

US EPA ARCHIVE DOCUMENT

MAR 24 1981

SUBJECT: EPA Reg.# 3125-GGN & 3125-GGR, the registration of two new products,, Oftanol 1.5% Granular and Oftanol 5% Granular, for use on turf for control of certain insects. CASWELL#447AB

FROM: Charles Frick, Toxicologist *e. Frick* *JDC* *3/23/81*  
Toxicology Branch, HED (TS-769) *3/23/81*

TO: William Miller (16) *WMD for WLB*  
Registration Division (TS-767)

THRU: Bill Burnam, Deputy Chief *C. J. Harrison*  
Toxicology Branch, HED (TS-769)

Petitioner: Mobay Chemical Corp.  
Agricultural Division

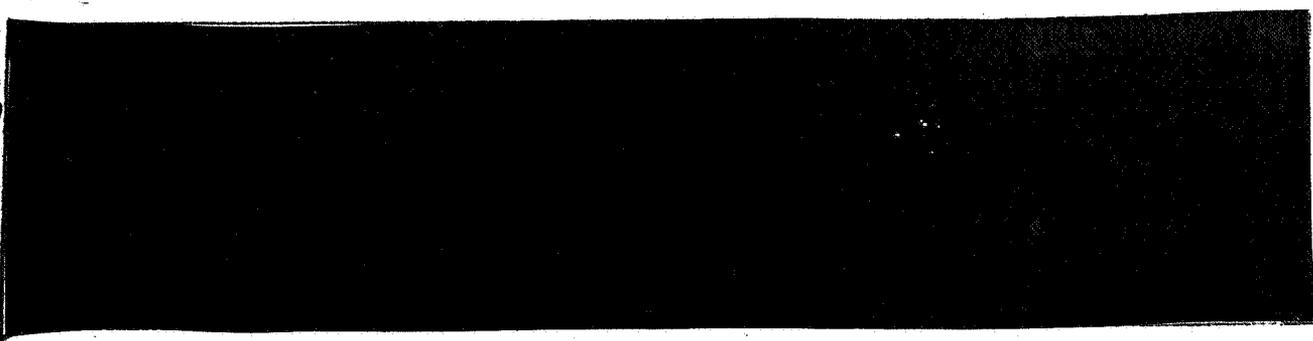
Conclusion: All data requirements have been fulfilled.

Formulation: Oftanol 1.5% Granular

<u>Component</u>	<u>Amount in lbs.</u>	<u>Percent</u>	<u>Purpose</u>
Amaze (Tech. 90% A.I.)	18	1.8	A.I.

Chemical Name - 1-Methylethyl 2-[[ethoxy[C-methylethyl)amino]phosphinothioyl]oxy[benzoate]

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Toxicology Data - The following studies were performed using Amaze 1.5% Granular.

Acute Oral Toxicity of Amaze 1.5% Granular to Rats

Testing performed by Mobay Chemical Corp., Stanley Research Center, Stillwell, Kansas; Report No. 68532, signed by E.J. Hixson; Report Date: 2/15/80; Date of Study: Initiated: 12/21/79; Terminated: 1/4/80 Study#74AOR14

Protocol

Adult male and female Sprague-Dawley derived rats were used for testing. Using carbowax as the excipient, the test compound was administered orally to groups of ten males and ten females. The animals were fasted for 19 hours prior to and at least one hour after dosing. The test material was given at 1000, 1700, 2890, and 4913 mg/kg to both sexes. Male rats ranged in weight from 199 to 246 grams and females from 183 to 235 grams.

Rats were observed for mortality and symptoms of toxicity at 0.5, 1.0 and 4 hours post treatment and at least daily for 14 days after treatment. The animals were weighed on the day of treatment and on days 7 and 14 post treatment. Survivors were sacrificed on day 14. Animals were examined for gross lesions at the time of death or at day 14 sacrifice. LD<sub>50</sub> values were calculated by the method of probit analysis.

Results

The incidence of symptoms and mortality was dose-related in both sexes. Symptoms observed included diarrhea, lacrimation, pilo-erection, tremors, ataxia, and convulsions. Average body weights of surviving male rats exhibited weight gain on days 7 and 14 after all but the highest dosage. Average body weights of surviving females receiving 1700 or 2890 mg/kg were lower at day 7 than initial body weights. One of two females surviving 2890 mg/kg had not regained her initial body weight by day 14.

No gross lesions were observed at the time of death or day 14 sacrifice in males receiving 1000 mg/kg or in females receiving 1000 or 1700 mg/kg. Congested lungs were observed in one of ten males and one of ten females receiving 2890 mg/kg; both had been found dead. Congested lungs were also observed in four of ten males and one of ten females receiving 4913 mg/kg; three of the four males and the female were found dead. Polycystic kidneys were observed in two males at 1700 mg/kg and one male at 2890 mg/kg. The importance of this observation is unclear because the incidence was not dose related.

Under the conditions of this study, the oral LD<sub>50</sub> of AMAZE 1.5% Granular = 3398 mg/kg (2733-4252 mg/kg, 95% C.L.) in male rats and 1911 mg/kg (1499-2423) mg/kg, 95% C.L.) in female rats.

Toxicity Category - III  
Core-Classification: Core-Guidelines

Acute Dermal LD<sub>50</sub> - Rabbit

Study performed by Mobay Chemical Corp., Stanley Research Center, Stillwell, Kansas; Report No. 68536, signed by E.J. Hixson; Report Date: 2/29/80; Date of Study: Initiated: 12/20/79; Terminated: 1/3/80  
Study No. 79ADL11

Protocol

The back of New Zealand white rabbits were shaved free of hair. Plastic collars were placed on the animals to be treated and the test material, moistened with physiologic saline, was applied as a paste to the shaven area. After 24 hours the covering was removed and the test material was moistened and wiped from the backs. The dose groups consisted of five males and five females treated with 2000 mg/kg. Four males and females were used as untreated controls.

Rabbits were observed twice daily (once daily on weekends) for 14 days for mortality and symptoms of toxicity. Rabbits were weighted on days 0, 7, and 14. Survivors were sacrificed on day 14. All rabbits were examined for gross lesions at the time of death or at day 14 sacrifice. Tissue samples were taken from both treated and untreated areas of skin on the backs of test animals and corresponding areas of control animals. Also tissue from notable gross lesions were taken. All tissue was taken for histopathology examination.

Results:

No symptoms of toxicity or mortality were observed in the treated or control animals. Treated rabbits appeared to gain weight at the same rate as control rabbits.

No significant gross lesions were noted. Microscopically there were minimal to mild focal areas of dermatitis in both the control and test animals. The dermatitis was noted in both treated and untreated areas of skin. The dermatitis was characterized by small accumulations of mononuclear inflammatory cells in the subepidermal connective tissue and sometimes only around the hair follicles.

The minor inflammatory changes noted were probably not related to the dermal application of test compound as the findings were similar in both control and test animals.

LD<sub>50</sub> = > 2000 mg/kg  
Toxicity Category - III  
Core Classification: Core-Minimum Data

#### Primary Dermal and Eye Irritation - Rabbit

Study conducted by Mobay Chemical Corp., Stanley Research Center; Stillwell, Kansas; Report No. 68537; signed by E.J. Hixson; Report Date: 2/29/80; Date of Study: Initiated 1/7/80; Terminated: 1/18/80; Study No. 800401 and 800501

#### Protocol

New Zealand white rabbit were used in both studies.

#### Eye Irritation

Nine rabbits eyes were examined using fluorescein dye and an ultraviolet light for defects or irritation. The rabbits were treated by placing 100 mg of test material in the left eye. The treated eyes of three rabbits were washed 45 seconds after the test material was administered with water. The treated eyes of the remaining six rabbits were not washed.

On days 1, 2, 3, 4 and 7, the treated eyes were examined for lesions of the cornea, iris, and conjunctival. The reactions were graded according to Draize

#### Dermal Irritation

The backs and sides of six rabbits were shaved. Four test sites were used on each animal. Two sites were abraded through the stratum corneum, the other two sites were left intact. The test material (0.5 grams) was moistened with saline applied to each test site on each animal under one inch square gauze patches. After 24 hours the patches were removed and the test material removed.

The test areas were evaluated 24 and 72 hours after the test material was applied according to the method of Draize.

#### Results: Eye Irritation

Wash Group: Slight erythema and chemosis were observed in three animals and a slight discharge in one of the rabbits. Erythema and discharge were absent by day 3 and chemosis was absent by day 7. No corneal lesions were observed.

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No Wash Group - Corneal lesions were observed in only one of six animals and were absent by day 2. This rabbits also exhibited moderate erythema on day 1; the remaining five rabbits exhibited mild erythema that was no longer apparent on day 2 (two rabbits), day 3 (two rabbits) on day 7 (one rabbit). Slight chemosis was observed in all six rabbits that cleared by day 7 at the latest. The rabbit with corneal lesions showed considerable discharge on day 1 that gradually subsided and was absent on day 7. The remaining five rabbits exhibited slight discharge that cleared by day 7 at the latest.

Toxicity Category - III  
Core-Classification: Core-Guideline

Dermal Irritation

Very slight erythema was observed on abraded skin sites of three rabbits at 24 hours but was not seen at 72 hours. Five rabbits (including the three with erythema) exhibited very slight edema on abraded skin sites at 24 hours but not at 72 hours. The sixth rabbit showed no response on abraded skin at either examination. The intact skin sites on all six rabbits showed no response to the test material at either 24 or 72 hours.

The Primary Irritation Index for Amaze 1.5% Granular was 0.67.

Toxicity Category - IV  
Core-Classification: Core-Guideline

Acute Inhalation LC50 - Rats

Study conducted by Mobay Chemical Corp., Stanley Research Center; Stillwell, Kansas; Study No. 80-041-05; Report No. 68914; Date of Study: Initiated: 5/8/80; Terminated: 5/22/80.

Protocol

Young adult male and female Sprague-Dawley rats were used. The initial (prior to exposure) body weights of males ranged from 216 to 243 grams and of females from 179 to 212 grams. Control group (same number and sex were utilized).

Ten animals of each sex were exposed for one hour to a single concentration of 20,000 ug (20 mg) granular formulation/liter of air.

Animals (treated and control) were observed for mortality and symptoms of toxicity during the exposure period, at 0.5, 1 and 4 hours post-exposure and twice daily for 14 days after the day of exposure. Animals were weighted prior to exposure and on days 1, 3, 7 and 14 of the post-exposure observation period.

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On day 14 all animals were sacrificed and subjected to a complete necropsy for gross abnormalities. The tissues of lungs (with bronchi and trachea), liver and kidney were taken and fixed for histopathological processing and examination.

### Results

No signs of toxicity were seen in the group of animals exposed to Amaze 1.5% Granular during the exposure or observation periods. On days 1 and 3 the average body weights of exposed female rats were similar to the initial body weights and showed an increase on days 7 and 14. The overall increase in body weights of the exposed females was slightly lower than the control group.

The average body weights of the exposed group of males showed slightly lower body weights than those of the control group on all days of the observation period. The overall increase in the body weights of the exposed group of males was significantly lower than the control group.

Gross examination of the male rats revealed pulmonary congestion in one male control and unilateral reduction in testicular size in another male. No microscopic lesions were found in male control.

On gross examination of female rats, it was found that the spleen, lumbar, cervical and mesentric lymph nodes were enlarged in one animal. Microscopic examination revealed moderate lymphoid hyperplasia in lymph nodes of one female control and mild mineralization in kidneys of another female control.

### Conclusion:

One hour exposure of rats to Amaze 1.5% Granular at a concentration of 20,000 ug (nominal) showed no signs of toxicity and no gross changes were observed. Histological examination of tissues (lung, liver, and kidney) showed no changes related to the exposure.

LC<sub>50</sub> = > 20 mg/liter

Toxicity Category - IV

Core-Classification: Core-Minimum Data

The following were conducted using Amaze 5% Granular Formulation.

Oftanol 5% Granular

<u>Component</u>	<u>Amount lbs.</u>	<u>Percent by Wt.</u>	<u>Purpose</u>
Amaze (Tech. 90 A.I. basis)	55.6	5.56	Active Ingredient

Dose 1000 mg/kg



Acute Oral LD50 - Rats

Study conducted by Mobay Chemical Corp.; Stanley Research Center; Stillwell, Kanasa; Report No. 67996; Study No. 79A0R06; Date of Study: Initiated: 6/19/79; Terminated: 7/3/79

Protocol

Sprague-Dawley derived rat were used in this study. Ten animals were used for each dose level. A geometric scale of 1.47 was used to determine the following levels:

Male and Female: 323, 475, 698, 1027, 1510, 2220 and 3263 mg/kg.

After dosing, the animals were observed twice daily over a 14-day period for mortality and signs of toxicity. Body weights were taken on days 0, 7 and 14. Necropsies were performed on all of the animals on the 14th day or at the time of death.

Results:

Signs of toxicity for males were diarrhea, salivation, lacrimation, tremors, decreased activity, convulsions, and unthrifty appearance. Average body weights were seen on all levels except for day 7 (1027 mg/kg). Gross necropsies at death or day 14 sacrifice revealed congested lungs (1/10 at 475, 1/10 at 698, 6/10 at 1027 mg/kg) and hemorrhagic enteritis (4/10 at 1510 and 3/10 at 2220 mg/kg).

Signs of toxicity for females were diarrhea, lacrimation, tremors, convulsions, decreased activity, and unthrifty appearance.

Average weight gains were seen on all levels except for 475 and 698 mg/kg on day 7.

Gross necropsies at the time of death or on day 14 sacrifice revealed congested lungs (1/10 at 475, 7/10 at 698, 9/10 at 1027; 1510, and 10/10 at 2220 mg/kg) and hemorrhagic enteritis (1/10 at 475, 1/10 at 698, and 2/10 at 1027 mg/kg).

Conclusions:

Under the conditions of this study, the following LD<sub>50</sub> values were determined for Amaze 5% Granular:

Males: 614 mg/kg (524 to 720 mg/kg) 95% C.L.  
Females: 576 mg/kg (498 to 666 mg/kg) 95% C.L.

Toxicity Category - III  
Core-Classification: Core-Guidelines

Eye and Dermal Irritation - Rabbit

Study conducted by Mobay Chemical Corp., Stanley Research Center; Stillwell, Kansas; Date of Study: Initiated: 9/18/79; Terminated: 9/28/79; Study No. 79EIL04 and 79DIL05; Study Director: E.J. Hixson; Report No. 68269

Protocol

New Zealand white rabbit were used in these studies.

Eye Irritation

Nine rabbits' eyes were examined using fluorescein dye in U.V. light for defects. The animals were treated by placing 100 mg of the test material in the left eye. The treated eyes of three rabbits were washed 45 seconds after the test material was administered using approximately 200 ml of water. The treated eyes of the remaining six rabbits were not washed.

Observations

On days 1, 2, 3, 4, 7, 8 and 9, the treated eyes were examined for lesions of the cornea, iris, and conjunctivae.

Dermal Irritation

The backs and sides of six rabbits were shaved. Four test sites were used on each animal. Two sites were abraded, the other two sites were left intact. The test material (0.5 gm) was moistened with saline and applied to each test site and each animal under one inch square gauze patches. After 24 hours the patches were removed.

Observations

The test areas were evaluated 24 and 72 hours after the test material was applied according to the method of Draize.

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Results: Eye Irritation

In the wash group, one rabbits' eye exhibited slight discharge one day after treatment but was clear thereafter; the remaining two rabbits eyes were clear throughout the observation period. In the no wash group, corneal lesions were observed in only one rabbit of this group; lesions had cleared by the second day post-treatment. Iritis was observed in three animals on day one but not thereafter. Erythema was observed in all six rabbits and chemosis in five of six on day 1; chemosis and erythema had cleared by day four in all but one animal which was clear on day 9.

Dermal Irritation

No erythema was observed in any treated animal at 24 or 72 hours after treatment.

The Primary Irritation Index for Amaze 5% Granular = 0.0

Conclusion:

Under conditions of these studies, AMAZE 5% Granular was found to be a mild eye irritant with lesions clear within seven days. This formulation was not an irritant on rabbit skin.

Core Classification

Eye Irritation - Core-Minimum Data  
Dermal Irritation - Core-Minimum Data

Toxicity Category

Eye Irritation - III  
Dermal Irritation - IV

Dermal LD50 - Rabbit

Study conducted by Mobay Chemical Corp., Stanley Research Center; Stillwell, Kansas; Date of Study: Initiated: 9/17/79; Terminated: 10/1/79; Study No. 79ADL07; Study Director: E.J. Hixson

Protocol

Male and female New Zealand White rabbits were used in this study.

The backs of the rabbits were shaved and then abraded. Plastic collars were placed on the animals and the test material moistened with saline, was applied as a paste to the shaved areas. The test sites were covered with plastic which was secured with tape. After 24 hours the coverings were removed and the test compound removed by wiping.

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Groups of five males and five females were treated with 2000 mg/kg. Four males and four females were used as controls.

### Observations

Rabbits were observed twice daily for 14 days for mortality and symptoms of toxicity. Rabbits were weighted on days 0, 7 and 14. Survivors were sacrificed on day 14. All animals were examined for gross lesions at the time of death or at day 14 sacrifice.

### Results:

No symptoms of toxicity or mortality were observed throughout the 14-day post treatment observation period. Weight gain of the treated group was comparable to that of concurrent untreated control animals.

No gross lesions were observed at day 14 sacrifice. Microscopically there was a minimal to mild focal dermatitis in the sections from both control and test animals.

The LD<sub>50</sub> = > 2000 mg/kg

Toxicity Category - III  
Core-Classification: Core-Minimum Data

### Acute Inhalation LC<sub>50</sub> - Amaze-20% Granular

Study conducted by Mobay Chemical Corp., Stanley Research Center; Stillwell, Kansas; Date of Study: Initiated: 1/30/80; terminated: 3/18/80; Study No. 80-411-01; Report No. 68762; Study Director: G.K. Sangha

### Protocol

Male and female Sprague-Dawley rats were used in this study. Male rats ranged in weight from 218-287 gm and females from 175-224 gm.

Animals were exposed (10 males and 10 females) for one hour to an exposure concentration of 20.0 mg formulation/liter of air. It was stated that the formulation was placed in the drum (See original data for apparatus design) and the drum was rotated during the exposure period so that any respirable dust generated by the granules was well distributed in the drum atmosphere.

Animals (treated and control) were observed for mortality and symptoms of toxicity during the exposure period and at 0.5, 1 and 4 hours of post-exposure period and twice daily for 14 days after the day of exposure except on weekends when they were observed only once during the day.

Animals were weighed prior to exposure and on day 7 and 14 after the exposure. On day 14 animals were sacrificed and were subjected to complete necropsy. Tissues from the lung, liver, and kidney were taken for histopathology.

Results:

No signs of toxicity were observed during the exposure and observation periods. The average body weights of the exposed groups of animals were similar to those of the control group.

At necropsy, pulmonary and hepatic congestion was observed in all control males. Pulmonary congestion was seen in all treated males. Microscopic examination of lungs, liver and kidneys revealed no histopathologic lesions in either the control or treated male animals.

Pulmonary hemorrhage was seen in 3 treated females; pulmonary congestion alone was seen in 3 treated females. Microscopic examination of lungs, liver and kidneys revealed no lesions in either control or treated females. Particle size was not determined.

LC50 = > 20 mg/liter

Toxicity Category - IV  
Core Classification: Core-Minimum Data

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