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DATA EVALUATION REPORT

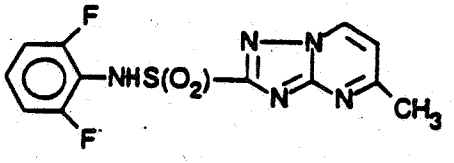
STUDY TYPE: Dermal Sensitization in the Guinea Pig (Guideline 81-6)

EPA IDENTIFICATION NOS.:
MRID NO.: 419938-09
HED PROJECT NO.: 1-2384
CASWELL NO.: 889

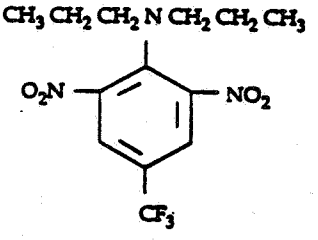
TEST MATERIAL: XRM-5313

SYNONYMS: Formulation containing: 2.6% XRD-498 [N-(2,6-difluorophenyl)-5-methyl(1,2,4)triazolo(1,5a) pyrimidine-2-sulfonamide] and 35.8% Trifluralin (Treflan; α,α,α-trifluoro-2,6-dinitro-N,N-dipropyl-p-toluidine)

XRD-498:



Trifluralin:



STUDY NUMBER: M-005313-002E

SPONSOR: DowElanco
9002 Purdue Road
Indianapolis, Indiana 44268-1189

TESTING FACILITY: The Toxicology Research Laboratory
Health and Environmental Sciences
The Dow Chemical Company
Midland, Michigan 48674

TITLE OF REPORT: XRM-5313: Dermal Sensitization Potential in the Hartley Albino Guinea Pig

AUTHORS: N.M. Berdasco

DATE REPORT ISSUED: May 31, 1991

SUMMARY/CONCLUSION: A 0.4 ml aliquot of a 50% solution of the test material in dipropylene glycol monomethyl ether, XRM-5313, was applied (once weekly for a total of 3 weeks) to the shaved skin of 10 Hartley albino guinea pigs. After 30 days, a challenge dose (0.4 ml of a 50% solution) was applied and dermal reactions were scored. The test material produced slight to moderate erythema in all ten animals tested and was judged to be a sensitizing agent under the conditions of this study. It was suggested by the study author that the

potential of XRM-5313 to cause a delayed hypersensitivity reaction in the guinea pig may be related to the reported sensitization activity of one of the active ingredients of the test substance, trifluralin.

Core Classification: Minimum

MATERIALS:

1. Test compound: Description: Orange liquid
   Sample reference: AGR 291670
   Source: DowElanco, Midland, Michigan
   Active ingredients: 2.6% XRD-498 and
   35.8% Trifluralin

2. Vehicle control: Material: Dipropylene glycol monomethyl ether
   Source: Not provided

3. Positive control: Material: DER 331 epoxy resin
   Vehicle: Dipropylene glycol monomethyl ether
   Source: Not provided
   Description: Not provided
   Purity: 10% solution

4. Test animals: Species: Guinea pig
   Strain: Hartley albino
   Source: Charles River Breeding Laboratories, Inc.
   Kingston, Michigan
   Age: Not provided
   Weight: 312-369 g
   Sex: Male

METHODS:

Range-finding primary irritation study:

Dose selections for the induction and challenge phases were based on the results of a range-finding test in which 0.4 ml aliquots of either 100%, 50%, 25%, or 10% XRM-5313 in dipropylene glycol monomethyl ether were topically applied to the skin of two guinea pigs for 6 hours. The treated skin was examined for erythema and edema approximately 24 and 48 hours posttreatment.

Induction phase:

Approximately 24 hours prior to the first test substance application, the left side of each guinea pig was clipped free of hair. A 0.4 ml aliquot of 50% XRM-5313 was applied to the left side of ten guinea pigs in Hill Top Chambers. A 10% solution of DER 331 epoxy resin in dipropylene glycol monomethyl ether was applied in a similar manner to another group of 10 guinea pigs and served as the positive control. The chambers were secured with non-irritating tape and removed after approximately 6 hours. Observations of erythema and edema were recorded the following day. The treatment regimen as described above was repeated once weekly for a total of three consecutive weeks.

Challenge phase:

Approximately two weeks after the last induction application, the right side of the animals was clipped free of hair and the 50% test solution or 7.5% DER 331 was applied to the right side of the guinea pigs in the same manner as in the induction phase. (The concentration of DER 331 was decreased from 10% to 7.5% due to erythema observed at the application site of seven animals following the third induction dose.) The chambers were removed after approximately 6 hours of exposure, and the following day the application sites were depilitated. Blind observations and gradings for sensitization response were conducted approximately 24 and 48 hours postchallenge.

Initial (Day 1) and terminal (Day 30) body weight values were recorded.

RESULTS:

Range-finding primary irritation study:

At 24-hours posttreatment, slight erythema was observed in guinea pigs treated with 0.4 ml of undiluted XRM-5313. Solutions of 50%, 25%, and 10% did not produce signs of irritation. A 50% solution of the test material in dipropylene glycol monomethyl ether was selected for induction treatment in the main sensitization study.

Main test for sensitization:

Body weight data:

Mean body weight values were similar between control and treated animals (Table 1). All animals gained weight during the duration of the study.

Table 1. Mean body weight values (g)

Dose group		Day 1	Day 30
Test material: 50% XRM-5313	Mean	336.8	505.2
	S.D.	12.3	39.3
	N	10	10
Positive control: 10%/7.5% DER 331	Mean	327.8	514.0
	S.D.	16.7	55.6
	N	10	10

Note: Data were extracted from report No. M-005313-002E, page 14.

Dermal observations:

Dermal scores are presented in Table 2.

During the induction phase of the study (observations performed one day after application on Weeks 1-3), no signs of dermal irritation were noted in guinea pigs treated with a 50% solution of the test substance. Slight to marked erythema was noted on the DER 331-treated skin.

Following challenge treatment on Day 30 of the study, examination at 24 and 48 hours posttreatment showed slight to moderate erythema on the treatment sites of guinea pigs treated with the test substance and the positive control material.

Table 2. Individual dermal observations

Treatment Group	Erythema/Edema After Induction			Erythema/Edema After Challenge		Animal Response
	Week 1	Week 2	Week 3	24 Hrs	48 Hrs	
50% XRM-5313	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	2/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
10%/7.5%a DER 331	0/0	0/0	1/0	1/0	1/0	+
	0/0	0/0	0/0	0/0	0/0	-
	0/0	0/0	1/0	1/0	1/0	+
	0/0	0/0	1/0	1/0	1/0	+
	0/0	0/0	1/0	1/0	1/0	+
	0/0	0/0	1/0	2/0	1/0	+
	0/0	0/0	0/0	1/0	1/0	+
	0/0	0/0	2/1	2/0	1/0	+
	0/0	0/0	0/0	0/0	1/0	+
	0/0	0/0	1/0	1/0	1/0	+

Erythema/Edema
0 = None
1 = Slight
2 = Moderate
3 = Marked

Response
- = Negative
+ = Positive

a A 10% solution of the positive control (DER 331) material was applied for the induction phase; this was decreased to 7.5% for the challenge phase.
Note: Data were extracted from report No. M-005313-002E, page 15.

STUDY DEVIATIONS:

The source of the positive control and vehicle materials was not provided as required by EPA FIFRA GLP.

COMPLIANCE:

The following signed and dated statements were included:
Statement of No Data Confidentiality
GLP Compliance Statement
Flagging Statement (negative)
Quality Assurance Statement

DISCUSSION:

The criteria used to determine whether or not a substance was considered to be a sensitizing agent were that 2 or more of the 10 treatment animals show a positive reaction. Therefore, DER 331, the positive control material, showed clear evidence of sensitization, and the test material, XRM-5313, also met those criteria. The test substance was considered to be a sensitizing agent under the conditions of this study.

According to the study author, "one of the active ingredients, trifluralin, has been shown to cause dermal sensitization in guinea pigs (E. Adams, DowElanco, personal communication)."