



# Hoechst



Hoechst Aktiengesellschaft  
Pharma Research  
Toxicology  
3rd December 1979

Primary Skin Irritation of a preparation of  
0.5 % Octopirox, 12.5 % Steinapol SBFA 30 (40 %),  
0.11 % citric acid and 86.89 % water (pH 7.0)  
in rabbits (patch test).  
Report No 735/79

Summary:

A patch test for skin tolerance carried out under the experimental conditions laid down in the FDA guide lines showed this preparation to be slightly irritant to the skin.

The Steinapol-water mixture used as a control proved to be slightly irritant to the skin.

Materials and methods

Albino Himalayan rabbits (Stock: Hoe: HIMK (SPFWiga); own breed) of 1.5 to 2.0 kg were used as experimental animals. They were kept in cages on their own and received standard feed ERKA 8300 (supplied by Robert Koch OHG, Hamm/Westf.). Feed and water was offered in unlimited quantities.

The substance Octopirox<sup>R</sup> = H 72 6146 A was supplied as a 0.5 % solution in 12.5 % Steinapol, 0.11 % citric acid and 86.89 % water. The pH was adjusted to 7.0. The vehicle Steinapol SBFA 30, 40 % in water was used as a control on the same animals.

The experiment was carried out during the period 05.11. to 08.11.1979.

Experimental procedure:

An area of at least 6 x 3 cm on both flanks of six rabbits was shaved with an electric razor. One half of each shaved area was, in addition, abraded with a scarifier. The substance under test and the vehicle on its own were applied in 0.5 ml quantities to pieces of gauze sized 2.5 x 2.5 cm. They were attached to the prepared skin with strips of adhesive plaster and covered with inert, impervious PVC film, 6 - 8 cm wide; an elastic bandage was then wound round the animals' trunks. The period of Application was 24 hours, at the end of which time the bandages were removed and the first inspection carried out, followed by further assessment at 24 and 72 hours.

The findings were used to determine the primary irritation score according to para 1500.41 of Federal Register 38, No 187, 27.09.1973, p 27019 (Appendix 1).

Results:

The application of the material under test produced an index of irritation of 2.0, so that Octopirox<sup>R</sup>, 0.5 % in a Steinapol-water mixture, must be considered as slightly irritant to the skin.

The 40 % mixture in water of Steinapol SBFA 30 (12.5 % : 87.5 %) used as a control produced similar oedema and erythema formation, but in addition the skin of all the animals was dry, rough and coarsely scaled. In two animals there were also deep fissures in the skin and in one the skin was raised at the site of application. The primary irritation score caused by the vehicle alone was 2.8, thus indicating that the Steinapol-water mixture has a slight propensity to irritate the skin.

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Appendix  
Classification

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)

Annex  
Report No. 735/79  
December 3rd, 1979

DERMAL TOLERANCE - PATCH TEST														Study No.:					
Substance: 12,5 % Steinapol SBFA 30, 40 % 87,5 % water							Dose: 2 x 0,5 ml/g on 3 x 3 cm skin surface							Investigator: Böcher / Vatter					
Concentration: Original			Application intact h flank 1 scarif. f flank				Species: Albino Himalayan rabbit				Study start: 05.11.1979								
Time after apol.		24 h					48 h					72 h							
Animal No.		288	289	290	291	292	517	288	289	290	291	292	517	288	289	290	291	292	517
scarified	Erythema	3	1	2	2	3	1	3	1	1	2	2	2	3	3	2	2	2	2
	Edema	2	2	1	2	2	3	1	0	0	0	1	2	1	0	0	0	0	2
intact	Erythema	0	1	2	2	2	1	0	1	0	2	0	2	0	3	2	2	1	2
	Edema	0	2	0	2	2	1	0	0	0	0	0	1	0	0	0	0	0	1
Sum		39					21					28							
Skin dry, rough								X	X			X	X	X	X	X	X	X	X
Skin with fine scales																			
Skin with coarse scales														X	X	X	X	X	X
Skin hardened																			
Skin raised																			X
Skin parchment-like																			
Skin chapped (superf.)																			
Skin chapped (deep)																			
Eschar formation														X					X
Necrosis																			
Desquamation, small-sized																			
Desquamation, large-sized																			
Open wound																			
Exudation (clear)																			
Exudation (reddish)																			
Scratch marks																			
Discolorations	isolated																		
	extensive																		
primary irritation index: Sum of all rabbits, 24 + 72 h-value=														67 : 24= 2,8					
Remarks:		h = hindflank			l = left			f = foreflank											

DERMAL TOLERANCE - PATCH TEST													Study No.:							
Substance: 12,5 % Steinapol SBFA 30, 40 % / water						Dose: 2 x 0,5 ml/g on 3 x 3 cm skin surface						Investigator: Böcher / Vatter								
Concentration: Original			Application intact h flank r scarif. f flank				Species: Albino Himalayan rabbit						Study start: 05.11.1979							
Time after appl.			24 h					48 h					72 h							
Animal No.			288	289	290	291	292	517	288	289	290	291	292	517	288	289	290	291	292	517
scarified	Erythema	3	2	1	3	3	1	3	2	0	2	3	0	2	2	0	1	2	0	
	Edema	2	1	0	2	2	1	0	0	0	0	1	0	0	0	0	0	1	0	
intact	Erythema	3	2	1	2	3	1	3	2	0	0	2	0	1	0	0	0	1	0	
	Edema	2	1	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	
Sum			39					18					10							
Skin dry, rough																				
Skin with fine scales																				
Skin with coarse scales																				
Skin hardened																				
Skin raised																				
Skin parchment-like																				
Skin chapped (superf.)																				
Skin chapped (deep)																				
Eschar formation																				
Necrosis																				
Desquamation, small-sized																				
Desquamation, large-sized																				
Open wound																				
Exudation (clear)																				
Exudation (reddish)																				
Scratch marks																				
Discolorations	isolated																			
	extensive																			

primary irritation index: Sum of all rabbits, 24 + 72 h-value= 49 : 24= 2,0

Remarks: h = hindflank                      r = right  
              f = foreflank