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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 20, 2006

MEMORANDUM:

Subject: EPA Reg. No.: 400-49/Alanap-L
DP Barcode: 333975
Case No.: 0183

From: Marianne Lewis, Biologist
Product Reregistration Branch
Special Review and Reregistration Division (7508C)

Marianne Lewis 11/20/06

To: Julia Stokes, CRM
Product Reregistration Branch
Special Review and Reregistration Division (7508C)

Applicant: Chemtura Corporation
199 Benson Road
Middlebury, CT 06749

FORMULATION FROM EPA Reg. No. 400-49 LABEL:

	% by wt.
Active Ingredient(s):	
Naptalam	23.7%
Inert Ingredient(s):	76.3%
Total	100.0%

BACKGROUND: In the 8 month response to the Naptalam RED, the registrant has submitted acute toxicity studies to support the reregistration of their product, EPA Reg. No. 400-49. The MRID's are as follows: 60405 (81-1), 60406 (81-2), 60407 (81-3), 78530 (81-4), 60408 (81-5), 157185 (81-6). Four (81-1, 81-2, 81-3, 81-5) of the studies were conducted by Product Safety Labs. The primary skin irritation study (81-5) was conducted Hazleton Laboratories America, Inc. The skin sensitization study (81-6) was conducted by Hill Top Research Inc. The test material used in each of the studies was the subject product.

The skin sensitization study (81-6) indicates that the subject product is a skin sensitizer. Therefore the subject product will be self validated as a skin sensitizer and a full review of this study will not be conducted at this time.

RECOMMENDATIONS:

- Two (81-1 & 81-2) of the studies submitted are acceptable to support the reregistration of EPA Reg. No. 400-49.
- The subject product has been self validated as a skin sensitizer.
- The primary eye irritation study (81-4) is unacceptable. However, based on information contained in the study and in the open literature, the Agency will assign the subject product to Toxicity Category III. A new study is not needed.
- The acute inhalation study is unacceptable. A new study should be cited or submitted.
- The primary skin irritation study (81-5) is unacceptable. A new study should be cited or submitted.

Procedural Deviations:

Acute Inhalation Study (81-3): The test animals were only exposed to the test material for 1hour. The test requirements are for a four hour exposure. The MMADs were not measured during the exposure. Studies that have not conducted particle size analysis at least twice during the exposure are not acceptable. Chamber concentration and particle size measurements should be made at least twice during the study at time points spaced well apart. This study is unacceptable. A new study following the OPPTS Guidelines should be cited or submitted.

Primary Eye Irritation Study (81-4): The laboratory conducted sodium fluorescein staining at 24 hours post-exposure. Although the Agency strongly encourages the use of sodium fluorescein staining, the Agency agrees that it is an optional tool that the laboratory can use in detecting cornea epithelial damage. However, if it is not done correctly it is not acceptable. Sodium fluorescein is a weak organic acid and it is very efficient in absorbing ultraviolet light and emitting fluorescent lights. The maximum absorption for this stain is 490μm (excitation) and its maximum emission is 520μm. Because this stain is highly fluorescent it can be detected at very low concentrations using UV light in biologic tissues & fluids. A regular incandescent light bulb would be inadequate to detect the majority of the staining. If the laboratory is going to conduct the sodium fluorescent staining, then the correct protocol should be followed. This study is unacceptable. However, based on the information available the Agency will classify this product as Toxicity Category III. A new study is not needed.

Primary Skin Irritation Study (81-5): Individual scores for irritation were not provided in the lab report, only summaries were given. The Agency needs to see all information/results generated by the studies, summaries are not adequate. This study is unacceptable. A new study should be cited or submitted.

The acute toxicity profile for EPA Reg. No. 400-49 is currently:

Acute Oral	IV	Acceptable
Acute Dermal	IV	Acceptable
Acute Inhalation		Unacceptable
Primary Eye	III	Unacceptable
Primary Dermal		Unacceptable
Skin Sensitization	skin sensitizer	Self Validated

NOTE: The labeling will be completed upon receipt of the required information.

DATA REVIEW FOR ACUTE ORAL TOXICITY (§81-1, 870.1100)

Product Manager: Jim Tompkins, 25
MRID No.: 60405

Reviewer: Marianne Lewis
Study Completion Date: 8/3/77
Report No.: T-234

Testing Facility: Product Safety Labs
Author: R. Shapiro

Quality Assurance (40 CFR §160.12): conducted prior to GLP

Test Material: Alanap Liquid, crystal clear burgundy colored solution

Species: Sprague Dawley derived albino rat
Age: young adult
Weight: males = 205 – 226 g; females = 200 – 215 g
Source: not given

Conclusion:

1. **LD_{50} (mg/kg):** > 5000 mg/kg

2. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviations from §81-1): none

Results:

Dosage (mg/kg)	Number Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: All rats appeared active and healthy throughout the 14 day test period.

Gross Necropsy: not given

DATA REVIEW FOR ACUTE DERMAL TOXICITY (§81-2, 870.1100)

Product Manager: Jim Tompkins, 25
MRID No.: 60406

Reviewer: Marianne Lewis
Study Completion Date: 7/20/77
Report No.: T216

Testing Facility: Product Safety Labs
Author: R. Shapiro

Quality Assurance (40 CFR §160.12): conducted prior to GLP

Test Material: Alanap Liquid, crystal clear burgundy colored solution
Species: New Zealand albino rabbit
Weight: males = 2.43 – 2.61 kg; females = 2.50 – 2.84 kg
Age: young adult
Source: not given

Summary:

1. **LD_{50} (mg/kg):** > 20,000 mg/kg

2. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviations From §81-2): none

Results:

DOSAGE (mg/kg)	Reported Mortality (number deaths/number tested)		
	Males	Females	Combined
20,000	1/5	0/5	1/10

Observations: The trunk was clipped free of hair. Two males and three females had epidermal abrasions made on the test sites. A patch containing the test material was placed over a 5 x 5 cm test site and secured with an elastic sleeve. After 24 hours, the patches were removed. One male that had epidermal abrasions died on day 14. All surviving animals appeared active and healthy.

Gross Necropsy Findings: The decedent had slight discoloration of one lobe of the liver and the right kidney, also evidence of lung hemorrhage and hemorrhage in right kidney. The survivors had no observable abnormalities noted.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3, 870.1300)

Product Manager: Meredith Laws, 04
MRID No.: Jim Tompkins, 25

Reviewer: Marianne Lewis
Study Completion Date: 8/5/77
Report No.: T-225

Testing Facility: Product Safety Labs
Author: R. Shapiro

Quality Assurance (40 CFR §160.12): conducted prior to GLP

Test Material: Alanap Liquid, crystal clear burgundy colored solution

Species: Wistar rat
Weight: males = 204 – 224 g; females = 203 – 272 g
Age: young adult
Source: not given

Summary:

Classification: Unacceptable

Procedure (Deviation From §81-3):

- One hour study
- No MMADs measured
- No measurement of chamber concentration

Results: **Reported Mortality**

Exposure Concentration	(number deaths/number tested)		
	Males	Females	combined
20 mg/L	0/5	0/5	0/10

Chamber Atmosphere		
Dose Level mg/L	MMAD	GSD
0.177	Not taken	Not taken

Nothing given about chamber concentrations/environment

Clinical Observations: "Slight tremor in several animals upon introduction to environmental chamber. No signs of gross toxicity during the 14 day observation period. No mortality."

Gross Necropsy Findings: "Unremarkable"

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: Meredith Laws, 04
MRID No.: 78530

Reviewer: Marianne Lewis
Study Completion Date: 4/26/78
Report No.: 198-182

Testing Facility: Hazleton Labs
Author:

Quality Assurance (40 CFR §160.12): conducted prior to GLP

Test Material: Alanap Liquid, pink liquid

Dosage: 0.1 mL
Species: New Zealand albino rabbit
Sex: not given
Weight: not given
Age: not given
Source: Bunnyville Farms

Summary:

Classification: Unacceptable

Procedure (Deviations From §81-4):

- UV light source not utilized during sodium fluorescein staining procedure

Results:

Observations	(number "positive"/number tested)		
	Hours		
	24	48	72
Corneal Opacity	3/6	1/6	0/6
Iris	0/6	0/6	0/6
Conjunctivae			
Redness	4/6	2/6	0/6
Chemosis	2/6	0/6	0/6
Discharge	1/6	0/6	0/6

At 24 hrs., 3/6 scattered diffuse opacity, 4/6 diffuse crimson red conjunctivae, 2/6 obvious swelling w/partial eversion of lids, & 1/6 discharge w/moistening of lids/hairs just adjacent to lids. At 48 hrs., 1/6 scattered diffuse opacity & 2/6 diffuse crimson red conjunctivae. By 72 hrs., all had cleared.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: Meredith Laws, 04
MRID No.: 60408

Reviewer: Marianne Lewis
Study Completion Date: 7/18/77
Report No.: T-210

Testing Facility: Product Safety Labs
Author: R.Shapiro

Quality Assurance (40 CFR §160.12): conducted prior to GLP

Test Material: Alanap Liquid, crystal clear burgundy colored solution

Dosage: 0.5 mL
Species: New Zealand albino rabbit
Sex: not given
Weight: range of 2.3 – 3.0 kg
Age: not given
Source: not given

Summary:

Classification: Unacceptable

Procedure (Deviations From §81-5):

- Individual results not given in report

Results: The trunks were clipped free of hair and epidermal abrasions were made on one test site per animal. Over both the intact and abraded test sites a 2.5 x 2.5 cm gauze patch was placed. The test material was introduced under each patch. The patches were then secured in place with tape and covered with a plastic trunk band. After 24 hours, the patches were removed.

ACUTE TOX ONE-LINER

1. PC CODE: 030703

2. CURRENT DATE: November 20, 2006

3. TEST MATERIAL: Alanap, crystal clear burgundy liquid, Naptalam: 23.7%

Study/Species/ Lab/Study#/Date	MRID #	Results	Tox. Cat.	Core Grade
acute oral toxicity/rat/Product Safety Labs/T-234/8-3-77	60405	LD_{50} > 5000 mg/kg	IV	A
acute dermal toxicity/rabbit/ Product Safety Labs/T-216/ 7-20-77	60406	LD_{50} > 20,000 mg/kg	IV	A
acute inhalation toxicity/rat/ Product Safety Labs/T-225/ 8-5-77	60407			U
primary eye irritation/rabbit/ Hazleton Labs/198-182/ 4-26-78	78530			U
primary dermal irritation/rabbit/ Product Safety Labs/T-210/ 7-18-77	60408			U
skin sensitization/guinea pig/ Hill Top Research/85-1583-21/ 12-26-85	47015925	Skin sensitizer	---	V

Core Grade Key:
A = Acceptable
S = Supplementary (upgradeable)
U = Unacceptable
V = self-Validated