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[redacted]

REPORT ON SKIN SENSITIZING (CONTACT ALLERGENIC) EFFECT IN GUINEA PIGS [redacted]

MAXIMIZATION TEST

The purpose of the study was to determine the sensitizing potential of [redacted] (TINUVIN 770).

[redacted]

(b) (4)

QUALITY ASSURANCE STATEMENT

Form 301 C

STUDY TITLE : (b) (4)

SKIN SENSITIZING (CONTACT ALLERGENIC) EFFECT IN GUINEA PIGS

MAXIMITATION TEST

Sponsor: KA

Study Ref./ Dispo.Nr.: (b) (4)

Study Director: (b) (4)

QA Inspector Name: (b) (4)

THE QUALITY ASSURANCE INSPECTION(S) WAS (WERE) PERFORMED ON THE FOLLOWING DATE(S) :

1	21.11.83	10	
2	19.12.83	11	
3	09.01.84 (final report audit)	12	
4		13	
5		14	
6		15	
7		16	
8		17	
9		18	

THE FINDINGS WERE REPORTED TO THE STUDY DIRECTOR AND TO THE MANAGEMENT ON THE FOLLOWING DATE(S) :

1	21.11.83	10	
2	19.12.83	11	
3	09.01.84	12	
4		13	
5		14	
6		15	
7		16	
8		17	
9		18	

(b) (4)

Date: 09.01.84

Signature: (b) (4)

DISTRIBUTION: ☒ Study Director

☒ GU 6.3 File

(b) (4)

(b) (4)

(b) (4)

To the best of my knowledge and belief, this study was conducted in compliance with Good Laboratory Practice regulations as set forth in the Principles of Good Laboratory Practice, adapted May 12, 1981, by the OECD Council.

(b) (4)

(b) (4)

REPORT ON SKIN SENSITIZING (CONTACT ALLERGENIC) EFFECT IN GUINEA PIGS OF (b) (4) (TINUVIN 770).

Sponsor: Plastics and Additives Division

Testing facility: (b) (4)

Study director: (b) (4)

Technical assistant:

Test material received: 18.07.1983

Validity: stable

Study initiated: 21.11.1983

Study completed: 22.12.1983

Summary and conclusion

No animal was sensitized by (b) (4) under the experimental conditions employed.

According to the maximization grading (b) (4) can be classified to the lowest grade of skin-sensitizing (contact allergenic) potential in albino guinea-pigs.

Study director: (b) (4)

signature:

date :

Approved by : (b) (4)

signature:

date :

Archive of protocol, raw data and final report: R 1062.307.

1. Material

Test material:	(b) (4) TINUVIN 770 Batch No. (b) (4)
Purity:	99.7%
Appearance:	white powder
Storage conditions:	room temperature
Validity:	stable
Stability under the condition of administration:	not determined
Auxiliary compounds:	Bacto Adjuvant, Complete Freund (Difco Lab., Detroit, Michigan USA) sesame oil (Siegfried, Zofingen) physiological saline (sterile solution, Hausmann) vaseline (Demopharm SA., Bienne)
Concentrations:	1% for intradermal application in sesame oil and saline adjuvant mixture 10% for epidermal application (Induction) in vaseline ~ 0.4 g per patch 1% for epidermal application (Challenge) in vaseline ~ 0.2 g per patch

2. Method

The test was carried out according to the maximization test of Magnusson and Kligman (J. invest. Dermatol. 52, 268-276, 1969), recommended in the OECD guidelines 1981 and in the EEC directive 79/831.

Animal strain: Guinea pigs of the Pirbright White strain (Tif: DHP), bred on our premises were used.

Animals received: 03.11.1983

Acclimatisation period: 18 days

The test was performed on 10 male and 10 female guinea pigs per group weighing between 332 and 478 g (~10 weeks old). It was impossible to select all animals within the weight range proposed in the protocol from the animals received for the test series.
The animals were housed individually in Macrolon cages (type 3), assigned to the different groups by means of random numbers generated by the random number generator incorporated in the Hewlett - Packard desk computer, identified with individual ear tags, kept at a constant room temperature of 21 ± 2°C, at a relative humidity of 50 ± 10% and on a 14 hours light cycle day. A 14 hours light cycle day is necessary to eliminate seasonal variation because the animal rooms are not totally protected from natural sunlight.
The animals received ad libitum standard guinea pig pellets - NAFAG No. 846, Gossau SG - and fresh water, supplemented with fresh carrots.
The sensitivity of the strain is controlled every six month with p - phenylenediamine.

The guinea pig is the animal of choice for sensitization studies.

Test procedure

Induction, intradermal application:

Two intradermal injections (0.1 ml per injection) were made into the neck of the guinea pigs with a mixture of adjuvant and saline, with the test compound (b) (4) in sesame oil and with the test compound (b) (4) in the adjuvant saline mixture.

Induction, epidermal application:

One week later (b) (4) was incorporated in vaseline and applied on a filterpaper patch to the neck of the animals (occlusive administration for 48 hours).

Challenge:

Two weeks after the epidermal induction application the animals were tested on the flank with 1% (b) (4) in vaseline and the vehicle alone (24 h occlusive application). Twenty four hours after removing the dressings the challenge reactions were graded according the Draize scoring scale (Appendix 1). The application sites were chemically depilated 3 hours before examination (Veet ®, ~ 5 minutes). A second evaluation is made 48 hours after removing the dressings.

The concentrations of the test compound for induction and challenge period were determined on separate animals.

A control group was treated with adjuvant and the vehicle during the induction period. During the challenge period the group was treated with the vehicle as well as with the test compound to control the maximal subirritant concentration of the test compound in adjuvant treated animals.

3. Results

The incidence of positive animals per group and the individual challenge reactions are listed in Table 1, 2 and 3.

The individual animal weights at start and end of test are listed in Table 4.

(b) (4) at the concentration of 1% in vaseline, did neither induce edema nor erythema reactions after epidermal challenge application.

(b) (4) can, therefore, be classified to the lowest sensitization class according to Magnusson and Kligman.

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1) in Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1959), the US Association of Food and Drug Officials (AFDO).
2) B. Magnusson, A.M. Kligman, J. invest. Dermatol. 52, 268-276, 1969.
Magnusson B. Identification of contact sensitizers by animal assay. Cont. Dermatitis 6, 46-50, 1980.

(b) (4) (b) (4)

Table 1

Incidence of positive animals per group after occlusive epicutaneous administration

	No. of positive animals/ No. of treated animals
after 24 hours	
Control group, vehicle application	0/20
(b) (4)	0/10
Test group, (b) (4)	0/20
vehicle application	0/20
after 48 hours	
Control group, vehicle application	0/20
(b) (4)	0/10
Test group, (b) (4)	0/20
vehicle application	0/20

(b) (4)

(b) (4) (b) (4)

Table 2

Challenge reactions after occlusive epicutaneous administration

Erythema (E) adn Edema (Ed.) scores 24 and 48 hours after removal of the dressings.

CONTROL GROUP

after 24 hours

Vehicle application

Animal No. m	401	402	403	404	405	406	407	408	409	410
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	411	412	413	414	415	416	417	418	419	420
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

(b) (4)

Animal No. m	401	402	403	404	405	406	407	408	409	410
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

after 48 hours

Vehicle application

Animal No. m	401	402	403	404	405	406	407	408	409	410
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	411	412	413	414	415	416	417	418	419	420
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

(b) (4)

Animal No. m	401	402	403	404	405	406	407	408	409	410
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

(b) (4)

Table 3

Challenge reactions after occlusive epicutaneous administration

Erythema (E) and Edema (Ed.) scores 24 and 48 hours after removal of the dressings.

TEST GROUP (b) (4)

after 24 hours

(b) (4)

Animal No. m	321	322	323	324	325	326	327	328	329	330
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	331	332	333	334	335	336	337	338	339	340
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Vehicle application

Animal No. m	321	322	323	324	325	326	327	328	329	330
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	331	332	333	334	335	336	337	338	339	340
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

after 48 hours

(b) (4)

Animal No. m	321	322	323	324	325	326	327	328	329	330
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	331	332	333	334	335	336	337	338	339	340
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Vehicle application

Animal No. m	321	322	323	324	325	326	327	328	329	330
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Animal No. f	331	332	333	334	335	336	337	338	339	340
Score E	0	0	0	0	0	0	0	0	0	0
Score Ed	0	0	0	0	0	0	0	0	0	0

Table 4

Individual animal weight in g

CONTROL GROUP			TEST GROUP (b) (4)		
Animal No.	weight at start	at end	Animal No.	weight at start	at end
401 m	354	561	321 m	392	472
402	426	562	322	361	525
403	332	420	323	421	576
404	394	588	324	435	628
405	442	645	325	414	664
406	400	594	326	460	616
407	478	583	327	441	577
408	423	598	328	472	635
409	391	492	329	418	608
410	431	567	330	473	635
411 f	406	494	331 f	439	484
412	343	470	332	405	528
413	391	505	333	437	606
414	416	518	334	425	529
415	390	455	335	410	504
416	403	494	336	465	604
417	432	572	337	390	490
418	390	466	338	404	547
419	381	539	339	368	485
420	382	565	340	382	481
$\bar{x}$	400.4	534.5		420.7	559.7
s	34.33	58.20		32.79	62.0

(b) (4) (b) (4)

Appendix 1

Evaluation of skin reactions according to Draize

(in Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1959), the US Association of Food and Drug Officials (AFDO).

	Score
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
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

(b) (4)

(b) (4)

(b) (4)

Appendix 2

Maximization grading

Sensitization rate (%)	Grade	Classification
0 - 8	I	weak
9 - 28	II	mild
29 - 64	III	moderate
65 - 80	IV	strong
81 - 100	V	extreme

(b) (4)