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Chemical:	**1H-1,2,4-Triazole, 1-((2-(2,4-dichloroph**
PC Code:	**122101**
HED File Code	**13000 Tox Reviews**
Memo Date:	**10/16/2001**
File ID:	**TX050197**
Accession Number:	**412-02-0281**

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05/10/2002

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

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: October 16, 2001

TXR #: 0050197

SUBJECT: Propiconazole

FROM: Abdallah Khasawinah, Ph.D., Toxicologist
Reregistration Branch 4
Health Effects Division (7509C)

TO: Eric Olson/Robert McNally (PM-60)
Reregistration Branch
Special Review and Reregistration Division (7508C)

THRU: Sanjivani Diwan, Ph.D., Senior Toxicologist
and
Susan V. Hummel, Branch Senior Scientist
Reregistration Branch 4
Health Effects Division (7509C)

TASK ID: DP Code:D272610 Submission: S591835
P.C. Code: 122101 MRID: 41594801 & 93194028

Registrant: Syngenta Crop Protection, Inc., 410 Swing Road, P.O. Box 18300, Greensboro, NC 27419

Action Requested: Prepare DER for acute inhalation study (MRIDs 41594801 & 93194028)

Agency's Response: HED toxicologists have reviewed the acute inhalation toxicity study of propiconazole in rats (See the attached DER). The study is classified **acceptable/guideline**. The LC_{50} of CGA 64250 (propiconazole) is >5.84 ± 0.19 mg/l for both male and female rats. CGA 64250 was placed in inhalation Toxicity Category IV. Below is the executive summary:

EXECUTIVE SUMMARY:

In an acute Inhalation toxicity study (MRID 41594801 & 93194028) Tif:Raif (SPF) rats (5/sex/dose) were exposed (nose only) for 4 hours to aerosols of CGA 64250 technical (91.9% purity; batch number op 412127) in absolute ethanol at 0 (control group) or 5.84 ± 0.19 mg/l (test group). The rats were observed during exposure and at regular intervals for 14 days for signs of toxicity and mortality. 57-64% of airborne aerosol particles were smaller than 3 μm in diameter.

All animals in the control and test group survived the treatments.

Slight to severe symptoms of ruffled fur, dyspnea, abnormal body positions and reduced spontaneous activity were seen in both sexes of the test material exposed group during the first 8 days of the post exposure. All animals exposed to the test article recovered on the 9th day and no symptoms were reported. Symptoms in the control group occurred during the exposure and recovered within a day.

The males exposed to the test article had significantly lower body weight gain than the controls (66% of the control group on day 7 and 83% of the controls on day 14). Female body weights of the treated group were comparable to the controls.

All animals were subjected to gross necropsy examination at day 14 and there were no adverse findings seen.

The LC_{50} of CGA 64250 is >5.84 ± 0.19 mg/l for both male and female rats. CGA 64250 was placed in Toxicity Category IV.

The study was classified **Acceptable** and it meets the Guideline requirements OPPTS 870.1300 [§81-3] for an acute inhalation toxicity in rats.

cc: Ray Kent, Branch chief HED RRB4

EPA Reviewer: Abdallah Khasawinah, Ph.D. A. Khasawinah Date Oct. 16, 2001
Reregistration Branch 4 (7509C)
EPA Secondary Reviewer: Sanjivani Diwan, Ph.D. S Diwan Date Oct 17, 2001
Reregistration Branch 4 (7509C)
TXR #: 0050197

DATA EVALUATION RECORD

STUDY TYPE: Acute Aerosol Inhalation Toxicity Study - Rat; OPPTS 870.1300 [§81-3]

DP BARCODE: D272610 SUBMISSION CODE:S591835
P.C. CODE:122101 TOX. CHEM. NO.:323EE

TEST MATERIAL (PURITY): CGA-64250 technical (91.1% purity)

SYNONYMS: Propiconazole, TILT, 1-[[2-(2',4'-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]-methyl]-1H-1,2,4-triazole

CITATION: Hartmann, H., 1988. CGA 64250 Technical: Acute Aerosol Inhalation Toxicity in Rats. Study No. 871471, Ciba-Geigy Ltd, Switzerland. January 14, 1988. MRID 41594801. Unpublished.

Gillis, J; Tisdel, M. 1990. Phase 3 Summary of MRID 41594801. Acute Inhalation Toxicity in the Rat. Study No. 871471. Prepared by Ciba- Geigy Ltd., July 10, 1990. MRID No. 93194028. Unpublished

SPONSOR: Ciba-Geigy Corporation

EXECUTIVE SUMMARY:

In an acute Inhalation toxicity study (MRID 41594801 & 93194028) Tif:Raif (SPF) rats (5/sex/dose) were exposed (nose only) for 4 hours to aerosols of CGA 64250 technical (91.9% purity; batch number op 412127) in absolute ethanol at 0 (control group) or 5.84 ± 0.19 mg/l (test group). The rats were observed during exposure and at regular intervals for 14 days for signs of toxicity and mortality. 57-64% of airborne aerosol particles were smaller than 3 µm in diameter.

All animals in the control and test group survived the treatments.

Slight to severe symptoms of ruffled fur, dyspnea, abnormal body

positions and reduced spontaneous activity were seen in both sexes of the test material exposed group during the first 8 days of the post exposure. All animals exposed to the test article recovered on the 9th day and no symptoms were reported. Symptoms in the control group occurred during the exposure and animals recovered within a day.

The males exposed to the test article had significantly lower body weight gain than the controls (66% of the control group on day 7 and 83% of the controls on day 14). Female body weights of the treated group were comparable to the controls.

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The LC_{50} of CGA 64250 is >5.84 ± 0.19 mg/l for both male and female rats. CGA 64250 was placed in Toxicity Category IV.

The study was classified **Acceptable** and it meets the Guideline requirements OPPTS 870.1300 [§81-3] for an acute inhalation toxicity in rats.

COMPLIANCE: GLP and confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:
   Description: viscous brown liquid, 110 ppm solubility in water at 20°C
   Batch #: op 412127
   Purity: 91.1%.
   CAS #: 60207-90-1
   Concentration/homogeneity was determined as described below for test atmospheres.

2. Test animals: Species: Rat (male and female)
   Strain: Tif:Raif (SPF) hybrid of RII/1 x RII/2
   Age and weight at dosing: Young adult 7-8 weeks old; 194-232 grams
   Source: bred and raised on premises.
   Acclimation period: Minimum of 5 days before exposure.
   Diet: Rat chow (NAFAG 890 Tox, Switzerland) ad libitum
   Water: Tap water ad libitum
   Photo period: 12 hour day light cycle
   Temperature: 22 ± 2°C
   Relative humidity : 66 ± 10%
   Air changes: 15 changes/hour

B. STUDY DESIGN and METHODS:

1. In life dates - start: November 18, 1987; end: December 9 1987

2. Exposure conditions: Animals were exposed to aerosol of CGA 64250 in a nose-only exposure unit (developed by Battelle Research) for a period of four hours. The chamber was maintained at an exactly balanced pressure to prevent leakage of the test atmosphere from the system, as well as dilution with outside air. The test material was dissolved in absolute ethanol at 30% (w/w) concentration. The aerosol was generated in two pneumatic nebulizers arranged in parrel. Both units had a small aspirating reservoir (1-2 ml) and an attached bulk fluid container. The nebulizers were operated at 6 l/minute each (input pressure 76 and 58 kpa) and the aerosol was diluted with filtered humidified air to yield a total flow

of 32 l/min. Coarse particles were removed from the aerosol by means of a glass cyclone. The throughput of the test material/vehicle mixture was determined by weighing the nebulizer, reservoir and cyclone before and after aerosol generation.

The air flow through the chamber was measured with Brooks Sho-Rate flow meters and maintained at 32 l/min.

The aerosol concentration in the chamber was determined gravimetrically 5 times during the exposure period. The average concentration was 5.84 ± 0.19 mg/l. The mass median aerodynamic diameter (MMAD) was 2.3-2.6 microns and the geometric standard deviation (GSD)was 2.0-2.2, with 57-64% less than 3 microns.

3. Animal assignment and treatment - the dose group consisted of 10 rats (5/sex), which were allocated by random selection and approximately matched in weight. A control group of 5 rats/sex was exposed to an inhalation of absolute ethanol GR (Merck).

4. Observations and Records - Rats were observed during exposure at 1, 2 and 4 hours as well as 2 hours after the exposure and daily thereafter until 14 days after dosing. Animals were weighed prior to exposure (day 0) and on study days 7, and 14 days after dosing.

Gross pathological examinations were performed on all animals, which were killed after 14 days by intravenous injection of Vetanarcol with particular attention to the respiratory tract.

5. Statistics - Inhalation LC_{50} was not calculated because there were no mortalities. The body weights of treated animals and the controls were compared by analysis of variance.

II. RESULTS AND DISCUSSION:

A. Mortality - All animals in the control and test group survived the treatments.

B. Clinical observations - slight to severe symptoms of ruffled fur, dyspnea, abnormal body positions and reduced spontaneous activity were seen in both sexes of the test material exposed group during the first 8 days of the post exposure. All animals exposed to the test article recovered within 9 days. Symptoms in the control group occurred during the exposure and animals recovered within a day.

C. Body Weight - The males exposed to the test article had significantly lower body weight gain than the controls (66% of the control group on day 7 and 83% of the controls on day 14). Female body weights of the treated group were comparable to the controls.

D. Necropsy - There were no adverse findings at gross necropsy in any of the animals in the treated or control groups.

The LC_{50} is >5.84 ± 0.19 mg/l for both males and females

E. Deficiencies - This study contains no deficiencies. It is considered a limit test.

The study was classified **Acceptable** as a limit test and it does meet the Guideline requirements OPPTS 870.1300 [§81-3] for an acute inhalation toxicity in rats.