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March 10, 1994

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Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator



88948000175

Subject: TSCA Section 8(e) Submission

RECEIVED
OFFICE OF TOXIC SUBSTANCES
ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Dear Sir/Madam:

Elf Atochem North America Inc. is submitting the attached study to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). This study provides information on 2-Ethylhexyl Thioglycolate (CAS No. 7659-86-1) and does not involve effects in humans. The title of the enclosed study report is 2-Ethylhexyl Thioglycolate Skin Sensitization Test in Guinea-Pigs (Maximization method of Magnusson, B. and Klingman, A.M.).

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

The following is a summary of the adverse effects observed in the skin sensitization test.

2-Ethylhexyl Thioglycolate was tested for potential to produce allergic skin reaction by intradermal injection and skin application to guinea pigs using a modified Magnusson and Klingman method. After challenge application, the test material produced evidence of a sensitization reaction in 50% (10/20) animals, and was classified as a moderate sensitizer.

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TSCA 8(e) Submission
2-Ethylhexyl Thioglycolate
March 10, 1994
Page 2

2

Elf Atochem has not previously filed any 8(e) notices or Premanufacture Notifications (PMNs) on the subject material.

Results from the study report will be incorporated into the current Elf Atochem Material Safety Data Sheet for 2-Ethylhexyl Thioglycolate.

Further questions regarding this submission may be directed to me at (610) 337-6892.

Sincerely,



C.H. Farr, PhD, DABT
Manager, Product Safety
and Toxicology

Enclosure

6-11-94

SPONSOR
Elf Atochem S.A.
La Défense 10
Cédex 42
92091 Paris-la-Défense
France

STUDY TITLE

SKIN SENSITIZATION TEST
IN GUINEA-PIGS
(Maximization method of
Magnusson, B. and Kligman, A.M.)

TEST SUBSTANCE

2-ETHYLHEXYL THIOGLYCOLATE

STUDY DIRECTOR

Jack Clouzeau

STUDY COMPLETION DATE

14th February 1994

PERFORMING LABORATORY

Centre International de Toxicologie (C.I.T.)
Miserey - 27005 Evreux - France

LABORATORY STUDY NUMBER

10268 TSG

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OFFICE OF TOXICOLOGY
ENVIRONMENTAL AND TOXICS

CONTENTS

STATEMENT OF THE STUDY DIRECTOR	4
OTHER SCIENTISTS INVOLVED IN THIS STUDY	4
STATEMENT OF THE QUALITY ASSURANCE UNIT	5
SUMMARY	6
1. INTRODUCTION	8
2. MATERIALS AND METHODS	8
2.1. TEST AND CONTROL SUBSTANCES	8
2.1.1 Test substance	8
2.1.2 Vehicle	8
2.1.3 Other substances	8
2.2. TEST SYSTEM	9
2.2.1 Animals	9
2.2.2 Environmental conditions	9
2.2.3 Food and water	9
2.3. TREATMENT	10
2.3.1 Preliminary test	10
2.3.2 Main study	10
2.3.2.1 Preparation of the animals	10
2.3.3 Induction phase by intradermal and cutaneous routes	10
2.3.3.1 Intradermal route	10
2.3.3.2 Cutaneous route	11
2.3.3.3 Challenge phase	11
2.4. SCORING OF CUTANEOUS REACTIONS	11
2.5. CLINICAL EXAMINATIONS	12
2.6. BODY WEIGHT	12
2.7. PATHOLOGY	12
2.7.1 Necropsy	12
2.7.2 Cutaneous samples	12
2.7.3 Microscopic examination	12
2.8. DETERMINATION OF THE ALLERGENICITY LEVEL	13
2.9. SUMMARY DIAGRAMS	14
Figure 1: control group	14
Figure 2: treated group	15
2.10. CHRONOLOGY OF THE STUDY	16
2.11. ARCHIVES	16

3. RESULTS	17
3.1. PRELIMINARY STUDY	17
3.1.1 Administration by intradermal route	17
3.1.2 Application by cutaneous route	17
3.2. MAIN STUDY	17
3.2.1 Clinical examinations	17
3.2.2 Scoring of cutaneous reactions	17
3.2.2.1 End of the induction period	17
3.2.2.2 Challenge application	18
4. CONCLUSION	18
Figure 3: Male body weight gain (g)	19
Figure 4: Female body weight gain (g)	20
APPENDICES	21
1. Test article description and certificate of analysis	22
2. Diet formula	25
3. Individual body weight values	27
4. Individual observation of cutaneous reactions	29
5. Positive control to check the sensitivity of Dunkin-Hartley guinea-pigs	31 and 32

STATEMENT OF THE STUDY DIRECTOR

This study was performed in accordance with the protocol agreed upon by Elf Atochem S.A., according to the maximization method of Magnusson and Kligman and according to:
. O.E.C.D. guideline No. 406, 12th May 1981.

The study was conducted in compliance with the principles of Good Laboratory Practice Regulations:

. O.E.C.D. Principles of Good Laboratory Practice, C(81)30(final) Annex 2. May 12, 1981.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained in the performance of the study.

There were no influences, impacts or circumstances noted which might have impaired the integrity of this study.

This study was performed at the Centre International de Toxicologie (C.I.T.), Miserey, 27005 Evreux, France.

Toxicology



J. Clouzeau
Biologist

Date: 14.2.94

OTHER SCIENTISTS INVOLVED IN THIS STUDY

Pharmacy

J. Richard
Doctor of Pharmacy

Toxicology

C. Pelcot
Study Supervisor

SUMMARY

At the request of Elf Atochem S.A., Paris-la-Défense, France, the potential of the test substance, 2-ETHYLHEXYL THIOGLYCOLATE, to induce delayed contact hypersensitivity following intradermal injection and cutaneous application was evaluated in guinea-pigs according to the maximization method of Magnusson and Kligman and O.E.C.D. (No. 406, 12th May 1981). The study was conducted in compliance with the Principles of Good Laboratory Practice Regulations.

Methods

Thirty guinea-pigs (15 males and 15 females) were allocated to 2 groups: a control group 1 (5 males and 5 females) and a treated group 2 (10 males and 10 females).

The sensitization potential of the test substance was evaluated after a 10-day induction period during which time the animals were treated with the vehicle (control group) or the test substance (treated group). On day 1, in presence of Freund's complete adjuvant, 0.1 ml of the test substance at a concentration of 25% in the vehicle was administered by intradermal route. On day 8, 0.5 ml of the test substance in its original form was applied by cutaneous route during 48 hours by means of an occlusive dressing. After a period of 12 days without treatment, a challenge cutaneous application of 0.5 ml of the vehicle (left flank) and 0.5 ml of the test substance in its original form (right flank) were administered to all animals.

The test substance and the vehicle were prepared on a dry compress then the dry compress was applied to the skin and held in place for 24 hours by means of an occlusive dressing. Cutaneous reactions on the challenge application sites were then evaluated 24 and 48 hours after removal of the dressing.

After the final scoring period, the animals were sacrificed and cutaneous samples were taken from the challenge application sites from all the animals. No histological examination was performed on the cutaneous samples.

The sensitivity of the guinea-pigs in C.I.T. experimental conditions were checked in a recent study with a positive sensitizer: Dinitro 2,4 Chlorobenzene. During induction period the test substance was applied at 0.05% (day 1) and 0.5% (day 8) concentrations. At cutaneous challenge application, 0.1% and 0.5% were tested on both flanks.

Results

No clinical signs and no deaths were noted during the study.

After the challenge application of the test substance, no cutaneous reactions were observed in the animals of the control group. A positive response characterised by a well-defined erythema was observed on the right flank of 10/20 and 5/20 treated animals after 24 and 48 hours, respectively. No oedema was noted. The reactions (very slight erythema) noted in 8/20 and 11/20 animals after 24 and 48 hours, respectively, were considered to be inconclusive evidence of sensitization.

The guinea-pigs which were used showed a satisfactory sensitization response in 100% animals using a positive sensitizer (appendix 5).

STATEMENT OF THE QUALITY ASSURANCE UNIT

The protocol, study (main) and report were inspected by the C.I.T. Quality Assurance Unit on the following dates:

<u>Inspection</u>	<u>Date of inspection</u>	<u>Date of inspection report</u>
Protocol	12.2.93	12.2.93
Test substance/preparation	10.9.93	10.9.93
Report (first typing)	10.1.94	10.1.94
Report (final)	14.2.94	14.2.94

The other stages (of the same type of studies) were inspected routinely on the following dates:

Animals/housing	8.9.93	8.9.93
Treatment	3.9.93	3.9.93

The inspections were performed in accordance with C.I.T. procedures and the principles of Good Laboratory Practice Regulations.



M. Labiche Date: 14.2.94
Pharmacist
Head of Quality Assurance Unit
and Scientific Archives

Conclusion

The test substance 2-ETHYLHEXYL THIOGLYCOLATE, induced positive skin sensitization cutaneous reactions in 10 out of 20, (50 %) guinea pigs. The allergenicity level of the test substance was (III) moderate in guinea-pigs.

1. INTRODUCTION

The objective of this study, performed according to maximization method established by Magnusson and Kligman (1), was to evaluate the potential of the test substance, 2-ETHYLHEXYL THIOGLYCOLATE, to induce delayed contact hypersensitivity in guinea-pigs.

The results of the study are of value in predicting the contact sensitization potential of the test material in Man.

During the induction period, the test substance was administered by intradermal route (together with an adjuvant to maximise potential reactions) and cutaneous route. After a rest period of 12 days, a challenge application with the test substance was performed in order to provoke a cutaneous sensitization reaction.

The study was conducted in compliance with:
. O.E.C.D. guideline No. 406, 12th May 1981.

2. MATERIALS AND METHODS

2.1. TEST AND CONTROL SUBSTANCES

2.1.1 Test substance

The test substance, 2-ETHYLHEXYL THIOGLYCOLATE, used in the study was supplied by Elf Atochem S.A.

Documentation supplied by the Sponsor identified the test substance as follows:

- . denomination: 2-ETHYLHEXYL THIOGLYCOLATE
- . batch number: 2401A
- . labelling: EHTG Lot 2401A, n° d'archivage CAL : 135/93
- . description: colourless liquid
- . quantity and container: a glass flask
- . date of receipt: 8.2.93
- . storage conditions: at room temperature, away from light
- . purity: 99.4%

Data relating to the characterization of the test substance are documented in a test article description and a certificate of analysis (presented in appendix 1) provided by the Sponsor.

2.1.2 Vehicle

The vehicle used was paraffin oil, batch No. 4547 (Coopérative Pharmaceutique Française, 77000 Melun, France).

2.1.3 Other substances

The other substances used were sterile isotonic aqueous NaCl solution, batch No. 3019 (Biosé-dra, 92240 Malakoff, France); Freund's complete adjuvant, batch No. 29829 (Osi, 75739 Paris, France); sodium laurylsulphate, batch No. 112H0485 (Aldrich, 67000 Strasbourg, France) and vaseline, batch No. 3006 (Monot, 21801 Quétigny, France).

- (1) Magnusson, B.; Kligman, A.M.: The identification of contact allergens by animal assay. The guinea-pig maximization test. *J. Invest. Derm.* 52: 268-276 (1969).

2.2. TEST SYSTEM

2.2.1 Animals

Species and strain: Dunkin-Hartley guinea-pigs.

Reason for this choice: species recommended by the international regulations for sensitization studies. The strain used has been shown to produce a satisfactory sensitization response using known positive sensitizers.

Breeder: Centre d'Élevage Lebeau, 78950 Gambais, France.

Number: 30 animals (15 males and 15 females).

Allocation of the animals to the groups: on day -1, the animals were weighed and randomly allocated to 2 groups: a control group 1 consisting of 10 animals (5 males and 5 females) and a treated group 2 consisting of 20 animals (10 males and 10 females).

Weight: on day 1, the animals had a mean body weight of 430 ± 22 g for the males and 429 ± 37 g for the females.

Acclimatization: at least 5 days before the beginning of the study.

Identification of the animals: the animals were identified individually by an ear-tattoo.

2.2.2 Environmental conditions

During the acclimatization period and throughout the study, the conditions in the animal room were as follows:

- . temperature: $22 \pm 3^\circ\text{C}$
- . relative humidity: $50 \pm 20\%$
- . light/dark cycle: 12 h/12 h

The air was non-recycled and filtered.

During the acclimatization period and throughout the study, the animals were housed individually in polycarbonate cages (48 x 27 x 20 cm) equipped with a polypropylene bottle. Sifted and dusted sawdust was provided as litter (SICSA, 92142 Alfortville, France). An analysis of potential residues and major contaminants is performed periodically (Laboratoire Wolff, 92110 Clichy, France).

2.2.3 Food and water

During the study, the animals had free access to "Guinea-pigs sustenance reference 106 diet" (U.A.R., 91360 Villemoisson-sur-Orge, France).

Food was periodically analysed (composition and contaminants) by the supplier.

The diet formula is presented in appendix 2.

Drinking water filtered by a F.G. Millipore membrane (0.22 micron) was contained in bottles.

Bacteriological and chemical analysis of the water and detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed periodically.

Results are archived at C.I.T.

There were no contaminants in the diet, water or sawdust at levels likely to have influenced the outcome of the study.

2.3. TREATMENT

2.3.1 Preliminary test

A preliminary test was performed to define the concentration to be tested in the main study.

By intradermal route

Determination of the Minimum Irritant Concentration (M.I.C.):

- . 24 hours before treatment, the dorsal region of the animals was clipped,
- . the test substance was prepared in an appropriate vehicle,
- . intradermal administration of the test substance (volume 0.1 ml) at increasing concentrations was performed in order to determine the maximum concentration which does not cause necrosis or ulceration, but a slight irritation,
- . evaluation of the potential cutaneous reactions, 24 and 48 hours after injection.

By cutaneous route

Determination of the Minimum Irritant Concentration (M.I.C.) and Maximum Non-Irritant Concentration (M.N.I.C.):

- . 24 hours before treatment, the dorsal region of the animals was clipped,
- . if necessary the test substance was diluted in an appropriate vehicle,
- . 0.5 ml of each concentration was applied to a gauze patch of approximately 4 cm² and then held in place by an occlusive dressing for 24 hours (2 concentrations per animal),
- . potential cutaneous reactions were evaluated 24 hours after removal of the gauze patches.

No residual test substance was observed upon removal of the dressings.

2.3.2 Main study

2.3.2.1 Preparation of the animals

For all animals and before each treatment, the application sites were:

- . clipped on days -1 and 7 (scapular area 4 x 2 cm),
- . clipped again on days 21 and 25 (each flank 2 x 2 cm) and shaved on day 21.

2.3.3 Induction phase by intradermal and cutaneous routes

2.3.3.1 Intradermal route

On day 1, 6 intradermal injections were made into a clipped area (4 x 2 cm) in the scapular region, using a needle (diameter: 0.50 x 16 mm, Terumo: C.M.L., 77140 Nemours, France) mounted on a 1 ml glass syringe (0.01 ml graduations, Record: Carrieri, 75005, Paris, France). Three injections of 0.1 ml were injected into each side of the animal, as follows:

Control group (figure 1)

- . Freund's complete adjuvant diluted to 50% with an injectable isotonic solution (NaCl 0.9%),
- . vehicle,
- . a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution and the vehicle.

Treated group (figure 2)

- . Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution,
- . test substance at a concentration of 25% in the vehicle,
- . a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution, and, the test substance at a concentration of 25% in the vehicle.

2.3.3.2 Cutaneous route

On day 7, the scapular area was clipped. As the test substance is shown to be non-irritant after occlusive cutaneous treatment during preliminary test, the animals were treated with 0.5 ml of sodium laurylsulphate (10%) in vaseline to provoke local irritation.

On day 8, a cutaneous application on the 6 injection areas (4 x 2 cm) of the scapular region was performed.

Control group

- . application of 0.5 ml of the vehicle.

Treated group

- . application of 0.5 ml of the test substance in its original form.

The test substance and the vehicle were prepared on a dry compress (Semes France, 54183 Heillecourt, France), which was then applied to the scapular region and held in place for 48 hours by means of an adhesive hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France). No residual test substance was observed at removal of the dressing.

One hour after removal of the occlusive dressing, cutaneous reactions were recorded.

2.3.3.3 Challenge phase

At the end of the rest period on day 22, the test substance was applied at the Maximum Non-Irritant Concentration (M.N.I.C.) i.e. in its original form.

On day 22, the animals from both groups received an application of 0.5 ml of the M.N.I.C. of the test substance on the posterior right flank, and 0.5 ml of the vehicle on the posterior left flank. This application was performed using a 1 ml plastic syringe (0.01 ml graduations, Terumo: C.M.L., 77140 Nemours, France). The articles were prepared on a dry compress (Semes France, 54183 Heillecourt, France), then applied to the skin. The compress was held in contact with the skin for 24 hours of means by an occlusive, hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France). No residual test substance was observed at removal of the dressing.

2.4. SCORING OF CUTANEOUS REACTIONS

Twenty-four and 48 hours after removal of the dressing from the challenge application site, the both flanks of the treated and control animals were observed in order to evaluate cutaneous reactions, according to the following scale:

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

Oedema formation

. No oedema	0
. Very slight oedema (barely perceptible)	1
. Slight oedema (visible swelling with well-defined edges)	2
. Moderate oedema (visible swelling raised more than 1 millimetre)	3
. Severe oedema (visible swelling raised more than 1 millimetre and extending beyond the area of exposure).....	4

Any other lesions were noted.

2.5. CLINICAL EXAMINATIONS

The animals were observed twice a day during the study in order to record clinical signs and to check for mortality.

2.6. BODY WEIGHT

The animals were weighed individually on the day of allocation into the groups, on the first day of the study (day 1), then on days 8, 15 and 25.

2.7. PATHOLOGY

2.7.1 Necropsy

On day 25, after the 48-hour observation period, the animals were sacrificed by CO₂ inhalation in excess.

2.7.2 Cutaneous samples

On day 25, a skin sample was taken from the treatment sites of the posterior left and right flanks of all animals. The samples were preserved in 10% buffered formalin.

2.7.3 Microscopic examination

No histological examinations were performed.

2.8. DETERMINATION OF THE ALLERGENICITY LEVEL

The treated animals show a positive reaction if macroscopic cutaneous reactions are clearly visible (erythema and/or oedema ≥ 2) and different from those of the control animals, or, if "doubtful" macroscopic reactions are confirmed at microscopic examination as being due to the sensitization process. Sensitization reactions are characterized at microscopic examination by basal spongiosis, reactional acanthosis of the epidermis and infiltration of mononucleated cells into the dermis ().

Determination of the allergenicity level

The allergenicity level of the test substance is calculated by comparing the number of animals showing positive reactions with the number of surviving treated animals at the end of the study.

% of animals showing a reaction	Allergenicity level	Classification
0 - 8	I	very weak
9 - 28	II	weak
29 - 64	III	moderate
65 - 80	IV	strong
81 - 100	V	very strong

According to the E.E.C. directive 91/325/E.E.C. published in the Journal Officiel des Communautés Européennes, when the reactions are positive in at least 30% of the treated animals, the test substance has sensitization properties and the sentence "R 43: May cause sensitization by skin contact" must be applied.

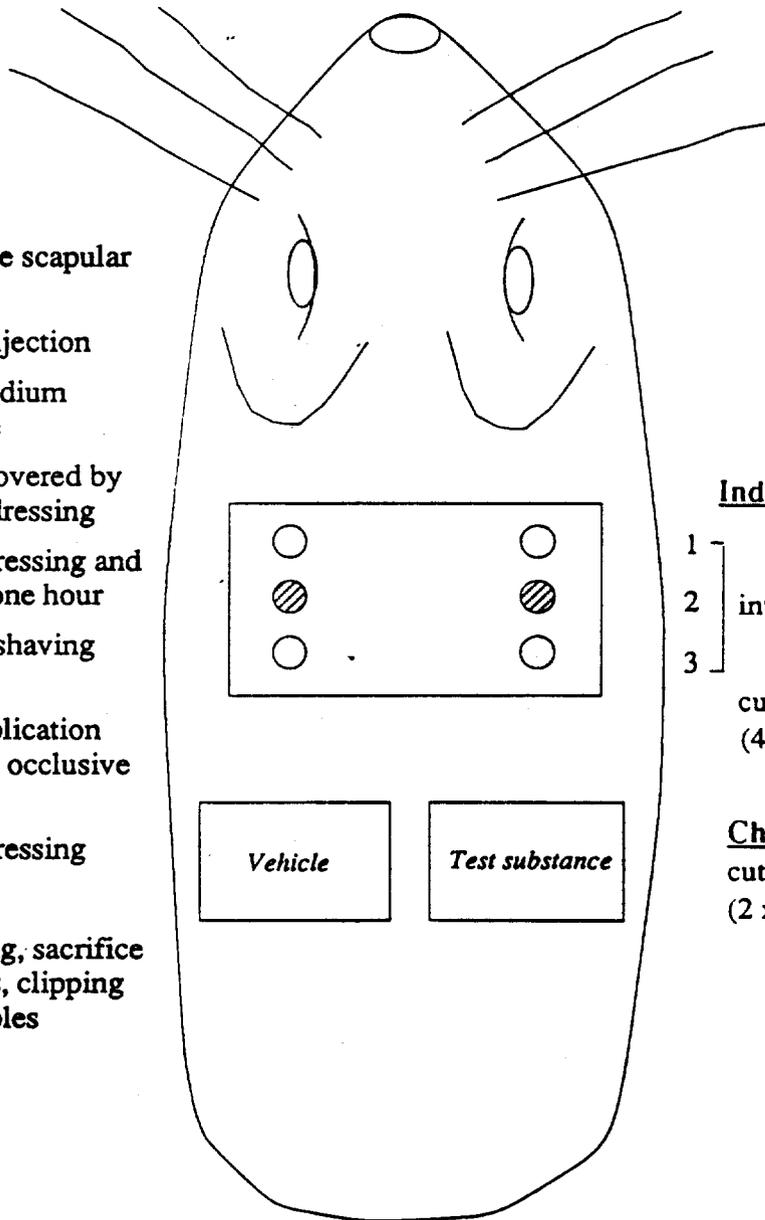
- (1) Duprat, P. ; Delsaut, L. ; Gradiski, D. ; Lepage, M. : Investigations histo-pathologiques et cytologiques lors de la mise en évidence, chez le cobaye, d'une allergie cutanée de type retardé. *Revue Méd. Vét.* 127: 7, 1083-1101 (1976).

2.9. SUMMARY DIAGRAMS

Figure 1: control group

Chronology

- Day -1 Clipping of the scapular region
- Day 1 Intradermal injection
- Day 7 Clipping + Sodium laurylsulphate
- Day 8 Application covered by an occlusive dressing
- Day 10 Removal of dressing and scoring after one hour
- Day 21 Clipping and shaving of the flanks
- Day 22 Challenge application covered by an occlusive dressing
- Day 23 Removal of dressing
- Day 24 First scoring
- Day 25 Second scoring, sacrifice of the animals, clipping and skin samples



Induction site

- 1
- 2 intradermal injections
- 3
- cutaneous application (4 x 2 cm)

Challenge application

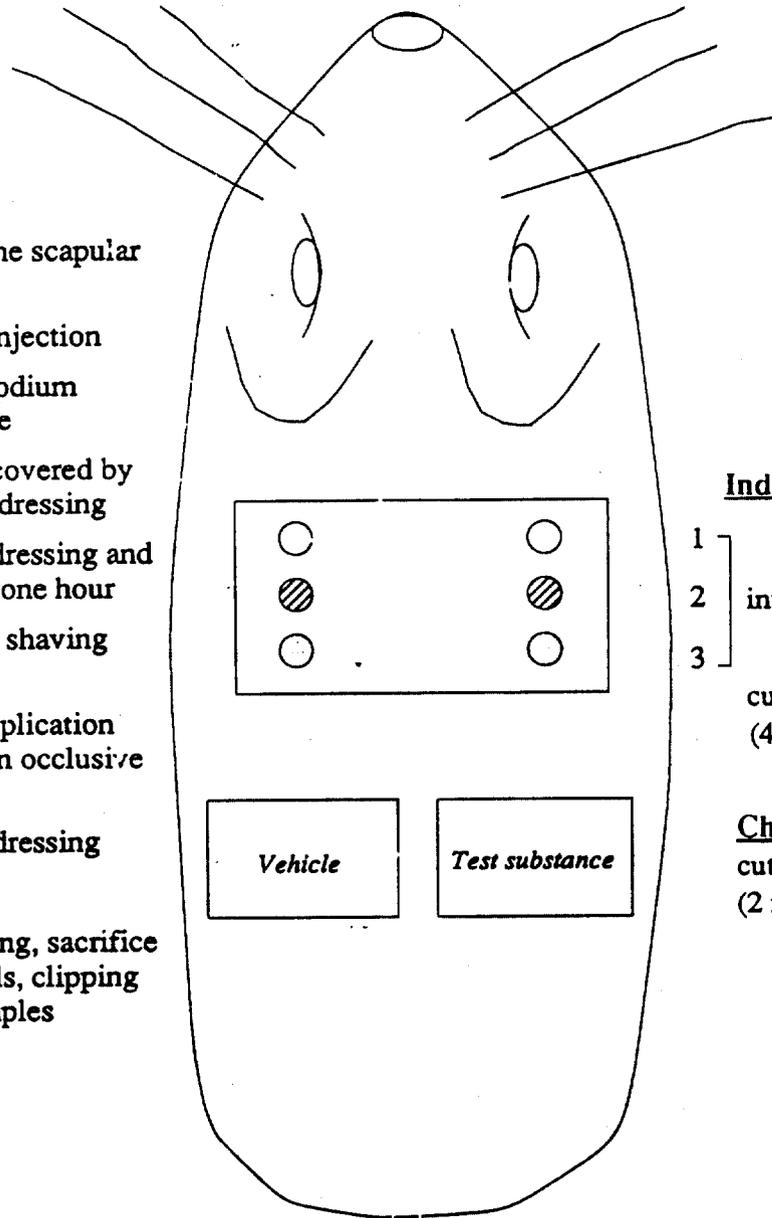
- cutaneous application (2 x 2 cm)

- 1 - 50% Freund's complete adjuvant and NaCl 0.9% solution
 - 2 - vehicle
 - 3 - 1 + 2, 50/50 (v/v)
- Intradermal injections

Figure 2: treated group

Chronology

- Day -1 Clipping of the scapular region
- Day 1 Intradermal injection
- Day 7 Clipping + Sodium laurylsulphate
- Day 8 Application covered by an occlusive dressing
- Day 10 Removal of dressing and scoring after one hour
- Day 21 Clipping and shaving of the flanks
- Day 22 Challenge application covered by an occlusive dressing
- Day 23 Removal of dressing
- Day 24 First scoring
- Day 25 Second scoring, sacrifice of the animals, clipping and skin samples



Induction site

- 1]
- 2] intradermal injection
- 3]
- cutaneous application (4 x 2 cm)

Challenge application
cutaneous application (2 x 2 cm)

- Intradermal injections
- 1] 50% Freund's complete adjuvant and NaCl 0.9% solution
 - ▨ 2] test substance and vehicle
 - 3] 1 + 2, 50/50 (v/v)

2.10. CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date	Day
Arrival of the animals	2.9.93	-8
Allocation of the animals into groups	9.9.93	-1
Weighing, induction by intradermal injection	10.9.93	1
Laurylsulfate application	16.9.93	7
Weighing, induction by cutaneous route	17.9.93	8
Removal of occlusive dressings and scoring of local reactions after 1 hour	19.9.93	10
Weighing	24.9.93	15
Challenge cutaneous application	1.10.93	22
Removal of occlusive dressings	2.10.93	23
Scoring of cutaneous reactions after . 24 hours	3.10.93	24
. 48 hours	4.10.93	25
Weighing, sacrifice of the animals and skin samples	4.10.93	25

2.11. ARCHIVES

The study archives:

- . protocol and possible amendments,
- . raw data,
- . correspondence,
- . final study report and possible amendments,
- . histological specimens:
 - tissues in preservative
 - possible blocks and slides

are stored in the premises of C.I.T., Miserey, 27005 Evreux, France, for 5 years after the end of the *in vivo* study. At the end of this period, the study archives will be returned to the Sponsor.

3. RESULTS

3.1. PRELIMINARY STUDY

3.1.1 Administration by intradermal route

The maximal administrable concentration by intradermal route was 50% of the test substance in the vehicle in presence of Freund's complete adjuvant. Several tests were performed to determine the minimal irritant concentration which did not provoke necrosis or ulceration.

Concentration of the test substance %	Scoring after treatment	
	24 hours	48 hours
1	irritation	irritation
10	irritation	irritation
25	irritation	irritation
50	necrosis	necrosis

M.I.C. is $\geq 25\%$.

Concentration used in the main study is 25% of the test substance.

3.1.2 Application by cutaneous route

The maximal applicable concentration by cutaneous route was 50% of the test substance in the vehicle. Several tests were performed to determine the M.I.C. and the M.N.I.C. after application of the test substance covered by an occlusive dressing for 24 hours.

Concentration of the test substance %	Scoring 24 hours after removal of the dressing (1)
50	no cutaneous reactions
100	no cutaneous reactions

M.N.I.C. is 100% of the test substance.

(1) No residual was observed.

3.2. MAIN STUDY

3.2.1 Clinical examinations

No clinical signs or mortalities were observed during the study.

The body weight gain of the treated animals was normal when compared to that of the control animals (figures 3 and 4, appendix 3).

3.2.2 Scoring of cutaneous reactions (appendix 4)

3.2.2.1 End of the induction period

On day 10, after removal of the dressing, slight irritation in the control and treated groups were observed at the intradermal injection sites.

3.2.2.2 Challenge application

After the challenge application, a very slight (1), well-defined (2) erythema was observed at the following frequency:

Erythema

Groups	Sex	Erythema score	Scoring of the cutaneous parameters			
			24 hours		48 hours	
			LF	RF	LF	RF
Control 1	Male	0	5/5	5/5	5/5	5/5
Treated 2	Male	0	10/10	-	10/10	1/10
		1	-	4/10	-	6/10
		2	-	6/10	-	3/10
Control 1	Female	0	5/5	5/5	5/5	5/5
Treated 2	Female	0	10/10	2/10	10/10	3/10
		1	-	4/10	-	5/10
		2	-	4/10	-	2/10

LF: left flank (control)

RF: right flank (treated)

After the challenge application of the test substance, no cutaneous reactions were observed in the animals of the control group. In the treated group, following cutaneous reactions were noted:

- very slight erythema in 8/20 animals after 24 hours and in 11/20 animals after 48 hours
- well-defined erythema in 10/20 animals after 24 hours and in 5/20 animals after 48 hours.

4. CONCLUSION

Under our experimental conditions and according to the maximization method established by Magnusson and Kligman, cutaneous reactions attributable to the sensitization potential of the test substance, 2-ETHYLHEXYL THIOGLYCOLATE, in its original form were observed in guinea-pigs.

Figure 3: Male body weight gain (g)

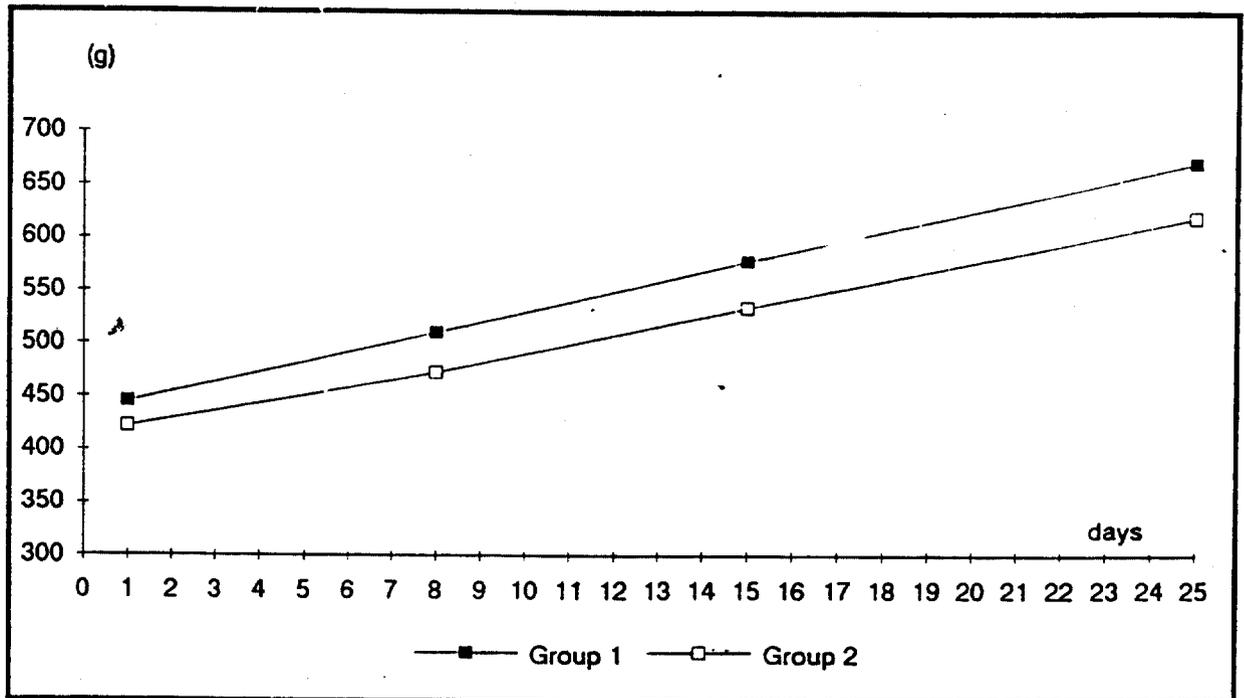
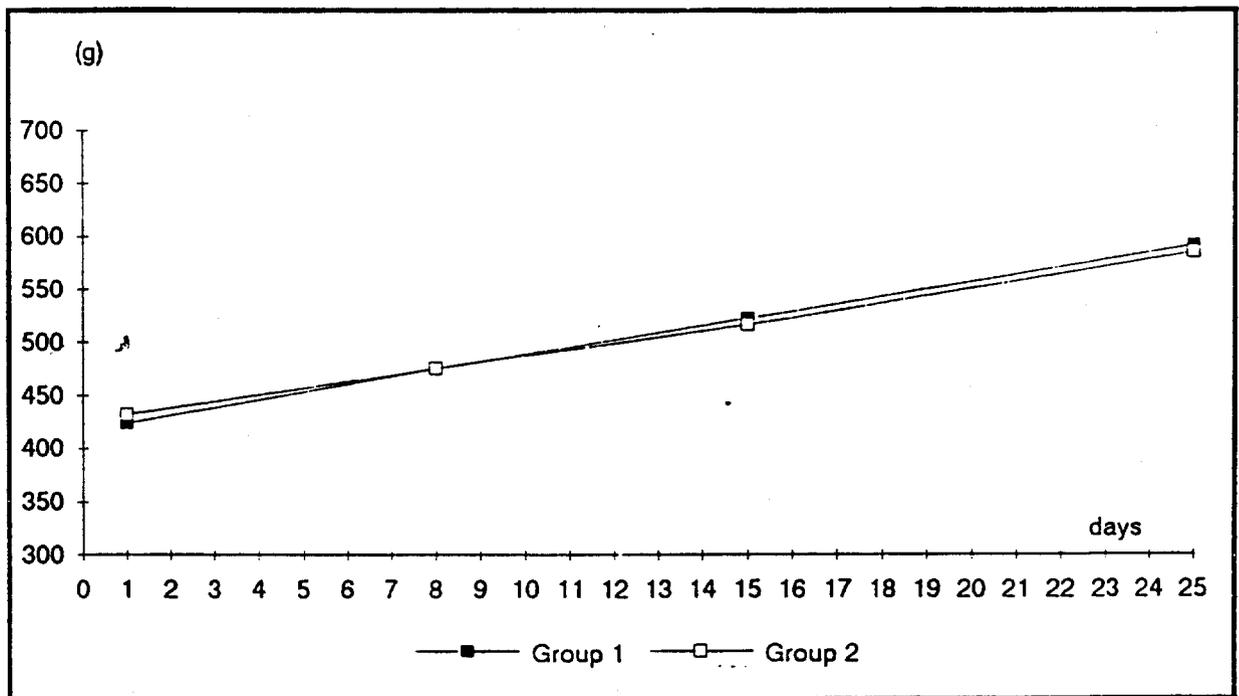


Figure 4: Female body weight gain (g)



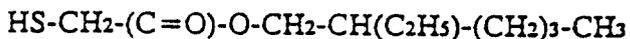
APPENDICES

1. Test article description and certificate of analysis

TEST ARTICLE DESCRIPTION

2-ETHYLHEXYL THIOGLYCOLATE

STRUCTURAL FORMULA



IDENTITY

Test article name	: 2-ethylhexyl thioglycolate (EHTG)
Chemical name	: Acetic acid, mercapto-, 2-ethylhexyl ester
CAS number	: 7659-86-1
EINECS number	: 2316264
Molecular formula	: C ₁₀ H ₂₀ O ₂ S
Molecular weight	: 204.32
Purity	: 99.4% (w/w)
Origin and batch	: SNEA(P), 2401A
ATOCHEM filing number	: CAL 135/93

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	: Colourless liquid
Viscosity	: 3.19 cP at 20°C
Specific gravity	: 0.974
Melting point	: < -31°C
Boiling point	: 133.5°C at 760 mm Hg
Vapor pressure	: 0.09 mbar at 20°C 0.397 mbar at 50°C
Flash point	: 119°C (ASTM D92)
Solubility	: insoluble in water soluble in ethylic alcohol

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

LD₅₀ / rat / oral = 303 mg/kg.

STORAGE AND DISPOSAL

Storage	: in dark and at room temperature
Expiry date	: January 1994
Disposal	: incineration

adresse postale :
BP 22 64170 Lacq
téléphone : - 33 - 59 92 22 22
téléc : petra 560053F

direction exploration production france

CENTRE ATOCHEM LEVALLOIS
95 rue DANTON
92303 LEVALLOIS-PERRET

FRANCE

ATTN: M. BOURALY

vitréf.

n/réf. RD 938002

objet : **ANALYSE - THIOGLYCOLATE D'ETHYL 2 HEXYLE (EHTG)**

CARACTERISTIQUES	ANALYSE
Pureté (%Pds)	99.40
SH (%Pds)	16.05
Indice d'acide (mg KOH/g)	0.04
Eau (ppm)	130
Alcool (%Pds)	0.149
Couleur APHA	≤ 10

Lacq le 5- 1-1993

M. DELOURME

2. Diet formula

Ref: 106
COMPLETE DIET
GUINEA-PIGS SUSTENANCE
 Appearance: 4.5 mm diameter pellets
 Conditioning: bags of 25 kgs

Daily portion: to sustain Guinea-pigs 35 - 50 g according to age and body weight, water ad libitum.

FORMULA %

Cereals, sugar	42
Milled vegetables	46
Vegetable proteins (pellets, yeast)	9
Mineral and vitamin composition	3

MEAN ANALYSIS %

Calorific value (Cal/kg)	2600
Water	10
Protids	17
Lipids	3
Carbohydrates (N.F.E.)	49
Cellulose (Weende)	13
Minerals	8

AMINO ACIDS (calculated in mg/kg)

Arginine	8500
Cystine	2500
Lysine	7200
Methionine	2100
Tryptophan	2000
Glycine	6000

MINERALS (calculated in mg/kg)			
	Nat. input	Input /MC	Total
P	7400	1400	8800
Ca	5400	5600	11000
K	12000	0	12000
Na	1300	1950	3250
Mg	3270	130	3400
Mn	60	40	100
Fe	170	150	320
Cu	10	15	25
Zn	40	45	85
Co	0.1	1.5	1.6

VITAMINS (calculated in kg)			
	Nat. input	Synth. input	Total
Vitamin A	3400 IU	6000 IU	9400 IU
Vitamin D3	30 IU	2000 IU	2030 IU
Vitamin B1	6 mg	6.40 mg	12.40 mg
Vitamin B2	5 mg	6.40 mg	11.40 mg
Vitamin B3	22 mg	26 mg	48 mg
Vitamin B6	0.70 mg	2.70 mg	3.40 mg
Vitamin B12	0.003 mg	0.012 mg	0.015 mg
Vitamin C	0 mg	200 mg	200 mg
Vitamin E	15 mg	60 mg	75 mg
Vitamin K3	5 mg	12.60 mg	17.60 mg
Vitamin PP	97 mg	14.50 mg	111.50 mg
Folic acid	2.20 mg	1.30 mg	3.50 mg
P.A.B. acid	0 mg	2.50 mg	2.50 mg
Biotin	0.02 mg	0.06 mg	0.08 mg
Choline	1010 mg	060 mg	1070 mg
Meso-Inositol	0 mg	62.50 mg	62.50 mg

This food is supplemented with stabilized coated vitamin C, avoiding the need of other food substances (greenery, ascorbic acid) if used within 4 months of date of manufacture.

U.A.R., 7 rue Galliéni, Villemoisson, 91360 Epinay-sur-Orge - Tel: 69.04.03.57
 Telex: UAR 691716F.

3. Individual body weight values

INDIVIDUAL BODY WEIGHT VALUES
(g)

Groups	Sex	Animals	Days								
			-1	1	(1)	8	(1)	15	(1)	25	
1	Male	01	435	440	49	489	71	560	112	672	
		02	424	428	86	514	55	569	96	665	
		03	448	435	77	512	121	633	13	646	
		04	453	463	50	513	47	560	174	734	
		05	462	461	64	525	44	569	71	640	
			M	444	445	65	511	68	578	93	671
			SD	15	16	16	13	32	31	59	37
		Female	16	412	425	13	438	60	498	61	559
			17	385	389	58	447	33	480	57	537
			18	447	448	62	510	38	548	58	606
			19	403	404	77	481	50	531	77	608
			20	439	452	51	503	53	556	94	650
			M	417	424	52	476	47	523	69	592
			SD	26	27	24	32	11	33	16	45
2	Male	06	409	404	63	467	55	522	95	617	
		07	427	432	55	487	48	535	77	612	
		08	358	464	-8	456	35	491	76	567	
		09	427	427	75	502	45	547	101	648	
		10	407	415	88	503	56	559	101	660	
		11	417	426	89	515	33	548	66	614	
		12	420	437	41	478	68	546	91	637	
		13	418	423	47	470	43	513	123	636	
		14	368	382	80	462	70	532	121	653	
		15	411	413	-27	386	163	549	10	559	
			M	406	422	50	473	62	534	86	620
			SD	24	22	40	36	38	21	33	34
		Female	21	452	460	50	510	53	563	55	618
			22	420	431	60	491	51	542	53	595
			23	351	336	38	374	77	451	98	549
			24	460	471	21	492	45	537	93	630
			25	432	443	36	479	11	490	53	543
			26	429	438	34	472	37	509	74	583
			27	402	408	49	457	49	506	60	566
			28	433	450	32	482	47	529	84	613
	29		468	481	49	530	24	554	91	645	
	30		415	404	64	468	19	487	26	513	
		M	426	432	43	476	41	517	69	586	
		SD	33	42	13	41	19	35	23	42	

(1) = Body weight gain
M = Mean
SD = Standard Deviation

4. Individual observation of cutaneous reactions

MACROSCOPIC EXAMINATION OF CUTANEOUS REACTIONS

Challenge application

Group	Sex	Animals	Day 24 scoring period (after 24 hours)				Day 25 scoring period (after 48 hours)			
			Erythema		Oedema		Erythema		Oedema	
			LF	RF	LF	RF	LF	RF	LF	RF
Control 1	Male	01	0	0	0	0	0	0	0	0
		02	0	0	0	0	0	0	0	0
		03	0	0	0	0	0	0	0	0
		04	0	0	0	0	0	0	0	0
		05	0	0	0	0	0	0	0	0
	Female	16	0	0	0	0	0	0	0	0
		17	0	0	0	0	0	0	0	0
		18	0	0	0	0	0	0	0	0
		19	0	0	0	0	0	0	0	0
		20	0	0	0	0	0	0	0	0
Treated 2	Male	06	0	1	0	0	0	0	0	0
		07	0	2	0	0	0	1	0	0
		08	0	2	0	0	0	2	0	0
		09	0	1	0	0	0	1	0	0
		10	0	2	0	0	0	1	0	0
		11	0	2	0	0	0	2	0	0
		12	0	2	0	0	0	1	0	0
		13	0	1	0	0	0	1	0	0
		14	0	2	0	0	0	2	0	0
		15	0	1	0	0	0	1	0	0
	Female	21	0	1	0	0	0	2	0	0
		22	0	1	0	0	0	1	0	0
		23	0	1	0	0	0	1	0	0
		24	0	0	0	0	0	0	0	0
		25	0	2	0	0	0	1	0	0
		26	0	2	0	0	0	1	0	0
		27	0	0	0	0	0	0	0	0
		28	0	2	0	0	0	1	0	0
		29	0	1	0	0	0	0	0	0
		30	0	2	0	0	0	2	0	0

LF: left flank (control)
RF: right flank (treated)

5. Positive control to check the sensitivity of Dunkin-Hartley guinea-pigs

Purpose: check the sensitivity of Dunkin-Hartley guinea-pigs to a positive control test article

Method : Magnusson and Kligman
Test substance : DINTRO 2.4 CHLOROBENZENE
C.I.T. Study - Date : July 1993 (CIT/Study No. 10829 TPG)
Number of animals : 5 females
Induction : 0.05% intradermal route day 1
 0.5% cutaneous route day 8
Challenge application: 0.1% right flank
 0.5% left flank

Conclusion

In our experimental conditions and according to the Magnusson and Kligman method, DINTRO 2.4 CHLOROBENZENE at a concentration of 0.5% induced positive skin sensitization reactions in 100% of the guinea-pigs.

**INDIVIDUAL REACTIONS: CHALLENGE PHASE
 MACROSCOPIC FINDINGS**

Group	Sex	Animals	24-hour scoring period				48-hour scoring period				Conclusion	
			Erythema		Oedema		Erythema		Oedema		LF	RF
			LF	RF	LF	RF	LF	RF	LF	RF		
Treated	Female	16	3	2	0	0	3/S	2/S	0	0	+	+
		17	3	2	0	0	3	1/S	0	0	+	+
		18	4	2	0	0	4	2/S	0	0	+	+
		19	4	2	0	0	4	1/S	0	0	+	+
		20	3	1	0	0	3/S	0	0	0	+	+/-

+ : hypersensitizing reaction
 S : dryness of the skin
 LF: left flank
 RF: right flank



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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Manager, Product Safety and Toxicology
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King of Prussia, Pennsylvania 19406-0018

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DEC 08 1994

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Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12933 A



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NON-CAP

CAP

Submission number: 12933A

TSCA Inventory: Y N D

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CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # BEHQ-0394-12933 SEQ. A
 TYPE: INT. SUPP FLWP
 SUBMITTER NAME: Elf Atochem North America, Inc.

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

VOLUNTARY ACTIONS:
 0601 NO ACTION REPORTED
 0602 STUDIES PLANNED (IN HUMAN)
 0603 NOTIFICATION OF WORKING CONDITIONS
 0604 LABELS/MSDS (HUMAN)
 0605 PROCESS/ANDI, INC. (HUMAN)
 0606 APPAUSE DISCONTINUED
 0607 PRODUCTION DISCONTINUED
 0608 CONFIDENTIAL

SUB. DATE: 03/10/94 OTS DATE: 03/15/94 CSRAD DATE: 05/09/94

CHEMICAL NAME: _____ CAS# 7659-86-1

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL. TRANS (IN VITRO)	01 02 04	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	ENV. OCCUR/REL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	RESPONSE REQUEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHIR. TOX. (HUMAN)	01 02 04	CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (HUMAN)	01 02 04		

TRIAJE DATA: NON-CEL INVENTORY YES (DROPPREF) NO IN HUMAN Non-Cap
 SPECIES: GP TOXICOLOGICAL CONCERN: LOW MED HIGH
 ONGOING REVIEW: YES (DROPPREF) NO (CONTINUE) REFR
 USE: _____ PRODUCTION: _____

0 0 0 >

<ID NUMBER>

8(e)-12933A >

<TOX CONCERN>

M >

<COMMENT>

DERMAL SENSITIZATION IN GUINEA PIGS IS OF MODERATE CONCERN. CHALLENGE APPLICATION PRODUCED, AT 24 HOURS, WELL-DEFINED ERYTHEMA IN 50% (10/20) OF ANIMALS, AND VERY SLIGHT ERYTHEMA IN 40% (8/20) OF ANIMALS. AT 48 HOURS, 25% (5/20) HAD WELL-DEFINED ERYTHEMA, AND 55% (11/20) HAD VERY SLIGHT ERYTHEMA. EDEMA WAS NOT SEEN. \$\$\$\$
-CPSS- 0406951403