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CASWELL FILE

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

JUN 15 1988

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& also 006747

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Acute Dermal and Intravenous Studies with Methylthioacetate (MTA), a Manufacturing Impurity in ORTHENE Technical (Acephate; EPA ID No. 239-2471)

FROM: Krystyna K. Locke, Toxicologist Krystyna K. Locke 6/1/88
Toxicology Branch
Hazard Evaluation Division (TS-769C)

TO: William H. Miller/Marilyn Mautz, PM Team 16
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Edwin Budd, Section Head
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Tox. Chem. No.: 584D (MTA)
Record No.: 204475
T. B. Project No.: 8-0158

Toxicology Branch has completed an evaluation of the following studies with MTA:

1. Acute dermal (rat)
   No. SOCAL 2314
   May 21, 1985
   MRID 261971
   LD_{50} = 1590 mg/kg (males)
   1580 mg/kg (females)
   Toxicity Category: II
   Classification: Core-Guideline

2. Acute dermal (rabbit)
   No. SOCAL 2207
   April 10, 1985
   MRID 261971
   LD_{50} = 300 mg/kg (approximate; males and females)
   Toxicity Category: II
   Classification: Core-Minimum

3. Acute dermal (monkey)
   No. 2107-121
   April 2, 1987
   MRID 40322601
   LD_{50} = > 6000 mg/kg (males)
   Toxicity Category: IV
   Classification: Core-Supplementary (females not tested)

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4. Acute intravenous (monkey)

No. 2107-121
April 12, 1987
MRID 40322601

LD_{50} : Not determined
Toxicity Category: Cannot be determined
Classification: Acceptable as Supplementary data

Studies No. 1 and 2, including histopathology of the visual system, were requested in the Registration Standard for acephate. Studies No. 3 and 4 were apparently submitted to show acute effects of MTA in yet another species, monkey.

Request for Studies No. 1 and 2 stemmed from an earlier report of gliosis, malacia, macrophage accumulation and papilledema of the optic nerve, observed in rabbits after an acute dermal exposure to MTA (Study No. 1534.8; 12/3/80).

In the currently evaluated studies, lesions in the optic nerve (gliosis and malacia) were observed only in the rabbits at the 250 mg/kg level (mid-dose group). No lesions were observed at the 100 mg/kg level (low-dose group), suggesting a no-effect level. All of the rabbits in the high-dose group (500 mg/kg) died within one hour after application of MTA directly on intact skin. The nonsurvivors had no lesions in the optic nerve, suggesting that these lesions do not develop spontaneously.

No histopathological changes were observed in the optic nerves or in the brain of rats and monkeys. The highest levels of MTA tested dermally were 3300 mg/kg in rats and 6000 mg/kg in monkeys.

Due to technical difficulties, exact doses administered intravenously to monkeys were unknown.

C06667

Reviewed by: Krystyna K. Locke
Section II, Tox. Branch (TS-769C)
Secondary reviewer: Edwin R. Budd
Section II, Tox. Branch (TS-769C)

KRL 6/1/88
Budd 6/14/88

DATA EVALUATION REPORT

Study Type: Acute dermal (rat)

Tox. Chem. No.: 584D
MRID No.: 261971
Project No.: 8-0158

Test Material: Methylthioacetate (SX-1500); clear liquid; purity: 99%

Study Number(s): SOCAL 2314

Sponsor: Chevron Chemical Company, Richmond, CA

Testing Facility: Chevron Environmental Health Center, Richmond, CA

Title of Report: The Acute Dermal Toxicity of Methylthioacetate (SX-1500) in Adult Male and Female Rats

Author(s): A. A. Carey, C. M. Cisson, W. R. Richter and Z. A. Wong

Report Issued: May 21, 1985

Conclusions:

LD_{50} = 1.59 g/kg (males)
1.58 g/kg (females)

Toxicity Category: II

Core Classification: Guideline

Methylthioacetate caused dermal irritation at the application site. Slight to severe erythema persisted in many animals throughout the study. Signs of toxicity observed during the study were ocular and nasal discharges, salivation, collapse and depression (lethargy). No histopathological changes were observed in the optic nerves or in the brain of any of the animals in this study. This suggests that, under the conditions of this study, methylthioacetate did not produce the optic neuropathy in the rat.

Experimental Procedures:

Sprague-Dawley rats were exposed dermally to the following levels of methylthioacetate (MTA): 0, 0.5, 1.5, 2.2, and 3.3 g/kg of body weight. Single doses of undiluted MTA were applied on intact skin, the occlusions removed after 24 hours of exposure, and the animals observed for toxic signs and mortality for 15 days. The application site was scored for irritation on days 1, 8, and 15 by the procedure of Draize et al. (1944)[1]. The LD_{50}, slope and 95% confidence limits were determined by the procedure of Berkson (1957)[2].

There were 5 males and 5 females in the control and the 3.3 g/kg groups, and 10 males and 10 females in each of the remaining groups. At the time of dosing, males and females were 49 or 50 days old, and weighed 229-305 g (males) and 157-225 g (females). The rats were:

1. Obtained from Bantin and Kingman, Inc., Fremont, CA;
2. Acclimated for 20-21 days;
3. Assigned randomly to groups;
4. Housed individually;
5. Fed unrestricted amounts of food (Purina Laboratory Rodent Chow #5001) and water;
6. Weighed on days 1, 2, 8 and 15; and
7. Examined (eyes) with a slit lamp and an ophthalmoscope before treatment and on day 15.

All animals on the study were examined grossly. The following organs and tissues were examined for gross pathological changes: skin, spleen, pancreas, stomach, small and large intestine, liver, adrenals, kidneys, gonads, uterus or seminal vesicles, bladder, heart, thymus, salivary glands, lungs, trachea, thyroid, eyes with optic nerve, brain with optic chiasma, and fat.

The following tissues and all tissues with gross abnormalities from all animals on the study were examined histopathologically: skin (application site), lungs, liver, kidneys, brain, eyes, and optic nerves. Tissue sections were evaluated by the Colorado Pathology Services, Inc., Fort Collins, Colorado.

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[1]Draize, J. H., Woodward, G., and Calvary, H. O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther. 82: 377-390, 1944.

[2]Berkson, J. Tables for use in estimating the normal distribution function by normit analysis. Biometrika 44: 411-435, 1957.

Results:

The following animals slipped out of their wraps immediately after dosing: 1 male and 2 females in each of the 1.5 g/kg and the 3.3 g/kg groups, and 1 male and 1 female in the 2.2 g/kg group. These animals remained on the study, but were excluded from calculations of the LD_{50} values.

Toxic signs

Treatment-related signs included salivation, lethargy and collapse. Treatment-unrelated signs (observed in both treated and untreated animals) included red ocular and nasal discharges.

Mortality

All males and females in the 3.3 g/kg group, and all males and 78% of the females in the 2.2 g/kg group died. Deaths occurred within 27 minutes to 2.5 hours after dosing. There were no deaths in the controls and 0.5 g/kg groups.

Skin irritation

At 24 hours after dosing, slight edema and slight to well defined erythema were observed in all treated groups, with the exception of the 0.5 g/kg group. Slight to severe erythema persisted in several of these animals (males and females) throughout the study.

Body weights

There were no significant differences in the mean body weight gains when the treated animals were compared with the controls. During the 15-day observation period, males in the control, 0.5 g/kg and 1.5 g/kg groups gained 76, 69, and 67 g, respectively. The corresponding weight gains for the females were 36, 41 and 35 g, respectively.

Ocular examination

No treatment-related abnormalities were observed.

Necropsy

Thickened, dry and flaky, and scabbed skin was observed at the application site in surviving animals treated with 1.5 and 2.2 g/kg of MTA; these changes appeared to be treatment-related. Other gross pathological observations included mottled and reddened thymus, diminished and reddened testis, dilated renal pelvis, reddened salivary glands, blanched liver with tan

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mottling, intratracheal foam, ocular opacities, urinary bladder calculi, liver with pitted surfaces, reddened walls in small intestine, and lungs with congestion and red mottling and foci; these abnormalities did not appear to be related to treatment with MTA.

Histopathology

Histologic changes were not observed in the brain, eyes and optic nerves of any animal. Treatment-related changes in other tissues included:

1. Tubular regeneration (basophilic staining), chronic inflammation and hydronephrosis in the kidneys;
2. Hematopoietic foci in the liver, and congestion and centrilobular vacuolation of hepatocytes; and
3. Pulmonary congestion, hemorrhage and edema.

The pulmonary congestion and edema were commonly observed in rats dying during the study and were most frequent in the 2.2 and 3.3 g/kg groups. The alveolar hemorrhage was seen in both control and treated rats and was likely inhaled blood, which apparently occasionally occurs during the necropsy procedure and should be considered incidental.

The histologic tissue alterations observed at the dermal application site included acanthosis, hyperkeratosis, dermal fibrosis, epidermal crusting, inflammation, and ulceration. These lesions were observed only in the treated rats from the 1.5 and 2.2 g/kg groups (rats from the 3.3 g/kg group died shortly after treatment). These dermal lesions appeared to be caused by the topical application of the test material.

LD_{50} (95% Confidence Limits)	Slope (95% Confidence Limits)
Males---1.59 (0.67-3.78) g/kg	1.81 (0.85-3.86)
Females-1.58 (0.72-3.43 g/kg	1.92 (0.78-4.71)

Toxicity category: II

Quality Assurance Statement, dated May 30, 1985, has been included in the report.

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Reviewed by: Krystyna K. Locke, Toxicologist RKL 6/1/88
Section II, Tox. Branch (TS-769C)
Secondary reviewer, Edwin R. Budd, Section Head
Section II, Tox. Branch (TS-769C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal (rabbit)

TOX. CHEM. NO.: 584D

MRID NO.: 261971

PROJECT NO.: 8-0158

TEST MATERIAL: Methylthioacetate (SX-1500); clear colorless liquid; purity: 99%

STUDY NUMBER(S): SOCAL 2207

SPONSOR: Chevron Chemical Company, Richmond, CA

TESTING FACILITY: Chevron Environmental Health Center, Richmond, CA

TITLE OF REPORT: The Acute Dermal Toxicity of Methylthioacetate (SX-1500) in Adult Male and Female Rabbits

AUTHOR(S): C. H. Bullock, C. M. Cisson, W. R. Richter and Z. A. Wong

REPORT ISSUED: April 10, 1985

CONCLUSIONS:

LD_{50} = 300 mg/kg (approximate; males and females combined)

Toxicity Category: II

Core Classification: Minimum

Four of the eight surviving rabbits in the mid-dose group (250 mg/kg) had lesions in the optic nerve. The lesions included gliosis and malacia (necrosis). No lesions were observed in the low-dose group (100 mg/kg), suggesting a no-effect level. All of the animals in the high-dose (500 mg/kg) and two in the mid-dose group died within one hour after application of the methylthioacetate directly on intact skin. The nonsurvivors did not have lesions in the optic nerve, indicating that these lesions do not develop spontaneously.

Signs of toxicity observed during the study in animals treated with 250 or 500 mg/kg were ataxia, weakness, dyspnea, rapid respiration, labored respiration, bloody oral and nasal

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discharge, decreased motor activity, collapse, convulsion, and death. Animals treated with 100 mg/kg showed only some signs of decreased motor activity.

EXPERIMENTAL PROCEDURES:

New Zealand rabbits, 5 of each sex per group, were exposed to single dermal application of undiluted methylthioacetate (MTA) for 24 hours and were sacrificed after 14 days of observation for physiological and behavioral abnormalities. The test material (0, 100, 250 or 500 mg/kg of body weight) was applied on the intact skin, occluded and then wiped off at the termination of the exposure. The 250 and 500 mg/kg groups were started on June 15, 1984, and the 100 mg/kg group on October 23, 1984. There was a concurrent control group at each time interval.

The rabbits were:

1. Obtained from L. I. T. Rabbitry, Whitehall, Montana;

2. Acclimated for 16 to 49 days;

3. Ten to thirteen weeks of age and weighed 2.4 to 2.9 kg at the time of dosing the 250 and 500 mg/kg groups;

4. Fifteen to seventeen weeks of age and weighed 2.7 to 3.2 kg at the time of dosing the 100 mg/kg group;

5. Housed individually;

6. Allocated randomly to groups;

7. Fed a daily ration of Purina Laboratory Rabbit Chow Certified HF #5325 and had free access to water;

8. Weighed prior to dosing and at 1, 2, 7 and 14 days after treatment; and

9. Examined for eye abnormalities prior to dosing and twice during the observation period; response to direct light, slit-lamp biomicroscope and indirect ophthalmoscope were used in these examinations.

The following organs and tissues from all animals were examined grossly: skin, spleen, pancreas, stomach, small and large intestine, liver, adrenals, kidneys, gonads, uterus or seminal vesicles, bladder, heart, thymus, salivary glands, lungs, trachea, thyroid, fat, brain, eyes, optic nerves, and sciatic nerve.

The brain, eye with optic nerve and tract attached, spinal cord, section of sciatic nerve, lungs, skin from the application

site, and any abnormal tissues were examined microscopically.

The LD_{50}, slope and 95% confidence limits were calculated by the procedure of Berkson[1]. The skin at the application site was scored for irritation at 1, 7, and 14 days after treatment by the procedure of Draize et al.[2]. The mean body weight gains of the treated animals were compared to those of the respective controls using the student t-test[3].

RESULTS:

Mortality

All animals treated with 500 mg/kg of the test material and two in the 250 mg/kg group died within one hour after treatment; no deaths occurred in animals treated with 100 mg/kg of the test material.

Toxic Signs

Decreased spontaneous motor activity was observed at all dose levels; at 250 mg/kg and 500 mg/kg, animals had collapsed. Ataxia, abnormal respiration, and pupil constriction or dilation, were also observed in animals treated with 250 or 500 mg/kg. In addition, convulsions (1 animal), bloody oral and nasal discharge (1 animal) and weakness (2 animals) were observed in the 250 mg/kg dose group.

Skin Irritation

Skin irritation was observed at the application site of animals in the 250 and 500 mg/kg groups. No skin irritation was noted in animals from other groups.

Body Weights

No significant differences in mean body weights were observed between males or females of the 100 mg/kg or 250 mg/kg groups and their respective controls.

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[1]Berkson, J. Tables for use in estimating the normal distribution function by normit analysis. Biometrika, 44: 411-435, 1957.

[2]Draize, J. H., Woodward, G., and Calvary, H. O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther., 82: 377-390, 1944.

[3]Sokal, R. R., and Rohlf, F. J. Biometry. W. H. Freeman and Company, San Francisco, pp. 175-252, 1969.

Clinical Ocular Examination

Abnormal pupil responses were observed in six of the eight surviving animals at the 250 mg/kg, in 1 female treated with 100 mg/kg, and in 4 of 20 control animals. No other clinical abnormalities were observed.

Gross Pathology

A high incidence of eschar and brown skin was observed at the application sites of animals in the 500 mg/kg group. Eschar was also observed in three animals from the 250 mg/kg group. According to the pathologist who examined the animals, these findings were probably treatment-related. Animals that died on test also had hemorrhaging, mottled and edematous lungs; grainy and discolored liver and kidneys; and discolored heart and pancreas. Nothing remarkable was observed in other tissues.

Histopathology

Four of the eight surviving rabbits (2 males and 2 females) in the 250 mg/kg group had lesions (gliosis, malacia) in the optic nerve. Lesions in the optic nerve were not observed in the controls, the 100 mg/kg group and the nonsurvivors.

Two rabbits in the 500 mg/kg group and one in the control group had dermal lesions. These lesions consisted of acute inflammation, acanthosis, hyperkeratosis, ulceration, crusting or fibrosis. Because the lesions were more severe in the control animal than in the treated animals, they were not attributed to the topical application of the test material.

Inflammatory lesions (acute or chronic inflammation, congestion) in the liver, kidneys and lungs were observed at all dose levels and were considered to be naturally occurring and unrelated to treatment.

COMMENTS:

This study is actually a composite of two studies. The study with the 250 and 500 mg/kg dose levels was begun on June 15, 1984, and completed on July 6, 1984. The study with the 100 mg/kg dose level was begun on October 23, 1984, and completed on November 6, 1984. Because there was a concurrent control at each time interval and because a primary reason for conducting this and other acute studies was to determine if MTA caused optic nerve lesions, this study is acceptable as an acute dermal study. None of the animals that died on test following treatment with 250 or 500 mg/kg of MTA had any lesions in the optic nerves, indicating that these lesions do not develop spontaneously.

A quality assurance statement dated April 22, 1985, was submitted with the report.

LD_{50}

The calculated LD_{50} and 95% confidence limits for males and females collectively was 297 (29.9 - 2951) mg/kg. The slope and 95% confidence limits was 1.67 (0.24 - 11.8). However, it was stated on pages 1 and 7 of the submission that the approximate LD_{50} for males and females combined was 300 mg/kg.

NOEL

None of the animals treated dermally with 100 mg/kg of MTA had any lesions in the optic nerve. Therefore, 100 mg/kg appears to be the no-effect level for optic nerve lesions induced by MTA in rabbits following acute dermal exposure.

TOXICITY CATEGORY: II

CORE CLASSIFICATION: Minimum

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Reviewed by: Krystyna K. Locke, Toxicologist KKL 6/1/88
Section II, Tox. Branch (TS-769C)
Secondary reviewer: Edwin R. Budd, Section Head ERB 6/14/88
Section II, Tox. Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: Acute dermal (Monkey)

TOX. Chem. No.: 584D
MRID No.: 40322601
Project No.: 8-0158

Test Material: Methylthioacetate (MTA)
Lot No. SX 1500; Purity: 99%

Study Number(s): 2107-121; P1163

Sponsor: Chevron Chemical Company, Richmond, CA.

Testing Facility: Hazelton Laboratories America, Inc., Vienna, VA.

Title of Report: Acute Dermal and Intravenous Toxicity of Methylthioacetate in Cynomolgus Monkeys

Author(s): Raymond H. Cox

Report Issued: April 2, 1987

Conclusions:

LD_{50} = > 6000 mg/kg (HDT in males only)

Toxic signs in the 3000 and/or 6000 mg/kg groups included dyspnea, limpness, mild cyanosis, subdued appearance, slow or no response to sound, and mydriasis. All animals appeared normal within 30 minutes after treatment. Ophthalmoscopy, necropsy and histopathology revealed no abnormalities.

Core Classification:

Supplementary (only males were used).

Toxicity Category: IV (males).

Experimental Procedures:

MTA was applied directly on the backs clipped free of hair (intact skin) of male cynomolgus monkeys (Macaca fascicularis) and the application sites were occluded with nonabsorbent binders for 24 hours. The levels of MTA used were 750 (Group 1), 1500 (Group 2), 3000 (Group 3) or 6000 (Group 4) mg/kg of body weight. During the exposure period, the monkeys (2/group) were

kept in restraint chairs. At the termination of the exposure, the binders were removed and the animals were observed for toxic signs and mortality for 42 days (Groups 1 and 2), 44 days (Group 3) and 56 days (Group 4). Only Group 4 was sacrificed at the termination of the observation period and examined grossly and histopathologically. The remaining animals were used in the study of acute intravenous toxicity of MTA (see separate review). The following tissues were examined histopathologically by Colorado Pathology Services, Inc.: brain (brainstem, cerebellum and cerebrum), eyes, optic nerve tracts, treated skin (application site), and all gross lesions.

The monkeys were purchased from Hazelton Research Primates, Inc. (HRP) and the test was performed in the same facility in which the monkeys were housed while owned by HRP. As a result, the quarantine period for the monkeys at HRP was considered adequate. At the initiation of treatment, the monkeys weighed 2.2 to 3.1 kg.

The monkeys were:

1. Assigned randomly to groups;
2. Identified by numbered ear tags;
3. Housed singly;
4. Fed Purina High Protein Monkey Chow #5048 and water ad libitum;
5. Weighed on days 1, 7, 14 and 56 (Groups 4 only) following treatment; and
6. Examined ophthalmoscopically before treatment and on days 13 to 20 and 46 (Group 4 only) after treatment.

The application sites were scored for irritation by the procedure of Draize et al. (1944[1]), but time intervals were not specified.

Results:

The testing laboratory selected monkey as the nonrodent species for this acute dermal toxicity study because of the considerable experience with that species.

There were no deaths and dermal irritation was not observed at any does level. Clinical signs included squirming and vocalization during treatment by most animals. One animal in 3000 mg/kg groups had dyspnea, limpness and mild cyanosis. In the 6000 mg/kg group, mydriasis and subdued appearance was observed in both animals; slow response to sound and little

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[1] Draize, J. H., Woodward, G., and Calvary, H. O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmaco. Exp. Ther. 82: 377-390, 1944.

spontaneous movement in one animal; and dyspnea and no response to sound in another animal. All monkeys appeared normal within 30 minutes after treatment.

Body weights did not appear to be treatment-related. On the observation day 14, the weight profile was as follows:

Group	Animal number	Weight gain or loss, g*
1	J00117	+ 200
	J00118	+ 100
2	J00119	- 100
	J00120	- 100
3	J00121	0**
	J00122	+ 100
4	J00123	- 100
	J00124	+ 100

*When compared with initial weight.
**Initial and final weights were the same.

The animals in Group 4 were also weighed on the observation day 56, just before sacrifice, and each gained weight. However, a comment was made in the report that "the weights recorded as terminal weights were from fasted monkeys and were not evaluated with the remaining body weights".

Ophthalmological examinations revealed no abnormalities. Necropsy and histopathology, performed only on Group 4, also revealed no abnormalities.

A certificate of compliance with FIFRA good laboratory practice standards (dated April 20, 1987) and a quality assurance statement (dated May 20, 1986) were included in the report.

LD_{50} = > 6000 mg/kg/day (males only)

Toxicity Category: IV

Classification of Study: Supplementary (because only males were used)

Reviewed by: Krystyna K. Locke, Toxicologist
Section II, Tox. Branch (TS-769C)
Secondary Reviewer: Edwin R. Budd, Section Head
Section II, Tox. Branch (TS-769C)

RRL 6/1/88
6/14/88

DATA EVALUATION REPORT

Study Type: Acute Intravenous (Monkey)

TOX. Chem. No.: 584D
MRID NO.: 40322601
Project No.: 8-0158

Test Material: Methylthioacetate (MTA)
Lot No. SX 1500; Purity: 99%.

Study Number(s): 2107-121

Sponsor: Chevron Chemical Company, Richmond, CA.

Testing Facility: Hazelton Laboratories America, Inc., Vienna, VA.

Title of Report: Acute Dermal Toxicity and Intravenous Toxicity: Methylthioacetate in Cynomolgus Monkeys

Author(s): Raymond K. Cox

Report Issued: April 2, 1987

Conclusions:

Due to technical difficulties, exact doses of MTA administered intravenously to 6 male cynomolgus monkeys were unknown and LD_{50} was not determined. The approximate single doses estimated for 4 animals (39.1, 53.6, 57.7 or 64.0 mg/kg), as well as 2 unknown doses ("smaller than 100 mg/kg"), caused toxic signs of short duration (3 to 30 minutes), but no weight loss, gross abnormalities (other than eye opacity in one animal), or histopathological tissue changes. Toxic signs included loss of reflexes, tremors, irregular breathing and limpness. There was one treatment-unrelated death.

Classification of Study: Acceptable as supplementary data.

Toxicity Category: Cannot be determined from these data.

Experimental Procedures:

Six male cynomolgus monkeys (body weight: 2.3-2.8 kg) were injected intravenously with MTA (single doses) and sacrificed

after the observation period of 14 to 16 days. These monkeys were first used in an acute dermal toxicity study in which they were treated with 750, 1,500 or 3,000 mg of MTA/kg of body weight. The I.V. injections were given on days 42 or 44 after dermal exposure.

According to the protocol, each monkey was to be injected with 100 mg of MTA/kg of body weight. However, because of technical difficulties, dosing could not be completed, resulting in lower exposure levels are follows:

Animal Number	Approximate (Estimated) Dose (mg/kg of Body Weight)
J00117	Not determined, but < 100 mg/kg
J00118	Not determined, but < 100 mg/kg
J00119	53.6
J00120	57.7
J00121	39.1
J00122	64.0

The monkeys were (1) observed frequently on the day of dosing and once daily thereafter; (2) examined ophthalmologically on days 4 to 6 after dosing; (3) weighed on days 1 and 7 after treatment, and at the termination of the study; (4) housed singly; and (5) given unrestricted amounts of food and water. All animals were necropsied and the following tissues were examined histopathologically: brain (brainstem, cerebellum and cerebrum), eyes, optic nerve and gross lesions.

Results:

Toxic Signs: See Conclusions on page 1.

Mortality: One animal (No. J00120) died at 7 minutes after dosing. The cause of death was not determined.

Body Weight: All animals gained weight.

Ophthalmoscopy: One animal (No. J00121) had corneal opacity which was not observed at the pretreatment examination.

Necropsy: Nothing remarkable was observed.

Histopathology: Mild perivascular inflammation in the cerebrum and brainstem was observed in the monkey which died

shortly after dosing (No. J00120). These lesions were regarded as being of insufficient magnitude to cause death and were not attributed to treatment.

LD_{50}: Not determined.

Classification of Study: Acceptable as Supplementary Data (Doses unknown or approximate and only males were used).

Toxicity Category: Cannot be determined (inadequate data).

A statement of compliance with FIFRA good laboratory practice standards (dated April 20, 1987) and a quality assurance statement (dated May 20, 1986) were included in the report.