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

005291

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUL 10 [illegible]

MEMORANDUM

SUBJECT: ASANA Insecticide 1.9 EC (24.0% ai)
EPA File Symbol 201-URI

and

Technical ASANA Insecticide (75.0% ai)
EPA File Symbol 201-URO

Accession No. 261477
Tox. Chem. #77A

FROM: William B. Greear, M.P.H. William B. Greear 7/7/86
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

TO: Adam Heyward, PM Team 15
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Albin B. Kocialski, Ph.D. ABK 7/7/86
Supervisory Pharmacologist
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

and

Theodore, M. Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769C)

Under a cover letter dated February 18, 1986, the Shell Chemical Company has submitted the results of several studies and a response to a question raised by the Toxicology Branch (TB) in the initial evaluation of EPA File Symbols 201-URO and 201-URI (see memorandum of W. Greear dated September 25, 1985). The studies that were submitted are indicated below together with their "Core" classification and toxicity category assignment.

1/15

ASANA Insecticide 1.9 EC

Study	Toxicity Category	Classification
Acute Oral LD_{50}*	II	Guideline
Acute Dermal LD_{50}*	III	Guideline
Acute Inhalation LC_{50}	II	Guideline
Primary Eye Irritation*	I	Guideline
Primary Dermal Irritation*	I	Minimum Data
Dermal Sensitization*	Sensitizer	Minimum Data

Technical ASANA Insecticide

Study	Toxicity Category	Classification
Acute Oral LD_{50}*	II	Guideline
Acute Dermal LD_{50}	III	Minimum Data
Primary Eye Irritation	III	Guideline
Primary Dermal Irritation	IV	Guideline
Subchronic Oral - Rat* (3-month)	NOEL = 50 ppm	Minimum Data

As requested, the petitioner has also provided information describing the "self-inflicted trauma" observed in rats in the 13-week study with MO 70616 (Report #227A-101-030-84). The self-inflicted trauma was a result of contact with the cage during convulsions produced by administration of the test material. This explanation is satisfactory.

The data requirements for the registration of Technical ASANA Insecticide and ASANA Insecticide 1.9 EC have been satisfied.

Labeling

The following precautionary statements should appear on the labels for ASANA Insecticide 1.9 EC and Technical ASANA Insecticide:

ASANA Insecticide 1.9 EC

> Corrosive. Causes eye damage and skin burns. May be fatal if swallowed or inhaled. Do not get in eyes, on skin, or on clothing. Wear goggles or face shield, protective clothing, and rubber gloves when handling. Wash thoroughly with soap and

*(See memorandum of W. Greear dated September 25, 1985)

water after handling. Remove contaminated clothing and wash before reuse. May cause allergic reactions.

Technical ASANA Insecticide

May be fatal if swallowed. Do not breathe vapors. Causes eye irritation. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

At this time, TB wishes to express concern over the use of the new A-alpha enriched Pydrin technical (Technical ASANA Insecticide) and its associated formulation.

The current Pydrin technical is a racemic mixture composed of four stereoisomers present in equal proportions. However, only one of the four stereoisomers possesses significant insecticidal activity. This stereoisomer is referred to as the A-alpha isomer. The current Pydrin technical contains a minimum of 18 percent of the A-alpha isomer. The new Pydrin technical contains a minimum of 75 percent of the A-alpha isomer. The acceptable daily intake (ADI) for fenvalerate was previously based on the results of a 2-year feeding study in rats with the current Pydrin technical and was 0.125 mg/kg/day. Because the petitioner decided to develop the use of the new Pydrin technical, TB decided to request an additional 90-day feeding study in the rat with the new Pydrin technical in order to determine the difference in the potency that might exist between the new and currently used Pydrin technicals. The new Pydrin technical produced a no-observable-effect level (NOEL) of 50 ppm in rats compared to a NOEL of 250 ppm in rats using the currently registered Pydrin technical. Thus, in anticipation of the registration of the new Pydrin technical, the ADI of 0.125 mg/kg, which is based on the degree of toxicity associated with the use of the currently registered Pydrin technical, was reduced by a factor of 5 to 0.025 mg/kg in order to reflect the increased degree of toxicity (potency) associated with the new Pydrin technical. (This is the same as saying that a residue level, for example of 2.0 ppm, with the new formulation will be able to produce the same toxic effects as 10 ppm of the current formulation, or that 100 ppm of the new formulation will be able to cause the same toxic effects as 500 ppm of the current formulation. Therefore, residue levels of 2.0 ppm and 100 ppm with the current formulation cannot simply be equated on a numerical basis with the new formulation, or stated in another way - 2.0 ppm of the current formulation is not the same as 2.0 ppm of the new formulation from a toxicological viewpoint.) Furthermore, this situation is not simply a matter of exceeding

100 percent of the ADI by adding more commodities and tolerances to an already long list and incrementally raising the percent of the ADI utilized. The situation as it may evolve means that if the new formulation is registered and the current tolerances remain in effect (and are not reduced accordingly) every commodity will theoretically carry residues which are five times stronger (more potent). As a result, when the new Pydrin technical is registered, the ADI will be exceeded by approximately 550 percent in nonnursing infants less than 1 year old [calculations using the Tolerance Assessment System (TAS)]. At present, it has been calculated that the ADI has been exceeded by approximately 11 percent using the TAS in this population subgroup. The ADI would also be exceeded by approximately 325 percent in children 1 to 6, by approximately 175 percent in children 7 to 12, etc., using the TAS, when the new Pydrin technical is registered.

Recommendations

1. The toxicological data requirements for the registration of Technical ASANA Insecticide (EPA File Symbol 201-URO) and ASANA Insecticide 1.9 EC (EPA File Symbol 201-URI) have been satisfied. TB has no objection to their registration provided the precautionary statements for the technical and formulation are changed as recommended above in the body of this memorandum.

2. TB expresses concern over the use of this new enriched A-alpha Pydrin technical and corresponding formulation with respect to its impact on the ADI as addressed above in the body of the memorandum.

3. The registrant should be informed that the 1-year dog feeding study with the new A-alpha enriched Pydrin technical is still outstanding.

005291

DATA EVALUATION RECORD

Subject: "Acute Dermal Toxicity of MO 70616 Technical in the Rabbit"

Test Material: MO 70616 Technical, purity 98.7% (83.7% A-alpha isomer) Lot #2-3-0-0, a viscous amber liquid.

EPA File Symbol: 201-URO

Accession No.: 261477

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Report No./Date: 3881-85/December 13, 1985

Authors: J.L. Maedgen and E.J. Sabol

Classification: Minimum

Toxicity Category: Category III

Materials and Methods:

Thirty male and thirty female New Zealand White albino rabbits weighing 1.80 to 2.65 kg were obtained from Ray Nichols Rabbitry, Lumberton, Texas. The rabbits were allowed to acclimatize to laboratory conditions for at least 8 days. The rabbits were housed in suspended wire bottom stainless steel cages. The cages were cleaned weekly. Purina Rabbit Chow and water were available ad libitum. The rabbits were prepared by clipping the back of the trunk free of hair to expose an area of 12 x 17 cm approximately 24 hours prior to treatment. Ten males and ten females weighing 2.00 to 2.65 kg were selected and distributed to a control and a test group using a stratified randomization procedure in such a way that the average weights and average weight distribution for each group were similar. The test material was applied at a rate of 2.00 g/kg to the exposure area of each animal and was held in contact with the skin with surgical gauze and adhesive tape. The trunk of each animal was then wrapped with polyethylene film to retard evaporation of volatile substances. An Ace bandage was then wrapped around the trunk of the animal. Animals in the control group were treated in an identical manner except that they were treated with 2.00 g/kg of water. Twenty-four hours after treatment the bindings were removed and the backs were wiped with a moist cloth to remove any excess test material. The rabbits were observed at 1, 2, 4, 6, and 24 hours after treatment and at least twice per day thereafter for 14 days for toxic effects. Individual body weights were determined initially and at 7 and 14 days. A gross necropsy was conducted on all animals. Skin irritation was scored immediately after the 24-hour exposure period and at 7 and 14 days.

Results:

Two animals in the control group died on day 13. One animal in the test group died on day 2. The test animals exhibited ataxia, body tremors, constricted pupils, muscle tremors, poor hindlimb coordination, and small feces. Mild erythema and edema of the skin of test animals was observed immediately after the 24-hour exposure period. At necropsy, the test animal that died during the study had signs of diarrhea, emaciation, nasal discharge, salivation, gastrointestinal (GI) tract distended with gas, and discoloration of the contents of the GI tract. The necropsy of the test animal that died differed from the controls only in that it was emaciated and showed signs of salivation. One test animal of the nine that survived had signs of diarrhea.

Toxicity Category: Category III

Conclusions: LD_{50} > 2000 mg/kg

Classification: Minimum

Justification for Classification:

Although the requirements of the limit test of a "guideline" study were not met because deaths occurred at the 2000 mg/kg dose level, more deaths occurred in the control group. Therefore, it is considered that the study was sufficiently close to fulfilling the "limit-test" clause of the guideline and, thus, fulfills the regulatory requirements.

DATA EVALUATION RECORD 005291

Subject: "Eye Irritation of MO 70616 Technical in the Rabbit"

Test Material: MO 70616 Technical, purity 98.7% (83.7% A-alpha isomer) Lot #2-3-0-0, a viscous amber liquid

EPA File Symbol: 201-URO

Accession No.: 261477

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Report No./Date: 3882-85/December 10, 1985

Authors: J.L. Maedgen and E.J. Sabol

Classification: Guideline

Toxicity Category: Category III

8 271

Materials and Methods:

Nine New Zealand White albino rabbits weighing 2.05 to 2.80 kg were obtained from Ray Nichols Rabbitry, Lumberton, Texas and were allowed to acclimate to laboratory conditions for 7 to 14 days. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The cages were cleaned weekly. Purina Rabbit Chow and water were available ad libitum. The rabbits' eyes were examined at least 24 hours prior to treatment with the aid of 0.2 percent sodium fluorescein. One tenth mL of the test material was placed into the conjunctival sac of the right eye of each rabbit. Then the lids were held together for a few seconds. Three of the nine treated eyes were each flushed with 300 mL of tap water 30 seconds after treatment. Ocular examinations were made at 1, 24, 48, and 72 hours and at 7 days after treatment. After 24, 48, and 72 hours and 7 days, the corneas were examined with the aid of 0.2 percent sodium fluorescein and an ultraviolet light source.

Results:

Conjunctivitis was observed at 1, 24, 48, and 72 hours in rabbits with washed (mean maximum score 10.0/110) and unwashed (mean maximum score 12.0/110) eyes. Corneal opacity was not observed. The eyes of all rabbits were clear by day 7.

Conclusions:

The test material causes mild ocular irritation in washed and unwashed rabbits' eyes.

Toxicity Category: Category III

Classification: Guideline

Materials and Methods:

Nine New Zealand White albino rabbits weighing 2.05 to 2.80 kg were obtained from Ray Nichols Rabbitry, Lumberton, Texas and were allowed to acclimate to laboratory conditions for 7 to 14 days. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The cages were cleaned weekly. Purina Rabbit Chow and water were available ad libitum. The rabbits' eyes were examined at least 24 hours prior to treatment with the aid of 0.2 percent sodium fluorescein. One tenth mL of the test material was placed into the conjunctival sac of the right eye of each rabbit. Then the lids were held together for a few seconds. Three of the nine treated eyes were each flushed with 300 mL of tap water 30 seconds after treatment. Ocular examinations were made at 1, 24, 48, and 72 hours and at 7 days after treatment. After 24, 48, and 72 hours and 7 days, the corneas were examined with the aid of 0.2 percent sodium fluorescein and an ultraviolet light source.

Results:

Conjunctivitis was observed at 1, 24, 48, and 72 hours in rabbits with washed (mean maximum score 10.0/110) and unwashed (mean maximum score 12.0/110) eyes. Corneal opacity was not observed. The eyes of all rabbits were clear by day 7.

Conclusions:

The test material causes mild ocular irritation in washed and unwashed rabbits' eyes.

Toxicity Category: Category III

Classification: Guideline

005291

DATA EVALUATION RECORD

Subject: "Primary Skin Irritation of MO 70616 Technical in the Rabbit"

Test Material: MO 70616 Technical, purity 98.7% (83.7% A-alpha isomer) Lot #2-3-0-0, a viscous amber liquid.

EPA File Symbol: 201-URO

Accession No.: 261477

Testing Facility: Stillmeadow, Inc.
Biological Testing Laboratory
Houston, TX 77036

Report No./Date: 3883-85/December 19, 1985

Authors: J.L. Maedgen and E.J. Sabol

Classification: Guideline

Toxicity Category: Category IV

11 214

Materials and Methods:

Three male and three female New Zealand White albino rabbits weighing 1.8 to 2.9 kg were obtained from Ray Nichols Rabbitry, Lumberton, Texas and were allowed to acclimate to laboratory conditions for 8 to 15 days. The rabbits were individually housed in suspended wire bottom galvanized steel cages. The cages were cleaned weekly. Purina Rabbit Chow and tap water were available ad libitum. The back of the trunk of each rabbit was clipped free of hair to reveal an 8 x 8 cm area approximately 24 hours prior to treatment. There was only one (intact) test site per animal. One half mL of the test material was placed on the test site under a 1 x 1 inch square surgical gauze patch. Each patch was secured with a piece of adhesive tape. The trunk of the animal was wrapped with clear polyethylene film to retard evaporation of the test material. Then an elastic Ace® bandage was wrapped around the trunk of the animal. Four hours after treatment the dressings were removed and the test sites were wiped with a moist cloth to remove the excess test material. The test sites were scored for irritation 1 hour after removal of the dressings and at 24, 48, and 72 hours after treatment. Observations for toxic/pharmacologic signs were made daily throughout the study.

Results:

Mild erythema and edema were observed in one animal 1 hour after removal of the dressing.

Conclusions:

The test material was practically nonirritating.

Toxicity Category: Category IV

Classification: Guideline

DATA EVALUATION RECORD 005291

Subject: "Acute 4-Hour Inhalation Study in Rats with MO 70616 1.9 EC"

Test Material: MO 70616 1.9 EC (24.0% ai) described as a yellow liquid Lot # 2-4-13-2

EPA File Symbol: 201-URI

Accession No.: 261477

Testing Facility: Westhollow Research Center
Houston, TX 77082

Report No./Date: 6155M/WTP-331/February 1986

Authors: L.A. Malley; K.I. Darmer, Jr.; R.G. Helman; D.G. Stevens

Classification: Guideline

Toxicity Category: Category II

Materials and Methods:

Eighty-four Fischer 344 rats weighing 180 to 233 g (males) and 139 to 172 g (females) were obtained from Harlan Industries, Indianapolis, Indiana and were housed individually in hanging polycarbonate cages with wire mesh bottoms. Rats were provided standard laboratory rat chow and water ad libitum except during exposure. The rats were transferred to clean cages once per week. The rats were acclimated to the laboratory for a period of at least 12 days prior to test. The animals were housed in rooms with a temperature of 20 ± 1.1 °C and relative humidity of 40 to 70 percent. A 12-hour-on and 12-hour-off light cycle was maintained. Twenty-four male and twenty-four female rats were randomly distributed to the following four groups according to body weight.

Exposure Concentration (%)	No. Males	No. Females
5	6	6
15	6	6
20	6	6
25	6	6

(Note: A preliminary study was performed in which two rats/sex were exposed to undiluted, 50 percent w/w and 5 percent w/w of the test material in water. All rats exposed to undiluted and 50 percent w/w of the test material died. No deaths occurred at the 5 percent dilution.)

The rats were exposed for a period of 4 hours in a 1000 L Hazleton model 1000 stainless steel/glass exposure chamber. The chamber temperature was kept at 22 ± 2 °C. Chamber airflow was maintained at 10 air changes per hour. Chamber temperature, humidity, and airflow were recorded every 30 minutes. Water dilutions of MO 70616 1.9 EC were generated into an aerosol by using a Heat Systems Ultrasonic Spray Nozzle, Model 600-2. Actual concentrations of the test material in the atmosphere were determined every half hour from the breathing zone of the animals. Test material concentrations were sampled by drawing air across preweighed filters. The filters were weighed for gravimetric determinations of concentrations, and then extracted and analyzed by liquid chromatography. Aerodynamic particle size analysis was done by sampling with an eight-stage Sierra cascade impactor, Model 2110-K. The rats were observed after exposure and then twice daily for the next 14 days for mortality and clinical signs of toxicity. Body weights were recorded initially and on days 7 and 14 of the observation period. Body weights were also recorded for rats that died, at the time of their death. All rats received a gross macroscopic examination.

Results:

Liquid chromatographic analysis of the atmospheric concentration produced with the 5, 15, 20, and 25 percent exposure levels were 0.1623, 0.613, 0.9141, and 1.1701 mg/L of the undiluted test material. The mass median aerodynamic diameter for all exposures was between 1.25 and 2.0 micrometers. No deaths occurred in the 5 and 15 percent exposure groups. In the 20 percent exposure groups, four of six males and three of six females died within 24 hours of exposure. In the 25 percent exposure group, six of six males and three of six females died within 6 hours of exposure. The following toxic signs were observed in animals of all test groups: chromodacryorrhea, hunched posture, tip toe gait, chewing claws and scratching the cage bottom, and coarse tremors. In the 5, 15, and 20 percent groups the animals also exhibited burrowing, excessive hunched posture leading to a rearing position, and scratching the nose and facial area. Rats in the 15, 20, and 25 percent group also had a red discharge around the nose and mouth, wetness in the genital area, prostration, splayed hind limbs, hypoactivity, and unsteady stance. Rats in the 20 and 25 percent groups also exhibited elevated hind limbs. Body weights were decreased in male rats in the 15 percent group and in surviving male and female rats exposed to 20 percent of the test material at day 7. Body weights of all surviving rats on day 14 exceeded day 0 weights. Gross necropsy of rats dying within 24 hours after exposure revealed pulmonary edema, hemorrhage from nasal or oral cavity, bloodstained fur around the nose and/or mouth, and expectoration of blood through the nose and mouth. At the day 14 necropsy, focal areas of atelectasis was observed in three rats exposed to 15 percent of the test material and pulmonary edema in two rats exposed to 25 percent of the test material.

Conclusions:

*LC_{t50} (males) = 19% w/w	for t = 4 hours
*LC_{t50} (females) = 22% w/w	for t = 4 hours
*LC_{t50} (combined) = 20% w/w (0.9141 mg/L)	for t = 4 hours

* estimated

Toxicity Category: Category II

Classification: Guideline

15
278