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RE: Submission of Final Report Pertinent to Previous Notice of
Substantial Risk filed under TSCA Section 8(e)
2,6-Dinitrotoluene CASRN: 606-20-2

Dear Sir/Madam:

The Chemical Manufacturers Association Dinitrotoluenes Panel
submits the following final report entitled "2,6-Dinitrotoluenes Acute
(6-Hour) Inhalation Toxicity Study in Rats" on behalf of the sponsors
listed in Attachment A.

On August 16, 1991, the CMA Dinitrotoluenes Panel notified the EPA
TSCA Section 8(e) Office that results of the referenced report appeared
to meet the criteria for reporting, based on the acute LC50 value
obtained. The submission letter is enclosed as Attachment B.

If you have any questions regarding this submission, please
contact me at (202) 887-1314.

Sincerely,

Barbara O. Francis

Barbara O. Francis
Manager
Dinitrotoluenes Panel

cc: C. Auer, EPA
G. Timm, EPA
Dinitrotoluenes Panel



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CMA 4/901844

2,6 DINITROTOLUENE
ACUTE (6-HOUR) INHALATION TOXICITY
STUDY IN RATS

Addressee:

Chemical Manufacturers Association,
2501 M Street, N.W.,
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Report issued: 25 September 1991.

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Colin J. Hardy.

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This report was produced in the

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P.O. Box 2, Huntingdon, PE18 6ES,
England.**

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CONFIDENTIALITY STATEMENT

This report contains the unpublished results of research sponsored by CHEMICAL MANUFACTURERS ASSOCIATION. These results may not be published, either wholly or in part, or reviewed or quoted in any other publication without the prior authorisation of the Sponsor.

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

HRC Report No. CMA 4/901844

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:

Good Laboratory Practice, The United Kingdom Compliance Programme, Department of Health & Social Security 1986 and subsequent revision, Department of Health, 1989.

United States Environmental Protection Agency, (TSCA), Title 40 Code of Federal Regulations Part 792, Federal Register, 29 November 1983 and subsequent amendment Federal Register 17 August 1989.

Japan Ministry of International Trade and Industry, Directive 31 March 1984 (Kanpogyo No. 39 Environmental Agency, Kikyoku No. 85 MITI).

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

G. P. Jackson

Graham C. Jackson, B.A., L.R.S.C.,
Study Director
Huntingdon Research Centre Ltd.

25 September 1991

Date

D. Neville Kellett

D. Neville Kellett, B.Pharm., Ph.D.,
M.R.Pharm.S.,
For Laboratory Management

Barbara O. Francis

Barbara O. Francis,
Chemical Manufacturers Association

27 September 1991

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.

G. C. Jackson

Graham C. Jackson, B.A., L.R.S.C.,
Study Director,
Department of Inhalation Toxicology

C. J. Hardy

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QUALITY ASSURANCE STATEMENT

HRC Report No. CMA 4/901844

Certain studies 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 Department 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 HRC Quality Assurance Department. It is considered to be an accurate description of the procedures and practices employed during the course of the study and an accurate presentation of the findings.

Date of inspection

15.02.90

Date of reporting Inspection
Findings to the Study Director
and HRC Management

16.6.90

Date of reporting Audit Findings
to the Study Director
and HRC Management

03.09.91



Peter H.C.V. Richold, B.Sc.,
Senior Systems Compliance Auditor,
Department of Quality Assurance,
Huntingdon Research Centre Ltd.

24-9-91

ABSTRACT

An acute inhalation study was carried out in order to determine the acute inhalation toxicity of 2,6-DINITROTOLUENE (2,6 DNT). The data from this study were used to calculate an LC_{50} (6-hour) and to assist in selection of exposure levels for a metabolism study on this material.

A group of 10 rats (5 males and 5 females) was exposed to the maximum vapour concentration of 2,6 DNT. There were no deaths following this exposure therefore, further groups were exposed at higher levels. The higher exposure levels were achieved by atomising a solution of 2,6 DNT in acetone/PEG 200.

All exposures were carried out using a nose-only exposure system, in order to minimise skin contact and were of 6 hours duration. Following exposure, blood samples were taken at intervals for up to 7 days to measure the concentration of methaemoglobin.

The exposure levels and mortality data were:

	<u>Exposure level</u> (mg/l)	<u>Deaths</u>	
		<u>Male</u>	<u>Female</u>
Vapour	0.026	0	0
Aerosol	0.196	2	0
	0.473	4	0
	0.694	5	3

No clinical signs were seen during exposure. At exposure levels of 0.196 mg/l and above, exaggerated respiratory movements, ataxia, lethargy and deaths occurred for several days post-exposure.

Food consumption and bodyweight gain were reduced in a dose-related fashion for several days following exposure.

No clear increase in methaemoglobin was seen.

Congestion of the lungs was seen in most rats that died as a result of the exposure.

The LC_{50} (6-hour) calculated from the mortality data for the rats exposed to aerosol was:

0.43 mg per litre of air. (95% confidence limits
0.23 - 0.63 mg/l)

For male and female rats considered separately, the LC_{50} (6-hour) values were 0.24 and 0.66 mg per litre of air respectively.

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SUMMARY

Test substance: A yellow solid identified as 2,6 DINITROTOLUENE (2,6 DNT).

Test animals: Albino rats, (Fischer 344). One air control group, 1 vehicle group and 4 test groups each of 5 male and 5 female rats.

Route of administration: By inhalation of the vapour of 2,6 DNT or by inhalation of a test atmosphere containing an aerosol generated from a solution of the test substance in acetone/PEG 200.

Duration of exposure: 6 hours continuous nose-only exposure.

Observation period: 14 days post exposure.

Results

Exposure levels and mortality:	Level (mg/l)	Mortality		Total
		Males	Females	
	0.026*	0/5	0/5	0/10
	0.196	2/5	0/5	2/10
	0.473	4/5	0/5	4/10
	0.694	5/5	3/5	8/10

* Vapour only

Clinical signs: (a) During exposure: there were no clinical signs related to exposure to 2,6 DNT.

- 11
- (b) During observation period: signs seen in rats exposed to aerosols of 2,6 DNT included abnormal respiration, brown staining around the snout and jaws, lethargy and death.

There were no clinical signs in rats exposed to the vapour of 2,6 DNT.

Recovery from the effects of exposure to aerosols of 2,6 DNT was seen from Day 4 of observation and the majority of the surviving rats had recovered by Day 5 of the observation period.

Eye damage, as a result of taking blood samples, was evident in a proportion of rats.

Bodyweight:

Reduced bodyweight or rate of bodyweight gain for up to 3 days in female rats and for up to 6 days in male rats exposed to 2,6 DNT. Reduced bodyweight, attributable to the method of constraint, was also observed in the control groups.

Food and water consumption:

Food consumption was reduced for up to 4 days following exposure to 2,6 DNT.

Water consumption was variable and increased in male rats following exposure to 2,6 DNT.

Methaemoglobin:

There was a possible small increase in methaemoglobin levels in rats exposed to 2,6 DNT. All values found for exposed rats were close to the values found for the control rats.

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Lung weight to bodyweight ratio: The lung weight to bodyweight ratios for the majority of rats that died as a result of exposure were higher than control values. The lung weight to bodyweight ratios for rats that survived exposure to 2,6 DNT were within normal limits.

Macroscopic pathology: The lungs of the majority of rats that died as a result of exposure were congested. A dark appearance of the liver was noted for a proportion of decedents.

There were no macroscopic abnormalities related to exposure to 2,6 DNT in rats that survived exposure.

CONCLUSION

The LC_{50} (6-hour) for 2,6 DNT is estimated at 0.24 mg/l of air for male rats (95% confidence limits 0.08 - 0.40 mg/l) and 0.66 mg/l of air for female rats (95% confidence limits 0.49 - 0.83 mg/l).

INTRODUCTION

The acute inhalation toxicity of 2,6 DNT was assessed by exposing 3 groups of rats to aerosols produced from solutions of the test substance in acetone and 1 group to the vapour of the test substance. Each group was exposed for a period of 6 hours in a nose-only exposure system. Two further groups were exposed to air or acetone vapour only.

This study on 2,6-dinitrotoluene was conducted as part of the first bilateral agreement between the U.S. and Germany to share data and testing costs on existing chemicals. German and American producers of dinitrotoluenes agreed to conduct an inhalation study, and a cooperative testing program was set up with the assistance of the Verband der Chemischen Industrie (the German chemical industry trade association) and the Chemical Manufacturers Association. Companies participating in the cooperative effort include Air Products and Chemicals, Inc.; Bayer AG; E.I. du Pont de Nemours and Co.; ICI Americas, Inc.; and Mobay Corporation.

The study was conducted at the Huntingdon Research Centre during the period 17 January 1990 to 21 March 1990.

The protocol for the study was approved by the Study Director and HRC Management on 19 October 1989 and approved by the Sponsor on 9 November 1989.

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

MATERIALS AND METHODS

Test substance

The test substance was a pale yellow solid identified as:

2,6 DINITROTOLUENE.

The sample was received on 17 November 1989 and was stored in the dark at 4°C and in the original containers.

The data supplied by the Sponsor indicated that the test substance was >99% pure and was stable under normal conditions of use.

Animals and maintenance

Thirty male and thirty female albino rats (Fischer 334), about 9 weeks old, were selected from 3 consignments of rats obtained from Charles River UK Limited, Manston Road, Margate, Kent, England. The dates of delivery and the number of rats selected were 17 January 1990 (10♂ and 10♀), 21 February 1990 (10♂ and 10♀) and 28 February (10♂ and 10♀).

The rats were selected so that males and females would be as close as possible to the weights specified in the protocol by the day of exposure.

On arrival the rats were allocated to 1 of 6 groups, each of 5 males and 5 females, and were identified individually by a number tattooed on the ears. The rats were housed 5 of like sex to a cage and acclimatised to laboratory conditions for at least 5 days before the day of exposure.

The holding cages (size 38 cm x 56 cm x 18 cm height) were made of polypropylene with welded wire mesh forming the top and floor. The cages were suspended on a movable rack. While in their cages all rats had free access to a measured excess amount of food (SDS LAD1) 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 6-hour exposure and an overnight post exposure period when the rats in the test group were kept in a ventilated cabinet to allow dispersal of any residual test substance.

The temperature of the holding area during the study remained within the limits of 18°C to 24°C except for 1 occasion when a temperature of 25°C was recorded.

The relative humidity was between the expected limits of 35% to 65% during most of the study period. Low humidities of between 22% and 34% were recorded on 15 occasions during January 1990 and on 1 occasion during March 1990.

Inhalation exposures

Three groups of rats were exposed continuously for 6 hours to test atmospheres containing an aerosol generated from 2,6 DNT and 1 group was exposed to vapour of 2,6 DNT.

Further groups acting as controls received either clean air only or acetone vapour only for 6 hours.

The group identifications and dates of exposure for the groups were:

Group 1	(Control 1)	:	24 January 1990.
Group 2	(Test)	:	24 January 1990.
Group 3	(Control 2)	:	28 February 1990.
Group 4	(Test)	:	28 February 1990.
Group 5	(Test)	:	6 March 1990.
Group 6	(Test)	:	7 March 1990.

Group 2 was exposed at the maximum attainable vapour concentration of the test substance in air. No deaths occurred in Group 2 and therefore, further exposures were carried out at higher concentrations of test substance in air. The higher concentrations were achieved by atomising a solution of 2,6 DNT and forming an aerosol.

Exposure system

Vapour generator (Group 2)

The vapour generator was constructed from a 1 litre 2-necked flask, an air inlet tube and glass distillation column which connected the flask to the inlet port on the exposure chamber. The flask was maintained at approximately 90°C in a hot water bath. The glass column connecting the flask to the exposure chamber was filled with glass wool to act as a particulate trap and also allowed the test atmosphere to cool to approximately 26°C before entering the exposure chamber.

Aerosol generator (Groups 4, 5 and 6)

The aerosol generator, shown in Figure 1, was designed to produce and maintain an atmosphere containing a high proportion of respirable droplets. The generator was comprised of a concentric jet atomiser and a plastic elutriation column. All parts of the generator in contact with the test substance were made of stainless steel or glass.

The solution of test substance in acetone was supplied to the generator from a syringe driven at a constant rate by a syringe pump. The compressed air supply to the generator was dried, filtered and oil-free.

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Exposure chambers

The nose-only exposure chambers were of cylindrical form (35.5 cm i.d., 38.5 cm height) and made of perspex. The chambers were fitted with a hemispherical perspex top giving an enclosed volume of approximately 50 litres. The rats were held for exposure in perspex restraining tubes (22 cm x 6 cm i.d.) which were attached at evenly spaced ports in the cylindrical section of the chamber, and were designed to allow only the snout to project into the chamber. Each rat was restrained in a forward position by an adjustable plastic stopper which also provided a seal for the tube.

The test atmosphere entered through a tube located at the base centre of the chamber and passed out through small holes in the lower edge of the cylindrical section. Each chamber was installed in a large fume cupboard exhausting to atmosphere through an absolute filter.

The exposure system is shown in Figure 2.

Procedure (Group 2)

Fifty grams of 2,6 DNT were placed into the generator flask. The distillation column was packed loosely with glass wool, to provide a particulate trap, and connected between the generator flask and the exposure chamber. A supply of clean dried air was connected to the air inlet tube and the supply pressure was adjusted to give a flow rate of 25 litres per minute measured at the generator outlet. The generator flask was heated in a water bath to maintain the 2,6 DNT in a molten condition at approximately 90°C.

Procedure (Groups 4, 5 and 6)

A supply of clean dried air was connected to the aerosol generator and the supply pressure was adjusted to give a flow rate of 25 litres per minute measured at the generator outlet tube. An in-line flow meter was used to monitor air flow throughout the exposure.

A solution for aerosolisation was prepared by dissolving 15 g 2,6 DNT and 5 g polyethylene glycol 200 (PEG 200) in sufficient acetone to make 100 ml of solution. The PEG 200 was necessary to eliminate crystallisation of 2,6 DNT at the tip of the concentric jet atomiser.

A syringe filled with the solution of the test substance was fitted to the syringe pump and connected to the generator with PTFE tubing. An initial flow rate of 0.11 ml/minute was selected for the exposure. This flow rate was expected to give a concentration of 2,6 DNT that would produce at least one death during the exposure.

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

The syringe pump was switched on and the exposure timed for 6 hours, following a 5-minute⁽¹⁾ equilibration period, from the appearance of an aerosol from the generator outlet. The syringe was replaced with a filled syringe and the flow rate adjusted if required during the exposure.

After 6 hours the supply of test substance was discontinued and the exposure chamber was allowed to clear before the rats were removed for examination.

The procedure was repeated, with flow rates of 2,6 DNT solution of 0.2 or 0.3 ml/minute for the other test groups.

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

The control groups were treated similarly but exposed to air only (Control 1) or to acetone vapour (Control 2). The flow rate of acetone into the control chamber air was 0.3 ml/minute (initially 0.1 ml/min, increased to 0.3 at 25 mins).

The control rats were returned to the holding room at the end of the exposure procedures.

Chamber atmosphere analyses

Seven air samples were taken from the chamber during each exposure and the collected material was analysed to determine the concentration of 2,6 DNT in the chamber air.

Each air sample was withdrawn, at 4 litres per minute, through a weighed glass fibre filter (Whatman GF/A) mounted in an open face filter holder (Groups 4, 5 and 6) or, at 2 litres per minute, through a gas absorption trap containing approximately 20 ml of acetone (Group 2). The trap was cooled to 0°C during sampling.

The volume of the air samples was measured with a wet-type gas meter.

(1) 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

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Three additional air samples were taken during the exposure of Groups 4, 5 and 6 using an Andersen cascade impactor⁽¹⁾. The samples were taken approximately 1.5, 3.5 and 5.5 hours after the start of exposure.

The material collected on the stages of the sampler was analysed to determine the particle size distribution of 2,6 DNT in the test atmospheres.

The collection characteristics for the sampler used at a sampling rate of 1.4 litres per minute are shown in Table 2.

The method of analysis for 2,6 DNT is described in Appendix 1.

During the exposure of Group 2, a check for particles was made using an optical particle counter (Royco model 218).

Chamber air temperature

The air temperature in the exposure chamber was measured with a mercury-in-glass thermometer and recorded at the start of exposure and then at 30-minute intervals during the 6-hour exposure.

Observations

Clinical signs

The rats were observed continuously for signs of reaction to the test substance during exposure and at least twice daily throughout the observation period. The clinical signs were recorded at the end of the chamber equilibration period, at 0.25, 0.5 and 1.0 hours and then at hourly intervals during the exposure. During the observation period the clinical signs were recorded once in the morning and then, as necessary, following a later check for clinical signs.

Bodyweight

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

(1) Andersen 200 Inc.

Food and water consumption

The amount of food and water consumed by each cage of rats was measured daily from the day following arrival. The daily mean intakes of food and water for each rat were calculated from the recorded data.

Methaemoglobin levels

Samples of blood were taken from the orbital sinuses, under light anaesthesia, from all rats at approximately 24 hours before exposure and then at 1 hour, 24 hours and 48 hours post exposure. The samples were analysed for methaemoglobin using the method of Van Kampen and Zijlstra (Advances in Clinical Chemistry 1975, 5th Ed., p 140). Additional samples were taken at 7 days post exposure for selected groups.

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 that died as a result of exposure and those killed at the end of the observation period 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 for possible future microscopic examination.

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Estimation of the LC₅₀ (6-hour) and standard error

The concentration of the test substance likely to cause death in 50% of exposed rats following a single 4-hour exposure was calculated by the log probit method of Miller and Tainter⁽¹⁾.

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 - 6.5).

The 95% confidence limits were calculated as $LC_{50} \pm 1.96 SE$.

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

RESULTS

CHAMBER ATMOSPHERE CONDITIONSConcentrations of 2,6 DNT

The analysis results for the air samples taken during the exposures are shown in Table 1 (page 29).

The mean concentrations of 2,6 DNT in the chamber air and the variations in concentration (range x 100/mean) for each group were:

Group	2,6 DNT in air (mg/l)	Variation (%)
2	0.026	50
4	0.196	39
5	0.473	25
6	0.694	34

Particle size distribution

The results for the air samples taken for determination of the particle size distribution of 2,6 DNT are shown in Table 2 (page 30 - 32).

The results show that approximately 85 % to 96 % of the 2,6 DNT present in the chamber atmosphere was in the form of particles of respirable size (<5.5 μ m aerodynamic diameter).

The results obtained with the Royco particle counter indicated that there were very few particles in the test atmosphere for Group 2.

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Chamber air temperature

The mean chamber air temperatures and the standard deviation of the means, during exposure of the groups were:

Group	Temperature (°C)	
	Mean	SD
1 (Control 1)	24	0.9
2 (0.026 mg/l)	26	1.1
3 (Control 2)	22	0.0
4 (0.196 mg/l)	23	0.7
5 (0.473 mg/l)	23	0.4
6 (0.694 mg/l)	23	0.3

SD = Standard deviation

There were no differences in temperature considered likely to influence the results of the study.

CLINICAL OBSERVATIONS

Mortality

The mortality is summarised below:

Group	Deaths		Total
	Male	Female	
1 (Control 1)	0/5	0/5	0/10
2 (0.026 mg/l)	0/5	0/5	0/10
3 (Control 2)	0/5	0/5	0/10
4 (0.196 mg/l)	2/5	0/5	2/10
5 (0.473 mg/l)	4/5	0/5	4/10
6 (0.694 mg/l)	5/5	3/5	8/10

In Group 4 (0.196 mg/l), two male rats were found dead on Day 2 (a.m.) of the observation period.

In Group 5 (0.473 mg/l), four male rats were found dead on Day 2 (a.m.) of the observation period.

In Group 6 (0.694 mg/l), five male rats and two female rats were found dead on Day 2 (a.m.) and one female rat was found dead on Day 3 (a.m.) of the observation period.

Clinical signs

(a) During the exposure

The incidence of clinical signs observed during exposure is shown in Table 3 (page 33 - 34). There were no clinical signs related to exposure to 2,6 DNT. Soiling of the fur by excreta was observed in the control and test groups during exposure.

(b) During the observation period

The incidence of clinical signs seen during the observation period is shown in Table 4 (page 35 - 39). Column 0 of this table shows the observations made when the rats were removed from the exposure chamber. At this time signs evident, in rats exposed to 2,6 DNT at 0.196 mg/l or higher levels, were brown staining around the snout and jaws, in Groups 4, 5 and 6 and exaggerated respiratory movements in Groups 5 and 6. Clinical signs seen on Day 1 and later in the observation period were brown staining over various parts of the body, matted fur, exaggerated respiratory movements, lethargy, ataxia and death. Injuries to the eyes as a consequence of taking the blood samples were evident in a number of control and test rats.

Recovery from the effects of exposure was seen from Day 4 of observation and complete in most surviving rats by Day 5 of the observation period.

Methaemoglobin levels

The methaemoglobin analysis results are shown in Table 9 (page 47 - 49). There was a slight increase in some treated groups during the first 24 hours following exposure. However, all values were close to the values found for the control rats.

Bodyweight

The group mean and individual bodyweights are shown in Table 5 (page 40) and Figures 3a and 3b.

Moderate to marked decreases of bodyweight or reductions in the rate of bodyweight gain were observed in exposed female rats for up to 3 days and in exposed male rats for up to 6 days following exposure. The weight gain of the control rats was also affected for up to 3 days following the exposure procedures.

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Food consumption

The food consumption data are presented in Table 6 (page 43).

Food consumption was reduced for 1 day in rats exposed at 0.026 mg/l and for up to 4 days following exposure to 2,6 DNT at concentrations of 0.196 to 0.694 mg/l of air.

Water consumption

The water consumption data are presented in Table 7 (page 43). Water consumption was not affected in female rats but variable and increased in male rats following exposure to 2,6 DNT at concentrations of 0.196 to 0.473 mg/l of air.

TERMINAL STUDIES

Lung weight to bodyweight ratio

The lung weight to bodyweight ratio for individual rats is shown in Table 8 (page 44 - 46).

The lung weight to bodyweight ratios were higher than control values in a proportion of rats that died as a result of exposure to 2,6 DNT. The ratios were within normal limits for the control rats and for the rats that survived exposure to 2,6 DNT.

Estimation of the LC₅₀ (6-hour) for 2,6 DNT

From the mortality data for Groups 4, 5 and 6 the LC₅₀ (6-hour) for 2,6 DNT, without regard to the sex of the rats, was established at:

0.43 mg per litre of air.

The standard error (SE) of the estimate was 0.102 mg per litre of air.

The 95% confidence limits were 0.23 - 0.63

For male and female rats considered separately the LC₅₀ values were:

Male rats: 0.24 mg per litre of air. SE 0.080 (95% confidence limits 0.08 - 0.40)

Female rats: 0.66 mg per litre of air. SE 0.085 (95% confidence limits 0.49 - 0.83)

Macroscopic pathology

The macroscopic pathological findings for individual rats are included in Appendix 2 (page 52 - 54).

The findings for rats that died as a result of exposure to 2,6 DNT were typified by congestion of the lungs. A dark appearance of the liver was noted for a number of rats that died as a result of exposure.

There were no treatment-related macroscopic abnormalities in rats that survived exposure to 2,6 DNT.

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CMA/4

FIGURE 1
Aerosol generator

- a. Plastic elutriating column
- b. Compressed air supply.
- c. Feed tube with adjustment screw.
- d. Venturi atomising jet.
- e. Drain tubes.

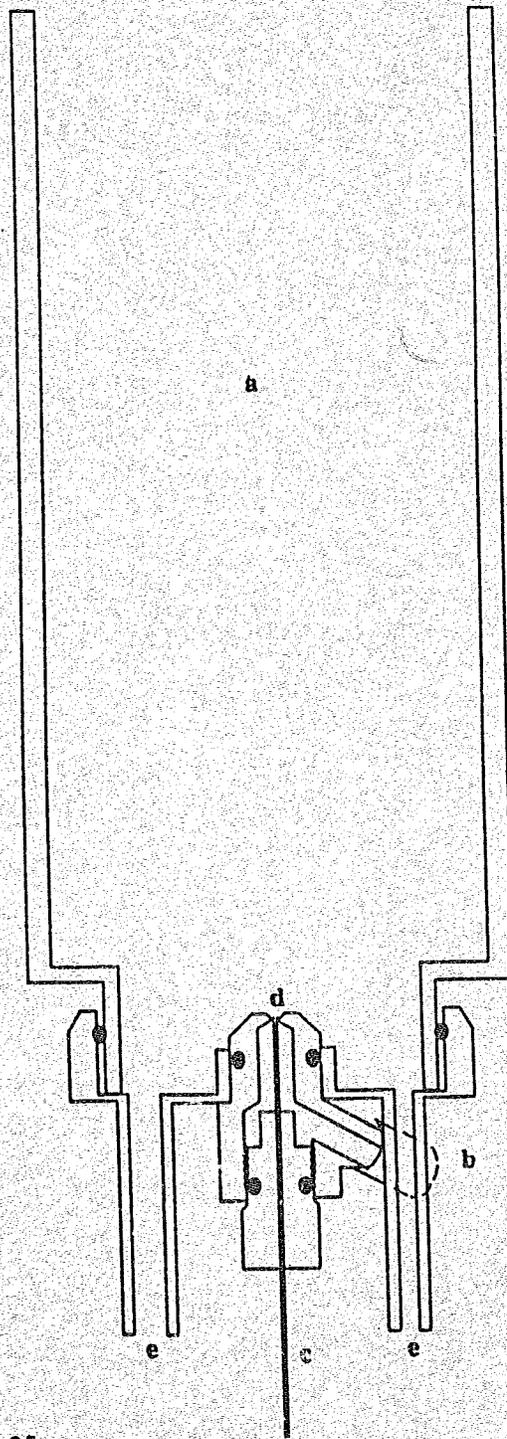
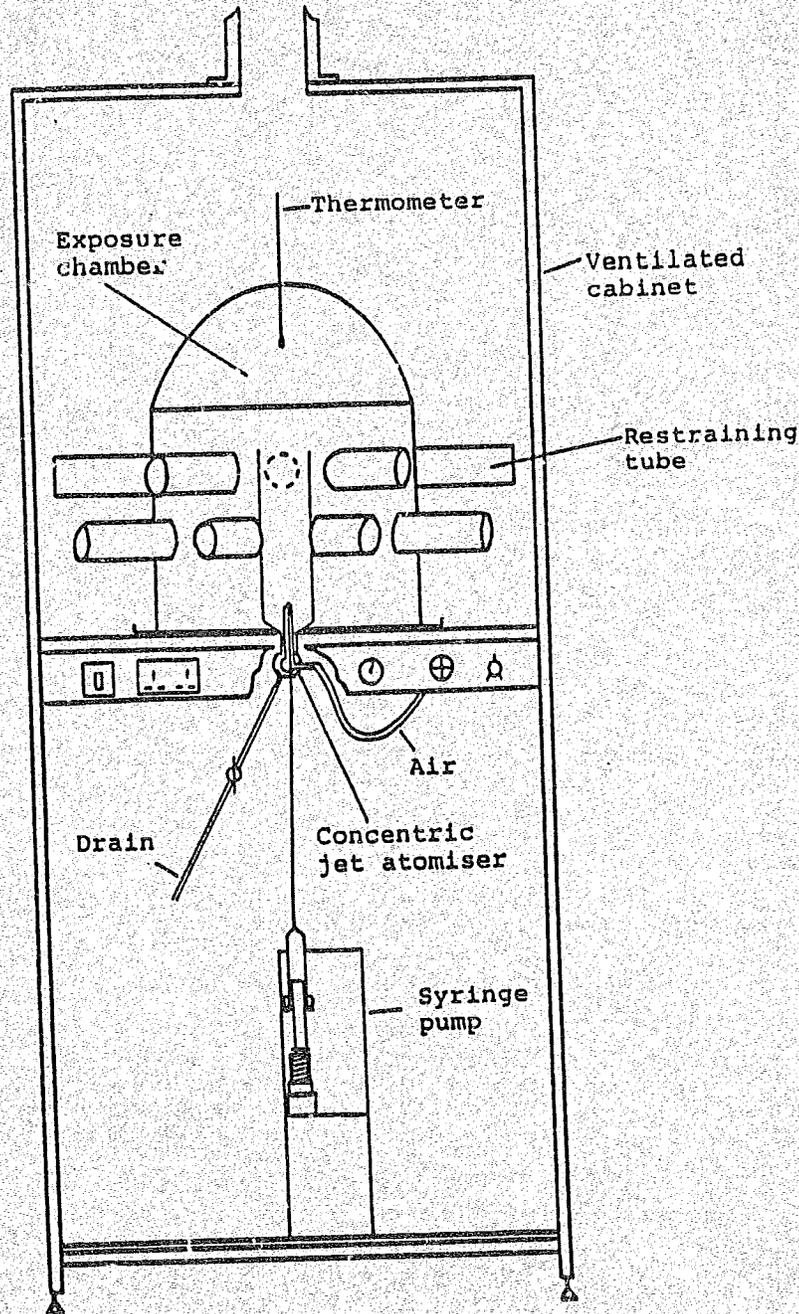


FIGURE 2
Exposure system



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FIGURE 3a

Group mean bodyweights: males

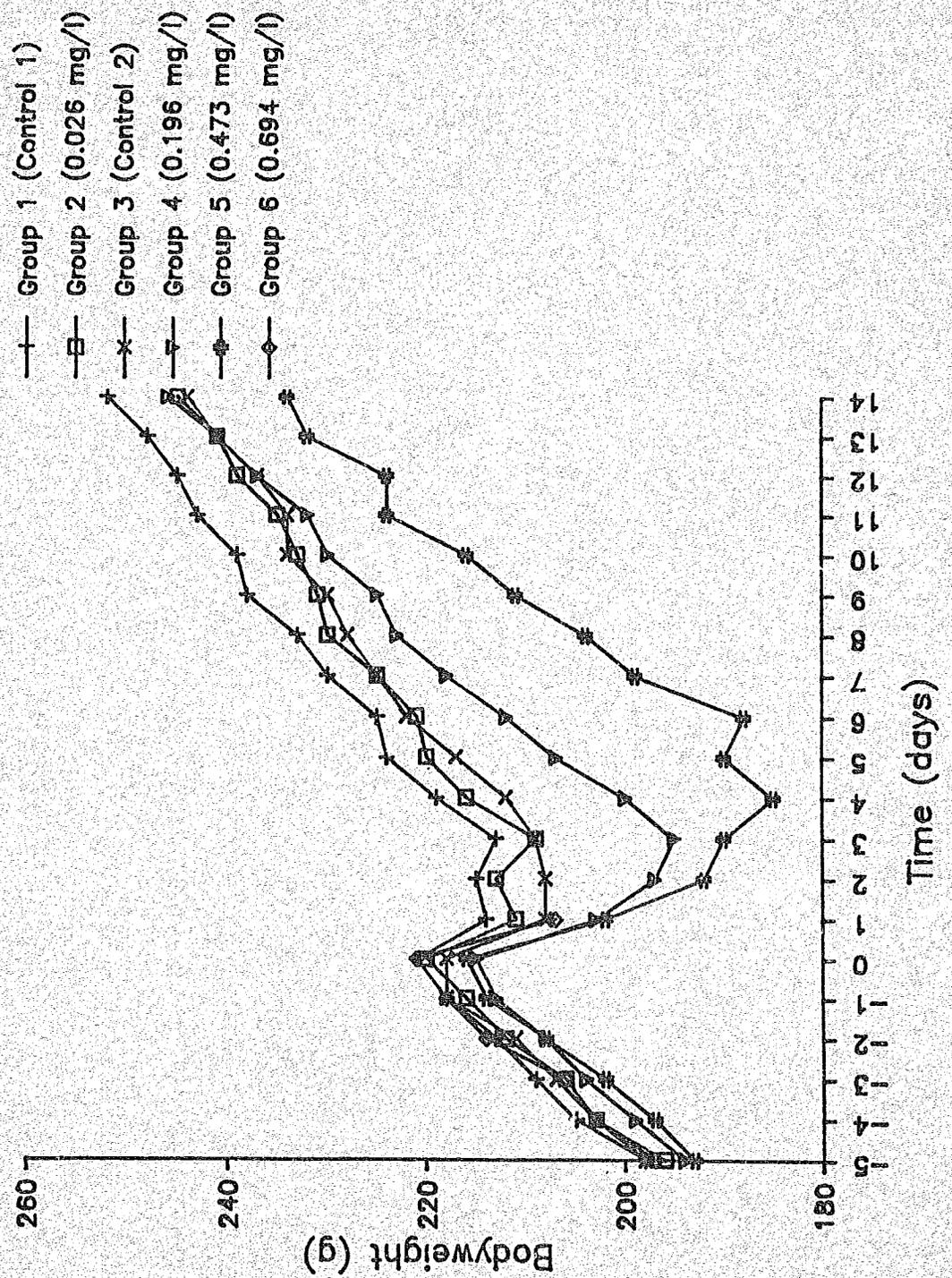


FIGURE 3b

Group mean bodyweights: females

