



# Hoechst



Hoechst Aktiengesellschaft  
Pharma Research  
Toxicology  
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Skin tolerance of a preparation  
of 1 % Octopirox (Op. E 001), 0.3 % citric acid  
and 98.7 % 1,2-propylene glycol (pH 7)  
in New Zealand rabbits  
Report No. 765/79

## Summary

Under the experimental conditions described, skin tolerance tested by the patch test shows that according to FDA standards the present preparation is slightly irritant to the skin.

The 1,2-propylene glycol used as control was not irritant to the skin by FDA standards.

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Material and method:

Albino New Zealand rabbits (supplier P Erkrath) weighing 2.19 to 2.75 kg ( $\bar{x}$  = 2.54 kg) were used for the experiment. The animals were kept in individual cages and received a standard feed ERKA 8300 (Futtermittelwerk Robert Koch OHG, Hamm/Westf.). Feed and water were supplied ad libitum.

The preparation of 1 % Octopirox<sup>R</sup> - H 72 6146 A, 0.3 % citric acid and 98.7 % 1,2-propylene glycol was a clear solution. The pH was adjusted to 7. The vehicle, 1,2-propylene glycol was tested as control in the same animals.

The experiment was carried out from 26.11. to 29.11.1979.

Procedure:

Areas of at least 6 x 3 cm on both flanks of 6 rabbits were depilated with electric hair clippers. One half of the shorn area was also scarified.

0.5 ml of the solution or the vehicle were applied on pieces of gauze each 2.5 x 2.5 cm in size. The gauze was fixed to the prepared skin with a strip of adhesive plaster and covered with a sheet of inert, impervious PVC 6 - 8 cm wide. Finally a permanent elastic bandage (Dauerbinde<sup>R</sup> K) was wrapped round the body of the animal. Exposure time was 24 hours. The first assessment of the irritant effect was made immediately after taking off the dressing; further assessments were made at 48 and 72 hours after application.

The irritability index was calculated from the results in accordance with the classification described under § 1500.41 in the Federal Register 38, No. 187, 27.09.1973, p 27019 (Appendix 1).

Result:

After application of the Octopirox preparation an irritation index of 2.0 was found. In addition the skin of one animal was dry and chapped, with coarse

scales. Consequently the preparation is classed as slightly irritant to the skin.

After treatment with the vehicle an irritation index of 0.5 was obtained. 4 animals showed a barely perceptible erythema and oedema. 1,2-propylene glycol is not considered irritant to the skin by FDA standards.

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Appendix  
Assessments

Evaluation of Primary Skin Irritation  
(Patch Test after FDA)

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The table is reproduced from U.S. Code of Federal Regulations § 1500.41 "Method of testing primary irritant substances" as published in Federal Register 38, 27019 (1973).

	<u>Value</u>
1. Erythema and Eschar Formation	
No erythema .....	0
Very slight erythema (barely perceptible) .....	1
Well defined erythema .....	2
Moderate to severe erythema .....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth) .....	4
2. Edema Formation	
No edema .....	0
Very slight edema (barely perceptible) .....	1
Slight edema (edges of area well defined by definite raising) .....	2
Moderate edema (raised approximately 1 mm) .....	3
Severe edema (raised more than 1 mm and extending beyond area of exposure) .....	4

"The 'value' recorded for each reading is the average value of the six or more animals subject to the test.

Add the values for erythema and eschar formation at 24 and 72 hours for intact skin to the values on abraded skin at 24 and 72 hours (four values). Similarly, add the values for edema formation at 24 and 72 hours for intact and abraded skin (four values). The total of the eight values is divided by four to give the primary irritation score."

Evaluation

0.0 - 0.5	Non-irritant	(nicht reizend)
0.6 - 3.0	Slightly irritant	(leicht reizend)
3.1 - 5.0	Moderately irritant	(mäßig reizend)
5.1 - 8.0	Severely irritant	(stark reizend)