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ELF ATOCHEM NORTH AMERICA, INC.

900 First Avenue, P.O. Box 1536
King of Prussia, PA 19406-0018

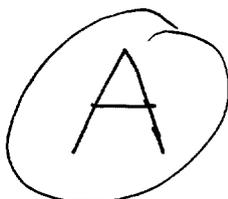
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U.S. Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460

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

RE: Report Submitted Pursuant to the TSCA Section 8(e)
Compliance Audit Program

CAP Identification Number: 8ECAP-0026

Dear Sir/Madam:

Pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by Elf Atochem North America Inc. (Atochem) and Environmental Protection Agency (EPA), Atochem is submitting the enclosed four-hour vapor inhalation study to the EPA. This study does not involve effects in humans.

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

The enclosed study provides information on the chemical Telogen D. Its exact chemical name is 1,1,2-trichloro-2,2-difluoro-1-iodoethane and its CAS number is 677-48-5.

The title of the enclosed report is Telogen D Acute Inhalation Toxicity in Rats. 4-Hour Exposure. The following is a summary of the adverse effects observed in this study.

Groups of five male and five female albino rats were exposed to vapors of Telogen D at concentrations of 0.17, 0.25, 0.42, 0.86 and 0.97 mg/l for four hours. The 4-hour inhalation LC₅₀ was estimated to be 0.47 mg/l.



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61 pgs.

TSCA CAP
Telogen D
October 12, 1992
Page Two

To our knowledge, Atochem has not previously submitted any TSCA Section 8(e) notices or premanufacture notifications on the subject chemical.

Further questions regarding this submission may be directed to me at 215 337-6892.

Sincerely,



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

Enclosures

Contains No CBI

CONFIDENTIAL

PWT 47/8727

6/17/87

6/17/87

2983

On Microfilm

TELOGEN D

ACUTE INHALATION TOXICITY

IN RATS

4-HOUR EXPOSURE

F-799

Addressee:

Dr. Joel A. Seckar,
Manager, Toxicology,
Safety, Health and Environmental
Affairs,
Pennwalt Corporation,
900 First Avenue,
P.O. Box C,
King of Prussia,
Pennsylvania 19406-0018,
U.S.A

Authors:

Graham C. Jackson,
Colin J. Hardy,
Saleh K. Majeed,
Chirukandath Gopinath.

Huntingdon Research Centre Ltd.,
Huntingdon,
Cambridgeshire,
PE18 6ES,
ENGLAND.

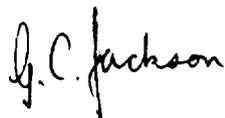
11 June 1987

CAS: 677-48-5

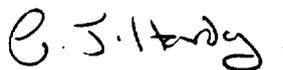
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England

We the undersigned, hereby declare that the work was performed under our supervision according to the procedures herein described, and that this report provides a correct and faithful record of the results obtained.



Graham C. Jackson, B.A., L.R.S.C.,
Senior Scientific Officer,
Department of Inhalation Toxicology



Colin J. Hardy, B.Sc., Ph.D., M.I.Biol., Dip.R.C.Path.,
Head of Industrial Chemicals Unit,
Department of Inhalation Toxicology

HRC REPORT No. PWT 47/8727

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

To the best of my knowledge and belief the study described in this report was conducted in compliance with the following Good Laboratory Practice Standards:

United States Environmental Protection Agency,
Title 40 Code of Federal Regulations Part 792,
Federal Register, 29 November 1983

Organization for Economic Co-operation and Development
ISBN 92-64-12367-9, Paris 1982

B. J. Hardy
C.J. Hardy, B.Sc., Ph.D., M.I.Biol., Dip.R.C.Path.,
Study Director

7.1.87
Date

QUALITY ASSURANCE STATEMENT

Certain studies of short duration, such as that described in this report, are conducted at HRC in a setting which involves frequent repetition of similar or identical procedures. At or about the time the study described in this report was in progress, 'process-based' inspections were made by the Quality Assurance Unit of critical procedures relevant to this study type. For the inspection of any given procedure, at least one study was selected without bias. The findings of these inspections were reported promptly to the Study Director and to HRC management.

This report has been audited by the HRC Quality Assurance Unit. It is considered to be an accurate presentation of the procedures and practices employed during the course of the study and an accurate presentation of the findings.

P. H. C. V. Richold
Peter H.C.V. Richold, B.Sc.,
Systems Compliance Auditor,
Quality Assurance Unit.

2.6.87
Date

SUMMARY	i	-	ii
INTRODUCTION			1
MATERIALS AND METHODS			
Test substance			2
Animals and maintenance	2	-	3
Inhalation exposures			3
Exposure system	3	-	4
Procedure	4	-	5
Chamber atmosphere analyses			5
Particle analysis			5
Chamber temperature			5
Observations	5	-	6
Terminal studies			6
Estimation of the LC ₅₀ (4-hour) and standard error			6
RESULTS			
Chamber atmosphere conditions			
Concentrations of TELOGEN D			7
Particle analysis			7
Chamber air temperature	7	-	8
Clinical observations			
Mortality			8
Clinical signs	8	-	9
Bodyweight			9
Food and water consumption			9
Terminal studies			
Lung weight to bodyweight ratio	9	-	10
Estimation of the LC ₅₀ (4-hour) for TELOGEN D			10
Macroscopic pathology			10
Microscopic pathology			10
FIGURES			
1. Exposure system			11
2a. Group mean bodyweights - male rats			12
2b. Group mean bodyweights - female rats			13

TABLES

1.	Concentration of TELOGEN D in air samples	14	
2.	-Particle counts	15	
3.	Clinical signs during exposure	16	- 17
4.	Clinical signs during observation period	18	- 19
5.	Individual and group mean bodyweights (g)	20	- 25
6.	Group mean daily food consumption (g/rat)	26	
7.	Group mean daily water consumption (g/rat)	27	
8.	Lung weight to bodyweight ratios	28	- 30

APPENDICES

1.	Method of analysis for TELOGEN D	31	- 32
2.	Pathological findings for individual rats	33	- 50

Test substance: TELOGEN D
1, 1, 2-Trichloro-2, 2-difluoro-1-iodoethane.

Test animals: Albino rats, (Sprague-Dawley).

Route of administration: By inhalation of test atmospheres containing vapour of test substance. Each test group was subjected to a single 4-hour continuous whole-body exposure.

Observation period: 14 days post exposure.

Results

Atmosphere concentrations of
TELOGEN D and mortality:

Group	Exposure level (mg/l)	Number dead/ number exposed		
		Males	Females	Total
1	Control	0/5	0/5	0/10
2	0.17	0/5	0/5	0/10
3*	0.25	5/5	0/5	5/10
4	0.97	5/5	5/5	10/10
5	0.42	2/5	0/5	2/10
6	0.86	5/5	4/5	9/10

* High variation in concentration

Clinical signs:

(a) During exposure

Signs observed in rats exposed to TELOGEN D, included partial closing of the eyes, disturbance to the breathing pattern and adoption of a hunched body posture.

(b) During the observation period

Signs observed in a proportion of test rats following exposure to TELOGEN D included disturbances to the breathing pattern, lethargy, pilo-erection, and discharge from the eyes.

Disturbances to the breathing pattern persisted for several days following exposure but most rats were normal by Day 3 and all were normal by Day 9.

Bodyweight: The rats that survived exposure to TELOGEN D lost weight or gained at a reduced rate for up to 6 days following exposure.

Subsequently the rate of bodyweight gain was similar to that of the control rats.

Food and water consumption: Food consumption was markedly reduced for 1-2 days and slightly reduced for a further 2-3 days following exposure.

Water consumption was reduced for 1-2 days following exposure.

Lung weight to bodyweight ratio: The ratio was higher than normal for all decedent rats and for 2/5 female survivors at 0.42 mg/l and 1/1 female survivor at 0.86 mg/l.

Estimate of the LC₅₀ (4-hour) for TELOGEN D: 0.47 mg/l of air (39 ppm).

Macroscopic pathology: Decedent rats had congested lungs and a frothy fluid in the trachea.

Survivors were within normal limits except for a pale and swollen appearance of the lungs of the 1 surviving female rat exposed at 0.86 mg/l

Microscopic pathology: No microscopic abnormalities in the lungs of rats that survived exposure to TELOGEN D.

The acute inhalation toxicity of the vapour of TELOGEN D was assessed by exposing groups of rats, each for a period of 4 hours, to atmospheres containing vapour of the test substance.

The study was conducted at the Huntingdon Research Centre during the period 13 August - 19 September 1986.

On completion of the study all data relating to the study, all preserved tissues and a copy of this report were lodged in the Huntingdon Research Centre Archives, Huntingdon, Cambridgeshire, England.

Other dates were:

Protocol Approval by Study Director: 14 February 1986

Protocol Approval by HRC Management: 10 February 1986

Protocol Approval by Sponsor: 20 June 1986

Test substance

The test substance was a dark brown/dark purple mixture of liquid and crystals supplied by the Sponsor, in glass bottles contained in steel tins.

The material was identified as:

1, 1, 2-Trichloro-2, 2-difluoro-1-iodoethane
(TELOGEN D)
Code number 6248-163-5

The test substance was received on 6 June 1986 and was stored at 4°C.

Information supplied by the Sponsor indicated that the material was sufficiently stable for use in this study and was 90 - 98% w/w pure.

The test substance is referred to as TELOGEN D in this report.

Animals and maintenance

Sixty 6-8 week old, 30 male and 30 female albino rats (Sprague-Dawley origin), were obtained in two consignments, from Charles River U.K. Limited, Manston Road, Margate, Kent, England.

The rats were ordered so that they would be approximately 200 g weight on the day of exposure. Deliveries were made on 13 August 1986 (25 male and 25 female rats) and 27 August 1986 (5 male and 5 female rats). The rats were allocated to one of 6 groups and each rat was identified by a number tattooed on the ears.

The rats were caged 5 males or 5 females to a cage and acclimatised to laboratory conditions for at least 5 days before exposure.

The cages were made of polypropylene (size 38 cm x 56 cm x 18 cm height) and had detachable wire mesh tops and floors. The cages were suspended on a movable rack. While in their cages all rats had free access to a measured amount of food (Labsure LAD 1) and tap water. Food and water supplies were analysed routinely to determine the levels of chemical or microbiological contaminants.

The rats remained in a holding room except for the 4-hour exposure and an overnight post exposure period when the rats were kept in a ventilated cabinet to allow dispersal of any residual test substance.

The mean maximum and minimum temperatures of the holding room during the period of the study are shown below:

Mean maximum temperature °C	Mean minimum temperature °C	Relative humidity %
25 (1.1)	20 (1.1)	54 (6.8)

The numbers in parentheses are standard deviations of the mean

Inhalation exposures

Five groups of 10 rats (5 male and 5 female), were exposed continuously for 4 hours to test atmospheres containing TELOGEN D in the form of vapour.

A further group of 10 rats (5 male and 5 female) was exposed to air alone using the same type of exposure system.

The groups were exposed on the following dates:

Group	Date of exposure
1 (Control)	19 August 1986
2 (Test)	19 August 1986
3 (Test)	20 August 1986
4 (Test)	21 August 1986
5 (Test)	22 August 1986
6 (Test)	5 September 1986

Exposure system

Vapour generation

Vapour of TELOGEN D was generated in the following ways:

For Group 2 an aliquot of TELOGEN D was placed in a round-bottomed flask which was held at 50°C in a water bath. Air was passed through the flask at 215 ml per minute and the vapour-laden air mixed with diluent air using a Y-piece to give a total flow of 25 litres per minute.

For Group 3 an aliquot of TELOGEN D was placed in a test tube and air was passed through the test substance at a rate of 150 ml per minute. The vapour-laden air was then mixed with diluent air using a Y-piece to give a total flow of 25 litres per minute.

For Group 4 an aliquot of TELOGEN D was mixed with glass wool and the glass wool impregnated with TELOGEN D was placed in a glass column. Air was passed through the glass column at 250 ml per minute and the vapour-laden air was mixed with diluent air using a Y-piece to give a total flow of 25 litres per minute.

For Group 5 an aliquot of TELOGEN D was melted and placed in a 5 ml syringe. The TELOGEN D was maintained in a molten state by a water jacket surrounding the syringe and held at 46-49°C. The syringe was placed on a syringe pump and connected to a glass concentric-jet atomiser. A supply of compressed air, heated by passing it through a coil in a water bath maintained at 45-48°C, was connected to the outer annulus of the atomiser. The air flow was set at 25 litres per minute. The TELOGEN D was atomised and subsequently evaporated to form vapour.

For Group 6 an aliquot of TELOGEN D was melted and placed in a 5 ml syringe. The TELOGEN D was maintained in a molten state by a water jacket surrounding the syringe and held at 49-50°C. The syringe was placed on a syringe pump and connected to a 1 metre long coiled glass column with a water-jacketed delivery tube. The glass column was placed in a water bath maintained at 49-50°C. Air was introduced into the glass column, at the same point as the molten TELOGEN D, at 25 litres per minute. The air/TELOGEN D mixture then passed through the column in which the TELOGEN D was vaporised. The vapour-laden air was then passed into the exposure chamber.

Exposure chambers

The whole-body exposure chambers used for the exposures were of square section and were fitted with pyramidal tops. The chambers were made of perspex and had an internal volume of approximately 115 litres. Each chamber was divided by wire mesh partitions to provide 10 separate animal compartments.

The test atmosphere entered through a port at the base centre of the chamber and passed through small holes in the lower edge of the square section. Each chamber was positioned inside a large cabinet equipped with an extract fan exhausting to atmosphere through a collection filter.

The exposure system is shown in Figure 1.

Procedure

The vaporisation system was established as described above.

The rats to be exposed were placed into separate compartments of the exposure cage.

The vapour generator was switched on and the exposure timed for 4 hours, following a 10.5-minute¹ equilibration period.

After 4 hours the supply of test vapour to the exposure chamber was discontinued and the exposure chamber was allowed to clear before the rats were removed for examination.

¹ 10.5 minutes is the theoretical time required for the concentration of aerosol in the chamber to reach 90% of its final value under the conditions of exposure employed.

The procedure was repeated, with appropriate vapour generation equipment, for each of the other test groups.

The control group was treated similarly but exposed to air only.

Following exposure the rats were returned to the holding cages and food and water supplies were restored. The rats were kept in a ventilated cabinet overnight and then returned to the holding room for the remainder of the observation period.

Chamber atmosphere analyses

Five air samples were taken from the chamber during each exposure and analysed to determine the concentration of TELOGEN D in the chamber atmosphere. The method of analysis for TELOGEN D is described in Appendix 1.

The samples were drawn through a sintered glass bubbler containing 2, 2, 4, trimethyl pentane as the trapping agent, at 2 litres per minute. The volume of the air samples was measured with a wet-type gas meter.

Particle analysis

Twice during each exposure samples were withdrawn from the exposure chamber using a Royco model 218 optical particle analyser in order to monitor the test atmosphere for the presence of particles of the test substance.

Chamber temperature

The temperature in each exposure chamber was measured with a mercury bulb thermometer and recorded at the start of the exposure and at 30-minute intervals during the exposure.

Observations

Clinical signs

The rats were observed continuously during the exposure for signs of reaction to the test substance and at least twice daily during the observation period.

Bodyweight

All rats were weighed daily from the day of delivery to the Huntingdon Research Centre until the end of the observation period.

Food and water consumption

Food and water consumption were determined daily by weight loss from the food hoppers and water bottles.

Terminal studies

At the end of the 14-day observation period the surviving rats were anaesthetised by intraperitoneal injection of pentobarbitone sodium and killed by exsanguination.

All rats dying as a result of exposure or killed at termination were subjected to a detailed macroscopic examination. The lungs were removed, dissected clear of surrounding tissue and weighed in order to calculate the lung weight to bodyweight ratio.

The lungs were infused with and preserved in buffered 10% formalin together with samples of the liver and kidneys.

The lungs of the rats in Groups 2, 3, 5 and 6 that survived exposure to TELOGEN D and the lungs of the control rats were processed for microscopic examination. The fixed tissues were embedded in paraffin wax, sectioned at 5 μ m, stained which haematoxylin and eosin and examined under the light microscope.

Estimation of the LC₅₀ (4-hour) and standard error

The concentration of TELOGEN D likely to cause death in 50% of exposed rats within 14 days following a single 4-hour exposure was calculated by the log probit method of Miller and Tainter¹.

The standard error was calculated from the formula:

$$SE \text{ of } LC_{50} = \frac{2s}{\sqrt{2N}}$$

Where 2s is the estimated increment in concentration of the test substance between probits 4.0 and 6.0 corresponding to 16% and 84% mortality and N is the total number of rats in groups with mortality between 6.7% and 93.3% (Probits 3.5 and 6.5).

¹ Miller, L.C. and Tainter, M.L. Proc. Soc. Exp. Biol. Med. 57, (2), 1944, pp 261-264

CHAMBER ATMOSPHERE CONDITIONSConcentrations of TELOGEN D

The analytical results for each air sample are shown in Table 1.

The mean concentrations determined for each exposure and the standard deviations of the means are shown below:

Group	TELOGEN D (mg/l)	Standard deviation
2	0.17	0.031
3	0.25	0.158
4	0.97	0.215
5	0.42	0.068
6	0.86	0.035

The variation in concentration was greater than is normally seen. This was considered to be due to technical difficulties associated with production of the test atmospheres.

The control of the exposure levels was considered adequate for the evaluation of the biological response to TELOGEN D for all groups except Group 3. The data from this group has not been used in establishing the LC₅₀ (4-hour).

Particle analysis

The results of the particle counts are presented in Table 2.

The highest count was 3636 particles in a 1-minute (283 ml) sample. Assuming a particle diameter of 1 μ m and a density of TELOGEN D of 2.4 g/cc this represents a concentration of 1.6×10^{-5} mg/l. The total concentration of TELOGEN D present in the air from which the sample was taken was 0.97 mg/l. Thus the amount of TELOGEN D present as particles was less than 0.0017% and for all practical purposes was negligible.

Chamber air temperature

The means and standard deviation (SD) of the means for the temperatures recorded during the exposure of the groups were:

Group	Mean ($^{\circ}$ C)	SD
1(Control)	23.1	1.98
2(0.17 mg/l)	22.8	1.81
3(0.25 mg/l)	23.8	1.06
4(0.97 mg/l)	23.7	0.94
5(0.42 mg/l)	28.7	1.89
6(0.86 mg/l)	29.4	0.82

The differences in temperature were considered unlikely to have influenced the results of the study. The higher temperatures for Groups 5 and 6 were due to the method of vapour generation used.

CLINICAL OBSERVATIONS

Mortality

The mortality is summarised in the following table:

Group	Concentration of TELOGEN D (mg/l)	Mortality		
		♂	♀	Total
1	(Control)	0/5	0/5	0/10
2	0.17	0/5	0/5	0/10
3	0.25	5/5	0/5	5/10
4	0.97	5/5	5/5	10/10
5	0.42	2/5	0/5	2/10
6	0.86	5/5	4/5	9/10

In Group 3 (0.25 mg/l), 1 male rat (21) died within 1 hour of the end of the exposure and 4 male rats (22, 23, 24, 25) were found dead on the morning of Day 1.

In Group 4 (0.97 mg/l) 5 male rats (31, 32, 33, 34, 35) and 3 female rats (36, 37, 39) died during exposure and 2 female rats (38, 40) died within 15 minutes of the end of the exposure.

In Group 5 (0.42 mg/l) 2 male rats (42, 44) died on Day 1.

In Group 6 (0.86 mg/l) 5 male rats (91, 92, 93, 94, 95) and 3 female rats (97, 98, 99) died during the exposure and 1 female rat (96) was found dead on the morning of Day 1.

Clinical signs

(a) During the exposure

The incidence of clinical signs seen during the exposures to TELOGEN D is shown in Table 3.

Signs seen during the exposure were considered typical of the response to an irritant vapour and included partial closing of the eyes, disturbances to the breathing pattern and adoption of hunched body posture.

(b) During the observation period

The incidence of clinical signs seen during the observation period is shown in Table 4. Column 0 of this table shows the observations made when the rats were removed from the exposure chambers. Clinical signs evident at this time in rats exposed to TELOGEN D included disturbances to the breathing pattern, lethargy, pilo-erection and discharge from the eyes.

Disturbances to the breathing pattern persisted for seven days following exposure but all rats that survived exposure to TELOGEN D were normal in appearance by Day 9 of the observation period and most were normal by Day 3.

Bodyweight

The individual and group mean bodyweights are shown in Table 5. The group mean bodyweights are also shown in Figures 2a and 2b for male and female rats respectively.

The rats that survived the effects of exposure to TELOGEN D lost weight or gained at a reduced rate for up to 6 days following exposure. Subsequently the rate of bodyweight gain was similar to that of the control rats.

Food and water consumption

The food and water consumption data are given in Tables 6 and 7 respectively.

Food consumption by rats that survived exposure to TELOGEN D was markedly reduced for 1-2 days following exposure and slightly reduced for a further 2-3 days in male rats and 3 days in female rats of Groups 2, 3 and 5. The single surviving female rat in Group 6 had variable food consumption following exposure but on average consumed an amount similar to that of the control rats from Day 7 of the observation period.

Water consumption was markedly reduced on Day 1 of the observation period and slightly reduced on Day 2. Subsequently water consumption was variable but generally similar to that for control rats.

TERMINAL STUDIES

Lung weight to bodyweight ratio

The lung weight to bodyweight ratios for individual rats are presented in Table 8.

The ratio was higher than normal for all decedent rats and within normal limits for most rats that survived exposure to TELOGEN D. Higher than normal lung weights were seen for 2/5 females that survived exposure at 0.42 mg/l and for the single female rat that survived exposure at 0.86 mg/l.

Estimation of the LC₅₀ (4-hour) for TELOGEN D

From the mortality data for Groups 2, 4, 5 and 6 the LC₅₀ (4-hour) for TELOGEN D was established at:

0.47 mg per litre of air (39 ppm)

The standard error of the estimate was 0.07 mg/l.

Macroscopic pathology

The macroscopic findings for individual rats are included in Appendix 2.

There were no findings attributable to exposure to TELOGEN D in rats that survived exposure except for a pale and swollen appearance of the lungs of rat 100 ? that survived exposure at 0.86 mg/l.

The lungs of the rats that died as a result of exposure were congested and frothy fluid was seen in the trachea.

Microscopic pathology

All changes seen are recorded in detail as individual reports (see Appendix 2). The following comments are made in summary.

PART A

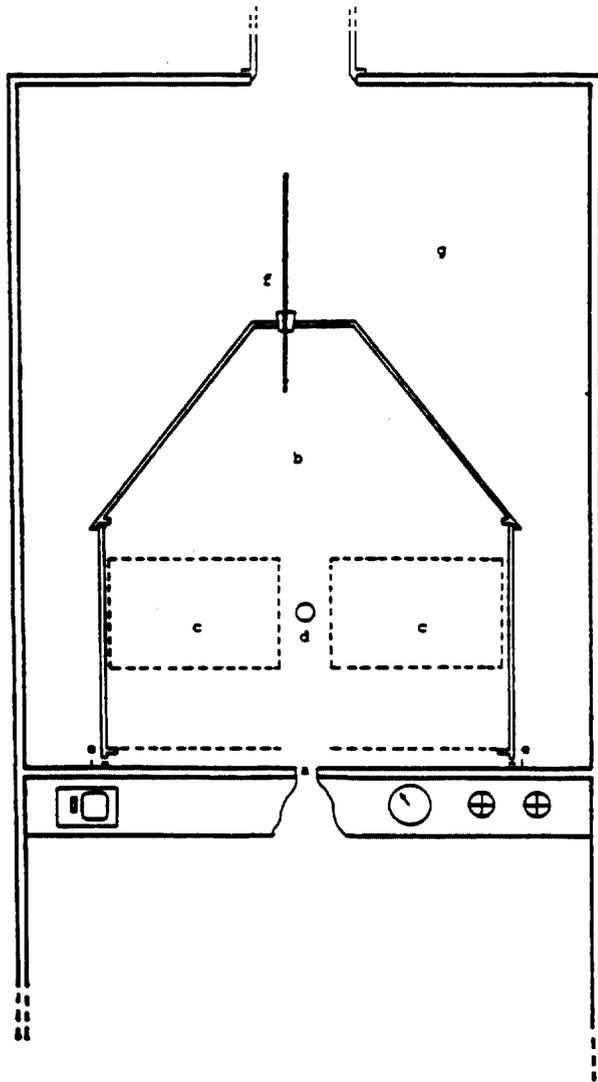
Treatment-related changes were not detected in the lungs.

PART B

Minor changes reported, which were considered of spontaneous origin and of no toxicological significance.

FIGURE 1
Exposure system

PWT/47

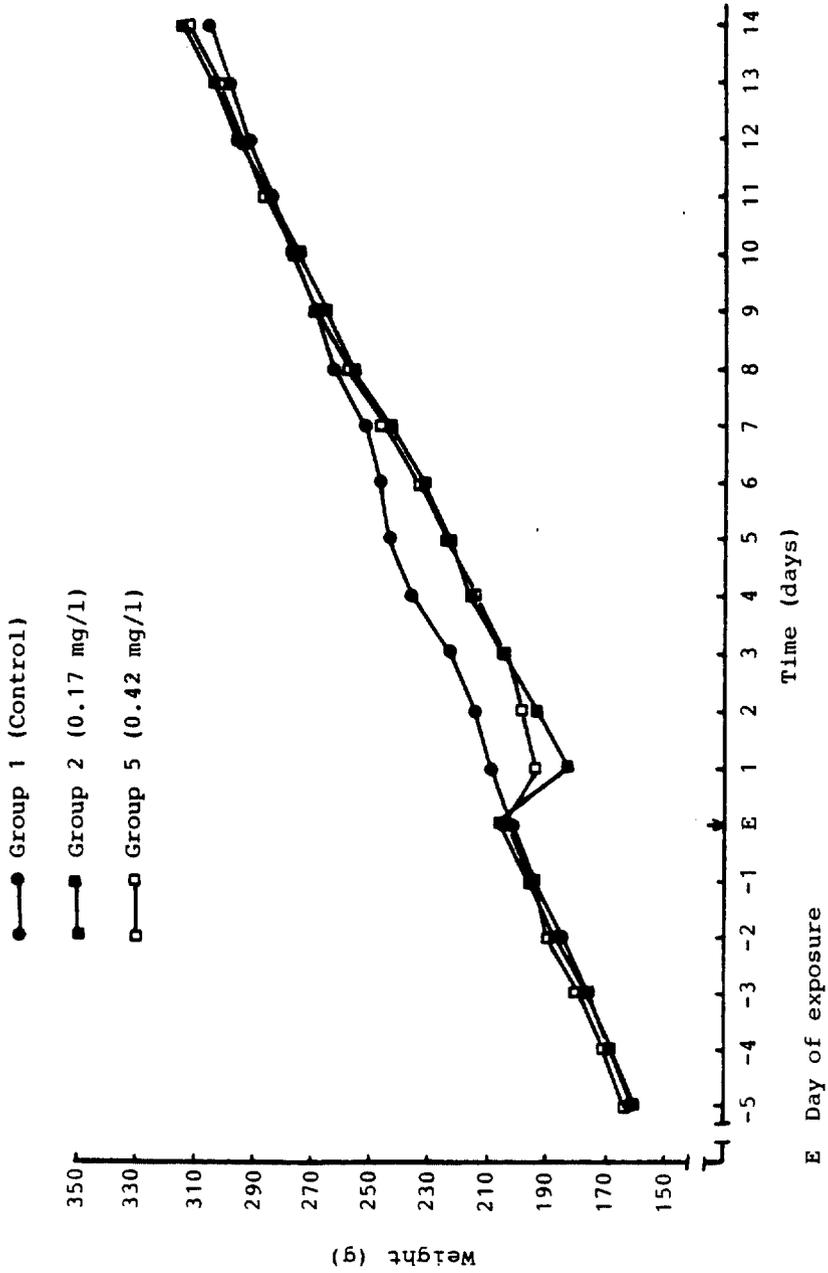


- | | |
|-------------------------|------------------------|
| (a) Vapour entry port | (e) Outlet vents |
| (b) Exposure chamber | (f) Thermometer |
| (c) Animal compartments | (g) Extraction chamber |
| (d) Sampling port | |

21

FIGURE 2a

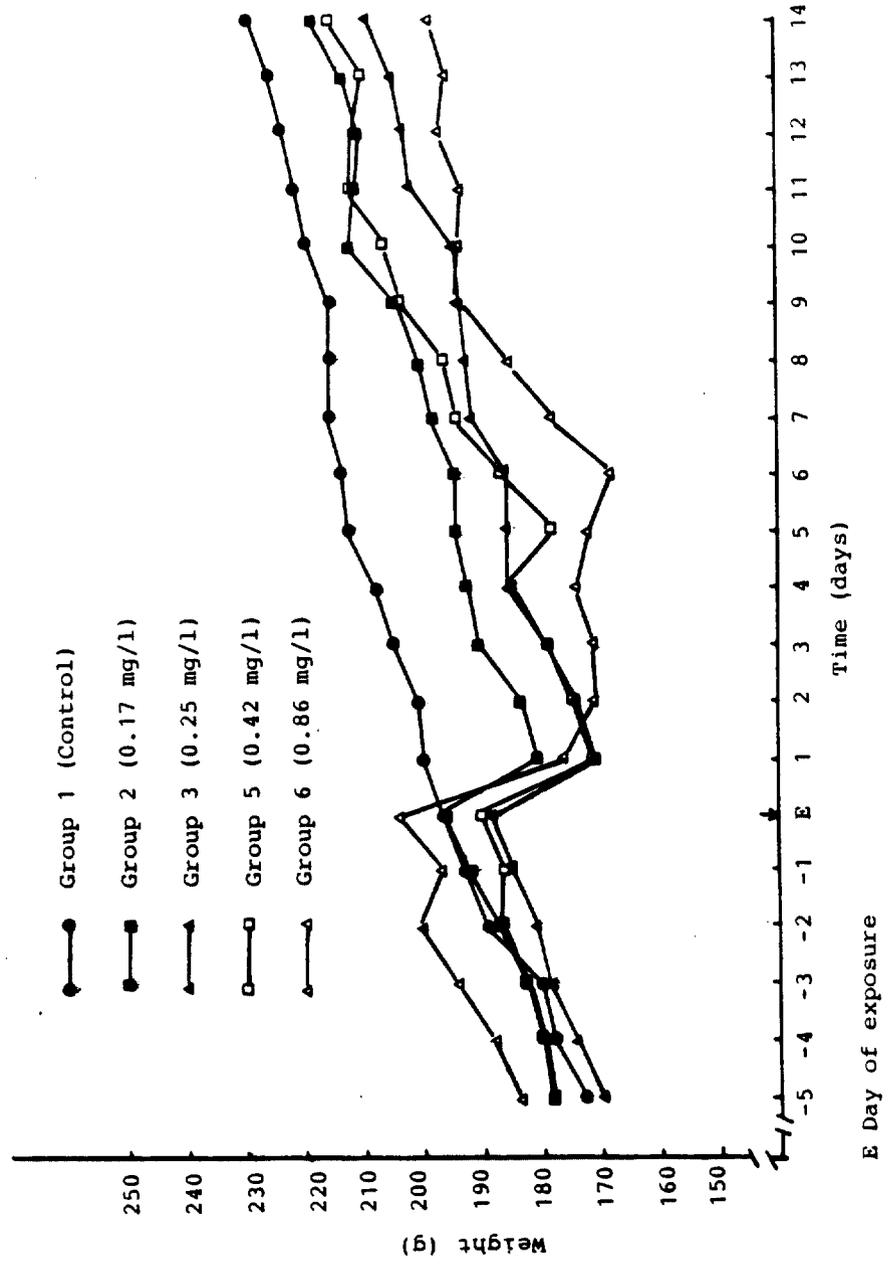
Group mean bodyweights - male rats



22

FIGURE 2b

Group mean bodyweights - female rats



23

TABLE 1

PWT/47

Concentration of TELOGEN D in air samples

Group	Sample	Time taken	TELOGEN D in air (mg/l)
2	2.1	0h : 30m	0.14
	2.2	1h : 00m	0.15
	2.3	2h : 00m	0.17
	2.4	3h : 00m	0.16
	2.5	3h : 50m	0.22
			Mean 0.17 SD 0.031
3	3.1	0h : 30m	0.10
	3.2	1h : 00m	0.13
	3.3	2h : 00m	0.28
	3.4	3h : 00m	0.26
	3.5	3h : 50m	0.50
			Mean 0.25 SD 0.158
4	4.1	0h : 30m	1.12
	4.2	1h : 00m	1.24
	4.3	2h : 00m	0.93
	4.4	3h : 00m	0.83
	4.5	3h : 50m	0.71
			Mean 0.97 SD 0.215
5	5.1	0h : 30m	0.45
	5.2	1h : 00m	0.53
	5.3	2h : 00m	0.37
	5.4	3h : 00m	0.38
	5.5	3h : 50m	0.38
			Mean 0.42 SD 0.068
6	6.1	0h : 30m	0.84
	6.2	1h : 00m	0.86
	6.3	2h : 00m	0.90
	6.4	3h : 00m	0.88
	6.5	3h : 50m	0.81
			Mean 0.86 SD 0.035

SD Standard deviation

TABLE 2

PWT/47

Particle counts

Group	Count	Time taken	Number of particles greater than size stated in a 1-minute count (Mean of 3 readings)			
			>0.5 μ	>1 μ	>2 μ	>3 μ
1	1.1	2h : 00m	189	38	20	2
	1.2	3h : 30m	75	21	7	1
2	2.1	1h : 30m	1382	59	12	0
	2.2	3h : 30m	549	0	0	0
3	3.1	1h : 30m	415	6	5	0
	3.2	3h : 30m	266	6	0	0
4	4.1	1h : 30m	3636	21	0	0
	4.2	3h : 30m	224	21	0	1
5	5.1	1h : 30m	69	2	0	0
	5.2	3h : 30m	54	1	0	0
6	6.1	1h : 30m	10	0	0	0
	6.2	3h : 30m	15	0	0	0

TABLE 3

PWT/47

Clinical signs during exposure

Group	Signs	Number showing signs						
		Time in hours						
		0*	0.25	0.5	1.0	2.0	3.0	4.0
1♂ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5
1♀ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5
2♂ (0.17 mg/l)	Wet around eyes Eyes partially closed Reduced respiratory rate Irregular respiratory pattern Exaggerated respiratory movements Hunched posture	5 5	5 5 5	5 5 5	5 5 5	5 5 5	5 5 3 4	5 5 5 5 5 4
2♀ (0.17 mg/l)	Wet around eyes Eyes partially closed Reduced respiratory rate Irregular respiratory pattern Exaggerated respiratory movements Hunched posture Arched back posture	5 5	5 5 5	5 5 5	5 5 5	5 5 5	5 5 2 2 5 3	5 5 5 5 5 3
3♂ (0.25 mg/l)	Wet around eyes Eyes partially closed Clear discharge from snout Reduced respiratory rate Mouth opening upon inhalation Exaggerated respiratory movements Hunched posture	5 5	5 1 5	5 5 5	5 5 5	1 5 5	5 5 5 5 5	5 5 5 1 5 5
3♀ (0.25 mg/l)	Wet around eyes Eyes partially closed Reduced respiratory rate Exaggerated respiratory movements Hunched posture	5 5	5 5	5 5	5 5	2 5 5 5	5 5 5 5 5	5 5 5 5 5
4♂ (0.97 mg/l)	Wet around eyes Eyes partially closed Reduced respiratory rate Mouth opening upon inhalation Exaggerated respiratory movement Hunched posture Dead (Total)	5 5	5 5	5 5	5 4 1	5 4 1	1 1 1 5 3 4	5 5 5 5 5 5
4♀ (0.97 mg/l)	Wet around eyes Eyes partially closed Reduced respiratory rate Mouth opening upon inhalation Exaggerated respiratory movements Hunched posture Dead	5 5	5 5	5 5	5 5 1	5 5 4	5 5 5 5 2	2 2 2 2 2 3

* During the equilibration period

(Clinical signs - continued)

Group	Signs	Number showing signs						
		Time in hours						
		0*	0.25	0.5	1.0	2.0	3.0	4.0
5♂ (0.42 mg/l)	Eyes partially closed	5	5	5	5	5	5	5
	Reduced respiratory rate	2	5	5	5	5	5	5
	Exaggerated respiratory movement		5	5	5	5	5	5
	Prone posture					1		
	Hunched posture						4	5
5♀ (0.42 mg/l)	Eyes partially closed	5	5	5	5	5	5	5
	Increased respiratory rate	1						
	Reduced respiratory rate	2	5	5	5	5	5	5
	Exaggerated respiratory movements		2	5	5	5	5	5
	Hunched posture				1		4	5
6♂ (0.86 mg/l)	Eyes partially closed	5	5	5	5	4		
	Reduced respiratory rate		5	5	5	4		
	Exaggerated respiratory movements		5	5	5	4		
	Hunched posture	3	4	5	5	4		
	Dead (total)					1	5	5
6♀ (0.86 mg/l)	Eyes partially closed	5	5	5	5	5		2
	Reduced respiratory rate		5	5	5	5		2
	Exaggerated respiratory movements		5	5	5	5		2
	Hunched posture	4	4	5	5	5		2
	Dead (Total)						2	3

* During the equilibration period

TABLE 4

PWT/47

Clinical signs during observation period

Group	Signs	Number showing signs															
		Day of observation period															
		0*	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1♂ (Control)	Normal appearance and behaviour Waxy tail	5	5	5	5	5	5	5	5	5	5	5	5	5	5	1	4
1♀ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
2♂ (0.17 mg/l)	Normal appearance and behaviour Reduced respiratory rate Exaggerated respiratory movements Lethargic Clear discharge from eyes Irregular respiratory pattern	5		5	5	5	5	5	5	5	5	5	5	5	5	5	5
2♀ (0.17 mg/l)	Normal appearance and behaviour Reduced respiratory rate Exaggerated respiratory movements Lethargic Clear discharge from eyes Irregular respiratory pattern Pilo-erection	5		5	5	5	5	5	5	5	5	5	5	5	5	5	5
3♂ (0.25 mg/l)	Reduced respiratory rate Exaggerated respiratory movement Lethargic Clear discharge from eyes Dead (Total)	4															
3♀ (0.25 mg/l)	Normal appearance and behaviour Reduced respiratory rate Exaggerated respiratory pattern Lethargic Clear discharge from eyes Brown staining on head Yellow staining around urogenital region	5	5	3	5	5	5	5	4	4	4	5	5	5	5		
4♂ (0.97 mg/l)	Dead (total)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
4♀ (0.97 mg/l)	Dead (total)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
5♂ (0.42 mg/l)	Normal appearance and behaviour Reduced respiratory rate Exaggerated respiratory movement	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3

* After exposure on day of exposure

TABLE 4

PWT/47

(Clinical signs - continued)

Group	Signs	Number showing signs														
		Day of observation period														
		0*	1	2	3	4	5	6	7	8	9	10	11	12	13	14
5♂ (continued)	Lethargic	3	3													
	Clear discharge from eyes	3														
	Dead (total)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
5♀ (0.42 mg/l)	Normal appearance and behaviour				5	5	5	5	5	5	5	5	5	5	5	5
	Reduced respiratory rate	5	5	5												
	Exaggerated respiratory movement	5	5	5												
	Lethargic	5	5													
	Clear discharge from eyes	5														
6♂ (0.36 mg/l)	Dead (total)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
6♀ (0.36 mg/l)	Normal appearance and behaviour										1	1	1	1	1	1
	Wet fur around jaws	2														
	Irregular respiratory movement	2	1	1	1											
	Reduced respiratory rate	2	1	1	1											
	Lethargic	2														
	Exaggerated respiratory pattern					1	1	1	1	1						
	Dead (total)	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4

* After exposure on day of exposure

TABLE 5
Individual and group mean bodyweights (g)

Group	Rat no.	Pre-exposure					E	Day of observation													
		-5	-4	-3	-2	-1		1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂ (Control)	1	160	165	175	184	192	202	206	213	222	234	241	244	247	256	262	267	276	282	287	292
	2	160	165	174	180	189	194	202	205	220	230	235	242	246	254	260	266	274	277	283	290
	3	159	170	176	182	192	200	208	216	218	234	241	245	252	260	266	274	279	287	296	304
	4	164	170	176	190	200	212	218	221	234	244	251	256	258	276	278	290	296	307	314	318
	5	164	170	177	185	196	204	210	215	221	237	245	250	257	266	276	283	286	300	306	315
	Mean	161	168	176	184	194	202	209	214	223	236	243	247	252	262	268	276	282	291	297	304
1♀ (Control)	6	180	182	184	192	196	202	206	206	210	210	217	220	222	217	222	226	231	222	233	240
	7	170	178	182	194	196	202	207	207	215	212	220	222	224	222	224	230	232	237	232	239
	8	170	178	181	190	190	190	192	190	188	197	200	200	197	206	200	206	204	205	212	212
	9	175	178	181	188	189	194	197	195	202	208	206	206	210	216	216	216	219	227	226	230
	10	170	172	173	182	196	198	200	205	209	214	220	224	226	220	220	224	226	229	227	230
	Mean	173	178	180	189	193	197	200	201	205	208	213	214	216	216	216	220	222	224	226	230

E Day of exposure

30

TABLE 5
(Bodyweights - continued)

Group	Rat no.	Pre-exposure					E	Day of observation													
		-5	-4	-3	-2	-1		1	2	3	4	5	6	7	8	9	10	11	12	13	14
2 ^d (0.17 mg/l)	11	161	170	174	185	197	204	180	185	196	207	207	216	226	242	252	260	267	277	284	294
	12	155	160	170	185	189	195	177	186	200	208	215	224	236	244	251	257	264	274	278	284
	13	160	170	178	190	197	211	190	202	214	228	238	251	260	274	280	294	307	318	326	340
	14	160	171	178	190	197	208	186	200	214	227	239	244	254	267	279	294	304	316	324	346
	15	162	172	180	190	198	210	184	187	194	206	212	220	234	246	257	267	274	285	292	302
	Mean	160	169	176	188	196	206	183	192	204	215	222	231	242	255	264	274	283	294	301	313
2 ^e (0.17 mg/l)	16	185	186	188	191	196	196	180	185	192	192	192	192	194	194	197	214	207	204	210	216
	17	183	186	188	189	194	200	177	184	192	190	200	198	206	204	207	223	219	214	219	224
	18	183	186	189	189	194	201	190	192	197	200	200	200	208	209	219	219	224	224	226	232
	19	170	172	175	185	190	196	186	187	188	192	194	194	194	200	202	206	204	209	216	218
	20	172	172	175	186	190	191	174	173	184	189	191	193	194	200	200	202	202	204	204	204
	Mean	179	180	183	188	193	197	181	184	191	193	195	195	199	201	205	213	212	211	215	220

E Day of exposure

TABLE 5
(Bodyweights - continued)

Group	Rat no.	Pre-exposure					E	Day of observation													
		-5	-4	-3	-2	-1		1	2	3	4	5	6	7	8	9	10	11	12	13	14
5 σ (0.42 mg/l)	41	172	184	192	197	207	190	193	204	217	232	237	252	260	272	281	288	296	306	316	
	42	160	167	173	182	189	200	DEAD													
	43	163	172	185	194	199	210	198	203	207	214	222	230	247	254	272	277	290	293	302	314
	44	160	169	175	185	189	197	DEAD													
	45	162	172	181	192	197	205	192	197	203	213	218	235	246	256	264	268	282	284	294	306
	Mean	162	170	180	189	194	204	193	198	205	215	224	234	248	257	269	275	287	291	301	312
5 ϕ (0.42 mg/l)	46	172	174	177	182	180	182	172	174	186	179	189	197	201	210	214	219	215	214	220	
	47	178	180	187	190	187	190	174	178	183	189	180	196	204	211	220	227	227	216	220	
	48	178	180	184	184	191	193	167	165	172	180	167	174	179	184	192	192	200	209	204	210
	49	178	180	181	188	187	194	181	184	184	187	186	194	199	195	202	207	211	213	217	220
	50	184	182	185	190	185	190	172	175	184	184	176	184	189	193	195	197	201	207	204	210
	Mean	178	179	183	187	186	190	173	175	179	185	178	187	194	197	204	207	212	211	216	

E Day of exposure

TABLE 6

PWT/47

Group mean daily food consumption (g/rat)

Group	Exposure level (mg/l)	Days																		
		Pre-exposure					Post exposure													
		-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂	Control	19	19	20	21	20	21	22	23	22	23	22	22	24	25	23	25	25	23	24
2♂	0.17	20	20	22	21	23	0	13	18	21	20	24	25	27	28	27	25	29	29	27
3♂	0.25	20	21	20	20	21	0													
4♂	0.97	21	21	21	22	24														
5♂	0.42	20	21	20	21	20	3	8	19	21	23	25	27	25	26	27	26	26	29	28
6♂	0.86	20	21	22	23	23														
1♀	Control	18	17	19	19	18	19	18	17	16	19	19	17	15	17	17	16	17	17	17
2♀	0.17	16	17	16	18	17	3	11	15	15	14	16	16	14	18	18	16	14	18	18
3♀	0.25	17	18	16	17	17	2	7	12	17	15	16	16	18	14	16	18	17	17	16
4♀	0.97	18	19	17	17	17														
5♀	0.42	18	17	18	18	16	2	4	13	15	11	17	19	18	20	21	20	17	18	20
6♀	0.86	19	17	19	17	19	0	4	4	11	10	6	18	18	14	16	21	13	11	27

TABLE 7

PWT/47

Group mean daily water consumption (g/rat)

Group	Exposure level (mg/l)	Days																		
		Pre-exposure					Post exposure													
		-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂	Control	24	25	25	26	28	26	28	30	29	29	29	33	31	32	29	31	31	30	30
2♂	0.17	25	23	25	25	24	2	24	27	28	23	31	29	30	30	30	29	29	30	30
3♂	0.25	25	25	24	25	24														
4♂	0.97	24	24	25	25	28														
5♂	0.42	23	23	23	24	26	5	22	28	29	24	32	29	28	28	29	30	30	29	31
6♂	0.86	24	25	26	25	28														
1♀	Control	24	25	26	25	26	27	24	26	26	27	26	27	21	24	23	24	25	24	26
2♀	0.17	21	23	22	23	23	6	22	25	22	21	25	24	20	26	26	23	18	26	26
3♀	0.25	21	22	20	23	18	5	16	24	28	26	24	25	22	17	20	24	24	20	23
4♀	0.97	26	25	25	24	25														
5♀	0.42	28	19	31	16	34	10	17	32	31	20	35	34	33	33	34	33	24	32	39
6♀	0.86	24	23	26	20	25	6	10	27	34	21	12	31	20	22	23	21	18	18	24

TABLE 8

PWT/47

Lung weight to bodyweight ratios

Group	Rat no.	Lung weight (g)	Bodyweight (g)	Lung to bodyweight ratio (LW/BW) x 100	
				Survivors	Decedents
1 σ (Control)	1	1.14	292	0.39	
	2	1.26	290	0.43	
	3	1.28	304	0.42	
	4	1.44	318	0.45	
	5	1.30	315	0.41	
				Mean	0.42
				SD	0.022
1 ρ (Control)	6	1.21	240	0.50	
	7	1.13	239	0.47	
	8	0.97	212	0.46	
	9	1.35	230	0.59	
	10	1.34	230	0.58	
				Mean	0.52
				SD	0.061
2 σ (0.17 mg/l)	11	1.45	294	0.49	
	12	1.31	284	0.46	
	13	1.40	340	0.41	
	14	1.32	346	0.38	
	15	1.43	302	0.47	
				Mean	0.44
				SD	0.045
2 ρ (0.17 mg/l)	16	1.30	216	0.60	
	17	1.23	224	0.55	
	18	1.46	232	0.63	
	19	1.11	218	0.51	
	20	1.02	212	0.48	
				Mean	0.55
				SD	0.062

SD Standard deviation

(Lung weight to bodyweight ratios - continued)

Group	Rat no.	Lung weight (g)	Bodyweight (g)	Lung to bodyweight ratio (LW/BW) x 100	
				Survivors	Decedents
3♂ (0.25 mg/l)	21	3.78	210		1.80
	22	2.67	200		1.34
	23	3.30	192		1.72
	24	4.12	208		1.98
	25	4.78	200		2.39
			Mean		1.85
			SD		0.383
3♀ (0.25 mg/l)	26	1.30	200	0.65	
	27	1.32	207	0.64	
	28	1.14	215	0.53	
	29	1.22	214	0.57	
	30	1.31	215	0.61	
			Mean	0.60	
			SD	0.050	
4♂ (0.96 mg/l)	31	4.28	210		2.04
	32	4.41	209		2.11
	33	3.75	208		1.80
	34	3.95	222		1.78
	35	3.65	211		1.73
			Mean		1.89
			SD		0.171
4♀ (0.96 mg/l)	36	4.50	194		2.32
	37	3.87	201		1.93
	38	3.91	200		1.96
	39	4.05	194		2.09
	40	3.98	199		2.00
			Mean		2.06
			SD		0.157

SD Standard deviation

TABLE 8

PWT/47

(Lung weight to bodyweight ratios - continued)

Group	Rat no.	Lung weight (g)	Bodyweight (g)	Lung to bodyweight ratio (LW/BW) x 100	
				Survivors	Decedents
5♂ (0.42 mg/l)	41	1.54	316	0.49	
	42	3.61	200		1.81
	43	1.62	314	0.52	
	44	4.53	197		2.30
	45	1.51	306	0.49	
			Mean	0.50	2.06
			SD		
5♀ (0.42 mg/l)	46	1.32	220	0.60	
	47	1.50	220	0.68	
	48	1.60	210	0.76	
	49	1.28	220	0.58	
	50	1.34	210	0.64	
			Mean	0.65	
			SD	0.072	
6♂ (0.86 mg/l)	91	4.52	212		2.13
	92	4.99	200		2.50
	93	3.25	203		1.60
	94	4.81	214		2.25
	95	5.42	221		2.45
			Mean		2.19
			SD		0.360
6♀ (0.86 mg/l)	96	3.70	206		1.80
	97	5.71	206		2.77
	98	5.64	208		2.71
	99	6.52	210		3.10
	100	1.72	199	0.86	
			Mean	0.86	2.60
			SD		0.557

SD Standard deviation

40

APPENDICES

Method of analysis for TELOGEN D

1. Instrumentation and apparatus

Gas chromatograph: Pye Unicam Series 304 with S8 autojector.

Integrator: Pye Unicam CDP4 computing integrator.

Apparatus: Volumetric flasks and pipettes.

2. Reagents

2, 2, 4 Trimethyl pentane: Fisons.

TELOGEN D: Supplied by Sponsor.

3. Preparation of sample solutions

The contents of the bubblers were transferred to 20 or 25 ml volumetric flasks and diluted to volume with trimethyl pentane.

4. Gas chromatography4.1. GLC operating conditions

Column: 1 m x 3 mm i.d. pyrex glass packed with 10% OV 101.

Temperatures: Column - 100°C
Injector - 100°C
Detector - 140°C

Gases: Helium 30 ml/minute
Hydrogen 33 ml/minute
Air 300 ml/minute

Retention time for
TELOGEN D: Typically 2.6 minutes

(Method of analysis - continued)

4.2. Analysis of samples

A 3 μ l aliquot of each sample solution was injected onto the GLC column using the autojector. The concentration of TELOGEN D in the sample solutions was evaluated from the expression:

$$C_x = \frac{A_x}{A_s}$$

Where C_x = concentration of TELOGEN D in aliquot (mg/ml)
 A_x = peak area due to TELOGEN D
 A_s = response factor (area/unit concentration) for
TELOGEN D

Samples were analysed as quickly as possible after collection

4.3. Standardisation

Approximately 250 mg of TELOGEN D was accurately weighed into a 50 ml volumetric flask, dissolved in trimethyl and diluted to volume with pentane. The solution was diluted to obtain standard solutions containing TELOGEN D at concentrations within the range of 0.5 and 5 mg/ml. Aliquots of the standard solutions were injected and the mean peak areas for TELOGEN D were calculated for each standard concentration. The mean response factor (A_s) for TELOGEN D was calculated from the mean peak areas by regression analysis.

Pathological findings for individual rats

Group 1Rat 1♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

Rat 2♂

Macroscopic findings:
 External appearance: Waxy tail.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.
 An area of alveolar macrophages.

Rat 3♂

Macroscopic findings:
 External appearance: Waxy tail.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

Rat 4♂

Macroscopic findings:
 External appearance: Waxy tail.
 Lungs: Few red areas (up to 1 x 1 mm).
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

(Pathology - continued)

Group 1 (continued)

Rat 50

Macroscopic findings:

External appearance: Waxy tail.

Microscopic findings:

Lungs: Minimal lymphoid aggregates.

45

(Pathology - continued)

Group 1 (continued)Rat 69Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 79Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 89Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 99Macroscopic findings:

Lungs:

Minimal congestion.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.
Medial calcification in blood
vessels.Rat 109Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

(Pathology - continued)

Group 2Rat 11♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 12♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 13♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 14♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 15♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

(Pathology - continued)

Group 2 (continued)Rat 16?Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 17?Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 18?Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.
Occasional areas of alveolar
macrophages.Rat 19?Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

Rat 20?Macroscopic findings:

No abnormalities detected.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.

(Pathology - continued)

Group 3*Rat 21♂Macroscopic findings:

External appearance: Yellow stained fur. Wet fur in urogenital region. Tail stained brown/black.

Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 22♂Macroscopic findings:

External appearance: Yellow stained abdominal fur. Frothy discharge from nostrils and in mouth. Slight brown staining around snout.

Lungs: Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 23♂Macroscopic findings:

External appearance: Frothy fluid discharge from nostrils and in mouth.

Lungs: Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 24♂Macroscopic findings:

External appearance: Wet fur around snout and jaws. Frothy fluid discharge from nostrils and in mouth. Tail stained brown/black.

Lungs: Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

49

(Pathology - continued)

Group 3 (continued)*Rat 25♂Macroscopic findings:

External appearance: Yellow staining in urogenital region.
Tail stained brown/black.

Lungs: Congested, appeared swollen. Frothy
fluid in trachea.

Microscopic findings:

No tissues processed as per
experimental protocol.

* Decedent

50

(Pathology - continued)

Group 3 (continued)Rat 26?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 27?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 28?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 29?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.

Rat 30?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
Lungs: Minimal lymphoid aggregates.
An area of alveolar macrophages.

(Pathology - continued)

Group 4*Rat 31♂Macroscopic findings:

External appearance: Wet around snout.
 Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 32♂Macroscopic findings:

External appearance: Wet around snout.
 Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 33♂Macroscopic findings:

External appearance: Wet around snout.
 Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 34♂Macroscopic findings:

External appearance: Frothy fluid discharge from nostrils.
 Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

(Pathology - continued)

Group 4 (continued)*Rat 35σMacroscopic findings:

External appearance:

Wet around snout and jaws. Frothy fluid discharge from nostrils.

Lungs:

Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

(Pathology - continued)

Group 4 (continued)*Rat 36?Macroscopic findings:

External appearance: Wet around snout and jaws.
Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 37?Macroscopic findings:

External appearance: Wet around snout and jaws. Frothy fluid discharge from nostrils.
Lungs: Congested. Appeared swollen. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 38?Macroscopic findings:

External appearance: Wet fur around snout and jaws. Frothy fluid discharge from nostrils.
Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 39?Macroscopic findings:

External appearance: Wet around snout and jaws. Frothy fluid discharge from nostrils.
Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

54

(Pathology - continued)

Group 4 (continued)*Rat 408Macroscopic findings:

External appearance: Wet around snout and jaws.
Lungs: Appeared swollen. Congested. Frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

55

(Pathology - continued)

Group 5Rat 41♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

*Rat 42♂

Macroscopic findings:
 External appearance: Wet around snout.
 Lungs: Congestion. Frothy fluid in trachea.
Microscopic findings: No tissues processed as per experimental protocol.

Rat 43♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

*Rat 44♂

Macroscopic findings:
 Lungs: Congestion. Frothy fluid in trachea.
Microscopic findings: No tissues processed as per experimental protocol.

Rat 45♂

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

* Decedent

56

(Pathology - continued)

Group 5 (continued)Rat 46?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

Rat 47?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

Rat 48?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Occasional areas of alveolar macrophages.

Rat 49?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.

Rat 50?

Macroscopic findings: No abnormalities detected.
Microscopic findings:
 Lungs: Minimal lymphoid aggregates.
 An area of alveolar macrophages.

(Pathology - continued)

Group 6*Rat 91♂Macroscopic findings:

External appearance: Clear discharge from mouth.

Lungs: Congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 92♂Macroscopic findings:

External appearance: Clear discharge from snout.

Lungs: Congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 93♂Macroscopic findings:

External appearance: Clear discharge from snout. Clear frothy discharge from trachea.

Lungs: Severe congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 94♂Macroscopic findings:

External appearance: Clear discharge from snout. Clear frothy discharge from trachea.

Lungs: Severe congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

(Pathology - continued)

Group 6 (continued)*Rat 95*Macroscopic findings:

External appearance: Clear discharge from snout. Clear frothy discharge from trachea.

Lungs: Severe congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

(Pathology - continued)

Group 6 (continued)*Rat 96?Macroscopic findings:

Lungs:

Appeared swollen. Congestion. Clear frothy fluid in trachea.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 97?Macroscopic findings:

External appearance:

Clear discharge from snout. Clear frothy discharge from trachea.

Lungs:

Severe patchy congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 98?Macroscopic findings:

External appearance:

Clear discharge from snout. Clear frothy discharge from trachea.

Lungs:

Severe patchy congestion.

Microscopic findings:

No tissues processed as per experimental protocol.

*Rat 99?Macroscopic findings:

External appearance:

Clear discharge from trachea.

Lungs:

Severe patchy congestion.
Clear frothy discharge from trachea.Microscopic findings:

No tissues processed as per experimental protocol.

* Decedent

60

(Pathology - continued)

Group 6 (continued)

Rat 1009

Macroscopic findings:

Lungs:

Appeared pale and swollen.

Microscopic findings:

Lungs:

Minimal lymphoid aggregates.
Occasional foci of alveolar
macrophages.



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

C. H. Farr, PhD, DABT
Manager, Product Safety and Toxicology
Atochem North America, Inc.
900 First Avenue
P.O. Box 1536
King of Prussia, Pennsylvania 19406-0018

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

FEB 27 1995

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Sincerely,

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

Enclosure

12316A



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Triage of 8(e) Submissions

Date sent to triage: FEB 24 1995

NON-CAP

CAP

Submission number: 12316 A

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



Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

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

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entire document: 0 1 2 pages 1, 2 pages 1, 2, tabs

Notes:

Contractor reviewer : LPS Date: 1/5/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:

Submission # 8E110-1092-12316 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: EF Atochem North America, Inc.

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0639 REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION OF WORKER RIGHTS
- 0404 LABEL/MSDS CHANGES
- 0405 PROCESS/HANDLING CHANGES
- 0406 APP/USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 10/12/92 OTS DATE: 10/26/92 CSRAD DATE: 09/22/94

CHEMICAL NAME:

Ethane, 1,1,2-trichloro-2,2-difluoro-1-iodo-
Telogen D

CAS#

677-48-5
677-48-5

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	<u>0242</u> IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	<u>0243</u> 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. OCCUR/REL/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 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	<u>0224</u> 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	0299 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
<u>0212</u> 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 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAGE DATA:

NON-CBI INVENTORY

ONGOING REVIEW

SPECIES

TOXICOLOGICAL CONCERN:

USE:

PRODUCTION:

YES

YES (DROP/REFER)

RAT

LOW

CAS SR

NO

NO (CONTINUE)

MED

DETERMINE

REFER:

HIGH

COMMENTS:

-CPSS- 0724951115

0 0 0 0 0 0 0 0 0 0 0

> <ID NUMBER>

8(E)-12316A

> <TOX CONCERN>

H

> <COMMENT>

ACUTE INHALATION TOXICITY IN RATS IS HIGH CONCERN BASED ON AN LC50 OF 0.47 MG/L (39 PPM) FOR A 4-HOUR EXPOSURE. DOSE (MG/L) AND MORTALITY: 0.17 (0/5 M, 0/5 F), 0.25 (5/5 M, 0/5 F), 0.97 (5/5 M, 5/5 F), 0.42 (2/5 M, 0/5 F), AND 0.86 (5/5 M, 4/5 F). CLINICAL SIGNS INCLUDED CHANGES IN BREATHING PATTERN, HUNCHED POSTURE, LETHARGY, PILO-ERECTION, DISCHARGE FROM EYES, WEIGHT LOSS OR REDUCTION IN WEIGHT GAIN, AND REDUCED FOOD AND WATER COMSUMPTION. PATHOLOGIC EXAM REVEALED CONGESTED LUNGS AND A FROTHY FLUID IN THE TRACHEA OF DECEDENTS, AND PALE, SWOLLEN LUNGS IN 1-SURVIVOR.

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