

(TXR 013599)

(8-3-99) 18

[CGA 279202 technical (trifloxystrobin)] Subchronic Oral Study (82-1)

EPA Reviewer: William B. Greear, MPH, DABT
Toxicology Branch II (7509C) Date:
EPA Secondary Reviewer: Jessica Kidwell, M.S.
Registration Action Branch 1 (7509C) Date:

DATA EVALUATION RECORD

STUDY TYPE: Subchronic Oral Toxicity-feeding-mouse
OPPTS 870.3100 [82-1]

DP BARCODE: D244009
P.C. CODE: 129112

SUBMISSION CODE: S538790
TOX. CHEM. NO.: N/A

TEST MATERIAL (PURITY): CGA 279202 technical (trifloxystrobin,
96.2%)

SYNONYMS: N/A

COMPLIANCE: Signed and dated GLP, Quality Assur
Confidentiality, and Flagging statements were in

CITATION: Gerspach, R. (1994) 3-Month Range Finding Toxicity
Study in Mice (Administration in Food): Short/Long-
term Toxicology, Novartis Crop Protection, AG, 4332
Stein, Switzerland. Test No. 933165, Novartis Nexus
No. 502-94, November 14, 1994. MRID 44496641.
Unpublished.

SPONSOR: Novartis Crop Protection, Inc., Greensboro, NC 27419

EXECUTIVE SUMMARY:

In a subchronic toxicity study (MRID 44496641) CGA 279202
technical (Batch KGL4617/5, 96.2%) was administered to 10 Tif:
MAGf (SPF) mice/sex/dose in the diet at dose levels of 0, 500,
2,000 or 7,000 ppm (0, 76.9, 315 or 1,275 mg/kg/day (M); 110, 425
or 1,649 mg/kg/day (F)) for 3 months. Survival, clinical signs,
body weight, food consumption, water consumption, hematology,
organ weights, gross necropsy and histopathology were determined.

One female in the 500 ppm group died on day 92, however,
according to the pathologist's report the death was not
treatment-related. Water consumption was increased in females at
7,000 ppm. Liver weight was increased in the 2,000 ppm (M-23%,
F-39%) and 7,000 ppm (M-30%, F-51%) groups. While the increase
was not significant in males at 2,000 ppm, there was a positive
trend by Jonkheere's test in this sex. Relative liver weight was
significantly increased in the 2,000 (M-15%, F-30%) and 7,000 (M-
40%, F-49%) ppm groups. Enlarged livers were observed in 2
females at 7,000 ppm. Enlarged spleens were observed in 2 females
at 2,000 ppm and in 6 females at 7,000 ppm. Hypertrophy of the
hepatocytes was observed in males (7) and females (10) at 7,000
ppm. Necrosis of hepatocytes was observed in males (3) and
females (2) in the 2,000 ppm group and in males (3) and
females (4) in the 7,000 ppm group. Splenic hemosiderosis was

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observed in males (5) and females (8) in the 7,000 ppm group. Splenic extramedullary hematopoiesis was observed in males (7) and females (9) at 7,000 ppm and in males (6) at 2,000 ppm, however, the biological significance in relationship to treatment is not known. The LOAEL is 2,000 ppm (315-425 mg/kg/day), based on increased absolute and relative liver weights in males and females and necrosis of hepatocytes in both sexes. The NOAEL is 500 ppm (76.9-110 mg/kg/day).

This subchronic toxicity study is classified **UNACCEPTABLE** because clinical chemistry values were not determined. The study does not satisfy the guideline requirement for a subchronic oral study (82-1) in mice. The study is not upgradable because of the absence of required clinical chemistry determinations and ophthalmological evaluation.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

COMMENTS:

There were no indications of neurotoxicity, immunotoxicity, endocrine disruption or increased sensitivity based on the age of the animal.

APPENDIX:

Study Date:

8/3/89

Study Period:

01-1989

MEAN ORGAN WEIGHTS				
Males				
Trifloxystrobin (ppm)				
Organ	0	500	2,000	7,000
Liver (g)	2.403	2.541	2.962 ⁺	3.112 ^{*+}
Females				
Trifloxystrobin (ppm)				
Organ	0	500	2,000	7,000
Liver (g)	1.824	1.999	2.531 ^{*+}	2.748 ^{*+}

Data taken from pp. 67-68 of 231, MRID# 44496641.

*p<0.01 (Lepage test)

+p<0.01 (Jonckheere's test)

[CGA 279202 technical (trifloxystrobin)]

Subchronic Oral Study (82-1)

SignOff Date: 8/3/99
DP Barcode: D243979
HED DOC Number: 013599
Toxicology Branch: TOX2