10/15/90

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

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OCT 15

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Review of response to EPA toxicology review of June 11, 1990 for Clethodim Technical
MRID Nos. 416236-00 to -03
ID No. 059639-G Clethodim
Tox Chem No. 721F
HED Project No. 0-1939

From: James N. Rowe, Ph.D. James N. Rowe 10/9/90
Toxicology Branch II
Health Effects Division (H7509C)

To: Ms. Joanne I. Miller/Ms. M. Erumsele-Matzer
Product Manager, Team 23
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: Marcia van Gemert, Ph.D., Chief Marcia van Gemert 10/11/90
Toxicology Branch II
Health Effects Division (H7509C)

ACTION: Review rebuttal comments and additional data submitted by the registrant, Valent U.S.A. Corporation for Clethodim Technical and Select 2EC formulation.

RECOMMENDATIONS:

1. Select 2EC

The acute inhalation study is Core Guideline data. Category III.

2. Clethodim Technical

a. 90-day subchronic dog study (MRID # 410301-06)

With the submission of this additional analytical data and information on preparation and storage of the test material, this study is upgraded to Core Minimum.

a. One-year oral dog study (MRID # 410301-11)

With the submission of this additional analytical data and information on preparation and storage of the test material, this

study is upgraded to Core Minimum.

DISCUSSION:

1. Select 2EC

See attached D.E.R. and one-liner.

2. Clethodim Technical

a. Analytical Support for Ninety-Day Dog Study with RE-45601 Technical

Background:

Supplemental analytical data (MRID No. 416236-02; Title, "Analytical Support for a Ninety-Day Dog Study with RE-45601 Technical") was submitted in regard to a 90-day subchronic oral toxicity study in dogs (MRID #410301-06). This data was requested by EPA since the report did not establish the stability of test material administered in gelatin capsules.

Results:

The registrant indicates that no data are available on the stability of the test material in the capsules but a sample of RE-45601 was analyzed prior to shipment to the testing laboratory and following study termination. The pre-study purity was 83.3% and the post-study purity was 81.6% (98% of pre-study concentration).

In addition, it was noted that the bulk of the material was stored in a freezer, in sealed containers and protected from sunlight. Once prepared, capsules containing the material were stored refrigerated in a sealed container.

Conclusions:

There does not appear to be any significant degradation of test sample over the period of study in the 90-day study and the laboratory has taken reasonable precautions to ensure that the nominal dosages used in the gelatin capsules were actually administered to the dogs.

b. Analytical Support for a One Year Dog Study with RE-45601 Technical

Background:

Supplemental analytical data (MRID No. 416236-03; Title, "Analytical Support for a One Year Dog Study with RE-45601 Technical") was submitted in regard to a 1-year dog oral toxicity study in dogs (MRID #410301-11). This data was requested by EPA since the report did not establish the stability of test material administered in gelatin capsules.

3

Results:

The registrant indicates that no data are available on the stability of the test material in the capsules but a sample of RE-45601 was analyzed prior to shipment to the testing laboratory, approximately midway through the study and following study termination. The pre-study purity was 83.4%, the mid-study purity was 83.5% and the post-study purity was 83.5%.

In addition, it was noted that while at Hazleton Laboratories, the test material was stored in a freezer, in sealed containers and protected from sunlight. Once prepared, capsules containing the material were stored refrigerated in a sealed desiccated container and protected from sunlight.

Conclusions:

There does not appear to be any degradation of test sample over the period of study in the one-year dog study and the laboratory has taken reasonable precautions to ensure that the nominal dosages used in the gelatin capsules were actually administered to the dogs.

4

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Reviewed by: James N. Rowe, Ph.D. James N. Rowe 10/4/90
Section III, Tox. Branch II(H7509C)
Secondary reviewer: Marcia vanGemert, Ph.D. Marcia vanGemert 10/11/90
Chief, Tox. Branch II(H75099C)

DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation (81-3) TOX. CHEM NO: 721F

ACCESSION NUMBER: MRID NO.: 416236-01

TEST MATERIAL: Select 2EC

SYNONYMS: CC-14900

STUDY NUMBER: CEHC 3141/CEHC 89-436

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Boulevard, Walnut Creek, CA 94596

TESTING FACILITY: Chevron Environmental Health Center, Inc., 15299 San Pablo Avenue, P.O. Box 4054, Richmond, CA 94804-0054

TITLE OF REPORT: The Acute Inhalation Toxicity of Select 2.0 EC (CC-14900) in Rats

AUTHOR(S): Bagos, A.C., Stine, E.R.

REPORT ISSUED: July 2, 1990

CONCLUSION:

Inhalation exposure to an aerosol (1.6 mg/L) of Select 2EC for 240 minutes to five male and five female rats produced no increase in mortality. Clinical signs of note for all exposed animals were an immediate reduction in motor activity during and immediately following exposure, ataxia up to 75 minutes post-exposure (PE) and abnormal respiratory sounds lasting up 12 days PE.

Toxicity Category: III

Core Classification: Guideline.

LC_{50} > 1.6 mg/L

MATERIALS:

1. Test compound: Description - amber liquid. Batch # - SX-1839, Purity -26.6% by weight.

2. Test animals: Species: rat, Strain: Sprague-Dawley, Age: (at time of exposure), males = 85 days, females = 82, Weight: males = 382-429 g, females = 230-261 g, Source: Bantin and Kingman, Inc., Fremont, California.

5

METHODS:

A copy of the materials and methods is attached. Five rats of each sex were exposed (whole-body) for 240 minutes to an aerosol of undiluted test material. The aerosol was produced with an Ohio High Output Pneumatic Nebulizer. The amount of total aerosol in the chamber was estimated gravimetrically. The concentration of RE-45601 in the chamber atmosphere was determined from samples of air taken during the exposure. Particle size of the aerosol was determined by drawing chamber atmosphere through a multijet cascade impactor. Animals were observed, approximately every 30 minutes during exposure, following removal from the exposure caging and twice daily thereafter for a total of 14 days. Rats were weighed before the exposure and on days 2, 7 and 14 post-exposure. Gross necropsy was performed on all animals (none died) on study on day 15. Histopathology was performed on the lungs and trachea of all animals.

Signed and dated statements for GLPs and Quality Assurance were included.

RESULTS:

The average total aerosol concentration was 4.4 mg/L and the the average concentration of Cab-14900 was 2.4 mg/L. The concentration in the test chamber was 1.6 mg/L. The average mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD), established by gravimetric analysis, were 2.9 μm and 2.0 μm, respectively. The average MMAD and GSD, based on chemical analysis, were 2.8 and 2.0 μm, respectively. Approximately 97% of the aerosol was smaller than 10 μm based upon results from both analyses. Thus, the test material was quite respirable.

Test chamber temperatures ranged from 21.0 to 21.5°C and the relative humidities ranged from 49 to 52%. These ranges are quite acceptable.

No deaths were noted during the study. The only clinical sign of toxicity noted at 25 minutes into exposure up to 25 minutes postexposure (PE) was decreased motor activity (5males/5 females). Wet fur due to aerosol deposition (all animals), colorless nasal discharge (2 males/5 females) and ataxia (all animals) were noted from 5 to 75 minutes PE. Salivation residue was observed in all animals from 5 minutes PE till 1 day PE. Longer lasting toxicological signs observed up to 12 days PE included abnormal respiratory sounds (all animals), red nasal discharge (all animals), yellow anogenital discharge (4 males/5 males), colorless anogenital discharge (2 males), unkempt appearance (all rats), hyperactivity (1 male), diarrhea (3 females) and red ocular discharge (1 male/1 female). All animals appeared normal by 10 (males) to 13 days (females) PE.

Mean body weights were decreased at day 2 in both sexes as compared to pre-exposure values (368 g/males, 221 g/females vs 408 g/males, 246/females, controls, respectively) but were somewhat elevated over pre-exposure values by day 14 (approximately 6%).

Gross necropsy showed that all animals were within normal limits of appearance. Two of five males had a focal trace of vascular calcification upon microscopic examination of the lungs. No abnormal findings were observed in either sex for the trachea.

CLETHODIM

Page_____ is not included in this copy.

Pages 8 through 11 are not included.

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 quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X 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.