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

MEMORANDUM

AUG 24 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: SAB Review of Resubmission of Product Characterization and Toxicology Data from Association for Sensible Pest Control in Support of the Registration of Baculovirus cydia pomonella (Submission No.: S444079; ID No.: 058042-R; DP Barcode No.: D193271; MRID No's.: 428169-01, 428169-02, 425172-03).

To: Phillip Hutton/ Linda Hollis (PM 18)
Insecticide-Rodenticide Branch
Registration Division (H7505C)

From: Cindy Schaffer, Microbiologist *C. Schaffer*
Biological Pesticides Section
Science Analysis Branch
Health Effects Division (H7509C)

Through: Roy Sjoblad, Ph.D., Section Head *Tim 8/24/93*
6/ Biological Pesticides Section
Science Analysis Branch
Health Effects Division (H7509C)

Action: SAB has been asked to review product analysis and toxicology data resubmitted in support of the registration of Sensible Pest Control Inc.'s, SPECIFIC-T-1, with Baculovirus cydia pomonella as the active ingredient used to control Tortricid Species.

Discussion:

Although the acute toxicity studies were performed with purified CpGV, not with the TGAI, rationale was provided and accepted for this discrepancy. SAB considers the TGAI to be equal to the EP (i.e., CpGV + [redacted]); therefore a recommendation of no further testing with the TGAI or EP is needed since it is not considered to pose any health risks because it is common knowledge that the [redacted] and residual diet are not likely to pose any significant health risks. SAB suggests the use of an eye shield or face mask to prevent eye irritation by these ingredients.

SAB also found the following deficiencies still outstanding:
Product Identity: 1. A five batch analysis for potency determination (i.e., for CSF/label conversion from % A.I. to GIB/ml) was not presented as part of the analysis of samples by the registrant.

INERT INGREDIENT INFORMATION IS NOT INCLUDED



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Toxicology data: 1. The registrant has yet to evaluate the potential of the virus to infect, replicate, transform or cause toxicity, in a mammalian cell culture assay (see August 16, 1993 memorandum from T. McClintock to L. Hollis re: note in cell culture section regarding a challenge of "mammalian cell lines with CpGV alkaline-liberated virions and monitor the cells for any adverse effects by light microscopy").

SUMMARY OF DATA RESUBMITTED:

Product Identity (REN PROFILE ANALYSIS):

The Restriction Enzyme Profile was submitted. A high degree of similarity was noted between the CpGV-MB and CpGV-MD DNAs while the profile of CpGV-R was distinctly different. This information correlated with the biological activity of the isolates against the first instar larvae of *C. pomonella*. CpGV-MB and CpGV-MV exhibited an LD₅₀ of approximately, 5 to 10 capsules vs. 363 capsules of CpGV-R.

Acute Dermal Toxicity (152A-12):

One animal displayed mild erythema and edema within 24 hours post dosing. No other signs of irritation were noted. SAB upgrades this study to acceptable.

CLASSIFICATION: ACCEPTABLE - TOX CATEGORY IV

Acute Pulmonary Toxicity/Infectivity (152A-12):

Although *Baculovirus cydia pomonella* was not toxic to rats when 1×10^8 GIBs was administered intratracheally, the registrant should have carried out this study further to demonstrate clearance of the test organism.

CLASSIFICATION: ACCEPTABLE - TOX CATEGORY IV

Primary Eye Irritation (152A-14):

Clinical observations were initially submitted for this study. A slight ocular redness was observed. All clinical signs dissipated by day 18. SAB suggests the use of protective eyewear and upgrades this study to acceptable.

CLASSIFICATION: ACCEPTABLE - TOX CATEGORY II

DATA EVALUATION REPORT

Reviewed by: Cindy Schaffer, Microbiologist, SAB/HED S
Secondary Reviewer: J. Thomas McClintock, Ph.D., Microbiologist, JTM
SAB/HED

STUDY TYPE: Acute Pulmonary Toxicity/Pathogenicity-Rat (152A-12)
MRID NO: 425172-03
TEST MATERIAL: Baculovirus cydia pomonella
SYNONYMS: Codling Moth Granulosis Virus
PROJECT NO: UCB: PULMO-91; NVP Report No. XOL109G
SPONSOR: Agricultural Experiment Station, University of California, Berkeley, CA; Association for Sensible Pest Control, Inc., Clayton, CA
TESTING FACILITY: Insect Pathology Group, University of California, Berkeley, CA; Northview Pacific Laboratories, Inc., Berkeley, CA
TITLE OF REPORT: Baculovirus cydia pomonella Acute Pulmonary Toxicity/Pathogenicity Study (Tier I) in Rats.
AUTHOR(S): Louis A. Falcon, Ph.D.; Arthur Berlowitz, M.S.; Mary Jane Deenihan
STUDY COMPLETED: 23 September 1992
CONCLUSION: Although Baculovirus cydia pomonella was not toxic to rats when 1×10^8 GIBs was administered intratracheally, the registrant should have carried out this study further to demonstrate clearance of the test organism.
CLASSIFICATION: ACCEPTABLE- TOX CATEGORY IV

I. STUDY DESIGN

Test Material: The microbial pest control agent is Baculovirus cydia pomonella Mexican Strain 1964 in physiological saline. The homogeneity, purity and stability of the dosing solution was not determined by the testing facility. Each test animal received a 1.2 ml/kg dose (approximately 3.75×10^8 Granulosis Inclusion Bodies [GIBs]) intratracheally.

Test Animals: Thirty-four male and thirty-four female Sprague-Dawley rats, were obtained from Simonsen's Laboratories Gilroy, CA. The male rat's weight ranged from 210.3 gm to 242.2 gm and the female's weight ranged from 159.6 gm to 194.1 gm at the beginning of the study.

Methods: The animals were assigned as follows: The control animal group was comprised of twelve male and twelve female rats and was dosed with a 0.45% saline solution; the shelf control group consisted of two males and two females; and twenty male and twenty female rats were intratracheally injected

with the test substance. The rats were randomly weighed on the day of dosing, weekly and at the scheduled sacrifice times. Treated animals were observed for signs of toxicity at frequent intervals during the first day post dosing and daily thereafter. All rats of each sex in the treatment groups were sacrificed by ether inhalation. The treated animals were divided into groups based on their sacrifice times as follows: Groups A through F consisted of 3 male and 3 female treated rats and two male and two female controls, each sacrificed at 10 minutes post dosing, 24 hours post dosing, 4, 7, 15 and 22 days post dosing. The animals were examined by necropsy for any macroscopic abnormalities. Samples of the gastrointestinal tract, blood, heart, lungs, kidney, liver, spleen, feces and urine were evaluated for the presence of viable GIB observed in the organs by incorporating the animal tissues into the codling moth diet at a ratio of 1:10. One neonate codling moth larva was placed in each cup (in triplicate), with a known quantity of spiked diet incubated at 27.5 C until larva death. Dead larvae were individually examined for the presence of Baculovirus cydia pomonella GIBs. Positive and negative control tissues were also evaluated for the presence of GIBs.

II. RESULTS

A. Body Weights:

No abnormalities were noted in body weight gain.

B. Clinical Signs:

No apparant clinical signs were noted at any time during this study.

C. Viral clearance/infectivity:

The organism was found in the lungs at a level of 1×10^8 GIBs at 1, 7 and 14 days post dosing. No signs of clearance were observed.

D. Necropsy:

One control female from Group A displayed congested lungs 10 minutes post dosing.

One treated male and one control female from Group F exhibited small lesions on the liver.

III. **SAB DISCUSSION:** Although the registrant should have carried out this study further to demonstrate clearance of the test organism; no indication of adverse health effects were noted.