

## CODING FORMS FOR SRC INDEXING

Microfiche No.	OTS0559859		
New Doc ID	88000000052S	Old Doc ID	8EHQ-1299-14612S
Date Produced	12/01/99	Date Received	12/10/99
		TSCA Section	8E
Submitting Organization	CONFIDENTIAL		
Contractor	CONFIDENTIAL		
Document Title	INITIAL SUBMISSION: FINAL REPORT, DERMAL SENSITIZATION STUDY OF DIMETHYL AMINO ARYL OLEFIN DYE IN GUINEA PIGS - MAXIMIZATION TEST, WITH COVER LETTER DATED 120299 (SANITIZED)		
Chemical Category	DIMETHYL AMINO ARYL OLEFIN DYE		

INITIAL  
SUB-  
MISSION

8EHQ-1299-146125

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December 2, 1999

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Attn. Section 8(e) Coordinator  
Office of Toxic Substances  
Environmental Protection Agency  
401 M Street S.W.  
Washington, DC 20460

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00 JAN 11 AM 9:56

Dear Sir or Madam:

Enclosed is information submitted under section 8(e) of the Toxic Substances Control Act. We are requesting confidential treatment of the information appearing in brackets [ ]. We have also enclosed a sanitized version of this document.

The request of confidential treatment is limited to our corporate identity, the company internal name of the material, the supplier's identity, the test laboratory's identity, the dates of testing, names of the individuals who signed documents and the explanation for this submission.

If you have any questions, please feel free to call me at [ ] .

Sincerely,

8EHQ-99-14612  
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Company Sanitized

# SANITIZED

December 2, 1999

Document Processing Center (TS-790)  
Attn. Section 8(e) Coordinator  
Office of Toxic Substances  
Environmental Protection Agency  
401 M Street S.W.  
Washington, DC 20460

RE: NOTICE OF SUBSTANTIAL RISK UNDER TSCA 8(e)

Dear Sir or Madam:

We are reporting on a material, Dimethyl Amino Aryl Olefin Dye, CAS # 100237-71-6, under Section 8(e) of the Toxic Substances Control Act. The material is described in [ ] .

[ ] routinely conducts toxicity evaluation of materials being considered for new product development. The explanation for this submission is that the [ ]

[ ] Therefore, included in this submission are two separate studies and sanitized versions of each study.

Study summaries: In the first of two studies we received notification from [ ] that one of our test materials was related to the deaths of two animals during a Guinea Pig Maximization Test (GPMT). We later received verbal notice that a third animal had died.

In the GPMT, ten guinea pigs received intradermal injections of 0.05 ml of 5% (w/v) test material. The estimated intradermal dose was 18 to 28 mg/kg body weight. Two animals died the day after receiving the injection. Two new animals were added to the test; however one of the new animals also died the day after receiving the injection. No lesions were observed during necropsy and clinical signs of toxicity were not evident prior to the death of the animals. None of the surviving animals showed signs of dermal sensitization.

The material does not pose a risk to customers who will use the final product because the material is bound in a coating and present at low concentrations. A Buehler Patch test was performed using the final product and the test results were negative for dermal sensitization. No signs of toxicity were reported for the final product.

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Exposure to workers who manufacture and process raw materials and intermediates is possible. These risks can be mitigated, however, by appropriate personal protection equipment and engineering controls.

We believe that these results were indicative of toxicity; however, we recognized that subcutaneous injection is not likely to occur in the workplace. A second study was initiated to evaluate acute dermal lethality and the summary for that test follows.

The acute dermal lethality study was conducted by moistening the test material with water and applying it to rabbit skin at a dose of 2,000 mg/kg of body weight. The exposure period was 24 hours in duration and the animals were observed for clinical signs for 14 days.

No mortality was observed during the study and the estimated dermal LD<sub>50</sub> for rabbits was greater than 2,000 mg/kg of body weight. All animals appeared to be normal during the study. There was slight to moderate dermal irritation. There were no lesions observed upon necropsy.

We believe that the results of this second test indicate that the material does not pose a substantial risk to human health and is more accurate as to the likely route of exposure.

If you have any questions regarding this submission or the results, feel free to contact me.

Sincerely,

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- (7) **Husbandry**
- (a) **Housing**  
Individually, in suspended stainless steel cages
  - (b) **Food**  
A measured amount of Laboratory Rabbit Diet HF #5326 (PMI Feeds, Inc.). The food is routinely analyzed by the manufacturer for nutritional components and environmental contaminants.
  - (c) **Water**  
*Ad libitum* from an automatic system. Samples of the water are analyzed for total dissolved solids, specified microbiological content, selected elements, heavy metals, organophosphates, and chlorinated hydrocarbons
  - (d) **Contaminants**  
There are no known contaminants in the food or water that would interfere with this study.
  - (e) **Environment**  
Environmental controls for the animal room will be set to maintain a temperature of 16° to 22°C, a relative humidity of 50% ±20%, and a 12-hour light/12-hour dark cycle.
  - (f) **Acclimation**  
At least 7 days
- (8) **Selection of Test Animals**  
Based on health and body weight according to SOPs. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test.
- (9) **Justification for Species Selection**  
Historically, the New Zealand White albino rabbit has been the animal of choice because of the large amount of background information on this species.

SANITIZED [ ]

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Page 6**B. Dose Administration****(1) Dose Level**

A single dose of 2,000 mg/kg of body weight will be administered to the intact skin of five males and five females. If no test material-related mortality is produced at this level, no further testing will be required. If any mortality occurs at the 2,000 mg/kg level, additional dose levels may be added at the direction of the study director in order to meet the objectives of the study.

**(2) Preparation of Exposure Area**

On the day before test material application, the back of each rabbit will be clipped free of hair with an electric clipper. Approximately 20% of the total body surface area will be clipped. The animals will be clipped as needed throughout the study.

**(3) Dose Administration**

All animals will receive a single administration of test material on Day 0. The dose will be based upon the animal's body weight before test material administration. The area of application will be covered with as thin and uniform a layer as possible. The test material will be moistened with distilled water (amount to be documented in the raw data). The area of application will be covered with a 4-ply gauze patch (approximately 9.5-cm x 19-cm) secured with paper tape around all edges and overwrapped with Saran Wrap® and Elastoplast® tape to provide an occlusive dressing. The rabbits will be collared during the 24-hour application period.

**(4) Reason for Route of Administration**

Historically, the dermal route has been the route of choice based on the method of Draize.

**(5) Removal of Test Material**

Approximately 24 hours after test material application the patches and collars will be removed and the residual test material will be removed using water or an appropriate substance.

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Page 7**C. Observation of Animals****(1) Clinical Observations**

For clinical signs and mortality at approximately 1, 2.5, and 4 hours after test material administration and daily thereafter for clinical signs, and twice daily (a.m. and p.m.) for mortality for at least 14 days (a.m. mortality only on Day 14). Observations may be extended when directed by the study director.

**(2) Reading of Dermal Irritation**

Approximately 30 minutes after patch removal, the initial dermal irritation reading will be made and recorded as the Day 1 reading (Attachment 1). The untreated skin of each animal will serve as its own control. Additional dermal irritation readings will be made on Study Days 3, 7, 10, and 14. Individual dermal irritation records will be maintained for each animal.

**(3) Body Weights**

Before test material application (Day 0), on Days 7 and 14, or at death (when survival exceeds 1 day)

**D. Pathology**

At termination of the respective experimental phase (Day 14), surviving animals will be euthanized. All animals, whether dying during the study or sacrificed in a moribund condition, will be subjected to an abbreviated gross necropsy examination and all abnormalities will be recorded. After necropsy, the animals will be discarded and no tissues will be saved.

**E. Statistical Analyses**

When applicable, LD<sub>50</sub> calculations determined by a modified Behrens-Reed-Muench cumulant method when applicable will be conducted. No other statistical analyses are required.

**7. Report**

A final report including those items listed below will be submitted.

Description of the test material

Description of the test system

Procedures

Dates of experimental initiation and termination

Tabulation of mortality data by sex and dose level

Description of any toxic effects/dermal irritation

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Tabulation of mean body weights by sex and dose level  
 LD<sub>50</sub> values by sex with 95% confidence intervals (when applicable)  
 Gross pathology findings/gross pathology report

8. **Location of Raw Data, Records, and Final Report**

Original data, or copies thereof, will be available at [redacted] to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data, including those item listed below will be retained in the archives of [redacted] for a period of one year following signing of the final report. One year after signing of the final report, all of the aforementioned materials will be sent to the Sponsor and a return fee will be charged. The Sponsor may elect to have the materials retained in the [redacted] archives for an additional period of time and [redacted] will charge a storage fee. If the Sponsor chooses to have [redacted] dispose of the materials, a disposal fee will be charged.

Protocol and protocol amendments

Dose preparation records

In-life records

Body weights

Dose administration

Observations

Anatomical pathology records

Study correspondence

Final report (original signed copy)

The following supporting records will be retained at [redacted] but will not be archived with the study data.

Animal receipt/acclimation records

Water analysis records

Animal room temperature and humidity records

Refrigerator and freezer temperature records

Instrument calibration and maintenance records