(TXR 013599) (8-3-99)

[CGA 279202 WG50] Dermal Sensitization Study (81-6)

EPA Reviewer: Ayaad Assaad, DVM, Ph.D. _____, Date _____
Toxicology Branch II (7509C)
EPA Secondary Reviewer: _____, Date _____
Toxicology Branch __ (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Skin Sensitization Test in the *Guinea Pigs-Buehler Test*

OPPTS Number: 870.2600 OPP Guideline Number: §81-6

DP BARCODE: D244009 SUBMISSION CODE: S538790
P.C. CODE: 129112 TOX. CHEM. NO.: N/A

TEST MATERIAL (PURITY): CGA 279202 *WG50 (A-9360 B) (trifloxystrobin, 50.8% a.i)*

SYNONYMS: *N/A*

CITATION: Winkler, G. (1996). Skin Sensitization Test in the *Guinea Pig*-Buehler Test, Lot No. P.509005. Novartis Crop Protection AG, Stein, Switzerland. Laboratory Project identification #: 963043. June 10, 1996. MRID 44496638. Unpublished.

SPONSOR: Novartis Crop Protection, Inc., Greensboro, NC. (Project # 487-96).

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44496637) conducted with CGA 279202 *WG50 (trifloxystrobin, 50.8% a.i, Lot #P.509005), young adult* (Tif:DHP) albino *guinea pigs* were tested using the Buehler Method. Two animal groups were utilized in this study, a test group (n=20, 10 males and 10 females), and a control group (n=10, 5 males and 5 females). Test animals were induced 3 times with the test article for 3 consecutive weeks at 50% concentration. Following 13-15 days rest, the animals were challenged with the test article at 10% concentration.

No dermal irritation was observed 24 or 48 hours following challenge to either previously-induced or naive control animals. Historical positive control data were provided to validate the test methodology. **In this study,** CGA 279202 *WG50 (trifloxystrobin)* **is not a dermal sensitizer.**

This study is classified as *acceptable (81-6), and* satisfies the guideline requirements for a dermal sensitization (Buehler test) study in the *guinea pig*.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, were provided. Flagging statements were not provided (not required by the guideline).

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## I. MATERIALS AND METHODS

### A. MATERIALS:

1. Test Material: CGA 279202 *WG50 (trifloxystrobin)*
   Description: Granules
   Lot/Batch #: P.509005
   Purity: *50.8%* a.i
   CAS #: 145701-21-9

2. Vehicle and positive control:
   The test article was dissolved in distilled water and applied to the skin using Hilltop chamber and occlusive dressing. No positive control group was included in the study. Historical positive control data were provided to validate the test methodology.

3. Test animals: Species: Albino *Guinea Pigs*
   Strain: Pirbright white strain (Tif:DHP)
   Age and Sex: 6-9 weeks old, males and females
   Weight at start of treatment: 305-399 g
   Source: Ciba-Geigy Limited, laboratory animal breeding, 4332 Stein, Switzerland.
   Acclimation period: At least 7 days
   Diet: Standard *Guinea Pig Pellets, NAFAG No.845, Gossau SG,* ad libitum
   Water: Municipal tap water, ad libitum
   *Housing: Individually, in Macrolon cages (Type 3)*
   *Environmental conditions: Temperature: 22 ±3°C*
   *Humidity : 30 to 70%*
   *Air changes: Not provided*
   *Photoperiod: 12 hr. light, 12 hr. Dark*

B. STUDY DESIGN and METHODS:

1. In life dates - start: April 24, 1996
end: May 23, 1996

2. Animal assignment and treatment - The study was conducted according to the Buehler method [Buehler, E., and H. Ritz; Current Concepts in Cutaneous Toxicity, p. 28 (1980)].

Dosing for the epidermal application was based on the results of a preliminary irritation screening study conducted in two animals with three different concentrations of the test article dissolved in distilled water 10, 30 and 50%. The concentration of 50% was the highest possible in distilled water, while the 10% concentration was the non-irritant dose. Therefore, the 50% concentration was selected for epidermal induction, and the 10% for challenge.

The epidermal induction phase (Weeks 1, 2 and 3), consisted of three applications on the same skin site (right flank) of 50% solution of the test article in distilled water (~ 90 mg a.i/animal, calculated by the reviewer) for 6 hours each (weeks 1 to 3) and a rest period of 13-15 days, followed by a challenge at week 5. The test article was loaded into a 0.35 ml volume Hilltop chamber secured with self adhesive material to the site of epidermal application. The control group was treated identically with distilled water in the occlusive chamber.

For the challenge phase (Week 5), the test and control groups were tested similarly with 10% CGA 279202 WG50 dissolved in distilled water (~ 18 mg a.i/animal) on the test flank, and on the other flank with distilled water only.

The guinea pigs were observed for dermal reactions 24 and 48 hours after removing the dressings.

Skin reactions were scored according to the following modified Draize scale for erythema formation:

0 - No erythema
± - Patchy erythema (non-confluent), doubtful reaction
1 - Slight confluent erythema on less than two third of the application area
2 - Slight to moderate confluent erythema on at least two third of the application area
3 - Moderate to strong confluent erythema

±, 0 - Negative reactions
1, 2, 3 - Positive reaction

Body weights of all animals were recorded at the start and termination of the study.

II. **RESULTS AND DISCUSSION:**

A. Induction reactions and duration - *No dermal reactions were observed in the animals in the test group when administered the test material during the induction phase of this study.*

B. Challenge reactions and duration - No dermal irritation was observed 24 or 48 hours following challenge to either previously-induced or naive control animals. Based on the results of the current study, CGA 279202 *WG50* is not considered to be a dermal sensitizer in *guinea pigs when tested by the Buehler method.*

C. Positive control - No positive control group was included in this study, however, historical positive control data were provided.

D. Deficiencies - Except for omitting the actual dose of test compound used/animal, and calculated by the reviewer, *no major deficiencies were detected in the current study.*

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