

Textile Products Division
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CIBA-GEIGY

8EHR-92-12281
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Contains NO CBI

October 9, 1992

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M. Street, SW
Washington, DC 20460

Attention: Section 8(e) Coordinator (CAP Agreement)

RE: 8E CAP - 0024

Dear Section 8(e) Coordinator:

Enclosed are triplicate copies of a study CIBA-GEIGY Corporation is submitting pursuant to the TSCA Section 8(e) Compliance Audit Program and CAP Agreement number 8E CAP-0024. The information being submitted is not considered Confidential Business Information. We are submitting the following information, as required by the CAP Agreement:

Company Name: CIBA-GEIGY Corporation
444 Saw Mill River Road
Ardsley, New York 10502-2699

Attention: Mr. Anthony Di Battista
Manager, Regulatory Affairs & Toxic Substances
Compliance
Telephone (914) 479-2776

Tested Chemical: Octadecanamide, N-[2-(diethylamino)ethyl]-;
also identified as: FAT 76 008/A
and: SAPAMINE COB-ST

CAS No.: 16889-14-8

Report Title: Skin Sensitizing (Contact Allergenic) Effect in
Guinea Pigs of FAT 76 008/A (Exp. No. 76/7, dated 6/4/76).

Summary: The test was carried out according to the optimization method of Maurer, et. al. (Agents and Actions Vol. 5 (2), 174-179, 1975). Under the experimental conditions employed, significant differences between the test group and the vehicle treated controls were found with the test material. Following the intradermal challenge injection 16/20 treated animals showed positive responses (compared with 0/20 controls). Epicutaneous



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Textile Products Division

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4/4/95

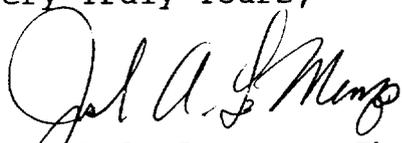
challenge resulted in 20/20 positive reactions to the test material (0/20 control positives). This study is submitted based on strong skin-sensitizing potential in guinea pigs and and potential human exposure that may have occurred. This material is no longer a commercial product.

Category: Unit II.B.2.b

Prior Reporting: Not applicable.

Please call the undersigned at telephone number (919) 632-2889 if you have any questions about this submittal.

Very Truly Yours,



Joseph A. LoMenzo, Ph.D.
Product Stewardship Director
Textile Products Division

Enclosures

2 copies of this letter

3 copies of the study

cc: A. Di Battista

I.D. # 04966

433

CIBA-GEIGY Limited
Basle, Switzerland
Toxicology/Pathology
PH 2.634

C I B A G E I G Y	Exp. No.: 76/7 June 4, 1976 OEK./TOX
	25. JUNI 1976

Industrial Medicine

MAR 14 1977

SKIN SENSITIZING (CONTACT ALLERGENIC) EFFECT IN GUINEA PIGS OF

FAT 76 008/A

SAPAMINE COB-ST = FAT 76008/A

1. Summary and Conclusion

Under the experimental conditions employed, highly significant differences between the test group and the vehicle treated controls were found with preparation FAT 76 008/A after intradermal and epidermal challenge application.

Preparation FAT 76 008/A is therefore considered to possess a marked skin-sensitizing (contact allergenic) potential in albino guinea pigs.

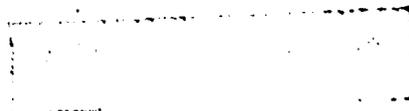
2. Method

The optimization test¹ was used, an intracutaneous sensitization procedure similar to the method recommended in the "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" (1959), the US Association of Food and Drug Officials (AFDO).

a) Animals

The test was performed on groups on 10 male and 10 female guinea pigs of the Pirbright white strain bred on our premises and weighing between 350 to 400 grams. The animals were housed individually in Macrolon cages, type 3, kept at a constant room temperature of 22±1°C, at a relative humidity of 55±5% and on a 14 hours light cycle day. The animals received ad libitum standard guinea pig pellets - NAFAG No. 830, Gossau SG - and fresh carrots.

¹ Maurer, Th., Thomann, P., Weirich, E.G. and Hess, R. (1975) The Optimization test in the guinea pig. A method for the predictive evaluation of the contact allergenicity of Chemicals. Agents and Actions Vol. 5 (2), 174-179, 1975



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b) Testing procedure

During the induction period the animals received one injection every second day (except weekends) to a total of 10 intracutaneous injections of a freshly prepared 0.1% suspension of FAT 76 008/A in physiological saline. One group was treated with the vehicle alone ("negative control").

On the first day, injections of 0,1 ml were administered into the shaven skin of the right flank and the back, while on the following days a single intracutaneous injection was given into the back.

During the second and third week of the induction period the test compounds were incorporated in a mixture²⁾ of the normal vehicle with complete Bacto Adjuvant (vehicle : adjuvant = 1 : 1).

Fourteen days after the last sensitizing injection, a challenge injection of 0,1 ml of a freshly prepared 0,1% suspension of FAT 76 008/A was administered into the skin of the left flank.

Twenty-four hours after each injection during the first week of the induction period and 24 hours after the challenge injection the reactions were recorded. Before examination, the reaction sites were depilated chemically (Butoquick[®], 5 minutes). The two largest perpendicular diameters (in mm) and the increase in the skin- fold thickness (in mm) were measured, and by multiplication of these values a "reaction volume" was obtained (in μ l) for each reading from each animal. The mean volume plus one standard deviation of the induction reactions observed in the individual animal in the first week was taken as representing the skin irritation "threshold" for each animal. Any challenge reaction greater than this threshold value in the induction period was graded as an allergic reaction and the animal termed "positive". The number of "positive" animals in the test group was compared with the number of animals in the control group (treated with the vehicle alone) that showed a non-specific reaction of at least the same magnitude ("negative control")³⁾.

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Ten days after the intracutaneous challenge injection, subirritant doses of the test compounds were applied epicutaneously under occlusive dressings which were left in place for 24 hours.

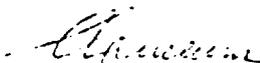
Results

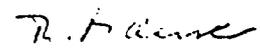
Intradermal injection of the vehicle alone failed to induce sensitization. No reactions were seen after application of the vehicle alone during the induction period and after the challenge application.

Table 1 summarizes the incidence of positive reactors after intradermal and epidermal challenge application.

Table 2 shows the reaction volumes for individual animals from the test group.

PH 2.634/TM/ma
June 4, 1976


Dr. P. Thomann


Dr. Th. Maurer

-
- 2) Bacto Adjuvant, complete Freund (Difco, Michigan, USA).
 - 3) The exact Fisher test for comparison of the basic probability of two binomial distributions; L. Sachs, Statistische Auswertungsmethoden, Thieme Verlag, Stuttgart, 1971. A probability of ≤ 0.01 was considered to indicate a significant difference.

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Table 1

A) Incidence of positive animals per group after intradermal challenge injection.

	No. of positive animals/ No. of treated animals	P
Vehicle control	0/20	
FAT 76 008/A	16/20	≪ 0.001

B) Incidence of positive animals per group after occlusive epicutaneous application.

	No. of positive animals/ No. of treated animals	P
Vehicle control	0/20	
1½ FAT 76 008/A	20/20	≪ 0.001

C) Challenge reactions after occlusive epicutaneous administration of the test compound.

Erythema score (Draize Score) 24 hours after removal of the dressing.

Animal No. m	1	2	3	4	5	6	7	8	9	10
Score	3	3	2	2	4	2	3	2	3	3
Animal No. f	11	12	13	14	15	16	17	18	19	20
Score	3	3	4	4	4	3	4	4	2	3

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Table 2 : Reaction volumes (μl) after intradermal injection of
FAT 76 008/A

Animal No.	Induction Application No.				Mean (\bar{x})	Standard deviation (s)	Treshold value ($\bar{x}+s$)	Challenge	+ = positive reactor
	1	2	3	4					
1 m	144	216	64	122	136.5	62.8	199.3	470	+
2	146	162	146	138	148.0	10.1	158.1	529	+
3	200	165	59	109	133.3	62.1	195.4	162	
4	210	190	64	55	129.8	81.6	211.4	186	
5	180	238	67	130	153.8	72.7	226.5	274	+
6	105	94	83	101	95.8	9.6	105.4	170	+
7	74	153	83	78	97.0	37.5	134.5	315	+
8	90	172	113	102	119.3	36.4	155.7	138	
9	154	178	83	144	139.8	40.4	180.2	270	+
10	73	321	21	146	140.3	131.0	271.3	317	+
11 f	210	170	90	122	148.0	52.8	200.8	390	+
12	101	96	115	106	104.5	8.1	112.6	230	+
13	109	108	101	105	105.8	3.6	109.4	317	+
14	162	200	162	64	147.0	58.2	205.2	363	+
15	83	82	138	154	114.3	37.2	151.5	418	+
16	101	62	138	109	102.5	31.3	133.8	230	+
17	56	122	160	113	112.8	43.0	155.8	120	
18	69	170	130	96	116.3	43.7	160.0	218	+
19	54	56	84	83	69.3	16.5	85.5	170	+
20	73	74	69	113	82.3	20.6	102.9	158	+
Group mean	119.7	151.5	98.5	109.5				272.3	16/20

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP

CAP

Submission number: 12281A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

		For Contractor Use Only			
entire document:	<u>0</u>	1	2	pages <u>1,2</u>	pages <u>1,2,3</u>
Notes:					
Contractor reviewer:	<u>LPS</u>			Date:	<u>5/11/95</u>

CECATS DATA
Submission # BEHQ-1092-12281 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Ciba-Geigy Corporation

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
0632 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/IN PROGRESS
0403 NOTIFICATION OF WORKING CONDITIONS
0404 LAB/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/09/92 OTS DATE: 11/02/92 CSRAD DATE: 04/04/95

CHEMICAL NAME:
FAT 76 008/A
SAPAMINE COB-ST

CASE
16889-14-8
16889-14-8

BEST COPY AVAILABLE

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLEN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0259 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0239 METAPHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAPHARMACO (HUMAN)	01 02 04		

TRACE DATA	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
<u>YES</u>		YES (DROP/REFER)	<u>GP</u>	LOW		
CAS SR	NO	NO (CONTINUE)		MED		
	IN TERMIN	REFER		<u>HIGH</u> Dermal Sensitization		

CONTACT:

#12281A
H

Dermal sensitization is of high concern based on positive reactions in 16/20 guinea pigs with intradermal challenge injection, and 20/20 with epicutaneous challenge.