8EHQ-0396-13603

Bayer

8(e) correc

Bayer Corporation
100 Bayer Road
Pittsburgh, PA 15205-9741
Phone: 412 777-2000

ORIGINAL

88-960000083

March 11, 1996

(B)

Document Processing Center (TS-790)
ATTN: Section 8(e) Coordinator
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Contains No CB

8EHQ-96-13603
SP001 03/20/96

RE: Correction to submission dated March 6, 1996
Incorrect study submitted, replace with attached

Dear Sir:

Bayer Corporation is submitting the results of a Dermal Sensitization study "Assessment of Contact Hypersensitivity to V159808 in the Albino Guinea Pig (Maximization Test)" on V159808 known as DBT, CAS# 168612-06-4: 1H-tetrazole-1-acetamide,N,N-dibutyl-2,5-dihydro-5-thioxo-, (LVE 96-33) that were concluded to be reportable under TSCA 8(e) as it was judged to be a strong sensitizer in this assay. We expect to import this material in the near future.

This information will be provided in our hazard communication literature and training programs. The information submitted in this report is not considered "Confidential Business Information". Please contact me if you have any questions.

89960000059

Sincerely,

Donald W Lamb

Donald W. Lamb, Ph.D
Vice President
Product Safety & Regulatory Affairs
412-777-7431

96-2-3.doc:vmk
Attachment
Certified Mail: P 921 654 946

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4/29/96

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REPORT

ASSESSMENT OF CONTACT HYPERSENSITIVITY TO

V159808

IN THE ALBINO GUINEA PIG

(MAXIMIZATION-TEST)

NOTOX Project 142818
NOTOX Substance 50373

NOTOX B.V., 's-Hertogenbosch, The Netherlands

The study described in this report was conducted in compliance with the most recent edition of:

OECD Principles of Good Laboratory Practice.

which are essentially in conformity with:

United States Food and Drug Administration. Title 21 Code of Federal Regulations Part 58.

United States Environmental Protection Agency, (FIFRA). Title 40 Code of Federal Regulations Part 160.

United States Environmental Protection Agency, (TSCA). Title 40 Code of Federal Regulations Part 792.

with the following exception:

Concentration, stability and homogeneity of test substance in vehicle used were not determined by analytical procedures.

Study Director: Dr.Ir. W.R. Pels Rijcken

i.a.

.....

Date: 07 July 1995

NOTOX B.V., 's-Hertogenbosch, The Netherlands

Study procedures were subject to periodic inspections and general non study specific processes were also inspected at periodic intervals.

This report was audited by the Quality Assurance Unit and the methods and results accurately reflect the raw data.

Dates of Q.A.U. Inspections/Audits	Reporting Date
22 March 1995	22 March 1995
09 May 1995	10 May 1995
15 May 1995	16 May 1995
03-04 July 1995	04 July 1995

Manager, Quality Assurance Unit C.J. Mitchell B.Sc.

Date: 7-7-95

STUDY DIRECTOR: Dr.Ir. W.R. Pels Rijcken

i.a.

.....

date: 07 July 1995

MANAGEMENT: Dr. I.C. Enninga
Technical Director

.....

date: 07/07/1995

SUMMARY

Assessment for Contact Hypersensitivity to V159808 in the Albino Guinea Pig (Maximization Test).

The study was carried out in accordance with the OECD Guideline No. 406, "Skin Sensitisation", the EEC Directive 92/69/EEC, Part B.6, "Skin Sensitisation" and based on the method described by Magnusson and Kligman, "Allergic Contact Dermatitis in the Guinea Pig - Identification of Contact Allergens".

Based on a test substance pretest, corn oil was selected as the most suitable vehicle for V159808.
Test substance concentrations selected for the Main study were based on the results of a preliminary study using five animals.
In the Main study, ten experimental animals were intradermally injected with a 1% concentration and epidermally exposed to a 50% concentration, while five control animals were similarly treated, but with omission of the test substance. Approximately 24 hours before the epidermal induction exposure all animals were treated with 10% SDS. Two weeks after the epidermal application all animals were challenged with a 50%, 25% and 10% test substance concentration and corn oil. A second challenge was performed one week later with test substance concentrations of 5%, 2% and 1% and the vehicle.

The skin reactions observed in response to the 2 and 1% test substance concentrations in seven (of the nine) experimental animals in the second challenge phase were considered indicative of sensitisation, based on the absence of any response in the control animals. These results lead to a sensitisation rate of 78 per cent.

Applying the rating of allergenicity described by Kligman A.M. (1966) on the results obtained in this test, V159808 is considered to have strong sensitising properties.

PREFACE

Sponsor	Agfa-Gevaert N.V. Septestraat 27 B-2640 MORTSEL Belgium
Study Monitors	Mr. G. Verbandt Dr. A. Suys Produktreglementeringen
Testing Facility	NOTOX B.V. Hambakenwetering 3 5231 DD 's-Hertogenbosch The Netherlands
Study Director	Dr.Ir. W.R. Pels Rijcken
Study Plan	Start : 01 May 1995 End : 09 June 1995

TEST SUBSTANCE

The sponsor is responsible for the completeness and GLP Compliance of all test substance data.

Identification	V159808
Description	Light pink solid
Batch	P 1 A
Purity	>99% (HPLC)
Instructions for test substance storage	At room temperature in the dark
Stability under storage conditions	Stable
Expiry date	January 01, 1997
Stability in vehicles	Stability in corn oil not indicated. Stable in polyethylene glycol for at least 4 hours.
Vehicles	Corn oil and polyethylene glycol 300.
Preparation	The test substance was ground to a powder using a mortar and pestle. The test substance formulations (w/w) were prepared prior to each treatment. No adjustment was made for specific gravity of vehicle. Homogeneity was obtained to visually acceptable levels.

PURPOSE AND RATIONALE

The purpose of this study was to evaluate whether V159808 induces skin hypersensitivity in guinea pigs after intradermal and epidermal exposure of the animals under the conditions described in this report.
This study should provide a rational basis for potential sensitising risk assessment in man.
The intradermal route of administration (first induction) was selected in order to obtain optimal contact between the test substance and elements of the immune system. The epidermal route of administration (second induction and challenge) was selected as it is a possible route of human exposure during manufacture, handling or use of the test substance.

GUIDELINES

The study procedures described in this report were based on the following guidelines and test method:

European Economic Community (EEC), Directive 92/69/EEC, Annex V of the EEC Directive 67/548/EEC, Part B.: Methods for the Determination of Toxicity; B.6: "Skin sensitisation", EEC Publication No L383, December 1992.

Organisation for Economic Co-operation Development (OECD), OECD "Guidelines for Testing of Chemicals", Guideline No 406 "Skin Sensitisation", Paris Cedex, adopted 17 July, 1992.

"Allergic Contact Dermatitis in the Guinea-Pig: Identification of Contact Allergens" Magnusson B. Kligman A.M., 1970 published by C.C. Thomas, Springfield, Illinois, USA.

ARCHIVING

NOTOX B.V. will archive the following data for at least 10 years:
protocol, report, a test substance reference sample and raw data.
All magnetic media produced on this study will be maintained indefinitely.

TEST SYSTEM

Species	Dunkin Hartley Crl: (HA)BR albino guinea pig (SPF-quality) Recognised by international guidelines as the recommended test system (e.g. OECD, EEC). Source : Charles River, Germany
Number of animals	Preliminary study : 5 females Experimental group : 10 females Control group : 5 females
Age at start of study	Approx. 6 or 7 weeks
Body weight prior to start	418 - 546 grams
Identification	Ear tag
Test system check	A positive control experiment is performed once every six months as a sensitivity check of the test system. The most recent test is summarised in the Appendix.

ANIMAL HUSBANDRY

Conditions:
Air-conditioned room with approximately 15 air changes per hour and the environment controlled with optimal conditions considered as being a temperature of 21°C and a relative humidity of 50%. Fluctuations from these optimal conditions were noted, but were considered not to have affected study integrity. Lighting was 12 hours artificial fluorescent light and 12 hours dark per day.

Accommodation:
Individually or in groups of 2 animals per labelled metal cage with wire-mesh floors and equipped with an automatic drinking system (ITL, Bergen, The Netherlands). The acclimatisation period was at least 5 days before start of treatment under laboratory conditions.

Diet:
Free access to standard guinea pig diet, including ascorbic acid (1600 mg/kg); LC 23-B, pellet diameter 4mm (Hope farms, Woerden, The Netherlands). Certificates of analysis were examined and retained in the NOTOX archives. In addition, hay (B.M.I., Helmond, The Netherlands) was provided once a week.

Water:
Free access to tap water, diluted with decalcified water. Certificates of analysis were examined and retained in the NOTOX archives.

PRELIMINARY STUDY

Initially, polyethylene glycol was chosen as the suitable vehicle for preparation of the test substance. The 25% test substance concentration in polyethylene glycol was the highest concentration that could be injected intradermally.
However, due to the fact that polyethylene glycol caused necrosis after intradermal injection, the vehicle was changed to corn oil.
The 1% test substance concentration in corn oil was the highest concentration suitable for intradermal injection.

Intradermal injections (three animals):
A 25% test substance concentration in polyethylene glycol was injected in one animal into two injection sites (0.1 ml each) in the left clipped shoulder region. A 10% and 5% concentration in polyethylene glycol were injected in a similar manner in a second animal in the right and left shoulder regions, respectively. A 1% concentration in polyethylene glycol and this vehicle were injected in a similar manner in a third animal. The resulting dermal reactions were assessed 24 and 48 hours later for erythema (see scale below), necrosis and diameter of necrosis.
The third animal then received intradermal injections of a 1% and 0.5% concentration in corn oil in a similar manner five days later. The resulting dermal reactions were assessed after 20 hours.

Epidermal application (the first two animals mentioned above):
A 50% test substance concentration in polyethylene glycol (0.5 ml) was applied epidermally on a shaved flank of one animal, using a Scotchpak-non-woven patch (2.5 x 2.2 cm) on Micropore tape (both 3M, St. Paul, USA) and held in place by Coban elastic bandage (3M, St. Paul, USA). A 25% concentration in polyethylene glycol was applied in a similar manner on the second animal. After 24 hours, the dressings was removed and the skin cleaned of residual test substance. The treated skin was assessed 24 and 48 hours later according to the scale described below.

Epidermal applications (two naive animals):
Four concentrations of the test substance in polyethylene glycol (50%, 25%, 10% and 5%, 0.05 ml each) were applied occlusively on a shaved flank of each of the two animals using Square chambers (v.d. Bend, Brielle, The Netherlands), mounted on Micropore tape and held in place by Coban elastic bandage. After 24 hours, the dressings were removed and the skin cleaned of residual test substance. The treated sites were assessed 24 and 48 hours later according to the scale described below.

Erythema and eschar formation:
No erythema 0
Slight erythema (barely perceptible) 1
Well-defined erythema 2
Moderate erythema 3
Severe erythema (beet redness) to slight eschar formation (injuries in depth) 4

Oedema formation:

No oedema 0
Slight oedema (barely perceptible) 1
Well-defined oedema (edges of area well-defined by definite raising) 2
Moderate oedema (raised approximately 1 millimeter)..... 3
Severe oedema (raised more than 1 millimeter and extending beyond the area of exposure) . 4

MAIN STUDY

INDUCTION - EXPERIMENTAL ANIMALS

Day 1 Three pairs of intradermal injections (0.1 ml/site) were made in the clipped scapular region as follows:
A) Freunds' Complete Adjuvant (Difco, Detroit, U.S.A.), 50:50 with water for injection (Ferensius AG, Bad Homburg, Germany).
B) The test substance at a 1% concentration corn oil.
C) The test substance, at twice the concentration used in (B), emulsified in a 50:50 mixture of Freunds' Complete Adjuvant.

Note: One of each pair was on each side of the midline and from cranial A) to caudal C).

Day 3 The dermal reactions caused by the intradermal injections were recorded.
Day 7: The clipped scapular area was rubbed with 10% sodium-dodecyl-sulfate (SDS, Boom, Meppel, The Netherlands) in vaseline using a spatula. This concentration of SDS provokes a mild inflammatory reaction.
Day 8 The clipped area between the injection sites was treated with 0.5 ml of a 50% test substance concentration using a Scotchpak-non-woven patch (2 x 4 cm) mounted on Micropore tape and secured with Coban elastic bandage.
Day 10 After 48 hours, the dressings were removed and the skin cleaned of residual test substance. Subsequently, all dermal reactions after epidermal application were recorded, according the scale presented above.

INDUCTION - CONTROL ANIMALS

Day 1 Intradermal injections were made similar to the method described above with the omission of the test substance.
Day 3 The dermal reactions caused by the intradermal injections were examined and a description of the local effects was recorded.
Day 7: SDS 10% treatment, as described above.
Day 8 Epidermal treatment with the vehicle only, using a similar patch as described above.
Day 10 After 48 hours, the dressings were removed and the skin cleaned. All dermal reactions were examined immediately after bandage removal and a description of the local effects was recorded.

CHALLENGE

Day 22 All animals were treated epidermally with 0.05 ml of each of a the following test substance concentrations, 50%, 25% and 10% and the vehicle on a clipped and shaved flank, using Square chambers, attached to Micropore tape and secured with Coban elastic bandage.
Day 23 After approximately 24 hours, the dressings were removed and the skin cleaned from residual test substance and vehicle. The treated sites were assessed for redness and swelling 24 and 48 hours after removal of the dressings, using the numerical grading system on page 10. After the first reading, the test sites were shaved with an electric razor.

No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Moderate erythema and swelling	3
Intense erythema and swelling	4

RE-CHALLENGE

Day 29: A second challenge was conducted one week after the first challenge. The method was similar to the first challenge for all animals except that the contralateral shaved flank of the animals was treated. The following test substance concentrations, 5%, 2% and 1%, and the vehicle were applied.

At the end of the study period all animals were killed by oxygen/carbon dioxide asphyxiation.

OBSERVATIONS

Mortality/Viability	Twice daily
Toxicity	At least once daily.
Body weights	Prior to start and at termination of the study.
Necropsy	Animal found dead was subjected to necropsy for gross macroscopic examination.

INTERPRETATION

The results for the experimental animals at the challenge application(s) were compared with the results for the control animals. Positive skin reactions (grade 1 or more) were considered signs of sensitisation, provided that such reactions are not observed in the control group.

A sensitisation rate (%) was calculated for each concentration as follows: the number of sensitised animals to one concentration in proportion to the total number of animals of the experimental group.
The highest sensitisation rate calculated was used to assign a classification according to Kligman (J. Invest. Dermatol. 47, 393-409, 1966).
Rating of sensitivity:

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

Preliminary Study

The results of the intradermal injections and epidermal exposures for the selection of suitable test substance concentrations for the main study are described in Tables 1 and 2.
No signs of systemic toxicity were observed during the preliminary study.

Based on the results, the test substance concentrations for the Main Study were selected to be a 1% concentration for the intradermal induction and a 50% concentration for the epidermal induction exposure. A 50%, 25% and 10% concentration were selected for the (first) challenge phase.
Corn oil was selected as the most suitable vehicle for the Main Study.

Main Study - Induction

Skin effects after intradermal injections (individual data not reported):

Injection sites B:
Experimental animals (1% test substance)
Slight/mild erythema was observed in seven animals on day 3 in the areas of injection. No abnormalities were seen in the other three animals.
Control animals (vehicle)
Slight/mild erythema was observed in two animals on day 3 in the areas of injection. No abnormalities were seen in the other three animals.

Injection sites A (1:1 mixture of FCA and water for injection):
All animals
Slight/mild or moderate/severe erythema was observed in the animals on day 3 in the areas of injection. One experimental animal also showed crust formation.

Injection sites C
Experimental animals (1:1 mixture of FCA and 2% test substance):
Slight/mild or moderate/severe erythema was observed in the animals on day 3.
Control animals (1:1 mixture of FCA and vehicle):
Slight/mild or moderate/severe erythema was observed in the animals on day 3.

Skin effects after epidermal induction:

The experimental animals showed slight, well defined or severe erythema with very small crusts or eschar formation after the 48 hours occluded epidermal induction exposure.
Three control animals showed slight or well defined erythema and four control animals showed small crusts after the 48 hours exposure period.

Main Study - Challenges

Control Group:
In the first challenge, two, five and two animals showed discrete/patchy or moderate/confluent erythema and scaliness in response to the 50%, 25% and 10% test substance concentrations, respectively.
In the second challenge, one animal showed discrete or patchy erythema in response to the 5% test substance concentration only.

Experimental Group:
In the first challenge, eight, ten and nine animals showed discrete/patchy or moderate/confluent erythema and scaliness in response to the 50%, 25% and 10% test substance concentrations, respectively.
In the second challenge, nine, seven and seven animals (of the nine) showed discrete/patchy or moderate/confluent erythema and scaliness or small crusts in response to the 5%, 2% and 1% test substance concentrations, respectively.

Toxicity Symptoms / Mortality

One experimental animal was found dead in the morning of day 30. As no clinical signs were observed, no macroscopic abnormalities were seen at necropsy and the dressing of the second challenge application had not been removed, it was considered likely that this animal died as a result of the application procedure.
No further mortality occurred and no symptoms of systemic toxicity were observed in the animals of the main study during the study period.

Body Weights

The average body weight of the experimental animals and the control animals was within an acceptable range at the beginning and at the end of the study.

CONCLUSION

The skin reactions observed in response to two test substance concentrations in seven (of the nine) experimental animals in the second challenge phase were considered indicative of sensitisation, based on the absence of any response in the control animals.
These results lead to a sensitisation rate of 78 per cent, which indicates that V159808 has strong sensitizing properties in this test applying the rating of allergenicity described by Kligman A.M. (1966).

TABLE 1: PRELIMINARY STUDY

INTRADERMAL INJECTIONS

Animal No.	Body Weight day -8 (gram)	Concentration % (w/w) in PEG	SKIN READINGS AFTER 24/48 HRS			Body Weight day -5 (gram)
			Erythema	Necrosis	Diameter (mm)	
553	442	25	1/1	yes/yes	6/6	438
554	465	10 5	1/1 1/0	yes/yes yes/yes	5/5 5/5	477
Animal No.	**Body Weight day -6 (gram)**	**Concentration % (w/w) in PEG**	**SKIN READINGS AFTER 24/48 HRS**			**Body Weight day -4 (gram)**
			Erythema	**Necrosis**	**Diameter (mm)**	
623	454	1 vehicle	1/1 1/1	yes/yes yes/yes	3/3 3/3	471
Animal No.	**Body Weight (gram)**	**Concentration % (w/w) in CO**	**SKIN READINGS AFTER 20 HOURS**			**Body Weight (gram)**
			Erythema	**Necrosis**	**Diameter (mm)**	
623		1 0.5	1 1	no no	- -	

EPIDERMAL APPLICATION USING SCOTCHPAK-NON-WOVEN PATCH

Animal No.	Body Weight day -8 (gram)	Concentration % (w/w) in PEG	SKIN READINGS AFTER BANDAGE REMOVAL				Body Weight day -5 (gram)
			After 24 hours		After 48 hours		
			Erythema	Oedema	Erythema	Oedema	
553	442	50	0	0	0	0	438
554	465	25	0	0	0	0	477
Systemic Symptoms Observed: No systemic symptoms observed.							

PEG = Polyethylene glycol
CO = Corn oil

TABLE 2: PRELIMINARY STUDY

EPIDERMAL APPLICATION USING SQUARE CHAMBERS

Animal No.	Body Weight day -8 (gram)	Concentration % (w/w) in PEG	SKIN READINGS AFTER BANDAGE REMOVAL				Body Weight day -5 (gram)
			After 24 hours		After 48 hours		
			Erythema	Oedema	Erythema	Oedema	
551	445	50	0	0	0	0	462
		25	0	0	0	0	
		10	0	0	0	0	
		5	0	0	0	0	
552	418	50	0	0	1	0	423
		25	0	0	0	0	
		10	0	0	0	0	
		5	0	0	0	0	

PEG = Polyethylene glycol

TABLE 3: INDUCTION AND FIRST CHALLENGE READINGS

ANIMAL NO.	INDUCTION DAY 10 READINGS 50a ER	50a OE	FIRST CHALLENGE DAY 24 READINGS 50a	25	10	0	DAY 25 READINGS 50a	25	10	0	COMMENTS
Experimental group											
536	1b	0	1	1	1	0	1	1s	1s	0	
537	4c	0	1s	2	1	0	1s	2s	1s	0	
538	1b	0	1	2	2	0	1s	1s	1s	0s	
539	0c	0	1	2	2	0	1s	2s	1s	0s	
540	1b	0	0	1	0	0	0s	1s	0s	0	
541	1b	0	0	1	1	0	0	1	1	0	
542	1	0	1	1	1	0	1	1	1	0	
543	2	0	0	1	1	0	1s	1s	1s	0	
544	1b	0	1	2	1	0	1	1	1	0	
545	2b	0	2	2	1	0	1	1	1	0	
Control group											
546	1b	0	0	0	0	0	0	1	0	0	
547	0	0	0	1	0	0	0	1	0	0	
548	2b	0	1	2	1	0	1	1	1	0	
549	0b	0	0	1	0	0	0s	1	0	0	
550	1b	0	1	1	0	0	1	1	1	0	

ER = Erythema.
OE = Oedema.
a = Concentrations (%) in corn oil.
b = This site also showed small crusts.
c = This site also showed eschar formation.
s = This site also showed scaliness.

TABLE 4: SECOND CHALLENGE READINGS

ANIMAL NO.	SECOND CHALLENGE DAY 31 READINGS 5a	2	1	0	DAY 32 READINGS 5a	2	1	0	COMMENTS
Experimental group									
536	1	0	1	0	1s	0	0	0	not sensitised
537	2bs	2	1	0	2bs	1s	1s	0	sensitised
538	1	1	1	0	2s	1s	1s	0	sensitised
539	-	-	-	-	-	-	-	-	c
540	1	0	0	0	1	0	0	0	not sensitised
541	1	1	1	0	1	1	1	0	sensitised
542	1	0	0	0	1	1	1	0	sensitised
543	0	0	0	0	1	1	1	0	sensitised
544	1	1	1	0	1s	1	1s	0	sensitised
545	2	2	1	0	2s	2	1	0	sensitised
Control group									
546	0	0	0	0	0	0	0	0	
547	0	0	0	0	0	0	0	0	
548	1	0	0	0	1	0	0	0	
549	0	0	0	0	0	0	0	0	
550	0	0	0	0	0	0	0	0	

a = Concentrations (%) in corn oil.
b = This site also showed small crusts.
c = This animal was found dead in the morning of day 30.
s = This site also showed scaliness.

Note
Animal 536 was considered as not sensitised, due to inconclusive results in response to the 1% test substance concentration.

TABLE 5: BODY WEIGHTS (gram)

GROUP / SEX	ANIMAL	DAY 1	DAY 32
GROUP 1 / FEMALES (EXPERIMENTAL)	536	546	712
	537	502	619
	538	513	706
	539	514	---
	540	499	699
	541	537	703
	542	447	567
	543	460	625
	544	528	664
	545	476	636
	MEAN	502	659
	ST.DEV.	33	50
	N	10	9
GROUP 2 / FEMALES (CONTROL)	546	514	687
	547	457	611
	548	495	676
	549	492	620
	550	467	599
	MEAN	485	639
	ST.DEV.	23	40
	N	5	5

Animal 539: Body weight at death was 663 grams.

APPENDIX

ASSESSMENT OF CONTACT HYPERSENSITIVITY TO

ALPHA-HEXYLCINNAMICALDEHYDE, TECH.85%,

IN THE ALBINO GUINEA PIG (MAXIMIZATION-TEST),

Positive Control Experiment.

NOTOX Project 028272

SUMMARY

A positive control experiment is carried out at regular intervals to check the reliability of the test system as used by NOTOX.
In this study, performed in December 1994, the Dunkin Hartley guinea pig was checked for the sensitivity to ALPHA-HEXYLCINNAMICALDEHYDE, TECH. 85%. The study was carried out in accordance with the OECD Guideline No. 406, the EEC Directive 92/69/EEC, Part B.6 and based on the method described by Magnusson and Kligman, "Allergic Contact Dermatitis in the Guinea Pig - Identification of Contact Allergens".
ALPHA-HEXYLCINNAMICALDEHYDE, TECH. 85%, was fabricated under lot no. 80281 and the purity was 99.4% (glc) (Aldrich Chemicals Co., Germany).

Concentrations selected for this study were:
Intradermal induction: 5% solution in physiological saline (w/w).
Epidermal induction: undiluted.
Challenge: a 50%, 25 and 10% solution in distilled water (w/w).

SKIN REACTIONS-IN THE CHALLENGE PHASE

NUMBER OF ANIMALS WITH SKIN REACTIONS

	ALPHA-HEXYLCINNAMICALDEHYDE Concentration			
	50%	25%	10%	vehicle
	24/48*	24/48	24/48	24/48
Experimental group (10 animals)				
Score 4	0/1	0/0	0/0	0/0
Score 3	2/4	1/2	1/3	0/0
Score 2	5/3	6/7	6/6	0/0
Score 1	3/2	3/1	3/1	0/0
Control group (5 animals)				
Score 1	1/2	1/3	1/1	0/0
No reactions	4/3	4/2	4/4	0/0

*. time (hours) after the challenge exposure

CONCLUSION

Taking into account the intensity of the responses and comparing these with the reactions seen in the control animals, it was concluded that nine (of ten) experimental animals showed positive reactions, indicative of sensitisation, in response to one or more of the three concentrations used in the challenge phase. These results lead to a sensitisation rate of 90 per cent, which indicates that ALPHA-HEXYLCINNAMICALDEHYDE, TECH.,85%, has extreme sensitizing properties in this test applying the rating of allergenicity described by Kligman A.M. (1966).

From these results, it was concluded that the Albino Dunkin Hartley strain of guinea pig is an appropriate animal model for the performance of studies designed to evaluate the sensitising potential of a substance.

The raw data and report from this study are kept in the NOTOX archives. The test described above was performed in accordance with NOTOX Standard Operating Procedures and the report was audited by the QA-unit.