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Study: Dermal Sensitization Test with SC-0224 Technical

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CASWELL FILE

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Material Tested: SC-0224 Technical (56.3%)

Animals: Guinea Pigs, Male (Hartley strain)

The purpose of this study was to evaluate the potential for SC-0224 to cause dermal sensitization.

Materials and Methods:

Husbandry: Standard GLP

The open epicutaneous test (OET) procedure, described in Appendix I, was followed.

This particular procedure, developed in accordance with EPA Guidelines, includes a primary irritation phase, a 26-day induction phase and two challenge phases, days 29 to 31 and 44 to 46. The material was applied topically and left uncovered.

Further details of the test procedure are quoted as follows:

"During the induction phase, the material was applied in a volume (liquid) or mass (petrolatum) of 100 ul or mg, respectively, to an approximate area of 2 cm². The primary irritation and challenge applications were made to smaller area, 1 cm², in a volume or mass of 25 ul or mg. During the induction phase, each animal was exposed daily, 5 days per week for 4 weeks, to a single concentration of material. The material was applied to the right flank. Each animal was then challenged with concurrent applications of several concentrations of the material applied to the left flank. To minimize variations in response due to flank location, the various concentrations of test material were rotated among different application sites. The skin reactions were evaluated for erythema (redness) and edema (swelling) according to an 8-point scoring system. These evaluations were made 24 hours after application in the primary irritation test, at weekly intervals during induction, and daily for the 3 days following challenge and rechallenge applications.

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"Known sensitizers, formaldehyde and 2-mercaptobenzothiazole (2-MBT), were used as positive controls (3). Deionized water was used as the vehicle for SC-0224 Technical and formaldehyde while petrolatum (Plough, Inc.) was used as the vehicle for 2-MBT). Control and test solutions were prepared at weekly intervals. Negative control groups (animals induced with vehicle and challenged with chemical) were included for each positive control material and SC-0224 Technical. In addition, each animal served as its own control because a vehicle site was included at challenge and rechallenge.

"A group was considered to have a positive response if one or more animals exhibited an erythema score of 2 or greater. The material was considered to be a sensitizer if the challenge reaction was positive and greater than the irritation reaction. Irritation was determined from the primary irritation results and the challenge response of the appropriate vehicle group." (pp 1-2)

Table 1 reproduced from the study (p. 8) summarizes the exposures the various groups of 8 animals each received, including the induction, challenge and rechallenge phases.

Table 1

Group	Concentrations Applied (%)		
	Induction	Challenge	Rechallenge
SC-0224 Technical			
I	100	30,10,3,1,d.w. ^a	30,10,3,d.w.
II	30	30,10,3,1,d.w. ^a	30,10,3,d.w.
III	10	30,10,3,1,d.w. ^a	30,10,3,d.w.
IV	3	30,10,3,1,d.w. ^a	30,10,3,d.w.
V	1	30,10,3,1,d.w. ^a	30,10,3,d.w.
VI	0.3	30,10,3,1,d.w. ^a	30,10,3,d.w.
VII	d.w.	30,10,3,1,d.w. ^a	30,10,3,d.w.

32
33
2

Table 1 (cont'd)

Controls			
VIII	1% HCHO ^b	1% HCHO, d.w.	1% HCHO, d.w.
IX	d.w.	1% HCHO, d.w.	1% HCHO, d.w.
X	3% 2-MBT ^c	3% 2-MBT, Pet	3% 2-MBT, Pet
XI	Pet ^d	3% 2-MBT, Pet	3% 2-MBT, Pet

a d.w. = Deionized Water

b HCHO = Formaldehyde

c 2-MBT = 2-Mercaptobenzothiazole

d Pet = Petrolatum

Results:

Induction (Table p. 12)

With respect to the total 26-day induction phase, it was found that by day 12 there was a positive response, in terms of erythema in all 8 animals of Group I (high dose), where the average score was 2.1. Erythema was also observed in approximately 50 percent of the Group II animals during days 12 to 26 (score 1.5 to 1.8). One animal of 8 in Group III exhibited a positive reaction. There were no responses to SC-0224 reported in any other dose groups.

Formaldehyde (1%) at days 12 to 19 elicited a positive erythema response (score 1.3 to 1.9) in 7/8 of the animals treated, with the incidence declining by day 26 to 3/8. 2-MBT (3%) yielded a response (score 2.0) in only 1 of 8 animals by day 12. Surprisingly, the vehicle for 2-MBT yielded a positive response which increased in frequency from 3/8 on day 5 to 8/8 on day 19, then decreasing to 4/8 by day 26, scores ranged 1.6 to 2.0.

In summary, during the induction phase, 100 percent and 30 percent SC-0224, 1 percent formaldehyde and petrolatum vehicle (for 2-MBT) gave positive skin responses. Responses to 10 percent SC-0224 and 3 percent 2-MBT were equivocal.

Challenge (Table, p. 13)

When induced animals were challenged with 30 percent, 10 percent, 3 percent, and 1 percent SC-0224 and vehicle control (water), a dose response for erythema was observed in

terms of frequency of response (but not magnitude which remained around 2) both as a function of challenge and induction doses. In most cases the response frequency was highest at 24 hours postchallenge, declining (exhibiting progressive decline) at the 48- and 72-hour observation times. A very definite response was seen in the formaldehyde challenge of formaldehyde induced guinea pigs. Also, it should be noted that the magnitude of the response to the vehicle (water) challenge in the formaldehyde case was surprisingly high. A meaningful challenge response was not seen in the case of 2-MBT (2%).

In summary, dermal sensitization studies in which guinea pigs were induced with SC-0224 and subsequently challenged with the same material, it was demonstrated that animals induced by the five highest doses were sensitized in a dose dependent manner and responded to challenge concentrations of SC-0224 of as low as 10 percent.

Rechallenge (Table 7)

When induced animals were rechallenged with 30 percent, 10 percent, 3 percent, and 1 percent SC-0224 and vehicle control (water), a dose response in terms of erythema (both frequency and magnitude of response) was observed as a function of the induction and rechallenge doses. In most cases, the response frequency was highest at 24-hour postrechallenge, as was true in the case of challenges. Also, as before, a very definite response was seen in the case of formaldehyde rechallenge. A striking response was not seen with 2-MBT (3%) rechallenge.

In summary, the rechallenge findings were essentially the same as those of the original challenge study, with the exception that the magnitude of the erythema response tended to decline from about 2.0 at high induction doses to 1.0 for the lower induction doses.

Additional Comments

Appendix III of the study submitted, skin response data for individual animals, shows that edema was not observed in any of the challenge or rechallenge tests, and, hence, does not constitute a positive finding in this study of SC-0224.

Weight gain of the guinea pigs over the 46-day period of study did not reveal any remarkable compound-related effects. It should be noted, perhaps, that there may have been a slight tendency for the higher dosed animals, those exposed to 30 to 100 percent test material, to gain less weight.