalation study is not validated. The lack of phosmet detection in chamber samples by chemical analysis raises serious questions concerning animal exposure.

3. Considerations of residue concentrations and their persistence in meat are deferred to the residue Chemistry Branch.

New Data:

Received with letter dated 1/18/82.

Starbar GX-118 (11.6% Phosmet):

Caswell No. 543

Reg. No. 27240-262

Acute Inhalation Toxicity:

This study is not validated. Analytically derived chamber concentrations taken during exposure suggest that the rats were not adequately exposed to phosmet.

Acute Oral LD50:

Ten rats per group (5 males, 5 female) were given by oral gavage 0, 250, 450, 500, 600, or 800 mg/kg GX-118. Rats were observed 14 days. Acute anticholinergic symptoms were reported. The following numerical results were reported. No animals died when given 450 mg/ml. All died which were given 800 mg/ml.

Combined LD_{50}: 362 (248-530) mg/kg
Male LD_{50}: 364 (201-660) mg/kg
Female LD_{50}: 337 (174-651) mg/kg

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Dose response curves:

Combined: y = 0.166 x - 16.1
Male: y = 0.158 x - 10.3
Female: y = 0.164 x - 13.5

x = dose mg/kg y = percent mortality

Acute Oral Toxicity Category II

Core: Guideline

Acute Dermal LD50:

Ten rabbits per group (5 abraded and 5 not) were dermally exposed to 2100 or 5100 mg/kg. These exposures were not concurrent but the protocol was the same. Doses were applied inside an impermiable plastic film and then wrapped with muslin cloth. At least 10% of the body surface was exposed for 24 hours after which the wrapping was removed and the skin was wiped to remove the test substance.

Signs observed were those from acute cholinesterase inhibition.

Induration of the skin persisted to the end of the study in rabbits given 2100 mg/kg. None of these died.

A rather severe superficial toxic epidermal necrosis was observed in rabbits given 5100 mg/kg. All of these animals had died by 41 hours after exposure.

LD_{50}: > 2100 mg/kg
< 5100 mg/kg

Acute Dermal Toxicity Category: III

Core: Guideline

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Primary Skin Irritation:

One half mg was applied to each of 4 areas (2 abraded, 2 not) on the back of each of 6 rabbits, then covered with gauze patches, and then covered with a plastic barrier and a muslin wrap. After 4 hours the wrap was removed and the skin wiped. Animals were observed for erythema and edema at 5 hours, 24 hours, 72 hours, 5 days, 6 days and 7 days after unwrapping.

Moderate erythema and edema was seen at 5 and 24 hours. Slight erythema remained at 72 hours. At 6 and 7 days sloughing of epidermis was observed with apparently healthy tissue underneath.

Primary Skin Irritation Category: III

Core: Guideline

Primary Eye Irritation:

Right eyes of 9 rabbits per group received 0.1 ml of undiluted GX-118, 1:2 dilution, or 1:49 dilution of GX-118 in water. Three of each group were washed after application. Six remained unwashed. Observations were made after 24, 48, and 72 hours and after 4 and 7 days. Observations for undiluted test were also made on days 13 and 21 and for 1:2 test on day 13. Results follow.

Undiluted: Opacity was not reversed after seven days in 3 of 6 unwashed and 1 of 3 washed eyes. Opacity remained in one washed eye after 21 days.

1:2 dilution: Opacity was reversed by the 7th day except in one unwashed eye in which it was not reversed by the 13th day.

1:49 dilution: No irritation

Toxicity Category (undiluted): I

Core: Guideline

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Swine Irritation Study:
Observations only.

Groups of 3 60-90 pound pigs were treated with one of the following:

Starbar GX-118 concentrate pour-on (1 oz/head):
1:2 dilution with water pour-on;
1:5 dilution with water pour-on;
1:7 dilution with water pour-on;
1:20 dilution spray
1:49 dilution spray

After treatment, groups were maintained in isolation for 24 hours and observed 1 hour, 3 hours, and 24 hours post treatment for significant eye or skin irritation.

No scurfiness or scaling developed during the 4 weeks post-treatment observation time.

Suckling and Weanling Pig Irritation Studies:
Observations only

The purpose of these studies was to determine whether or not adverse reactions would occur on sows, suckling pigs, and freshly weaned pigs when they were treated with GX-118 or its use dilutions.

Sixteen mature brood sows (300-400 lbs.), having an average of nine suckling pigs (3-7 days old) each, were divided into four treatment groups of 4 sows each. The four treatments were the following:

1. GX-118 diluted one volume to five volumes of water, applied as a pour-on. (2.0% A.I. solution).

2. GX-118 diluted one volume to two volumes of water, applied as a pour-on. (4% A.I. solution).

3. GX-118 diluted one volume to 100 volumes of water, applied as a spray. (0.125% A.I. solution).

4. GX-118 diluted one volume to 49 volumes of water, applied as a spray. (0.25% A.I. solution).

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Pour-on was applied at the rate of one ounce per hundred pounds of body weight along the backline from the neck line to the hips. Spray was applied until animals were completely wet nearly to the point of run off. Application were to the sows, not to suckling pigs.

Later, 144 one-month old (12 lb.) weaned pigs were treated. These were the same pigs previously included as suckling pigs of the treated sows.

Treatment consisted of spraying all pigs with GX-118 diluted one volume to 49 volumes of water (0.25% A.I. solution) until wet. Observations were made for any adverse effects to sows or sucklings and later to weaned pigs at one hour, 24 hours, 48 hours, 72 hours, 8 days and 14 days following treatments.

Two sows which received the 1:5 pour-on showed a slight reddening of the skin within one hour of treatment. This effect was not evident after 24 hours.

There were no other adverse effects to sows, suckling pigs or weaned pigs. It was reported that there were no adverse effects to persons making application.

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