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Atrazine/Review #21/9.7.78/9 pages

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DATE: September 7, 1978

SUBJECT: Addition of Data to the Files for the Following Formulations:

a) Banvel 4 (Dicamba; 3,6-Dichloro-o-anisic acid or 2-Methoxy-3,6-dichlorobenzoic acid) + Aatrex 80WP [Atrazine; 2-Chloro-4-(ethylamino)-6-isopropylamino)-s-triazine] + Princip WP [Simazine;2-Chloro-4,6-bis (ethylamino -s-triazine] + Paraquat 2EC (1,1 -Dimethyl-4,4'--bipyridinium dichloride).

b) Banvel 4S + Lasso 4 EC [Alachor;2-Chloro-2',6'-diethyl-N-(methoxymethyl) acetanilide].

c) Banvel + Eradicane 6.7 EC [Eptam; S-Ethyl dipropylthiocarbamate) + R-25788 (N,N-Diallyl-2,2'-dichloroacetamide)] . EPA Reg.#876-EUP33 Caswell#295, 63, 740, 634, 11, 284A, 435

FROM: Larry Anderson
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TO: Robert Taylor
Product Manager#25

Recommendations:

Eye irritation, skin irritation, acute dermal LD_{50}, and acute oral LD_{50} studies described in the present review sufficiently define the reported acute toxicity of the aforementioned formulations.

*No RPAR criteria have been exceeded. However, Aatrex 80 WP and Princip WP are products (triazines) which potentially contain nitrosamines, and Paraquat 2EC is an RPAR candidate based on inhalational, teratogenic, and chronic (lung) effects.

I Acute Toxicity Studies of Banvel 4 + Aatrex 80 WP -- Princip WP + Paraquat 2EC in Rats and Rabbits (International Research and Development Corp. 5/3/78, submitted by Velsicol Chemical Corp., 6/23/78, Acc. No. 234451)

A. Eye Irritation Study in the Rabbit

1. Procedure

Nine (3 males and 6 females) New Zealand White rabbit, 2.0-3.7 kg, were used. A 0.1 ml aliquot of test material was instilled into each right eye. Untreated left eyes served as controls. Eyes of 3 animals were flushed with 300 ml of water at 30 seconds following instillation of the method of Draize et al. (1944) at 24, 48 and 72 hours and 4 and 7 days post-treatment. Examinations with sodium fluorescein were done concurrently at 72 hours and 7 days.
according to a modification

2. Results

Eye Injuries:

i) Unwashed eyes: Conjunctivitis during 4 days post-treatment; clear discharge.
ii) Washed eyes: Unremarkable. Washing was beneficial.

3. Conclusions

a) Classification: Core Guidelines
b) TOX Category III

B. Skin Irritation Study in the Rabbits

1. Procedure

Six (3 males and 3 females) New Zealand White rabbits, 2017-2543g, were used. Onto the skin of each rabbit was applied 0.5 ml of test material under occlusive dressing. Skin of 3 rabbits was abraded before treatment. Dressing was removed at 24 hours following application, and test sites were washed. Irritation was scored according to a modification of the method of Draize et al. (1944) at 24 and 72 hours post-treatment.

2. Results

P.I. Index = 0.2/8.0

3. Conclusions

a) Classification: Core Minimum Data

i) Only 3 animals comprised groups with either intact or abraded test sites; however, the results are definitive.

b) TOX Category: IV

C. Acute Dermal LD_{50} in Rabbits

1. Procedure

Eight (4 males and 4 females) New Zealand White rabbits, 2.3-3.0 kg, received dermal applications of 20000 mg/kg of test material under occlusive dressing. The skin of 2 males and 2 females was abraded before treatment. Dressings were removed at 24 hours following application. Observations of mortality, toxic signs, and body weight changes were continued over 14 days post-treatment. Necropsies were performed.

2. Results

a) Mortality: None. LD_{50} > 20000 mg/kg
b) Toxic Signs: Diarrhea, hypoactivity, decreased limb tone, ataxia, dehydration, blood discharge from urogenital region, possible prolapsed uterus; erythema and edema at test sites.
c) Body Weight Changes: Loss at 7 days with recovery of gain by 14 days post-treatment.
d) Necropsy: Swollen urogenital region, pale kidneys.

3. Conclusions

a) Core Minimum Data

i) Because low dermal toxicity of the test compound was shown, use of 1 dosage level is acceptable.

ii) Body weights in conjunction with food intake were not determined daily.

b) TOX Category: IV

D. Acute Oral LD_{50} Study in Rats

1. Procedure

Ten (5 males and 5 females) Charles River CD rats, 202-250g, were given 5000 mg/kg of test material by gavage. Animals were observed for mortality, toxic signs, and body weight changes during 14 days post-treatment. Necropsies were done.

2. Results

a) Mortality: None. LD_{50} > 5000 mg/kg
b) Toxic Signs: Hypoactivity
c) Body Weight Changes: Unremarkable
d) Necropsy: Mottled kidneys, distension and thickened glandularmucosa of the stomach.

3. Conclusions

a) Classification: Core Minimum Data

i) Body weights in conjunction with food intake were not determined daily.

b) TOX Category:

E. Final Conclusions

The acute toxicity of the formulation, based on the studies reviewed within, is summarized follows:

Hazard Indicator	TOX Cat.
Eye Irritation	III
Skin Irritation	IV
Acute Dermal LD_{50}	IV
Acute Dermal LD_{50}	IV

II. Acute Toxicity Studies of Banvel + Eradicane 6.7 EC in Rabbits and Rats (International Research and Development Corp., 5/11/78, submitted by Velsicol Chemical Corp., 6/23/73, Acc. No.234449).

A. Eye Irritation Study Rabbits

1. Procedure

Nine (4 males and 5 females) New Zealand White rabbits, 2.3-2.7 kg, were used. A 0.1 ml aliquot of test substance was instilled into each right eye. Untreated left eyes served as controls. Eyes of 3 rabbits were washed with 300 ml of water at 30 seconds following treatment.

Injuries were scored according to a modification of the method of Draize et al. (1944) at 24, 48, 72, 96, and 168 hours post-treatment. Examinations with sodium fluorescein were done concurrently at 72 and 168 hours following instillation.

2. Results

a) Eye Injuries:

i) Unwashed eyes: Conjunctivitis during 48 hours post-treatment; no corneal opacities were observed.

ii) Washed eyes: Conjunctivitis during 24 hours post-treatment. Washing was beneficial.

b) Mortality: One rabbit with washed eyes died by 96 hours following instillation of undetermined causes.

3. Conclusions

a) Classification: Core Guidelines
b) TOX Cat: III

B. Skin Irritation Study in Rabbits

1. Procedure

Six (3 males and 3 females) New Zealand White rabbits, 2.2-2.8 kg, were used. Onto the skin of each rabbit was applied 0.5 ml of test substance under occlusive dressing. Test sites of 3 rabbits were abraded before treatment. Dressing was removed at 24 hours after application, and the skin was washed. Irritation was scored according to a modification of the method of Draize et al. (1944) at 24 and 72 hours post-treatment.

2. Results

P.I.. Index = 0/8

3. Conclusions

a). Classification: Core Minimum Data

i) .The test material should have been applied to intact and abraded skin on each rabbit, but the results of the present study are conclusive.

ii) Test sites should be wiped but not washed following treatment.

b) TOX Cat.: IV

C. Acute Dermal LD_{50} Study in Rabbits

1. Procedure

Eight (4 males and 4 females) New Zealand White rabbits, 2.3-2.8 kg, received dermal application of 20000mg/kg of test material under occlusive dressing. Skin of 2 males and 2 females was abraded before treatment. Dressing and residual test material were removed at 24 hours post-application. Animals were observed for mortality, toxic signs, and body weight changes during 14 days following treatment. Necropsies were done.

2. Results

a) Mortality: None $LD_{50} > 20000$mg/kg
b) Toxic Signs: Unremarkable except for erythema and edema at test sites.
c) Body Weight Changes: Unremarkable
d) Necropsy: Mottled and pitted kidneys.

3. Conclusions

a) Classification: Core Minimum Data

i) Body weights in conjunction with food intake were not determined daily.

b) TOX Cat: :IV

D. Acute Oral LD_{50} Study in Rats

1. Prodecure

Ten (5 males and 5 females) Charles River CD rats, 200-230g, were given 5000 mg/kg of test material by gavage. Observations of mortality, toxic signs, and body weight changes were conducted over 14 days post-treatment. Necropsies were done.

2. Results

a) Mortality: None. $LD_{50} > 5000$ mg/kg
b) Toxic Signs: Unremarkable
c) Body Weight Changes: Unremarkable
d) Necropsy: Mottled kidneys, hydrometra of the uterus, thickened glandular mucosa in the stomach.

3. Conclusions

a) Classification: Core Minimum Data

i) Body weights in conjunction with food intake were not determined daily.

b) TOX Cat.: IV

F. Final Conclusions

The acute toxicity of the formulation, described in the present review, is summarized as follow:

Hazard indicator	TOX Cat.
Eye Irritation	III
Skin Irritation	IV
Acute Dermal LD_{50}	IV
Acute Oral LD_{50}	IV

III. Acute Toxicity Studies of Banvel 4S + Lasso 4 EC in Rats and Rabbits (International Research and Development Corp., 5/23/78, submitted by Velsicol Chemical Corp., 6/23/78, Acc. No.234450).

A. Eye Irritation Study in Rabbits

1. Procedure

Nine (5 [illegible] & female New Zealand [illegible] rabbits, 2.1-3.0 kg, were used. Into each right eye was instilled 0.1 ml of test compound. Untreated left eyes served as controls.

(continued from Page 6)

Eyes of 3 rabbits were flushed with 300 ml of water at 30 seconds after treatment. Injuries were scored according to a modification of the method of Draize et al. (1944) at 24, 48, 72, 96, and 168 hours post-treatment. Examinations with sodium fluorescein were done simultaneously at 72 and 168 hours.

2. Results

a) Eye Injuries

i) Unwashed eyes: Conjunctivitis during 48 hours post-treatment. Corneal opacities were not evident.

ii) Washed eyes: Unremarkable. Washing was beneficial.

b) Mortality: One rabbit with washed eyes died of indetermined causes.

3. Conclusions

a) Classification: Core Guidelines
b) TOX Cat.: III

B. Skin Irritation Study in Rabbits

1) Procedure

Six (3 males and 3 females) New Zealand White rabbits, 2.9-3.7 kg, were used. A 0.5 ml aliquot of test substance was applied under occlusive dressing to the skin of each rabbit. Skin of 3 rabbits was abraded before treatment. Dressing was removed at 24 hours post-application, and test sites were washed. Irritation was scored according to a modification of the method of Draize et al. (1944) at 24 and 72 hours following treatment.

2. Results

P.I. Index = 0.4/8.0

3. Conclusions

a) Classification: Core Minimum Data

i) Although test material was not applied to intact and abraded skin on each rabbit, the results are definitive.

b) TOX Cat.: IV

C. Acute Dermal LD_{50} Study in Rabbits

1. Procedure

Eight (4 males and 4 females) New Zealand White rabbits, 2.3-2.8 kg, received dermal applications of 20000 mg/kg of test material under occlusive wrappings. Skin of 2 males and 2 females was abraded before treatment. Dressing and residual test material were removed at 24 hours post-application. Observations of mortality, toxic signs, and body weight changes were made for 14 days post-treatment. Necropsies were done.

2. Results

a) Mortality: None. $LD_{50} > 20000$mg/kg.
b) Toxic Signs: Unremarkable except for erythema and edema at test sites.
c) Body Weight Changes: Unremarkable
d) Necropsy: Mottled and pale kidneys, congested lungs, hyperemic stomach mucosa.

3. Conclusions

a) Classification: Core Minimum Data

i) Body weights in conjunction with food intake were not determined daily.

b) TOX Cat.: IV

D. Acute Oral LD_{50} Study in Rats

1. Procedure

Ten (5 males and 5 females) Charles River CD rats, 200-258g, were administered 5000 mg/kg of test material by gavage. Observations of mortality, toxic signs, and body weight changes were conducted over 14 days post-treatment. Necropsies were done.

2. Results

a) Mortality: None. $LD_{50} > 5000$ mg/kg
b) Toxic Signs: Hypoactivity
c) Body Weight Changes: Unremarkable
d) Necropsy: Hyperemic and thickened stomach mucosa, hydrometra of the uterus.

3. Conclusions

a) Classification: Core Minimum Data

i) Body weights in conjunction with food intake were not determined daily.

b) TOX Cat.: IV

E. Final Conclusions

The acute toxicity of the formulation according to the studies reviewed herein is summarized as follows:

Hazard Indicator	Tox Cat.
Eye Irritation	III
Skin Irritation	IV
Acute Dermal LD_{50}	IV
Acute Oral LD_{50}	IV

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