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

9-23-91

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 4581-292 / PENNCAP-M
Microencapsulated Insecticide

FROM: Ian Blackwell
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

E 9/23/91

TO: Dennis Edwards, Jr. PM 12
Insecticide-Rodenticide Branch
Registration Division (H7505C)

APPLICANT: ATOCHEM NORTH AMERICA, Inc.
Three Parkway
Philadelphia, PA 19102

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
O,O-Dimethyl O-p-nitrophenyl phosphorothioate*	20.9
Related isomers	1.1
Inert Ingredients:.....	78.0
Total	100.0%

*Methyl Parathion

053501

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BACKGROUND: The applicant has submitted an acute oral toxicity study to support a change in the signal word from WARNING to CAUTION. The registrant has also cited acute dermal, acute inhalation, primary eye irritation and primary dermal irritation studies which support this registration. The acute oral study was conducted by Northview Pacific Laboratories, Inc. and the MRID number is 418056-01. The acute dermal study was conducted by Oak Ridge North Animal Clinic and the data accession number is 2400-374-030. The acute inhalation study was conducted by WIL Research Laboratories, Inc. The primary eye irritation study was conducted by Welcome Independent Laboratories, Inc. The primary dermal irritation study was conducted by Cannon Laboratories, Inc. The TRID number for these studies are 460089-018 through -020.

RECOMMENDATION: RSB/PRS findings are as follows:

1. The acute oral toxicity study is acceptable and classified as core minimum data because the age and source of the test animals were not specified.

2. The acute dermal toxicity study is classified as supplementary and cannot be used to support this registration. The registrant must reconduct the study or cite other acceptable data. The study was classified as supplementary for the following reasons:
   a. The test procedures and study results including the observations and gross necropsy findings were not provided.
   b. An insufficient dosage was used to qualify as a limit test.
   c. An insufficient number of animals was tested and dosing was carried out at three different dates.
   d. The ages and sex of test animals were not specified.
   e. Observation period was insufficient (2 days, not required 14 days.

3. The acute inhalation toxicity study is classified as supplementary and cannot be used to support this registration. The registrant must reconduct the study, cite other acceptable data or request a waiver in accordance with 40 CFR 158.45. The study was classified as supplementary for the following reasons:
   a. The exposure period was insufficient (1 hour instead of required 4 hours).
   b. The Mass Median Aerodynamic Diameter (MMAD) was not provided.
   c. No females were tested.

4. The primary eye irritation study is acceptable and classified as core minimum data for the following reasons:
   a. The source and age of the animals were not provided.
   b. No quality assurance statement was provided.

5. The primary dermal irritation study is acceptable and classified as core minimum data for the following reasons:
   a. The exposure area was 1 in^2 and not 6 cm^2 as per guidelines.
   b. Observations were not conducted at 1 hour and at 48 hours after removal of wraps.

6. The registrant must submit a dermal sensitization study to support this registration.

7. PRS does not recommend approval of the proposed label changes at this time since the acute toxicity battery cited to support this registration is deficient. When the registrant provides a complete and acceptable acute tox battery to support this registration, the proposed labeling changes can be reconsidered.

LABELING:

Proposed label changes will be considered upon submission of outstanding data.

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

Product Manager: (19). Report Date: 1/24/85
Reviewer: Ian D. Blackwell Study No.: X4J007G
MRID No.: 418056-01 .
Testing Facility: Northview Pacific Laboratories, Inc. .
Author(s): M.J. Deenihan .

Species: Sprague-Dawley rats .
Sex: 111 male + female .
Age: Not specified .
Weight: approx. 150-300 g .
Source: Not specified .

Test Material: PENNCAP-M (microencapsulated methyl parathion)

Observation Days (Post Exposure): 14
Quality Assurance (40 CFR §160.12): Not specific

Conclusion:

1. LD50 (mg/kg): Males (M) = 600 (513-702) ;
Females (F) = 660 (545-799) ;
Combined(C) = .

2. Toxicity Category: III
Classification: core-minimum

Procedure (Deviations From §81-1):
Ages and sources of test animals not specified.

Results:

Reported Mortality

Dosage (mg/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
5	0/3	0/3	0/6
10	0/3	0/3	0/6
25	0/3	0/3	0/6
50	0/3	0/3	0/6
75	0/3	0/3	0/6
100	0/3	0/3	0/6
250	0/5	0/5	0/10
500	1/5	1/5	2/10
625	3/5	1/5	4/10
750	5/6	4/5	9/11
825	5/5	4/5	9/10
1000	5/5	5/5	10/10

Observations: See attached sheet.

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OBSERVATIONS FOR ACUTE ORAL TOXICITY OF PENNCAP-M:

Animals that received as little as 250 mg/kg went into convulsions within 5 minutes of dosing. Animals receiving high doses had severe convulsions which usually ended in death on the same evening as the dosing. Animals receiving 1500 mg/kg usually died within 15 minutes of dosing. Surviving animals usually continued to convulse, although this typically ended within two days. At doses from 500 to 625 mg/kg, animals displayed extremely bulged eyes that continued throughout the test period if the animal survived. Increased respiration rates and salivation were also common.

Necropsy of animals that died during the test period uncovered reddened lungs, stomachs distended with fluid and/or gas, intestines filled with a yellow substance and/or gas, and darkened adrenal glands.

Necropsy of test animals that survived dosing showed nothing unusual except for a few red areas on the lungs, reddened intestines and darkened adrenal glands.

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

Product Manager (PM): 12 .
Reviewer: Ian D. Blackwell Report No.: Not specified
DATA Acces #: 2400-374-030 . Report Date: Not specified

Testing Laboratory: Oak Ridge North Animal Clinic
Author(s): Tom O. Miessler, DVM

Species : rabbit .
Age : not specified .
Sex : not specified . Wt.: 0.862 to 1.588 kg
Source: not specified .

Test Material: PENNCAP-M Encapsulated Methyl Parathion .
Dosage: 1250 mg/kg

Quality Assurance (40 CFR §160.12): Not included

Summary:

LD50: _____
Toxicity Category: _____
Classification: core - supplementary

Procedure (Deviations From §81-2):
The study was neither a range study nor a limit test.
Procedures were not included in the submission.
The nine animals tested were tested three at a time on three different dates.
No observations of the test animals after dosing were given.
No gross necropsy was discussed.
The ages, sexes and source of the test animals were not specified.
Insufficient observation period (3 days instead of the required 14 days).

Results:

1. Reported Mortality

Dosage (mg/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
1250			0/9

2. Observations: None given.

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

Product Manager (PM): 12 .
Reviewer: Ian D. Blackwell Report No.: WIL-1056-77
TRID No.: 460089-020 . Report Date: 12/7/77 .

Testing Laboratory: WIL Research Laboratories, Inc. .
Author(s): not specified .
Species: rat .
Wt.: 212.2 to 255.5 g . Age : not specified .
Sex : 10 males .
Source: Harlan Industries, Inc..

Test Material : PENNCAP-M .
Conc. : 2,920 ppm .

Quality Assurance (40 CFR §160.12): Not included

Summary:

LC50: .
Toxicity Category: .
Classification: core - supplementary.

Procedure (Deviations From §81-3):
Exposure period was for one hour.
The percent of inhalable particles was not sufficient.
Mass Median Aerodynamic Dynameter was not determined.
Concentration was measured in parts per million (ppm).
Quality assurance was not included.
No females were used in the study.

Results:

1. Reported Mortality:

Concentration (ppm)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
2920 ppm	0/10	---	0/10

% particles ≤ 10 microns = 8%
MMAD = not specified

2. Observations: Dark red spots on the lungs of one male.

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

Product Manager (PM): 12 .
Reviewer: Ian D. Blackwell Project No.: WIL-1056-77
TRID No.: 460089-019 . Report Date: 8/2/77

Testing Laboratory: Welcome Independent Laboratories, Inc.

Author(s): Linda Jones .

Species: New Zealand Albino rabbit .
Source: not specified . Sex: 4 males + 5 females
Age: not specified . Weight: 2.55 to 3.05 kg

Test Material : PENNCAP M N.B. 77-120-3

Dosage: 0.1 ml .

Quality Assurance (40 CFR §160.12): Not included

Summary:

Toxicity Category: IV .
Classification: core - minimum.

Procedure (Deviation From §81-4):
Source and age of animals not specified.
No quality assurance was provided.

Results:

	Observations (number "positive"/number tested.							
	Hour 1	Days 1	2	3	4	7	14	21
Cornea	---	0/6	0/6	0/6	0/6	0/6	---	---
Iris	---	0/6	0/6	0/6	0/6	0/6	---	---
Conjunctivae								
Redness	---	0/6	0/6	0/6	0/6	0/6	---	---
Chemosis	---	0/6	0/6	0/6	0/6	0/6	---	---
Discharge	---	0/6	0/6	0/6	0/6	0/6	---	---

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DATA REVIEW FOR
DERMAL IRRITATION TESTING (§81-5)

Product Manager (PM): 12 .
Reviewer: Ian D. Blackwell
TRID No.: 460089-018 Report Date: 10/11/77
Report No.: 7E-7944

Testing Laboratory: Cannon Laboratories Inc. .

Author(s): not specified

Species: New Zealand albino rabbits .

Sex : six males
Age : not specified
Weight: 2.0 to 2.5 kg
Source : not specified

Test Material : PENNCAP-M
Dosage : 0.5 ml to 1 in^2 area

Quality Assurance (40 CFR §160.12): Not included

Summary: The Primary Irritation Index = ____

Toxicity Category: IV

Classification: core - minimum

Procedure (Deviations From §81-5):
No scores were taken at 30-60 minutes or 48 hours.
The exposure area was 1 in^2.
GLP statement not included.

Results: At 24 hours, 6/6 test animals displayed very slight erythema and no edema. At 72 hours, 1/6 animals displayed very slight erythema.

Tox Chem No. 372 File Last Updated _____ Current Date 9/5/91

Study/Animal/Lab/Date	Material	EPA Accession Number	Results: LD50, LC50, etc.	Tox. Cat.	CORE Grade
Acute oral toxicity/ X4J007G/ rat/ Northview Pacific Laboratories, Inc./ 1-24-85	0,0-Dimethyl 0-p-nitrophenyl phosphorothioate ....20.9% Related isomers 1.1%	418056-01	LD_{50} males = 600 mg/kg (513-702) females = 660 mg/kg (545-799)	III	minimum
Acute dermal toxicity/ not specified/ rabbit/ Oak Ridge North Animal Clinic/ Not specified		2400-374-030		---	supple-mentary
Acute inhalation tox. WIL-1056-77/ rat/ WIL Research Labs, Inc 12-7-77		460089-020		---	supple-mentary
Primary eye irritation WIL-1056-77/ rabbit/ Welcome Independent Laboratories, Inc. 8-2-77		460089-019	No irritation was observed.	IV	minimum
Primary dermal irrit. 7E-7944/ rabbit/ Cannon Laboratories, Inc./ 10-11-77		460089-018	At 72 hours, 1/6 displayed very slight erythema.	IV	minimum

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