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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: July 8, 1983

SUBJECT: Vitavax-RS
Acute inhalation rat and acute oral mouse studies.
Response to Standard data gaps. I.D.# 400-81.
Caswell #165A. Acc# 250158.

TO: Henry Jacoby. PM 21
Registration Division (TS-767)

FROM: Alex Arce,
Toxicology Branch

THRU: W. Butler - Section III Head
R. Coberly - Quality Control
W. Burnam - Chief, Toxicology Branch (TS-769)

Recommendation: The studies submitted in response to the data gaps have been reviewed and classified as follows

Rat LC_{50} >5.5 mg/L - Core Minimun data
mice LD_{50} pending further information. No core classification assigned yet.

Data Review

Study: "Acute Inhalation Toxicity of Technical VITAVAX in Sprague - Dawley Rats" Food & Drug Research Laboratories, Inc. # 7332B. Submitted to Uniroyal Chemical.

October 13, 1982

Product: Technical grade Vitavax

Time of exposure: 4 hours, whole body exposure.

Subjects: 5 male and 5 female adult rats

Concentration: 5.0 mg/L

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Method: EPA Proposed Guidelines - 43:No. 163 Augu st 22, 1978.

Date: From September 15 to 29, 1982

Chamber: 128L. acrylic exposure chamber with a particulate generator; using ambient air to dilute the aerosol. "The air flow rate was maintained at 35 L/minute"

Concentrations

Nominal and Gravimetric were calculated by standard methods:
$\frac{\text{Weight of material}}{\text{chamber air flow}}$ = CONCENTRATION
Particle size: analysed twice each hour.

Temperature and Humidity: Monitored using hygrometer, each hour.

Observations: For signs of Toxicity and body weights at various intervals. Signs of Toxicity - daily; Body weights - weekly

Necropsy: All animals were necropsied and the whole head, air pa sages, lungs, liver and kidney preserved.

Results

Mortality: No mortality occured.

Signs of Toxicity: Nasal discharge in 3 animals.

Body Weight: Slight decrease 2 days after exposure, otherwise normal.

Necropsy: Lungs described as dark. No other signs.

LC_{50} >5.5 mg/l.

Note: The investigator does not give the LC_{50}. He reports "failed to cause mortality."

This study meets the minimum requirements for an Inhalation Toxicity test.

Core: Core minimum data
Toxicology Category III

Note: The various tables submitted with the test have been inspected by this reviewer and found to be acceptable.

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Study

"Acute Oral LD_{50} Assay in Mice" FDRL No. 7581A, April 11, 1983.

Product: Vitavax Technical

Subject: Male and female adult mice CDI

Method: 43 CFR 163.81.1 (EPA-FIFRA)

Range finding study: 4 dose levels were used, LD_{50} finding Study; 5 dose levels of 1.0; 1.78; 3.16; 5.62; and 10 g/kg; 4 mice per dose level. Result 4/4 dead at, 5.6 g/kg. Thus, the final study used 5 dose levels as follows: 2.50; 3.11; 3.87; 4.82 and 6.00 g/kg, 10 male and 10 females per dose level.

Results

Mortality LD_{50} = Combined 3.55 g/kg (3.15 to 3.95)

Signs of Toxicity: Ataxia, convulsion, decreased activity.

Necropsy: Bloodlike fluid in the intestines.

Conclusion

Pending clarification of the method used for dosing the animals, such as intubation, gavage etc., we will be unable to grade the study. "Single oral dose," does not explain how the dose was administered.

DCR-11693:AlexArce:TOX29:jad:7/15/83

Note: Requirement 163.81.1 has been Totally satisfied - refer to attached Generic Data Requirements. The submitted "Acute Oral LD50 Assay in Mice" was not required.

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CARBOXIN

A-1. Generic Data Requirements: Toxicology (See Chapter VI)

Guidelines Citation	Name of Test	Composition	Does EPA Have Data to Partially or Totally Satisfy this Requirement?	Bibliographic Citation	Must Additional Data be Submitted Under FIFRA 3(c)(2)(B)? If So, due when?
163.81-1	Acute Oral Toxicity	Technical Grade of Active Ingredient	all	00003065	no
163.81-2	Acute Dermal Toxicity	Technical Grade of Active Ingredient	all	00003066	no
163.81-3	Acute Inhalation Toxicity	Technical Grade of Active Ingredient	partially 1/	0000311[illegible]	yes, 14 months
163.81-4	Primary Eye Irritation	Technical Grade of Active Ingredient	no	-	yes, 14 months
163.81-5	Primary Skin Irritation	Technical Grade of Active Ingredient	all	0003119	no
163.81-6	Dermal Sensitization	Technical Grade of Active Ingredient	no	-	yes, 14 months
163.82-1	Subchronic 21-Day Oral	Technical Grade of Active Ingredient	all	00003063 00003030	no
163.82-2	Subchronic 21-Day Dermal Toxicity	Technical Grade of Active Ingredient	all	00003216	no
163.82-4	Subchronic Inhalation Toxicity	Technical Grade of Active Ingredient	no	-	reserved 2/

These data requirements are current as of August, 1981. Refer to the guidance package for updated requirements.

1/ Since the study gave neither the particle size nor the actual concentration of carboxin in the inhalation chamber, further testing is required.

2/ Will depend on results of an acute inhalation test for technical carboxin.

CARBOXIN

A-2. Generic Data Requirements: Toxicology (See Chapter VI)

Guidelines Citation	Name of Test	Composition	Does EPA Have Data to Partially or Totally Satisfy this Requirement?	Bibliographic Citation	Must Additional Data be Submitted Under FIFRA 3(c)(2)(B)? If So, due when?
163.83-1	Chronic Feeding	Technical Grade of Active Ingredient	all	00003031 00003152	no
163.83-2	Oncogenicity	Technical Grade of Active Ingredient	partially	00003031 00003152	yes[1/], 38 months
163.83-3	Teratogenicity	Technical Grade of Active Ingredient	partially	00003120	yes[2/], 24 months
163.83-4	Reproduction	Technical Grade of Active Ingredient	all	00003032	no
163.84-2 through -4	Mutagenicity	Technical Grade of Active Ingredient	partially	00003118	yes[3/], 24 months
163.85-1	Metabolism (Identification of Metabolites)	Technical Grade of Active Ingredient	all	00002945 00002943 00002944	no

These data requirements are current as of August, 1981. Refer to the guidance package for updated requirements.

1/ An eighteen-month mouse oncogenicity study is needed to meet this requirement.

2/ A teratogenicity test is needed on a second mammalian species, i.e. in addition to the test on rats.

3/ Test choices within these categories must be accompanied with rationale.

(1) At least 1 more test for detecting gene mutations from among these types:
- Insects e.g. sex-linked recessive lethal test.
- Mammalian somatic cells in culture with and without metabolic activation.
- Mouse specific locus test.

(2) At least 3 test for detecting chromosomal aberrations (see 163.84-1(b)(2)(ii).

(3) At least 2 tests for detecting primary DNA damage (see 163.84-1(b)(2)(iii)).

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NOTE TO COBERLY AND FILE

The mice oral L D 50 study was not needed. the requirements for the standard have been fulfilled already . Thus , the mice L D 50 is not important .

In a Phone conversation with the REd of Uniroyal , I was told that the method used was " GAVAGF "; we can raise the classification to core minimum,although it is not important . waste of time .

The study was perfo-med overseas and this is the reason that mice were used . We do not use mice for oral tox in the states That is the reason of my questioning regarding the method used .

Alex

7-25-83

The phone conversation with Uniroyal was recieved today July, 25 (monday) 1983 as an naswer to my question to W. Kyle , Uniroyal Red.

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