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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES,

MEMORANDUM MAY 10 1983

TO: A.E. Castillo
Disenfectant Branch/RD (TS-767C)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

SUBJECT: Pine-Sol Cleaner Disenfectant
EPA-1730-LT
TOX. No. 665, No. 331A, No. 392H, [redacted] and
No. 613A.

Action Requested:

Toxicity data review of the rabbit and monkey eye irritation studies conducted with the Pine-Sol Cleaner Disenfectant.

Registrant:

American Cyanamid Co.

Recommendation:

This product is in toxicity Category II based on the monkey eye irritation study.

Consideration given to this Recommendation:

Assigning toxicity Category II labeling for this formulation based on the results of the monkey eye irritation study is a departure from the testing guidelines which recommend the rabbit as the species of choice for eye irritation studies. With reference to the revised NAS publication 1138 pg. 41, "The albino rabbit is the species of choice, with the monkey (especially the rhesus) as the preferred second species when comfirmatory data are necessary".

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formuation: No. CPRD 6630

ACTIVE INGREDIENTS

Pine Oil	14.91%
[redacted]	
Octyldecyldimethyl Ammonium Chloride	1.13%
Didecyldimethyl Ammonium Chloride	0.56
Dioctyl dimethyl Ammonium Chloride	0.56
Inert Ingredients	70.04%

Toxicity Data Review

The following toxicity studies were reviewed by James E. Wilson of the Disinfectants Branch/RD and Core evaluated by R. Landolt.

1. Eye Irritation - Cynomolgus Monkey
   Biosearch Inc. No. 81-2817A, Jan. 25, 1982, Acc. No. 247522

   a. Method

   A 0.1 ml aliquot of the test material was placed onto the cornea of the left eye of 9 monkeys with an automatic micropipette. Six of the treated eyes were not washed; three were washed for one minute, twenty seconds after contact. The eyes were examined for lesions by a veterinary opthalmologist at 0, 0.5, 1.0, 2.0, 4.0, 24, 48, and 72 hours and 7 days after instillation. If any animal(s) has effects present at 7 days, they were again examined at 9, 14, and 21 days. The animals were mildly sedated for these examinations to permit the eyes to be examined under magnification using a biomicroscope.

   b. Results

   Mild corneal opacity was observed after 30 minutes. The scores increased and peaked at 48 hours with an average score of 2. After 72 hours, 5/6 had a score of grade 1 and 1/6 was graded at 2. No opacity was observed on day 7; however, opacity was present in one eye at the day 14 reading. Conjunctival irritation was moderate after 24 hours. Most scores decreased after 48 hours and all conjunctival irritation was clear after 7 days except for grade 1 redness in 1 monkey which persisted through the day 14 reading.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Pigment ingrowth from the limbus into the cornea was observed in 5/6 during the hour 48 reading (this is the same eye which had prolonged redness). The results for the rinsed eyes were generally the same as those for the nonrinsed eyes, with somewhat diminished severity of signs.

c. Conclusion

The chemical produces opacity which clears in all eyes in 7 days; pigment ingrowth into the cornea is present in 5/6 after 7 days.

All conjunctival signs clear in 7 days except for redness in one monkey. Corneal opacity (mild) and pigment ingrowth reappear after 14 days in one eye. The mild corneal opacity reported for day 14, cleared by day 21 with the pigment ingrowth from the limbus into the cornea evident at day 21. Pigment migration* onto the cornea is the process of healing for corneal injury where the corneal epithelium heals by sliding of normal epithelium from an adjacent area.

Classification of Data - Core Guideline

Toxicity Category - II

*Green, W.R., J.B. Sullivan, R.M. Hehir, and L.G. Scharpf. 1976. A systematic comparison of chemically-induced eye injury in the albino rabbit and rhesus monkey. In: Soap and Detergent Association. Submission to the National Academy of Sciences by the Soap and Detergent Association on toxicity test procedures.

2. Eye Irritation - Rabbit
Biosearch Inc. No. 79-1809A-1, May 19, 1980 Acc. No. 244653

a. Method

Twenty-four New Zealand white rabbits were divided into four groups. The left eyes were examined for injuries and those with defects were discarded. Six animals were dosed at each of the following levels: 0.01, 0.03, 0.05 and 0.10 ml. The chemical was placed directly on the cornea. Readings were made at 1, 2, 3, 5, 7, 10, 14, 17, and 21 days.

b. Results

At 0.01 ml 3/6 developed mild corneal opacity, iritis and conjunctival irritation. All signs in this group disappeared by day 10. In the 0.03 and 0.05 groups 3/6 had opacity and iritis which lasted 21 days. At 0.1 ml, 2/6 showed moderate opacity and severe iritis after 21 days.

c. Conclusion

The chemical produces corneal opacity and iritis which are not reverisible in 21 days.

Classification of Data - Minimum

i. Deficiency: Washed eyes were not included in this study.

Toxicity Category - I

3. Skin Irritation
Biosearch Inc. No. 79-1809A. March 7, 1980. Acc. No. 244653

a. Method

Six adult albino rabbits were clipped free of dorsal fur. Two sites were selected on each animal and one of those sites was further prepared by abrading the skin. One-half of the test material was placed under a patch on each site. After 24 hours the patches were removed and degree of irritation scored then and again after 48 and 72 hours.

b. Results

Primary Irritation Score: 4.45
Scores for erythema and edema indicated moderate irritation (grades 2-3) for the 72 hr. observation period.

c. Conclusion

The product is a moderate skin irritant.

Classification of Data - Core Guideline

Toxicity Category - III

4. Oral Toxicity
Food and Drug Research Lab No. 6389, Jan. 16, 1980
Acc. No. 244653.

a. Method

Five groups of Sprague-Dawley rats, each group containing 5 males and 5 females, were fasted overnight then fed doses of 1.20, 1.71, 2.45, 3.50 and 5.00 g/kg of the test material. The animals were observed 14 days for signs of toxicity and mortality. Body weights were taken on days 0 and 14.

b. Results

There were no deaths at 1.20 and 1.71 g/kg. One female died at 2.45, 2 males and 3 females died at 3.50 and all test animals died at 5.10 g/kg. Decreased activity, ataxia and diarrhea were noted. Autopsy revealed pale lungs, liver, spleen and kidneys. Body weight gains were normal.

c. Conclusion

The oral (male and female) LD_{50} of the product is 3.17 (2.17-4.77) g/kg.

Classification of Data - Minimum

i. Deficiency: The LD_{50} for each sex was not determined.

Toxicity Category - III

5. Dermal Toxicity
Biosearch Inc. No. 80-1968A, May 29, 1980 Acc. No. 244653

a. Method

Ten albino rabbits, five male and five females, were clipped free of dorsal fur. The exposed area was further prepared by abrading the skin prior to application of 2.0 g/kg of the test material to the skin. A sleeve was placed on each animal, under which the material was introduced and allowed to remain in place for 4 hours. After the exposure period the coverings were removed along with any remaining chemical. The animals were observed for two weeks. Signs of toxicity, mortality and weight changes were recorded. All animals were autopsied for gross pathological changes in tissues and organs.

b. Results

Severe erythema and edema lasted several days. No other signs were noted. Gross necropsy findings were unremarkable.

c. Conclusion

The 4-hour exposure dermal LD_{50} of the chemical is greater than 2.0 g/kg.

Classification of Data - From Supplementary to Minimum

i. Deficiency

In the dermal study the chemical was kept in contact with the skin for four hours and not 24 as required. The report states that none of the material was absorbed and no signs of systemic toxicity were reported. Since the oral toxicity does not indicate that the chemical is highly toxic and it does not appear that the chemical is absorbed dermally, this reviewer recommends that the study be accepted in support of the product.

Toxicity Category - III

Raymond E. Landolt

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Review Section #1
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