

1/19/1996  
[81-6. Pirimicarb 500g/kg DG [inert ingredient information not included] Formulation: Dermal Sensitization-guinea pig/1991]

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#### DATA EVALUATION REPORT

**STUDY TYPE:** Dermal Sensitization - Guinea pig/81-6

**TOX. CHEM. NO.:** 359C

**P. C. NO.:** 106101

**MRID NO.:** 43498707

**TEST MATERIAL:** Pirimicarb 50 DG Formulation [inert ingredient information not included]

**SYNONYMS:** 2-(dimethylamino)-5,6-dimethyl-4-pyrimidinyl dimethylcarbamate

**STUDY/REPORT NUMBERS:** GG5292 (Main study) & GG5254 (Positive control)/CTL/P/3410

**SPONSOR:** Zeneca Inc.  
Wilmington, DE 19897

**TESTING FACILITY:** Imperial chemical Industries, PLC  
Alderley Park  
Macclesfield, Cheshire  
UK

**TITLE OF REPORT:** Pirimicarb: Skin Sensitization to the Guinea Pig of a 500g/kg DG Formulation

**AUTHOR:** R.J. Parr-Dobrzanski

**STUDY COMPLETION DATE:** June 17, 1991

**EXECUTIVE SUMMARY:** In a dermal sensitization study (Buehler method), thirty female guinea pigs were divided into two groups of 20 treated and 10 controls and were induced at weekly intervals for a total of 3 treatments with 0.4ml, 75% Pirimicarb 500g/kg DG Formulation [inert ingredient information is not included] in corn oil or corn oil only (control group). All guinea pigs (tested and control) were challenged 2 weeks after the last induction dose by applying 0.1 to 0.2 ml of 75% (w/v) and 30% (w/v) test substance in corn oil. Twenty-four and 48

INERT INGREDIENT INFORMATION IS NOT INCLUDED

hours after application of the challenge dose, the guinea pigs were evaluated for dermal reactions. Formaldehyde in deionized water was used as a positive control [MRID No.: 43498707; Study Nos.: GG5292 (main), GG5254 (positive control)].

Challenge with 75% (w/v) and 35% (w/v) of test substance in corn oil did not elicit a skin sensitization response in previously induced guinea pigs (score - 0). Positive control formaldehyde induced extreme skin sensitization response (17/20; 85%). **Based on the response, Pirimicarb 500 g/kg DG Formulation is not a sensitizer to guinea pig skin.**

This study is classified as **core-Acceptable** and **satisfies** the requirements, for a series § 81-6 dermal sensitization study in guinea pig.

#### **MATERIALS:**

1. **Test Compound:** Pirimicarb 500g/kg DG formulation, *[inert ingredient information not included]* Lot # was not given, however codified as sample ref: RS 641/H, Formulation Ref. YF7904; Purity: 49.6%, and described as blue/green solid, was used in this study. Formaldehyde (40% w/v aqueous solution) was used as positive control.
2. **Test Animals:** Species: Guinea pig, Strain: Young adult Dunkin Hartley, Weight: 333 - 421g females for the main study and 337 to 450g males for the positive control study, Source: ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK. The animals were housed individually in suspended cages and maintained at a temperature of 19°C ± 2°C, a relative humidity of 55 ± 10% and to a 12-hour dark/light cycles. Air was changed 20 - 30 times per hour. The guinea pigs were acclimated for 6 days to the laboratory environment. Labsure RGP guinea Pig Diet and water was provided ad libitum.

#### **METHODS:**

Thirty acclimated female guinea pigs were divided into two groups of twenty treated and ten controls. Doses selected for main study were based on preliminary investigations in which 75% suspension did not produce irritation. Positive controls (males) were run at a different time, utilized 20 test and 10 controls. The sensitizing properties of the test substance were assessed using the method described by Buehler (1965).

INERT INGREDIENT INFORMATION IS NOT INCLUDED

### Induction:

Induction phase consisted of treating guinea pigs with 0.4ml of either a 75% (w/v) preparation of the formulation in corn oil or corn oil only (control group) applied topically under a 2cm<sup>2</sup> lint pad to clipped (5cm<sup>2</sup>) scapular region and secured in place using occlusive dressing for 6 hours. The treatment was repeated weekly at the same site for a total 3 applications. Positive control 30% formaldehyde in deionized water was used but the study was run at different time but essentially followed the same procedure as used in the main study.

### Challenge:

After 2 weeks the test and naive animals were exposed to 0.1 to 0.2 ml of 75% (w/v) and 30% (w/v) preparation of formulation in corn oil to the shaved flank areas and was held in place using occlusive dressing for 6 hours; 75% formulation was always applied to the left flank area. The positive control animals received 10% formaldehyde in deionized water. Twenty-four and 48 hours after application of challenge dose, the guinea pigs were evaluated for dermal reactions on a 4 point scale (0 = no reaction, 1 = scattered mild redness, 2 = moderate diffuse redness, and 3 = intense redness and swelling).

The sensitivity response was expressed as percentage of the test animals that gave response greater than the maximum seen in control animals. Following is the evaluation criteria:

<u>% net response</u>	<u>description</u>
0	not a sensitizer
1-8	weak sensitizer
9-28	mild sensitizer
29-64	moderate sensitizer
65-80	strong sensitizer
81-100	extreme sensitizer

### QUALITY ASSURANCE:

A statement Quality Assurance Unit, a statement of GLP Compliance and a statement of Confidentiality of Data were attached.

### RESULTS:

Signs of moderate irritation including scabbing, thickening of the skin, desquamation, oedema, and erythema were seen in

test animals during the induction phase of the study. No signs of irritation were seen in any control animals. Following challenge with either 75% or a 30% w/v preparation in corn oil, no skin response was elicited in test or control animals (score - 0).

Positive control formaldehyde 10% w/v in aqueous solution produced mild redness to moderate diffuse redness in 17/20 animals; the % response is 85%.

#### DISCUSSION:

The data reporting was thorough and the summary means were supported by individual animal data. Positive control study was run at a different time than the main study; the date of the study was not provided. Although the studies were run at different times, the interpretation of the study was not compromised. Based on the results, Pirimicarb 500g/kg DG Formulation is not a sensitizer to guinea pig skin.

This study is classified as **core-Acceptable** and **satisfies** the requirement, for a series § 81-6 dermal sensitization study in guinea pig.

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