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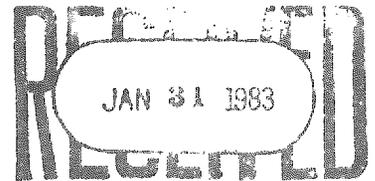
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878214021
August 18, 1964

CAS No. 17557-23-2

REPORT



TK 10412/1

REPETITIVE SKIN IRRITATION IN THE RABBIT AFTER FIVE CONSECUTIVE

APPLICATIONS

GU PROJECT NO. 820990

XB 2727 techn.

12 05 04 / Seifert

ISCA CONFIDENTIAL
BUSINESS INFORMATION

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1. INTRODUCTION

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At the request of the Plastics & Additives Division an subacute study in rabbits was conducted. The purpose was to determine the skin irritating potency of TK 10412/1 after five consecutive applications on the rabbit skin.

This report presents the results of the laboratory investigation as compiled by the undersigned.

Study Director

G. Seifert, T.O.G., Section Head

.....
date:

G. Seifert
August 18, 82

2. SUMMARY AND CONCLUSIONS

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Under the conditions of the present experiment TK 10412/1 was found to cause extreme irritation when applied to intact and abraded rabbit skin.

The calculated primary irritation index was 6.8.

3. PERSONNEL

Study Director:

G. Seifert, T.C.G., Section Head

Technical Personnel:

A. Buenzli
E. Fankhauser
E. Schaer
S. Winter

The job descriptions and the summaries of training and professional experience for all personnel participating in this study are filed in the archives of the test facility.

4. MATERIALS AND METHODS

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4.1 Test Article

Code No

TK 10412/1

Batch No.

Tank 8404 roh

Description

liquid

Stability

stable

Purity

not determined

Test Article Received:

28.06.82

4.2 Experimental Animals

Rationale

The albino rabbit has been selected for this test as being a standard species for the determination of skin irritation.

Species and strain

New Zealand White Rabbits

Source

Kleintierfarm Madoerin AG, CH-4414
Fuellinsdorf

Number of animals

3 male / 3 female

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Initial body weight range

2-3 kg

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Individual identification

ear tags

Husbandry

Animals were housed individually in metal cages.

The animal room was air conditioned: temperature $22 \pm 3^{\circ}$ C, relative humidity $55 \pm 15\%$; 12 hours light/day, approximately 15 air changes/h.

Diet

Rabbit food, NAFAG, No. 814 Tox, NAFAG AG, Gossau, SG (Switzerland), and water were provided ad libitum.

4.3 Design

Basis

The procedure used is based on the method of Draize, described in the "Appraisal of the Safety of Chemicals and Foods, Drugs and Cosmetics" (1959) of the US Association of Food and Drug Officials (AFDO).

Application of the substance

Before treatment the entire back and the flank of the rabbits were shaved with an electric clipper.

Gauze patches of 4 x 5 cm soaked with 0.5 ml of the test material were applied to the skin.

The patches were covered with an impermeable material and were fastened to the body of the rabbit with adhesive tape. The dressings were removed after 24 hours.

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The skin reaction was assessed after removal on the basis of the following evaluation scheme.

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SCORE FOR SKIN IRRITATION IN RABBITS

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
Total possible erythema score	4

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 more than 1 mm).....	3
Severe edema (raised more than 1 mm and extending beyond area of exposure).....	4
Total possible edema score	4

Primary reaction score = score after the first 24 hours = RAW*

Mean reaction score = average score on days 1-5 = RMW*

Final reaction score = score on day 5 of test = RW*

The severity of skin irritation was rated as follows :

0	= none	>2 - 4	= moderate
>0 - 1	= minimal	>4 - 6	= marked
>1 - 2	= slight	>6 - 8	= extreme

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A new patch was then applied to the same dorsal area, and the procedure was repeated for a total of 5 consecutive days. The fifth dressing was removed 8 hours after the application and the skin reaction was then recorded.

The skin reaction was recorded again on days 8, 9 and 10 (recovery period).

Bodyweights were recorded at -3 days, at initiation and day 3 and 5 of the treatment period and at day 8 and 10 of the observation period.

Toxic symptoms were recorded daily.

4.4 Procedure

Starting date of the experiment

19.07.82

End date of the experiment

28.07.82

5. RESULTS

Skin irritation

See Table 1

Under the experimental conditions the animals showed:

a primary reaction score of :

4.7

a mean reaction score of:

6.8

a final reaction score of:

8.0

After treatment with TK 10412/1 there was no tendency of recovery during the observation period.

The vehicle treated patches showed no irritation effect on the skin of rabbits.

Bodyweight

See Table 2

Symptoms

See Table 3

The rabbits had not recovered at the end of the observation period.

Autopsy

All animals were killed and autopsied after the 10 test days, and macroscopically examined.

No substance related gross organ changes were observed, which could be related to substance application.

The application sites in all animals showed extended erythemas and necroses during the test as well as the observation period.

6. ARCHIVES

Final Report

WST 454

Copy of the final report

WST 452

Raw Data

WST 454

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7. DISTRIBUTION

Sponsor

Archives

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8. TABLES

Table 1

Table 2

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EVALUATION OF THE SKIN REACTIONS

TABLE: **1**
 TEST MATERIAL:
 TEST No:

TK 10412 11
 820990

	After 1 day						After 2 days						After 3 days						After 4 days					
Sex	♂			♀			♂			♀			♂			♀			♂			♀		
Animal No.	115	116	117	118	119	120	115	116	117	118	119	120	115	116	117	118	119	120	115	116	117	118	119	120
Erythema	2	3	2	2	2	3	3	4	4	3	4	3	3	4	4	3	4	4	3	4	4	3	4	4
Edema	2	3	2	2	2	3	3	4	3	3	3	3	3	4	4	3	4	4	3	4	4	3	4	4
Total	4	6	4	4	4	6	6	8	7	6	7	6	6	8	8	6	8	8	6	8	8	6	8	8
Mean	4.7			4.7			7			6.3			7.3			7.3			7.3			7.3		
Group mean	4.7						6.7						7.3						7.3					
	After 5 days						After 8 days						After 9 days						After 10 days					
Sex	♂			♀			♂			♀			♂			♀			♂			♀		
Animal No.	115	116	117	118	119	120	115	116	117	118	119	120	115	116	117	118	119	120	115	116	117	118	119	120
Erythema	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Edema	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Total	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Mean	8			8			8			8			8			8			8			8		
Group mean	8						8						8						8					

Study conducted from 19.7.82 to 28.7.82

PH-Wert: 0.6 Appl. site NECROSIS in 6/6 animals
 Zucht: Mactörin SCAB FORMATION in animals
 Tox. Nr.: 54/82 EXTENDED ERYTHEMA in 6/6 animals

Date: 28.7.82 Visum: E. Fankhauer

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Gewichtsprotokoll

2

Test-Material: *TK 1041211*
 Test-Nr.: *820990*
 Dosis mg/kg:

Datum		19.7.82	21.7.82	23.7.82	26.7.82	28.7.82									
Tier No.	Sex														
115	♂	2490	2395	2340	2345	2360									
116	♂	2520	2425	2440	2460	2430									
117	♂	2590	2500	2455	2560	2635									
		2533	2440	2398	2455	2475									
		51	54	58	108	143									
118	♀	2500	2340	2300	2430	2470									
119	♀	2495	2425	2415	2495	2540									
120	♀	2525	2410	2410	2475	2510									
		2507	2392	2375	2467	2507									
		16	45	65	33	35									
Visum:		E.F.	E.F.	E.F.	E.F.	E.F.									

phys. Zustand:

Bemerkungen:

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Test-Material 72 104/1/1 | Test-Nr. 170550

KANINCHEN-SYMPTOME 3

TIER NR. 115-110 | APPL. ART 5 Tg Neutrition | DOSIS mg/kg

Visum: E. Frankfurter

DATUM	14	16	18	19	20.7	21.7	22.7	23.7	24.7	25.7	26.7	27.7	28.7						
Sedation																			
Dyspnoe								x	x	x	x	x	x						
Miosis																			
Exophthalmus																			
Bauchlage																			
Bauch-Seitenl.																			
gekr. Haltung																			
Seitenlage	S	S	S	S	S	S	S	S											
Ataxie	0	0	0	0	0	0	0	x	x	x									
Ruderbeweg.																			
Klon.ton. Kr.																			
Opisthotonus																			
Tremor								x	x	x	x	x	x						
Diarrhoe																			
gestr. Fell																			
Salivation																			
Hyperreflexe																			

Bemerkungen:

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