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DATA EVALUATION REPORT

Study Type: Repeated dose metabolism Tox. Chem No. 323EE

Accession No.: 265794

Test Material: CGA 64 250 fungicide

Synonyms: Tilt, propiconazole

Study Number: 12/86

Sponsor: Ciba Geigy

Testing Facility: Ciba Geigy Agricultural Division, Basle Switzerland

Title of Report: Effect of repeated oral administration of CGA 64 250 on the liver weight of male and female mice

Author: R. Bissig

Report Issued: Aug. 20, 1986

Conclusions:

Male and female mice were fed unlabeled CGA 64 250 for 21 days at doses of 5, 100, 2500 ppm CGA 64 250 followed by a single oral dose of 14C CGA 64250 at the corresponding dose level. Liver weights were recorded 4 days post ^{14}C dosing and were significantly increased in the high dose (2500 ppm) males and females. When presented as liver/body weight ratios, data for both males and females showed an increase in the high dose. A female animal treated with a single dose (equivalent to a daily dietary dose of 2500 ppm) only of ^{14}C CGA 64250 also showed an increase in absolute and relative liver weights.

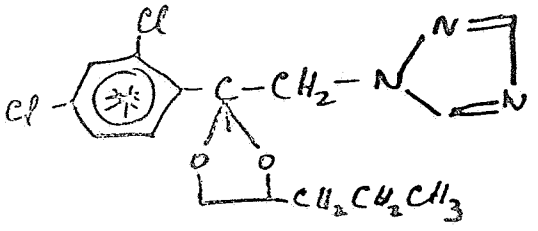
Core Classification: supplementary

A. Materials:

1. Test Compound:

Description: Labelled compound: Specific Activity = 56.9uCi/mg
Batch: GAN-VI-43
Supplier: H. Mory, N. Wigger
Purity: 92%, increased to 97% [redacted]

Structure:



Description: Unlabelled Compound:
Batch: OP 412127,
Purity: 91.1% [redacted]

Dilution of labelled compound to a specific activity of 18.9 uCi/mg and 17.8 uCi/mg for males and females respectively.

2. Test Animals:

Species: Mice

Strain: CD-1

Age: 4 weeks

Weight: 22-26 gms

Source: Charles River WIGA, GmbH, Switzerland, Germany

Study Design:

Animal assignments and study procedures:

Mice: 21 males (7/dose level) and 24 females (7/dose level at end of study). 2/sex were used as control. After dosing animals were kept in glass metabolism cages. Food containing the radioactive ^{14}C- test compound administration. After ^{14}C dosing animals were allowed food and water ad libitum. Urine and feces were collected at 24 hour intervals. 4 days post ^{14}C-dosing animals were killed and blood, liver, kidneys, lungs and remaining carcass were analyzed. Body weights were taken at weekly intervals.

Test Procedure:

Test material was mixed in the diet and given for 21 days. Test doses were 5, 100 and 2500 ppm. ^{14}C CGA 64 250 was dissolved in ethanol/polyethylene glycol 200/water (7/9/4 v/v). Dosing solution was 0.1 ml by stomach tube for mice. Labelled ^{14}C CGA 64 250 was equivalent to 5, 100 and 2500 ppm in the 24 hour food assuming a daily consumption of 5 gms for mice.
Livers were taken four days after ^{14}C dose was administered for comparison and two additional animals/group were maintained on standard diet for 21 days before being given a single oral dose of ^{14}C-CGA 64 250 corresponding to 2500 ppm in food.

Measurement of radioactivity is on appended pages 1-4. Procedures for thin layer chromatography, liquid chromatography, high performance liquid chromatography, spectroscopic methods, enzymatic hydrolysis and calculations are on appended pages 4-12.

Results:

Liver weights were significantly increased in high dose (2500 ppm) males and females. When presented as liver/body weight ratios, both high dose males and females showed increased liver weight ratios. The female animal treated with a single dose of only ^{14}C CGA 64 250 also showed an increase in absolute and relative liver weights. Data are on appended pages 1 and 2.

TILT CGA-64250 Reviews

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p. 4-5

The next 2 page(s) is/are not included in this copy of the TILT reviews.

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 commerical/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

X Detailed methods and results of a registrant submission.

___ Duplicate pages.

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