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DATA EVALUATION REPORT

STUDY TYPE:	Acute Dermal Sensitization Study (81-6)
MRID NUMBER:	410826-04
TEST MATERIAL:	INV-9360-7
STUDY NUMBER:	Medical Research No. 4581-469 Haskell Laboratory Report No. 429-87
HED PROJECT NUMBER:	9-2188
SPONSOR:	E.I. du Pont de Nemours and Company Inc.
TESTING FACILITY:	E.I. du Pont de Nemours and Company Inc. Haskell Laboratory for Toxicology and Industrial Medicine Elkton Road, P.O. Box 50 Newark, Delaware 19714
TITLE OF REPORT:	Closed-Patch Repeated Insult Dermal Sensitization Study (Buehler Method) with INV-9360-7 in Guinea Pigs
AUTHOR:	William J. Brock
REPORT ISSUED:	September 9, 1987 Date Revised: October 23, 1987
CONCLUSIONS:	It appears that no sensitization reaction occurred under the conditions of the study as described above. Classification of Data: Core-guideline

METHODS:

A liquid test formulation containing INV-9360-7 (a white powder, 94.9% pure, Medical Research No. 4581-469) as a 40% w/v suspension in 80% ethanol, was evaluated for dermal sensitization potential using the Buehler method.

Young adult male and female Duncan Hartley albino guinea pigs (Charles River Breeding Laboratories, Stone Ridge, New York) were used in this study. They were housed singly in suspended stainless steel cages with temperature, relative humidity and light cycle being regulated. The guinea pigs were weighed and observed for general health during a quarantine period of approximately one week. They were also weighed at the end of the study. All animals were euthanatized at the end of the study.

RANGE-FINDING STUDY

Initially a range-finding test was carried out with four guinea pigs ranging from 412 to 484g so as to determine the primary irritation potential of the test material. Aliquots of 0.4 ml of 40% (a maximal practical test concentration based on solubility), 20%, 10%, and 5% w/v suspension of the test material in 80% ethanol (in water) were applied onto the shaved intact skin of each animal's back in Hill Top Chambers. A piece of plastic wrap was placed over the patch and the animals were then wrapped with adhesive bandage. After a six-hour exposure period all wrappings and patches were removed, the test sites gently washed with warm water to remove excess test material. Irritation responses were scored approximately 24 hours post-treatment.

INDUCTION PHASE

Test article:

0.4 ml of a 40% w/v suspension of the test material in 80% ethanol (in water) was applied onto the shaved intact skin of twenty guinea pigs (ten male and ten female, weighing 363 to 556 g) in Hill Top Chambers (patches), covered with plastic wrap and secured with adhesive bandage. This procedure was performed once a week for three consecutive weeks, exposing the animals for six hours at a time, after which irritation responses were scored.

Vehicle controls:

The same procedure was adopted for five male and five female guinea pigs, weighing 379 to 551g, which were treated with 0.4 ml of 80% ethanol (in water).

Positive controls:

Approximately two weeks before the study was initiated, the same procedure was adopted for three male and two female guinea pigs (weighing 411 to 506g), which were treated with 1-chloro, 2,4 -dinitrobenzene (DNCB) as a 0.5% suspension in 80% ethanol (in water), following which irritation responses were scored 24 and 48 hours after treatment.

CHALLENGE PHASE

Test article:

The twenty guinea pigs were challenged two weeks after the last induction treatment by applying 0.4 ml of a 40% w/v suspension of the test material in 80% ethanol (in water), using the same procedure as outlined above.

Vehicle controls:

The same procedure as during the induction phase was repeated two weeks later for the "vehicle control" guinea pigs (five males and five females weighing 379 to 551 g).

Positive controls:

The same procedure,(using a concentration of 0.3% suspension of DNCB in 80% ethanol in water), as during the induction phase, was repeated two weeks before for the "positive control" guinea pigs (three males and two females).

Negative controls:

Two male and two female guinea pigs, weighing 417 to 455 g were treated with 0.4 ml of the 40% w/v of the test material in 80% ethanol (in water).

Subsequently the test sites were depilated with Neet Hair Cream Remover 22 hours post-treatment. Irritation responses were noted 2 hours after depilation and 48 hours post-treatment. The animals were rechallenged one week later (with the exception of the positive control animals) adopting the same procedures and the same concentrations used in the challenge phase.

RESULTS:

RANGE-FINDING STUDY

Since no dermal irritation was noted at concentrations tested, the researchers used a 40% suspension of the test material in 80% ethanol.

INDUCTION PHASE

Test article:

Slight patchy erythema was observed in four test guinea pigs (4/20) after the second and third induction treatments.

Vehicle controls:

No dermal irritation noted.

Positive controls:

Slight/confluent or moderate/patchy erythema to severe erythema with necrosis and/or edema was observed in all the "positive control" guinea pigs (5/5), 24 and 48 hours aft er the second and third induction with 0.5% DNCB. No irritation was noted after the first induction treatment. At 24 hours following the third induction treatment, severe erythema with edema and necrosis was observed in all of the positive control guinea pigs. These effects were still evident at 48 hours although the edema had resolved.

CHALLENGE PHASE

Test article:

Slight, patchy erythema to slight/confluent or moderate patchy erythema was observed in the test animals at 24 hours (14/20) and 48 hours (18/20).

Vehicle controls:

No dermal irritation noted.

Positive controls:

Severe erythema with necrosis, blanching or edema was observed in all the "positive control" animals at 24 and 48 hours post-challenge (5/5).

Negative controls:

Slight, patchy erythema was observed in three out of four negative controls guinea pigs at 24 hours and in all four guinea pigs (4/4) at 48 hours.

RECHALLLENGE PHASE

Upon rechallenge with INV-9360-7 slight patchy erythema was observed in 1) the test guinea pigs (11/20 at 24 hours and 12/20 at 48 hours).

2) the "negative control" guinea pigs showed the same results upon rechallenge as for the challenge phase (3/4 at 24 hours and 4/4 at 48 hours).

CONCLUSIONS:

It appears that no sensitization reaction occurred under the conditions of the study as described above.

Classification of Data: Core-guideline