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CB-407 XR-972

September 18, 1970

Mr. Henry S. Bussey, Head Registration Procedures Section Pesticides Regulation Division Agricuitural Research Service U. S. Department of Agricuiture Washington, D. C. 20250

Reg. No. 239-EGEA Referral Date - 4/2/70

Dear Mr. Bussey:

The toxicity data received from you on the product Ortho Monitor 6 Spray containing O.S-dienthy' phosphoramidothicate as the active ingredient have been reviewed.

We have no objection to the registration of this product for the proposed usage pattern.

If you have any questions regarding our comments, please contact us at your convience.

Sincerely,

Lamar B. Dale, Jr., Ph.D. Pharmacologist Pesticide Registration Branch Division of Pesticide Chemistry and Toxicology Office of Pesticides

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cc: BF-219 BF-219/THHarris XTOX FILE

> RDCoberly/LBDale/ccw 9/18/70

I. DATE OF REFL U. S. DEPARTMENT OF AGRICULTURE 3-31-70 12 05 % 000972 AGRICULTURAL RES TH SERVICE PESTICIDES REGULA...JN DIVISION WASHINGTON, D. C. 20230 2. FILE SYMBOL/REGISTRATION NO. INTERDEPARTMENTAL COORDINATION 239-ECFA OF S. DATE OF APPLICATION ACTIVITIES RELATING TO PESTICIDES Referral of Application for Registration under the 3-18-70 Federal Insecticide, Fungicide, and Rodenticide Act 5. PRODUCT NAME NAME & ADDRESS OF APPLICANT OR REGISTRANT OBTHO MOBITOR 6 SPRAY ONTHO DIV CHEVRON CHENICAL CO gho Bensley St 94804 Richmond, California COMMENTS BY COORDINATING AGENCY BEST AVAILABLE COPY 9. NAME OF AGENCY S. DATE BY (NAME) OTHER: BAFETY . HUMAN BAFETY - FISH AND WILDLIFE DATE INITIALS DATE INITIALS DATE INITIALS PR COMMENTS COMMENTS USE COMMENTS ONLY REPLACES PR FORM 9-290, PR FORM 9-291. 230 P. Mara

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Methamidophos toxicology review

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Pages	4	_ ti	hroug	1h <u>7</u>	are	e not	included	in	this	copy.

The material not included contains the following type of information:

- Identity of product inert ingredients
- Identity of product impurities
- Description of the product manufacturing process
- Description of product quality control procedures
- Identity of the source of product ingredients
- Sales or other commercial/financial information
- X A draft product label
- The product confidential statement of formula
- Information about a pending registration action
- FIFRA registration data
- The document is a duplicate of page(s)
- The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

7 RDCoberly/ccw - 9/18/70 000972 0,S-dimethyl phosphoramidothioate Chemical Name Monitor Trade Name RE-9006; ENT. 27396 : Alternate Name CH3 0 . Structural Formula CH2 " C2 H8 NO2 PS Empirical Formula 141.13 : Molecular Weight 39-41°C e. Melting Point 1.31 (melt) Density Pungent Odor _ Infinitely miscible with water and alcohol; less than 1% in Solubility kerosene; less than 10% in benzene or xylene. Low Volatility Approx 10-4 mm Hg at 20°C Vapor Pressure Normal at ambient temperatures Stability Insecticide for crops Use Chevron Company

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000972 MONITOR Male $LD_{50} = 15.6 \text{ mg/KG}$ Acute Rat Oral (95% Tech) Female $LD_{50} = 13.0 \text{ mg/KG}$ Typical cholinesterase inhibition signs were noted. Male $LD_{50} = 21 \text{ mg/kg}$ Acute Rat Oral (75% Tech) : Female LD₅₀ = 18.9 mg/kgMale $LD_{50} = 32.3 \text{ mg/KG}$ t Acute Rat Oral (6 S) Female $LD_{50} = 24.1 \text{ mg/KG}$ Tremors, salivation, dyspnea were noted, Female $LD_{50} = 16.2 \text{ mg/KG}$: Acute Mice Oral (95%) Tremors, salivation, dyspnea were noted Female $LD_{50} = 18.0 \text{ mg/KG}$ Acute Mice Oral (75%) Tremors, salivation, straub tail, dyspnea and rarely clonic convulsions were noted. No mortality occurred at 15 mg/KG or lower. Male $LD_{50} = 118 \text{ mg/KG}$. No gross pathological changes were noted. Acute Rabbit Dermal (Tech) Toxic signs noted were miosis, salivation, rhinorrhea, ataxia, and CNS depression.

MONITOR (i.j.) 000972 Acute Rabbit Dermal (Monitor 6 S) Male $LD_{50} = 125 \text{ mg/KG}$. No gross : pathological changes were noted. Toxic signs noted were miosis, diarrhea, salivation, rhinorrhea and death. An LC50 value was not established Acute Rat Inhalation (95%) because of the vapor method used. A slight effect was shown by a depression of both the RBC and plasma Ch.E. activity. Exposure was four hours. Acute Rat Inhalation (Monitor 6 S) No LC50 value could be estab-(4 hours) of vapors was made. No mortality or signs of intoxication was noted. A slight to moderate depression of the RBC level of Ch.E. activity was noted. 21 Day Subacute Rabbit Dermal Levels tested were 5.0 and 10 mg/KG. Two deaths were (75% Tech) noted at high level and one Sec. Sec. 6 at low level. Deaths were due to cholinergic reactions at the high level. Slight body weight loss was noted at the high level. No adverse findings were noted in hematologic and clinical blood chemistry studies. These findings are difficult to believe due to the dosage levels used.

MONITOR 000972 Levels tested were 0.3, 1.0, 90 Day Rat Feeding (75% Tech) : 3.0, and 10 ppm. Male showed plasma Ch.E. depression at 3.0 and 10 ppm; females at 10 ppm. .RBC Ch.E. depression was noted at 10 ppm. Brain Ch.E. depression was noted at 3.0 and 10 ppm. The no-effect level is approx. 1.0 ppm. Recovery was noted several weeks post treatment. Levels tested were 0.025, 0.075, and 0.25 mg/KG. No clear-cut or consistent pattern 90 Day Dog Feeding (75% Tech) : of effects on cholinesterase activity was observed. 21 Day Rat Paired Feeding Study Tested at 30 ppm. No body INVALID (97% Tech) IBT # B 6486 weight loss was indicated. 12/10/80 12/20/68 المعدم المراجع المراجع en cara de la cara composi-Two Year Dog Oral (RE~9006-111, :Levels tested were 0.075, 0.25 and 0.75 mg/KG seven days a week. No mortality was observed. No toxic effects were noted. Two Year Rat Feeding (RE 9006-111, SX-116) (97%) : Levels tested were 3.0, 10, and 30 ppm. Body weight loss was observed at 30 ppm (see 21 day rat feeding). The no effect level is greater than 30 ppm. 4.11

MOMATOR 000972 Three Generation Rat Reproduction The Flb litters of the 30 ppm Study (75%) level showed increased still-IBT 8 62 55 1/16/70 births a decrease in viable pups at day five and again at INVALID weaning. All test males showed 12/10/80 a decreased heart weight. Histopathology on parent animals was negative. The F2a and F2b litters, both test and control showed a higher than normal number of stillbirths. The 5 day survival index for the F2a and F2b litters of the 30 ppm were higher than the control value. A greater than 20% decrease in Ch.E. acitivity was noted in both sex of the Flb parents. Histopathological examination revealed no adverse finding. Microsomes accelerate the : Microsomal Oxidation hydrolysis of monitor to O,S-dimethyl phosphorothioate. a an an an an an an an an an Metabolism in the Rat. المراجع المراجع المراجع المحكوم والمراجع المراجع Approximately one-half of the dose was excreted within 24 hrs as CO₂ or in the urine. Neurotoxicity was not exhibited Neurotoxicity in Chickens (75% Tech): Atropine and ur 2-PAM are Antidotal Study antidotal

Thiono isomer impurity

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Acute Rat Oral (RE 9169)

Male $LD_{50} = 633 \text{ mg/KG}$ Female $LD_{50} = 549 \text{ mg/KG}$

Death was proceeded by signs of intoxication associated with central nervous system depression.

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Acute Rabbit Dermal (RE 9169) (SX 198)

 $LD_{50} = ~ 3.5 \text{ gm/KG on intact}$ skin. $LD_{50} = 1.57 \text{ gm/KG on}$ abraded skin. Toxic signs were weakening hyporeflexia, loss of reflexes and salivation.

Human Exposure Reports

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Sixty-six human contact reports, with various concentrates did not show significant effects.

SUMMARY

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This chemical exhibits lethal toxicity at low dosage levels and thus must be considered a highly toxic material. The subacute studies indicate the chemical is largely excreated from the body within 24 hours. The portion remaining does exhibit a continuous effect until intake is stopped. Recovery requires from one to three weeks after such a subacute exposure.

A singly or subacute non lethal levels do not produce constant histological.

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