(8-3-99)

[CGA 279202] (Tox# 013599) 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: Dermal Sensitization (Maximization Test)-*Guinea Pigs*
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 *Technical (trifloxystrobin, 96.4% a.i)*

SYNONYMS: *N/A*

CITATION: Marty, J. (1994). Skin Sensitization Test in the *Guinea Pig*-Maximization Test, Lot No. P.405009. Novartis Crop Protection AG, Stein, Switzerland. Laboratory Project identification #: 943047. September 28, 1994. MRID 44496637. Unpublished.

SPONSOR: Novartis Crop Protection, Inc., Greensboro, NC. (Project # 496-94).

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44496637) conducted with CGA 279202 *Technical (trifloxystrobin, 96.4% a.i, Lot #P.405009), young adult* (Tif:DHP) albino *guinea pigs* were tested using the Maximization Test. 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).

Dermal irritation and reactions, characterized by erythema and edema, were observed 24 and 48 hours in 85 and 80%, respectively, of the animals in the test group following challenge to previously-induced sites. Historical positive control data were provided to validate the test methodology. **According to the maximization grading of Magnusson and kligman utilized in this study, CGA 279202 *Technical (trifloxystrobin)* is a strong dermal-sensitizing chemical, with contact allergenic potential in the guinea pigs.**

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

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, were provided. Flagging statements were not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: CGA 279202 *Technical (trifloxystrobin)*
   Description: Light brown powder
   Lot/Batch #: P.405009
   Purity: *96.4%* a.i
   CAS #: 145701-21-9

2. Vehicle and positive control:
   Sterile physiological solution, complete Freund's adjuvant, white petroleum Vaseline, and oleum arachidis (peanut oil), were used individually or in the following mixtures to treat both test and control animals:
   a. Adjuvant/saline mixture 1:1 (v/v)
   b. 5% CGA 279202 tech. In oleum arachidis (w/v)
   c. 5% CGA 279202 tech. In the adjuvant/saline mix. (w/v)
   d. 50% CGA 279202 tech. In Vaseline
   e. 30% CGA 279202 tech. In Vaseline
   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: Young adults, males and females
   Weight at start of treatment: 350-436 g
   Source: Ciba-Geigy Limited, animal production, 4332 Stein, Switzerland.
   Acclimation period: At least 6 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: August 16, 1994
end: September 8, 1994

2. Animal assignment and treatment - The study was conducted according to the original protocol of Magnusson and Kligman (J. Invest. Dermatol. 52, 268-276, 1969; Contact Dermatology, 6, 46-50, 1980).

Dosing for the intradermal injections was selected based on the solubility of the test article in standard vehicles and its local and systemic tolerability in a pretest, no details were provided regarding that pretest. It was stated that 5% (w/v) of the test article in oleum arachidis could be injected, and well tolerated intradermally in the selected animal model. This concentration of the test article was used in the definitive study.

Dosing for the epidermal application was based on the results of a preliminary irritation screening study conducted in two animals with two different concentrations of the test article in Vaseline, 30 and 50%. Skin reactions were observed with 50% conc. Of the test article.

For the intradermal induction phase (Day 0), 3 pairs of intradermal injections (0.1 ml/each) were made simultaneously into the left and right side of the shaved neck of the test and control animals. For the test group, each pair of intradermal injection site received either: adjuvant/saline mixture 1:1 (v/v), 5% CGA 279202 tech. in oleum arachidis (w/v), or 5% CGA 279202 tech. in the adjuvant/saline mix. (w/v). The control group received either: adjuvant/saline mixture 1:1 (v/v), in the first and second sites, or oleum arachidis.

For the epidermal induction phase (Day 8), after cleansing the application sites 24 hours prior to epidermal application, animals in the test group received 0.4 g of the test article in Vaseline (50% w/w). The control group received Vaseline only. Both test article and control material were applied on a filter paper patch to the neck by occluded administration for 48 hours.

For the challenge phase (Day 21), the test and control groups were tested on one flank with 30% CGA 279202 tech. In Vaseline (w/w), and on the other flank with the vehicle only. Both materials were applied on a

filter paper patch (0.2 g/patch) by occluded administration for 24 hours.

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

Skin reactions were scored according to the following Draize for erythema and edema formation scoring scale:

Erythema and eschar formation:
0 - No erythema
1 - Very slight erythema
2 - Well defined erythema
3 - Moderate to severe erythema
4 - Severe erythema to slight eschar formation

Edema formation:
0 - No edema
1 - Very slight edema
2 - Slight edema
3 - Moderate edema
4 - Severe edema

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

II. **RESULTS AND DISCUSSION:**

A. Induction reactions and duration - *Dermal reactions were observed 48 hours following epidermal application (Day 10 of the study) in all animals in the test (20/20) and control (10/10) groups.*

B. Challenge reactions and duration - Dermal irritation and reactions, characterized by erythema and edema, were observed 24 and 48 hours in 85 and 80%, respectively, of the animals in the test group following challenge to previously-induced sites. Based on the results of the current study, and according **to the maximization grading of Magnusson and kligman utilized,** CGA 279202 *Technical (trifloxystrobin)* **is a strong dermal-sensitizing chemical, with contact allergenic potential in the guinea pigs.**

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

D. Deficiencies - *No major deficiencies were detected in the current study.*

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