DATE: September 24, 1981

SUBJECT: Gordon's Trimec® 450 Herbicide
EPA Registration No. 2217-624

FROM: Sherell A. Sterling
PB/ISS

TO: Richard Mountfort
Product Manager (23)

Applicant: PBI/Gordon Corporation
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Active Ingredient:
2,4-D-Dimethylamine salt .................. 23.12%
MCPP-dimethylamine salt ................. 24.70%
Dicamba-dimethylamine salt ...................... 6.18%
Inert Ingredients ............................... 46.00%

Background: The registrant is requesting a change in signal word from "DANGER" to "WARNING." In support of this, 37 eye studies were submitted and/or referenced for review.

Recommendations:

1. The following formulations are considered substantially similar to Trimec 450 Herbicide: 823, 881, EH 600, and EH 599 (see reviews 9, 14, 15, and 16). For each of these formulations, the eye irritation toxicity category is Tox. Cat. I, with corneal opacity through day 21.

2. Based on the Eye Irritation studies submitted, the appropriate signal word for this product remains "DANGER."
1. Rabbit Eye Irritation; Stillmeadow #1528-80; February 20, 1980; Acc. No. 245537 (2217-543, 5/7/80)

Procedure: 0.1 ml of "Fairway C-881 B-0129 1-3-80" was applied into one eye of each of 9 New Zealand white rabbits. Three rabbits had the treated eye washed with room temperature tap water for 1 minute beginning 30 seconds after treatment; 6 remaining eyes were treated and unwashed. Scoring at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, and 21 days.

Results: At 24 hours, unwashed eyes showed corneal opacity (2/6=5, 1/6=10, 1/6=20, 1/6=30) in 5/6; iris irritation in 6/6=10; conjunctival redness in 3/6=2, 3/6=3; chemosis in 5/6=4, 1/6=3; discharge in 5/6=2, 1/6=3; all showed necrosis. At 7 days, corneal opacity still observed in 5/6 eyes (2/6=5, 1/6=10, 1/6=20, 1/6=40); iris irritation in 4/6=10, 2/6=5; redness and chemosis in 6/6 eyes; discharge in 5/6; necrosis noted in 5/6. At 21 days, corneal opacity in 5/6 (1/6=10, 1/6=20, 2/6=30, 1/6=45); iris irritation and redness in 5/6 eyes; chemosis in 6/6 and discharge in 3/6 eyes. Symptoms observed also included pupil constriction, invasion of cornea by blood vessels, swollen cornea, corneal stippling, and vocalization upon instillation.

The washed eyes at 24 hours showed corneal opacity in 2/3 eyes (1/3=5, 1/3=40); iris irritation in 2/3=10, 1/3=5; conjunctival redness in 1/3=2, 2/3=3; chemosis in 2/3=3, 1/3=4; discharge in 3/3=2; necrosis in all animals. At 7 days, corneal opacity in 2/3=20; iris irritation, redness, and chemosis in 3/3 eyes; discharge in 2/3. By day 21, corneal opacity reduced to 1/3=5; redness and discharge observed in 1/3 each, chemosis in 2/3. Also observed: stippling, pupils constricted; apparent invasion of cornea by blood vessels.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

2. Rabbit Eye Irritation; Stillmeadow Project #1376-79; October 17, 1979. (2217-597; 1/21/80)

Procedure: 100 mg of untreated vermiculite was applied into one eye of each 9 New Zealand white rabbits. Three rabbits had the treated eye washed for 1 minute at 30 seconds post-treatment with room temperature deionized water; remaining 6 treated eyes were not irrigated. Scoring at 1, 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, no corneal opacity, iris irritation, or discharge observed in either group. The unwashed eye group showed 3/6 with redness (3/6=1) and 2/6 in the washed eye group showed redness (2/6=1); 6/6 unwashed eyes with chemosis (5/6=1, 1/6=2) and 3/3 in the washed eye group with chemosis (3/6=1). All appeared normal by 72 hours.
Study Classification: Core Guideline Data. Since the test substance was not EH594, this study cannot be used in support of EH594 formulation.

Toxicity Category: III - CAUTION. The toxicity category, as determined in this study, is for untreated vermiculite and not EH594.

3. Rabbit Eye Irritation; Stillmeadow #1376-79; October 17, 1979; Acc. No. 243058 (2217-AUN; 12/9/80)

Procedure: Nine New Zealand white rabbits each received 100 mg of untreated vermiculite in one eye. Thirty seconds after treatment, the treated eye of 3 animals was washed with deionized water for one minute. Scoring at 1, 24, 48, 72 hours; 4 and 7 days.

Results: In the unwashed eyes at 24 hours, the only irritation observed was redness in 3/6=1; chemosis in 5/6=1, 1/6=2. All irritation in unwashed eyes was clear by 72 hours. Washed eyes at 24 hours showed only redness in 2/3=1 and chemosis in 3/3=1. By 48 hours, all eyes were clear.

Study Classification: Core Guideline Data.

Toxicity Category: IV - CAUTION.

4. Rabbit Eye Irritation; Stillmeadow #1336-79; October 15, 1979; Acc. No. 243058 (2217-AUN; 12/9/80)

Procedure: Nine New Zealand white rabbits each received 100 mg of "DMB #2" in one eye. Subsequent to treatment, 3 of the eyes were rinsed for one minute with room temperature tap water. Scoring was at 1, 24, 48, 72 hours and 4, 7, 10, 13, 16, 19, 21 days.

Results: The unwashed eyes at 24 hours showed iris irritation in 2/6=5, 1/6=10; redness in 6/6=2; chemosis in 5/6=3, 1/6=4; discharge in 2/6=1, 4/6=2; stippling in 6/6 eyes. By day 7, unwashed eyes showed corneal opacity in 1/6=5; iris irritation in 1/6=5; redness in 2/6=1, 1/6=2, 1/6=3; chemosis in 3/6=1, 1/6=2, 2/6=3; discharge in 2/6=2. At day 21, corneal opacity in 2/6=5; conjunctival redness in 1/6=1; chemosis in 1/6=1, 1/6=2; discharge in 1/6=2.

Washed eyes at 24 hours were clear except for chemosis in 1/3=1. All eyes were clear by 72 hours.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION. The only corneal opacity seen was very mild in only 2 animals, developing 7 days post-treatment.

5. Primary Eye Irritation Studies in Rabbits: EH588; MRI Project #4823-B-(1); November 12, 1979. (2217-597; 1/21/80)
Procedure: 0.1 ml of EH588 was applied into one eye of each of 6 New Zealand white rabbits; no irritation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At instillation, 6/6 rabbits vocalized. At 24 hours, 6/6 showed corneal opacity (3/6=20, 3/6=40); 6/6 exhibited eye irritation (2/6=2, 4/6=1), 6/6 with conjunctival erythema (1/6=1, 3/6=2, 2/6=3); 6/6 with swelling (1/6=1, 1/6=2, 2/6=3, 2/6=4); 6/6 with discharge (4/6=2, 2/6=3). Fluorescein testing showed 6/6 had corneal involvement (2/6=5, 1/6=30, 2/6=45, 1/6=60). At 7 days, 1/6 with corneal opacity (1/6=20); 1/6 showed iritis irritation (1/6=1); 1/6 exhibited conjunctival erythema (1/6=1); 1/6 showed swelling (1/6=2); and 1/6 with discharge (1/6=1). Fluorescein testing revealed 1/6 with corneal involvement (1/6=40) at 7 days.

Study Classification: Core Minimum Data. An eyewash group was not tested. Since the test substance was not EH594, this study cannot be used in support of the EH594 formulation.

Toxicity Category: II - WARNING. The toxicity category, as determined in this study, is for EH588 and not EH594.

6. Primary Eye Irritation Studies in Rabbits: EH588; MRI Project #4823-B-(1); November 12, 1979. (2217-597, 1/21/80)

Procedure: 0.1 ml of EH589 was applied into one eye of each of 6 New Zealand white rabbits; no irritation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, 4/6 showed corneal opacity (1/6=20, 3/6=40); 4/6 exhibited iris irritation (3/6=1, 1/6=2); 5/6 exhibited conjunctival erythema (2/6=1, 3/6=2); 5/6 with swelling (2/6=1, 3/6=2); and 5/6 with discharge (1/6=1, 3/6=2, 1/6=3). Fluorescein testing showed 4/6 with corneal involvement (2/6=5, 1/6=45, 1/6=60).

Study Classification: Core Minimum Data. An eyewash group was not tested. Since the test substance was not EH594, this study cannot be used in support of the EH594 formulation.

Toxicity Category: IV - CAUTION. The toxicity category, as determined in this study, is for EH588 and not EH594.

7. Primary Eye Irritation Studies in Rabbits: EH596; MRI Project #4823-B-(1); November 12, 1979. (2217-597, 1/21/80)

Procedure: 0.1 ml of EH596 was applied into one eye of each of 6 New Zealand white rabbits; no irritation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, 5/6 showed corneal opacity (4/6=20, 1/6=40); 5/6 with iris irritation (5/6=1); 5/6 with conjunctival erythema (1/6=2, 4/6=3); 5/6 showed swelling and 6/6 with discharge (1/6=1, 5/6=2). Fluorescein test showed 4/6 with corneal involvement (3/5=5, 1/6=30). At 7 days, all eyes appeared normal.

At 7 days 1/6 showed corneal opacity (1/6=20), 1/6 with iritis irritation (1/6=1); 1/6 showed conjunctival erythema (1/6=1); 1/6 with swelling (1/6=2) and 1/6 with discharge (1/6=1).
Study Classification: Core Minimum Data. An eyewash group should have been studied. Since the test was conducted on EH596 and not EH594, this study cannot be used in support of the EH594 formulation.

Toxicity Category: II - WARNING. The toxicity category, as determined in this study, is for EH596 and not EH594.

8. Primary Eye Irritation Studies in Rabbits: EH594; MRI Project #4823-B-(1); November 12, 1979. (2217-597; 1/21/80)

Procedure: 0.1 ml of EH594 was applied into one eye of each of 6 New Zealand white rabbits; no irrigation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, 6/6 exhibited corneal opacity (6/6=40); 6/6 showed iris irritation; 5/6 with conjunctival erythema (4/6=1, 1/6=3); 6/6 with swelling (3/6=2, 3/6=3); and 5/6 with discharge (4/6=2, 1/6=3). Fluorescein testing showed 6/6 with corneal involvement (6/6=60).

At 7 days, 4/6 exhibited corneal opacity (2/6=20, 1/6=40, 1/6=80); 4/6 with iris irritation (3/6=1, 1/6=2); 4/6 showed conjunctival erythema (2/6=2, 2/6=3); 4/6 exhibited swelling (3/6=2, 1/6=4); and 4/6 with discharge (1/6=1, 2/6=2, 1/6=3). Fluorescein testing showed 4/6 with corneal involvement (2/6=5, 2/6=40).

Study Classification: Core Minimum Data. A treated-and-rinsed group was not tested.

Toxicity Category: I - DANGER.

9. Acute Eye Irritation - Rabbits; Hill Top Labs; July 1, 1979; Acc. No. 240898 (2217-624; 6/9/80)

Procedure: 0.1 ml of "823" was applied into one eye of each of 9 New Zealand white rabbits. Three rabbits had the treated eye flushed with lukewarm tap water, 30 seconds post-treatment, for 60 seconds. Draize scoring at 24, 48, 72 hours and 4, 7, 10, 13, 16, 19, and 21 days.

Results: Corneal opacity exhibited in 8/9 through day 21. Erythema, edema, and discharge observed in all animals through day 7. Other symptoms included blisters under eyelid (9/9), vascularization (8/9), loss of hair around eyes (5/9), vocalization at application (4/9), conjunctivae closing in around eye (1/9). Eye irritation, permanent damage more pronounced in eyes that had been washed.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.
10. Primary Eye Irritation Studies in Rabbits: EH595; MRI Project #4823-B-(1); November 12, 1979 (2217-597, 1/21/80)

Procedure: 0.1 ml of EH595 was applied into one eye of each of 6 New Zealand white rabbits; no irrigation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, no corneal opacity observed; 1/6 showed iris irritation (1/6=1); 6/6 with conjunctival erythema (2/6=1, 3/6=2, 1/6=3), 5/6 showed swelling (5/6=2); and 5/6 with discharge (1/6=1, 4/6=2). Fluorescin testing showed 3/6 with corneal involvement at 24 hours (3/6=5). All appeared normal by day 7.

Study Classification: Core Minimum Data. A treated and rinsed group was not tested. Please note that the test substance is EH595 and not EH594.

Toxicity Category: III - CAUTION.


Procedure: 100 mg of EH576 was applied into one eye of each of 9 New Zealand white rabbits. Three rabbits had the treated eye washed with room temperature tap water for one minute beginning 30 seconds post-treatment; remaining 6 treated eyes were not irrigated. Scoring at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, and 21 days.

Results: At 24 hours, the unwashed group exhibited no corneal opacity when examined; fluorescein examination revealed 5/6 with corneal involvement; 6/6 with corneal stippling. Iris irritation observed in 3/6 (2/6=1, 1/6=2) unwashed eyes at 24 hours; 6/6 showed redness (6/6=2); 6/6 with chemosis (5/6=3, 1/6=4); 6/6 with discharge (4/6=2, 2/6=1). At 24 hours, the "washed" eye group showed no corneal opacity and no iris irritation; 1/3 exhibited redness (1/3=3); 3/3 with chemosis (3/3=1).

At day 7, unirinsed eyes showed 1/6 with corneal opacity (1/6=5); 2/6 had positive fluorescein tests; 1/6 with corneal stippling; 1/6 with iris irritation (1/6=2); 4/6 showed redness (2/6=1, 1/6=2, 1/6=3); 6/6 with chemosis (3/6=1, 1/6=2, 2/6=3); 2/6 with discharge (2/6=2). In unirinsed group, 2/6 showed corneal opacity and conjunctival irritation through day 21. All rinsed eyes appeared normal by 72 hours.

Study Classification: Core Guideline Data. Since the test substance was not EH594, this study cannot be used in support of the EH594 formulation.

Toxicity Category: I - DANGER. This toxicity category, as determined in this study, is for EH576 and not EH594.
12. Primary Eye Irritation Studies in Rabbits Using PBI/Gordon Corporation Test Material EH595 and EH601; MRI #4823-B(2); January 2, 1980; Acc. No. 244753 (2217-597; 4/24/81)

Procedure: Nine New Zealand white rabbits each received 0.1 ml of "EH 601" in one eye. Three eyes were rinsed 30 seconds after treatment with room temperature tap water for one minute. Eyes scored at 24, 48, 72 hours; 4, 7, 8, 9, 11, 14, 15, 17, and 21 days.

Results: The unwashed eyes at 24 hours exhibited corneal opacity in 6/6=20; iris irritation in 2/6=5, 1/6=10; conjunctival redness in 4/6=2, 2/6=3; chemosis in 4/6=2, 2/6=3; discharge in 3/6=2, 3/6=3. Only 3 animals scored through day 21; other animals' irritation had cleared. At 21 days, corneal opacity observed in 3/3=20; iris irritation in 3/3=5; redness in 3/3=2; chemosis in 3/3=2; discharge in 2/3=2, 1/3=3.

At 24 hours, the rinsed eyes showed corneal opacity in 3/3=20; redness in 2/3=1, 1/3=2; chemosis in 2/3=2, 1/3=3; discharge in 1/3=1, 1/3=2, 1/3=3. By day 7, corneal opacity seen in 1/3=20; redness in 2/3=1, 1/3=2; chemosis in 2/3=2, 1/3=3; discharge in 1/3=1, 1/3=2, 1/3=3. At day 14 (the last scores recorded), only irritation noted was chemosis in 1/3=1.

Study Classification: Core Minimum Data.

Toxicity Category: I - DANGER.

13. Primary Eye Irritation Studies in Rabbits Using PBI/Gordon Corporation Test Materials 881 (Dimethylamine), 2,4-D (Dimethylamine), and 2,4-D (Iso-octyl ester); MRI #4823-B(1); Nov. 12, 1979; Acc. No. 244753 (2217-597; 4/24/81)

Procedure: Nine New Zealand white rabbits each received 0.1 ml of "881 (Iso-octyl ester)" in one eye. Three eyes were rinsed 30 seconds after treatment with room temperature tap water for one minute. Eyes scored at 24, 48, 72 hours; 7, 10, 13, 14, 17, 21 days.

Results: Unwashed eyes at 24 hours exhibited redness in 6/6=1; chemosis in 5/6=2, 1/6=3; discharge in 4/6=1, 1/6=2, 1/6=3. At 3 days, corneal opacity in 2/6=20, 2/6=40; iris irritation in 3/6=1; redness in 4/6=1; chemosis in 3/6=1, 2/6=2; discharge in 3/6=1; redness in 4/6=1; chemosis in 3/6=1, 2/6=2; discharge in 3/6=1, 2/6=2. All eyes appeared clear by day 7.

Washed eyes exhibited no irritation at 24 hours. At day 2, iris irritation in 1/3=5; redness in 1/3=1; chemosis in 1/3=1; discharge in 1/3=1. All eyes were clear by day 4.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.
14. Primary Eye Irritation Studies in Rabbits Using PBI/Gordon Corporation
Test Materials 881 (Iso-octyl ester), 881 (Dimethylamine), 2,4-D
(Dimethylamine, and 2,4-D (Iso-octyl ester)); MRC #48323-B(1); Nov. 12,
1979; Acc. No. 244753. (2217-597; 4/24/81)

Procedure: Nine New Zealand white rabbits each received 0.1 ml of "881
Dimethylamine" in one eye. Three eyes were rinsed 30 seconds after
 treatment with room temperature tap water for one minute. Eyes scored at
24, 48, 72 hours; 4, 7, 14, 21 days.

Results: At 24 hours, the unwashed eyes showed corneal opacity in 1/6=10,
3/6=40, 1/6=45; iris irritation in 3/6=5, 2/6=10; redness in 3/6=1,
3/6=2; chemosis in 1/6=2, 5/6=3; discharge in 6/6=3. By 21 days, corneal
opacity in 4/6=40, 1/6=80; iris irritation in 4/6=5, 1/6=10; redness in
4/6=2, 1/6=2; chemosis in 4/6=2, 1/6=4; discharge in 4/6=2, 1/6=3.

The washed eyes exhibited corneal opacity in 3/3=10; iris irritation in
1/3=5, 2/3=10; redness in 2/3=1, 1/3=3; chemosis in 1/3=2, 2/3=3; discharge
in 1/3=2, 2/3=3 at 24 hours. At 21 days, corneal opacity in 1/3=20; iris
irritation in 1/3=5; redness in 2/3=2; chemosis in 1/3=2; discharge in
1/3=2.

Study Classification: Core Guideline Data.
Toxicity Category: I - DANGER.

15. Rabbit Eye Irritation; Stillmeadow #1344-79; October 17, 1979; Acc. No.
244753 (2217-597; 4/24/81)

Procedure: Nine New Zealand white rabbits each received 0.1 ml of "EH 600"
in one eye. The test substance "EH 600" is composed of the following active
ingredients:

2,4-D, DEA salt .................. 23.54%
MCP, DEA salt .................. 15.69%
Banvel, DEA salt ................ 3.92%

Three eyes were rinsed 30 seconds after treatment with room temperature tap
water for one minute. Eyes scored through day 21.

Results: Upon instillation, 3/6 in unwashed group vocalized. All eyes
showed red blister in conjunctival sac at 1 hour. At 24 hours, the
unwashed eyes exhibited corneal opacity in 1/6=5, 2/6=20, 1/6=30; iris
irritation is 6/6=10; conjunctival redness in 6/6=2; chemosis in 2/6=3,
4/6=4; discharge in 4/6=2, 2/6=3; also noted were necrosis (6/6) and
corneal stippling (5/6). One animal found dead on day 7. Day 21,
unwashed eyes exhibited corneal opacity in 1/5=10, 1/5=20, 1/5=30,
1/5=40; iris irritation in 2/5=5, 3/5=10; redness in 2/5=1, 3/5=2;
chemosis in 2/5=2, 2/5=3, 1/5=4; discharge in 2/5=1, 3/5=2; also, cornea
invaded by blood vessels (5/5), corneal swelling (2/5); ptosis around
eye (1/5).
Upon instillation, 1/3 animals with washed eyes vocalized; red blisters seen in conjunctival sac of 3/3 rabbits. After 24 hours, washed eyes showed corneal opacity in 1/3=30, 2/3=40; iris irritation in 3/3=10; redness in 3/3=2; chemosis in 1/3=3, 2/3=4; discharge in 3/3=2; necrosis and corneal stippling in all rabbits. At 7 days, corneal opacity in 3/3=10, cornea invaded by blood vessels; iris irritation in 3/3=10; redness in 3/3=2; chemosis in 2/3=3, 1/3=4; discharge in 1/3=1, 1/3=2, 1/3=3; necrosis and stippling in 3/3. By day 21, corneal opacity in 1/3=5, 1/3=40; also, invasions of cornea by blood vessels, swollen cornea; iris irritation in 1/3=10; redness in 3/3=1, chemosis in 1/3=1, 2/3=2; discharge in 1/3=2.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

16. Rabbit Eye Irritation: Project #1340-79; October 15, 1979; Accession No. 241322. (2217-597, 4/24/81 and 2217-AGO, 6/10/80)

Procedure: 0.1 ml of "BH 599" was applied into one eye of each of 9 New Zealand white rabbits. Three rabbits had the treated eye flushed with room temperature tap water for 1 minute, 30 seconds post-treatment. Scoring at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, 21 days.

Results: In non-washed eyes at 24 hours, no corneal opacity; positive fluorescein staining in 6/6; stippling in 5/6; iris irritation in 6/6=10; conjunctival redness in 2/6=2, 4/6=3; chemosis in 6/6=4; discharge in 4/6=2, 2/6=3; necrosis in 6/6. By day 7, unrinshed eyes showed corneal opacity in 4/6=5 with invasion of cornea by blood vessels; stippling in 6/6; iris irritation in 6/6=10; redness in 5/6=2, 1/6=3; chemosis in 2/6=3, 4/6=4; discharge in 6/6=2; necrosis in 6/6. At day 21, unwashed eyes exhibited corneal opacity in 2/6=15, 1/6=20, 2/6=30, 1/6=40 with invasion of blood vessels into cornea and swelling of cornea; irritation to iris and conjunctiva continued in all animals.

In rinsed eyes at 24 hours, corneal opacity in 1/3=20, 1/3=40; positive fluorescein stain in 3/3; stippling in 3/3; iris irritation in 3/3=10; redness in 2/3=2, 1/3=3; chemosis in 1/3=3, 2/3=4, discharge in 1/3=2, 2/3=3; necrosis in 3/3. By day 7, rinsed eyes exhibited corneal opacity 1/3=5, 1/3=10, 1/3=45 with invasion by blood vessels; iris irritation in 1/3=5, 2/3=10; redness in 1/3=2, 2/3=3; chemosis in 1/3=3, 2/3=4; discharge in 1/3=1, 2/3=2; necrosis in 3/3. At day 21, corneal opacity in 1/3=20 and 1/3=40 with invasion by blood vessels and corneal swelling; iris and conjunctival irritation continued in 2/3 washed eyes.

8/9 eyes were worse from day 7 to day 21.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.
17. Primary Eye Irrit.  Studies in Rabbits: EH596; M. Project #4823-B(1); November 12, 1979. (2217-597; 1/21/80)
Procedure: 0.1 ml of EH596 was applied into one eye of each of 6 New Zealand white rabbits; no irrigation. Scoring at 24, 48, 72 hours, 4 and 7 days.

Results: At 24 hours, 5/6 showed corneal opacity (4/6=20, 1/6=40); 5/6 with iris irritation (5/6=1); 5/6 with conjunctival erythema (1/6=2, 4/6=3); 5/6 showed swelling and 6/6 with discharge (1/6=1, 5/6=2). Fluorescein test showed 4/6 with corneal involvement (3/5=5, 1/6=30). At 7 days, all eyes appeared normal.

Study Classification: Core Minimum Data. An eyewash group should have been studied. Since the test was conducted on EH596 and not EH594, this study cannot be used in support of the EH594 formulation.

Toxicity Category: II - WARNING. The toxicity category, as determined in this study, is for EH596 and not EH594.

18. Primary Eye Irritation Studies in Rabbits Using PBI/Gordon Corporation Test Materials 881 (Iso-octyl ester), 881 (Dimethylamine), 2,4-D (Dimethylamine), and 2,4-D (Iso-octyl ester); MRI #4823-B(1); Nov. 12, 1979; Acc. No. 244753 (2217-597; 4/24/81)
Procedure: Nine New Zealand white rabbits each received 0.1 ml of "2,4-D (dimethylamine)" in one eye. Three eyes were rinsed 30 seconds after treatment with room temperature tap water for one minute. Eyes scored at 24, 48, 72 hours; 4, 7, 14, and 21 days.

Results: At 24 hours, the unwashed eyes showed corneal opacity in 5/6=20; 1/6=40; iris irritation in 6/6=5; redness in 4/6=1, 2/6=2; chemosis in 4/6=2, 2/6=3; discharge in 1/6=1, 4/6=2, 1/6=3. By day 21, corneal opacity in 2/6=20, 1/6=60, 1/6=80; iris irritation in 2/6=1, 2/6=2; redness in 2/6=2, 2/6=3; chemosis in 2/6=2, 2/6=4; discharge in 2/6=2, 2/6=3.

The washed eyes at 24 hours exhibited corneal opacity in 2/3=20; iris irritation 2/3=5; redness in 1/3=1, 2/3=2; chemosis in 1/3=1, 1/3=2, 1/3=4; discharge in 3/3=3. Corneal opacity in 1/3=20; iris irritation in 1/3=5; redness in 1/3=2; chemosis in 1/3=2; discharge in 1/3=1 at 21 days.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

19. Eye Irritation Study; MRI #4823-B(3); July 31, 1980; Acc. No. 245537
Procedure: Nine New Zealand white rabbits each received 0.1 ml of EH552 (1# 2,4-D acid; MCPA acid; Dicamba) in one eye. Three treated eyes were subsequently rinsed 30 seconds post-application for one minute with lukewarm water. Eyes were examined at 24, 48, 72 hours; 7, 10, 13 days.
Results: One animal with a washed/treated eye and one with an un washed eye were inadvertently terminated on day 11. These animals were replaced. The animals that were terminated exhibited the most severe reaction to treatment.

The unwashed eyes at 24 hours exhibited corneal opacity in 1/7=10, 3/7=15, 1/7=20, 1/7=30, 1/7=40; redness in 2/7=1, 1/7=2, 4/7=3; chemosis in 1/7=1, 3/7=2, 1/7=3, 2/7=4; discharge in 2/7=2, 5/7=3. By day 7, the unwashed eyes exhibited corneal opacity only in 1/7=10; redness in 1/7=1. All unwashed eyes were clear at day 13.

Washed eyes at 24 hours exhibited corneal opacity in 1/4=5, 1/4=20, 1/4=60; iris irritation in 1/4=5; redness in 2/4=1, 1/4=2, 1/4=3; chemosis in 1/4=1, 2/4=2, 1/4=4; discharge in 1/4=2, 3/4=3. At day 7 chemosis in 1/4=1; discharge in 1/4=1. At day 10, the only irritation was discharge in 1/4=1; animal terminated on day 11.

Study Classification: Core Minimum Data. Two animals were inadvertently terminated.

Toxicity Category: III - CAUTION.

20. Eye Irritation Study; MRF #4823-B(3); Acc. #245537

Procedure: Nine New Zealand white rabbits each received 0.1 ml of BL 8000 in one eye. Three treated eyes were subsequently rinsed 30 seconds post-application for one minute with lukewarm water. Readings were taken at 24, 48, 72 hours; 4, 7 days.

Results: One animal (unwashed group) died on day 5; animal was replaced. In unwashed eyes at 24 hours, rabbits exhibited corneal opacity in 2/7=10, 1/7=15, 3/7=60; redness in 2/7=1, 3/7=2, 2/7=3; chemosis in 1/7=1, 6/7=3; discharge in 2/7=2, 5/7=3. All eyes were clear by day 7.

The washed eyes at 24 hours exhibited corneal opacity in 1/3=30, 2/3=60; redness in 2/3=2, 1/3=3; chemosis in 2/3=2, 1/3=3; discharge in 3/3=3. By day 7, all scores were clear.

Death was not attributed to test substance.

Study Classification: Core Guideline Data

Toxicity Category: III - CAUTION.

BL 8000 is equivalent to (by AOAC method):

2,4-D, dimethylamine salt .................. 6.3%
MCPP, dimethylamine salt .................. 3.02%
Dicamba, dimethylamine salt ................ 0.69%
21. Eye Irritation Study; MRI #4823-B(2); Dec. 31, 1979; Acc. #245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. No procedures were given. Test substance was EH604 (4# diethanolamine salts of 2,4-D/MCPP/Dicamba). Animals were scored on 1, 2, 3, 4, 7 days.

Results: At 24 hours, corneal opacity in 4/4 eyes = 40; iris irritation in 3/4=5; redness in 3/4=2, 1/4=3; chemosis in 3/4=3, 1/4=4, discharge in 4/4=3. At day 7, scores were identical.

Study Classification: Supplementary Data. Only 2 animals tested. Procedures must be reported.

22. Eye Irritation Study; MRI #4823-B(2); Dec. 31, 1979; Acc. No. 245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. Animals were scored on day 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH605 (4# triethanolamine salts of 2,4-D, MCPP, Dicamba).

Results: At 24 hours, corneal opacity in 4/4=20; iris irritation in 2/4=5; redness in 4/4=2; chemosis in 4/4=4; discharge in 4/4=3. At 7 days, corneal opacity in 1/4=2, 1/4=40; iris irritation in 1/4=10; redness in 2/4=1, 1/4=2, 1/4=3; chemosis in 3/4=2, 1/4=4; discharge in 1/4=1, 1/4=3.

Study Classification: Supplementary Data. Insufficient number of animals. Insufficient description of test.

23. Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. No. 245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH606 (4# DEA/TEA salts of 2,4-D/MCPP/Dicamba).

Results: At 24 hours, corneal opacity in 4/4=20; redness in 2/4=2, 2/4=3; chemosis in 2/4=2, 2/4=4; discharge 4/4=3. At day 7, corneal opacity in 1/4=40; iris irritation in 1/4=10; redness in 3/4=1, 1/4=3; chemosis in 3/4=2, 1/4=4; discharge in 3/4=1, 1/4=3.

Study Classification: Supplementary Data. Insufficient number of animals. Insufficient description of test.

24. Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. No. 245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. Animals were scored on day 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH607 (2# dimethylamine salts of 2,4-D/MCPP/Dicamba).
Results: At 24 hour corneal opacity in 4/4=20; ir... irritation in 2/4=5; redness in 2/4=2, 2/4=3; chemosis in 2/4=2, 2/4=4; discharge in 4/4=3. On day 7, corneal opacity in 2/4=40; iris irritation in 2/4=10; redness in 2/4=1, 2/4=3; chemosis in 2/4=2, 2/4=3; discharge in 2/4=3.

Study Classification: Supplementary Data. Insufficient number of animals. Insufficient description of test.

25. Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. No. 245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH608 (2# Diethanolamine salts of 2,4-D/MCPP/Dicamba).

Results: At 24 hours, corneal opacity exhibited in 4/4=20; redness in 2/4=2, 2/4=3; chemosis in 4/4=2; discharge in 4/4=3. At day 7, redness in 2/4=1, 2/4=2; chemosis in 4/4=2; discharge in 2/4=1.

Study Classification: Core Supplementary Data. Insufficient number of animals. Description of procedures was insufficient.

26. Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. #245537

Procedure: Two animals were used in this study; scores were reported for their right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH609 (2# DEA/TEA salts of 2,4-D/MCPP/Dicamba).

Results: At 24 hours, eyes exhibited corneal opacity in 4/4=20; redness in 4/4=3; chemosis in 4/3=3; discharge in 4/4=3. At day 7, corneal opacity in 1/4=40; iris irritation in 1/4=5; redness in 2/4=2, 1/4=3; chemosis in 4/4=2; discharge in 1/4=1, 1/4=3.

Study Classification: Supplementary Data. Number of animals was insufficient. Description of procedures was not adequate.

27. Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. #245537

Procedure: Two animals were used in this study; scores were reported for both the right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH610 (1# Dimethylamine salts of 2,4-D/MCPP/Dicamba).

Results: At 24 hours, eyes exhibited corneal opacity in 1/4=20, 1/4=40; iris irritation in 1/4=10; redness in 1/4=1, 3/4=2; chemosis in 4/4=2; discharge 3/4=2, 1/4=3. At 7 days, redness in 4/4=1; chemosis in 4/4=2.
28. **Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. #245537**

**Procedure:** Two animals were used in this study; scores were reported for both the right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substances was EH611 (1 # Diethanolamine salts of 2,4-D/MCPP/Dicamba).

**Results:** At 24 hours, animals exhibited redness in 1/4=2; chemosis in 4/4=2; discharge in 3/4=2, 1/4=3. At day 7, redness in 4/4=1; chemosis in 4/4=2; discharge in 2/4=1.

**Study Classification:** Supplementary Data. Insufficient number of animals. Description of procedures was inadequate.

29. **Eye Irritation Study; MRI #4823-B(2); December 31, 1979; Acc. No. 245537**

**Procedure:** Two animals were used in this study; scores were reported for both the right and left eyes. Animals were scored on days 1, 2, 3, 4, 7. No further procedures were given. Test substance was EH612 (1 #TEA/DEA salts of 2,4-D/MCPP/Dicamba).

**Results:** At 24 hours, redness was observed in 1/4=1, 3/4=2; chemosis in 4/4=2; discharge in 2/4=1, 2/4=3. On day 7, redness noted in 2/4=1; chemosis in 4/4=2.

**Study Classification:** Supplementary Data. Insufficient number of animals. Description of procedures was inadequate.

30. **Eye Irritation Study; Stillmeadow #2121-81; April 16, 1981; Acc. No. 245537**

**Procedure:** Nine New Zealand white rabbits each received 0.1 ml of "EH 680 BK 800" in one eye. Three treated eyes were rinsed with room temperature deionized water for one minute, 30 seconds post-treatment. Scores were recorded at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, 21 days.

**Results:** Unwashed eyes at 24 hours exhibited iris irritation in 5/6=5; redness in 1/6=1; 5/6=2; chemosis in 1/6=1; 4/6=2; discharge in 1/6=1, 1/6=3, 3/6=2. At 7 days, corneal opacity observed in 1/6=10; redness in 3/6=1; chemosis in 1/6=1. At 21 days, only corneal opacity observed in 1/6=10 with dulling.

The washed eyes at 24 hours exhibited redness in 1/3=1, 2/3=2; chemosis in 2/3=1, 1/3=3; discharge in 1/3=1, 1/3=2. On day 7, redness in 1/3=1. All eyes were clear by day 10.
31. Eye Irritation Study: Stillmeadow 2126-81; April 16, 1981; Acc. #245537

Procedure: Nine New Zealand white rabbits each received 0.1 ml of EH 681 (1/gal 2,4-DE BOE, 1/gal 2,4-D IOE, 1/gal Dicamba) in one eye. Three treated eyes were washed with room temperature deionized water for 1 minute beginning 30 seconds post-treatment. Eyes scored at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, 21 days.

Results: The unwashed eyes at 24 hours exhibited corneal opacity in 2/6=20; iris irritation in 6/6=5; redness in 5/6=2, 1/6=3; chemosis in 3/6=2, 3/6=3; discharge in 3/6=2, 3/6=3. At day 7, corneal invasion seen in 2/6=5, 1/6=10; iris irritation in 1/6=5; redness in 4/6=1, 1/6=2; chemosis in 2/6=1, 1/6=2; discharge in 1/6=3. At 21 days, the unwashed eyes exhibited corneal opacity in 1/6=5.

The washed eyes exhibited corneal opacity at 24 hours in 1/3=15, 1/3=20; redness in 3/3=2; chemosis in 1/3=1, 2/3=2; discharge in 1/3=1, 1/3=2, 1/3=3. On day 7, corneal opacity observed in 2/3=10 with dulling; iris irritation in 1/3=10; redness in 1/3=1, 1/3=2; chemosis in 1/3=2; discharge in 1/3=3. At day 21, the washed eyes exhibited corneal opacity in 1/3=5, 1/3=15.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

32. Rabbit Eye Irritation Study: Stillmeadow #2131-81; April 20, 1981; Acc. #245537

Procedure: Nine New Zealand white rabbits each received 0.1 ml of EH 683 Amine 2,4-D Acid (33.23% Dicamba) in one eye. Three treated eyes were subsequently washed with room temperature deionized water for one minute, 30 seconds post-treatment. Eyes were scored at 1, 24, 48, 72 hours; 4, 7, 10, 13, 16, 19, 21 days.

Results: At 24 hours, the unwashed eyes exhibited corneal opacity in 1/6=10, 1/6=15, 4/6=20; iris irritation in 6/6=10; redness in 6/6=2; chemosis in 6/6=3; discharge in 3/6=2, 3/6=3; also noted were corneal stippling and necrosis. The unwashed eyes on day 21 exhibited corneal opacity in 1/6=5, 1/6=10, 3/6=20, 1/6=40; iris irritation in 2/6=5, 3/6=10; redness in 3/6=1, 3/6=2; chemosis in 3/6=1, 2/6=3; discharge in 2/6=1, 1/6=3; also, invasion of blood vessels into cornea, dulling of cornea, nodule on cornea, hair loss.

The washed eyes at 24 hours exhibited corneal opacity in 1/3=5, 1/3=10, 1/3=20 with stippling; iris irritation in 1/3=5, 2/3=10; redness in 2/3=2, 1/3=3; chemosis in 2/3=2, 1/3=3; discharge in 2/3=2, 1/3=3; necrosis in 1/3. By day 21, corneal opacity observed in 2/3=10 with dulling, invasion by blood vessels, nodule; iris irritation in 1/3=10.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING.
Study Classification: Core Guideline.

Toxicity Category: I - DANGER.

33. Rabbit Eye Irritation; MRI #4823-B(3); August 27, 1980; Acc. #245537

Procedure: Nine New Zealand white rabbits each received 0.1 ml of EH552 (1#2,4-D Acid/MCPP Acid/Dicamba) in one eye. Three treated eyes were rinsed for 1 minute with lukewarm water, 30 seconds post-application. Eyes were examined 24, 48, 72 hours; 7, 10, 13 days. Two animals (one un洗ed, one washed) were inadvertently terminated on day 11; these animals were "replaced."

Results: The unwashed eyes at 24 hours exhibited corneal opacity in 1/7=10, 3/7=15, 1/7=20, 1/7=40; redness in 2/7=1, 1/7=2, 4/7=3; chemosis in 1/7=1, 3/7=2, 1/7=3, 2/7=4; discharge in 2/7=2, 5/7=3. By day 7, corneal opacity observed in 1/7=10; redness in 1/7=1 of the unwashed eye group.

The washed eyes exhibited corneal opacity in 1/4=5, 1/4=20, 1/4=60; iris irritation in 1/4=5; redness in 2/4=1, 1/4=2, 1/4=3; chemosis in 1/4=1, 2/4=2, 1/4=4; discharge in 1/4=2, 3/4=3. At day 7, only irritation was chemosis and discharge in 1/4=1 in animal that was subsequently "inadvertently terminated"; at day 10, this animal with very slight discharge.

Both animals that were inadvertently terminated showed the most irritation in their group.

Study Classification: Core Minimum Data.

Toxicity Category: III - CAUTION.

34. Eye Irritation Study; MRI #4823-B(1); October 15, 1979; Acc. #245537

Procedure: Six New Zealand rabbits each received 0.1 ml of EH590 in one eye. Eyes were examined at 24, 48, 72 hours; 4 and 7 days. None of the treated eyes were rinsed.

Results: At 24 hours, observations included corneal opacity in 6/6=40; iris irritation in 6/6=5; redness in 6/6=3; chemosis in 5/6=2, 1/6=3; discharge in 1/6=2, 5/6=3. By 7 days, corneal opacity exhibited in 1/6=20; iris irritation in 1/6=5; redness in 1/6=2; chemosis in 1/6=2; discharge in 1/6=2.

Study Classification: Core Minimum Data. An eyewash group was not tested.

Toxicity Category: III - CAUTION.
35. Eye Irritation Study; MRI #4823-B(1); October 15, 1979; Acc. #245537

Procedure: Six New Zealand white rabbits each received 0.1 ml of BH591 in one eye. Eyes were examined at 24, 48, 72 hours; 4 and 7 days. No eyes were rinsed.

Results: Corneal opacity observed at 24 hours in 3/6=40, 2/6=80; iris irritation in 3/6=5; 2/6=10; redness in 1/6=1, 5/6=3; chemosis in 4/6=2, 2/6=4; discharge in 1/6=1, 5/6=3. At day 7, corneal opacity noted in 3/6=20, 1/6=40; iris irritation in 3/6=5, 1/6=10; redness in 3/6=2, 1/6=3; chemosis in 4/6=2, 1/6=3; discharge in 1/6=1, 3/6=2, 1/6=3.

Study Classification: Core Minimum Data. An eyewash group was not tested.

Toxicity Category: I - DANGER.

36. Eye Irritation Study; MRI #4823-B(1); October 15, 1979; Acc. #245537

Procedure: Six New Zealand white rabbits each received 0.1 ml of BH597 in one eye. Eyes were examined at 24, 48, 72 hours; 4 and 7 days. None of the treated eyes were rinsed.

Results: At 24 hours, corneal opacity was seen in 4/6=20, 2/6=40; iris irritation in 6/6=2; redness in 1/6=2, 5/6=3; chemosis in 5/6=2, 1/6=3; discharge in 6/6=3. By day 7, corneal opacity exhibited in 1/6=20, 1/6=40; iris irritation in 1/6=5, 1/6=10; redness in 1/6=2, 1/6=3; chemosis in 2/6=2, 1/6=4; discharge in 1/6=1, 1/6=2, 1/6=3.

Study Classification: Core Minimum Data. An eyewash group was not tested.

Toxicity Category: I - DANGER.

37. Eye Irritation Study; MRI #4823-B(1); October 15, 1979; Acc. #245537

Procedure: Six New Zealand white rabbits each received 0.1 ml of BH598. Observations were made at 24, 48, 72, 4 and 7 days. None of the treated eyes were rinsed.

Results: At 24 hours, corneal opacity was exhibited in 1/6=60, 5/6=80; iris irritation in 6/6=10; redness in 6/6=3; chemosis in 6/6=4; discharge in 6/6=3. At 7 days, corneal opacity in 1/6=40, 5/6=60, iris irritation in 6/6=10; redness in 6/6=2; chemosis in 6/6=2; discharge in 6/6=2.

Study Classification: Core Minimum Data. An eyewash group was not treated.

Toxicity Category: I - DANGER.
STORAGE & DISPOSAL

Prohibited: Do not contaminate water, food or feed by storage, disposal or cleaning of equipment. Do not store new or other pesticides or seeds.

Pesticide Disposal: Pesticide, spray, mixture or rinse that cannot be used or chemically reprocessed should be disposed of in a landfill approved for pesticides or burned in a safe place away from water supplies.

Container Disposal: Triple rinse for equipment and offer for recycling, reconditioning or disposal in approved landfill, or bury in a safe place.

General Consult federal or local disposal authorities for approved alternative procedures.

USE PRECAUTIONS: OBSERVE CAREFULLY.

1. Avoid drift of spray onto vegetables, flowers, ornamental plants, shrubs, trees, and other desirable plants.
2. Be sure to apply only to weeds, grasses, or lawns or other areas to be sprayed.
3. Read and follow all directions and cautions on label.
4. Do not spray when winds are excessive. A wind speed of 10 miles per hour or more is likely to drift application.
5. Do not spray on days when temperature exceeds 85°F.
6. Do not spray when plants are wet with dew or rain. Application will be ineffective.
7. Do not contaminate domestic or irrigation waters.
8. Some injury may be expected to turf when used on new and sodding or young grass lawns. Spot sprays may use one or two leaves of grass. Check present conditions before application.
9. Do not use on lawns, shrubs, and vegetables with soil or irrigation waters. Properly dispose of sprayer, clean the sprayer, clean alternate between soak or dry cleaning, and thoroughly before leaving other plants.
10. Failure to observe the above precautions may result in injury.

USE INSTRUCTIONS:

ORNAMENTAL LAWNS AND TURF: Apply TRIMEC® 450 HERBICIDE at the rate of 2 to 3 pints per acre in sufficient water for adequate coverage. Maximum kill of weeds will be obtained from Spring or early Fall application when weeds are actively growing. Avoid applying during long excessively dry or hot periods unless adequate irrigation is available. Do not irrigate within 24 hours of application. Do not apply to newly seeded turf until after the second or third mowing. Grass seed can be safely sown 3 to 4 weeks after application at recommended rate. Do not use on dichondra.

WEEDS CONTROLLED: TRIMEC® 450 HERBICIDE is especially effective against weeds such as Sheep Sorrel, Knotweed, Spot, Spurge, Chickweed, Oxalis, and Henbit. In addition to these, it kills virtually all broadleaf weeds, some of which are listed below. Repeat applications if necessary.

- Bedstraw
- Black Nightshade
- Blackberry
- Buckhorn
- Burdock
- Chick
- Chickweed
- Clover
- Dandelion
- Dock
- Ground Ivy
- Heal-all
- Parsley
- Henbit
- Ragweed
- Knotweed
- Shepherd's
- Parsley
- Sorrel
- Spotted Spurge
- Chickweed
- Oxalis
- Henbit

NOTICE: Seller warrants that the product conforms to the ingredient statement. Since conditions of use, such as climate, soil, and applicability with other chemicals, plant varieties, and equipment may vary, no claims other than those stated on the label are made.