

13016

TSCA HEALTH & SAFETY STUDY COVER SHEET

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1.0 SUBMISSION TYPE - Contains CBI <input type="checkbox"/> 8(d) <input checked="" type="checkbox"/> 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify <u>8EHQ - 1298 - 14327</u> XX- Intial Submission - Follow-up Submission - Final Report Submission Previous EPA Submission Number or Title if update or follow-up: _____ Docket Number, if any: # _____ <input type="checkbox"/> continuation sheet attached		
2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI) <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID Cert# P 917006753 98-2-24	2.3 FOR EPA USE ONLY <div style="text-align: right; font-size: small;">98 DEC -4 PM 3:43</div>
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY -Contains CBI <i>Reported Chemical Name (specify nomenclature if other than CAS name):</i> CAS#: 54914-37-3 Aliphatic Polyamine Purity _____ % <input checked="" type="checkbox"/> Single Ingredient <input type="checkbox"/> Commerical/Tech Grade <input type="checkbox"/> Mixture Trade Name: <u>Desmophen PAC XP 7076</u> Common Name: _____ <div style="text-align: center; font-size: large; font-weight: bold; color: black;">Contains No CBI</div>		
4.0 REPORT/STUDY TITLE - Contains CBI Study on Acute Inhalation Toxicity on Rats, Report # 28048 <input type="checkbox"/> Continuation sheet attached		
5.1 STUDY/TSCATS INDEXING TERMS [CHECK ONE] HEALTH EFFECTS (HE): <input checked="" type="checkbox"/> ENVIRONMENTAL EFFECTS (EE): _____ ENVIRONMENTAL FATE (EF): _____		
5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes) STUDY SUBJECT ROUTE OF VEHICLE OF TYPE: <u>ATOX</u> ORGANISM (HE, EE only): <u>RATS</u> EXPOSURE (HE only): <u>ORAL</u> EXPOSURE (HE only) <u>INHL</u> Other: <u>Developmental</u> Other: _____ Other: <u>Gavage</u> Other: <u>Unknown</u>		
6.0 REPORT/STUDY INFORMATION <input type="checkbox"/> Contains CBI X- Study is GLP Laboratory <u>Bayer AG, Department of Tox, Wuppertal</u> Report/Study Date <u>10/21/98</u> Source of Data/Study Sponsor (if different than submitter) <u>Bayer AG</u> Number of pages <u>135</u> <input type="checkbox"/> continuation sheet attached		
7.0 SUBMITTER INFORMATION <input type="checkbox"/> Contains CBI Submitter: <u>Donald W. Lamb, Ph.D</u> Title: <u>V. P., Prod. Safety & Reg. Affrs</u> Phone: <u>412-777-7431</u> Company Name: <u>Bayer Corporation</u> Company Address: <u>100 Bayer Road</u> <u>Pittsburgh, PA 15205-9741</u> Submitter Address (if different): _____ Technical Contact: <u>Donald W. Lamb, Ph.D</u> Phone: <u>(412)777-7431</u> <input type="checkbox"/> continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <input type="checkbox"/> Contains CBI <div style="text-align: center;">  BEHQ-98-14327 </div> <input type="checkbox"/> continuation sheet attached		

Submitter Signature: Donald W Lamb Date: 11/30/98


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9.0 CONTINUATION SHEET

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CONTINUED FROM COVER SHEET SECTION # 2.1

The clinical sign of lethargy (defined on the clinical sign table on page 77 of the report as "motility reduced") occurred in three non-moribund animals, with the duration of the sign lasting three days. As this sign occurred in more than two non-moribund animals and the sign lasted for more than two days, this finding is a trigger for reporting.

Abstract

An acute inhalation toxicity study was conducted with Desmophen Pac XP 7076 using rats. Groups of rats were nose-only exposed for four hours to the average aerosol concentration of 583, 1400, 2727, and 4937 mg/m³ air.

Clinical observations: The exposure to a concentration to 583 mg/m³ air was tolerated without mortality, whereas higher concentration evoked mortalities. Signs were apparent in a concentration dependent manner and persisted up to the end of the 2-week post-exposure period. The duration of signs was contingent upon respiratory changes. The major signs observed are as follows: bradypnea, dyspnea, labored breathing pattern, sneezing, stridor, cyanosis, emaciation, bristled, and ungroomed hair-coat, limp, motility reduced, gait changes, nostrils/muzzle: reddened and with red encrustation, nasal discharge, decrease in body weight, hypothermia. Gross necropsy findings demonstrated lower respiratory tract damage (bloated lung, edema, and pleural effusions).

The LC₅₀ (4hr) for males = 1276 mg/m³ air and for females = 2392 mg/m³ air. The NO(A)EL for males and females was < 583 mg/m³ air.

In conclusion, the aerosolized Desmophen Pac XP 7076 causes moderate acute inhalation toxicity to rats, and experimental evidence suggests that mortality is causally related to lower respiratory tract irritation.

**BAYER AG
DEPARTMENT OF TOXICOLOGY
FRIEDRICH-EBERT-STR. 217-333
D - 42096 WUPPERTAL**

Report-No.: 28048

Date: 21.10.1998

**DESMOPHEN PAC XP 7076
(*Latent Aliphatic Polyamine*)**

**STUDY ON ACUTE INHALATION TOXICITY ON RATS
ACCORDING TO OECD No. 403,
EC Guideline 92/69/EEC and the TSCA § 798.1150**

by

PD Dr. J. Pauluhn

Study No.: T5067020

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with the OECD Principles of Good Laboratory Practice (as revised in 1997) and to the Principles of Good Laboratory Practice (GLP) according to Appendix 1 German Chemicals Act (Bundesgesetzblatt Part I, July 29, 1994). Quality Assurance (Dr. R. Rauchschalbe) mandates the following statements:

1. Data addressing the purity of test sample, including the responsible laboratory and study director, have not been provided by the sponsor.
2. Data addressing the duration (exact date) of the stability of test sample have not been provided by the sponsor.
3. The characterisation of test specimen is therefore incomplete or absent.
4. The statement made by the study director based on the information provided by the sponsor addressing the purity (pp. 11) is, according to QA, inadequately documented in the raw data.



PD Dr. J. Pauluhn D.A.B.T.
Board Approved Toxicologist (DGPT)
EUROTOX Registered Toxicologist
Study Director

Date: Oct. 7, 1998

**SPONSOR:
BAYER CORP.**

Dr. J. Thyssen
Head of Toxicology

Date: _____

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Quality Assurance Statement

Test Item : DESMOPHEN PAC XP-7076
Study No.: T5067020

Study-based inspections/audits were conducted by the Quality Assurance on the dates given below. Audit reports have been submitted in writing to the study director and, if necessary, also to the laboratory management, or other persons affected.

Date of audit**Date of report to study
director and/or management**

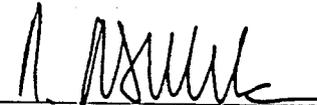
Jun. 02, 1998	(study plan)	Jun. 02, 1998
Jun. 09, 1998	(study conduct)	Jun. 09, 1998
Aug. 14, 1998 - Aug. 20, 1998	(first draft)	Aug. 26, 1998
Sept. 29, 1998	(final draft)	Oct. 12, 1998

The results of the study and the methods used have been correctly reported.

Quality Assurance Unit
PH-QA-C/GLP, Bayer AG

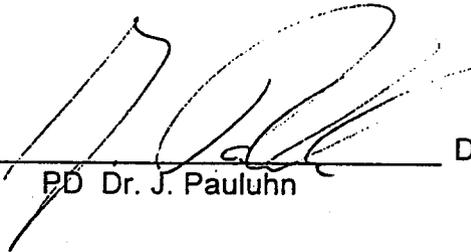
Date: Oct. 12, 1998

Responsible: _____


Dr. R. Rauchschalbe

3. SIGNATURES

Study
Director:



PD Dr. J. Pauluhn

Date: August 31, 1998

Analytical
Chemistry:



Dr. W. Rüngeler

Date: Sep. 2, 1998

Institute
Head:



Dr. L. Medicinal
Prof. G. Schlüter

Date: Sept 24, 1998

4. SUMMARY

A study of the acute inhalation toxicity of DESMOPHEN PAC XP 7076 (hereafter referred to as *test substance*) on rats has been conducted in accordance with OECD Guideline No. 403. The study conditions were adjusted so as to fulfill both the EC Guideline 92/69/EEC and the TSCA § 798.1150 (1989) guidelines. Groups of rats was nose-only exposed for four hours to the average aerosol concentrations of 583, 1400, 2727 and 4937 mg/m³ air. With regard to the respirability of the aerosol generated internationally recognized recommendations, such as of SOT (1992) were fulfilled, i.e. the MMAD was between \approx 1.1-1.5 μ m (GSD \approx 1.9). The results can be summarized as follows:

<p>LC₅₀ inhalation (aerosol, 4 hr) Males: 1276 (929-1752) mg/m³ air¹⁾ Females: 2392 (1742-3283) mg/m³ air</p>	<p>NO(A)EL Males & females: < 583 mg/m³ air</p>
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Clinical observations: The exposure to a concentration of 583 mg/m³ air was tolerated without mortality whereas higher concentrations evoked mortalities. Signs were apparent in a concentration-dependent manner and persisted up the end of the 2-week postexposure period. The duration of signs was contingent upon respiratory changes. The major signs observed are as follows: bradypnea, dyspnea, labored breathing pattern, sneezing, stridor, cyanosis, emaciation, bristled and ungroomed hair-coat, limp, motility reduced, gait changes, nostrils/muzzle: reddened and with red encrustations, nasal discharge, decrease in body weights, hypothermia. Gross necropsy findings demonstrated lower respiratory tract damage ('bloated lung', edema, pleural effusions).

Evaluation and Assessment

Thus the aerosolized test substance proved to have a moderate acute inhalation toxicity to rats and experimental evidence suggests that mortality is causally related to lower respiratory tract irritation.

¹ All concentration data represent actual concentrations of the test substance in the rats' breathing zone (filter analyses).

5. INTRODUCTION

This acute inhalation toxicity study was conducted in accordance with OECD Guideline No. 403 using DESMOPHEN PAC XP 7076 as a test substance. The study was performed on rats (single nose-only exposure over 4 hours to the aerosolized test substance, dynamic exposure conditions, 2 week observation period). This study served the purpose of product classification and to estimate the potential acute health hazard resulting from handling this product.

Testing facility:

Institute of Toxicology - Industrial Chemicals/Department of Occupational Toxicology, Bayer AG, D-42096 Wuppertal, Friedrich-Ebert-Straße 217 - 333, Germany.

Study/project identification:

Study no.: T5067020

Study period:

June 9, 1998 - July 1, 1998

Experimental starting date: June 8, 1998 (technical pre-trials)

Study completion date: see signature of study director (page 7)

Sponsor:

BAYER Corporation, Agriculture Division
P.O. Box 4913 Hawthorn Road
Kansas City, MO 64120-0013
U.S.A.

6. RESPONSIBILITIES

Air conditioning/air make-upDipl. Ing. G. Strietholt
Analytical characterization of test atmospheres:..... Dr. W. Rüngeler
Archiving the study data:..... Prof. G. Schlüter
Biometric evaluation:..... Dr. J. Pauluhn
Gross pathology:.....Dr. Rosenbruch
Head of Department:..... Prof. Dr. E. Löser
Laboratory Animal Services: Dr. Petersen v. Gehr
Quality Assurance:..... Dr. H. Lehn
Study Director and Report Author:..... Dr. J. Pauluhn
Test substance shipment / supply of data:..... D.W.Sturdivant/Bayer Corp. USA

7. MATERIALS AND METHODS

7.1. Test substance

Test substance: Desmophen PAC XP 7076
CAS#: 54914-37-3
Product code: DA -164
Manufacturer: BAYER Corp., Pittsburgh, U.S.A.
Lot-no.: BP 30889 , approval date: August 22, 1997
Purity: within specification. Sample returned to sponsor for re-analysis.
Storage conditions: at room temperature / darkness
Appearance: pale yellow liquid
Chemical family: Latent Aliphatic Polyamine

7.2. Test System and Housing of Animals

Species and species justification: The study was carried out in rats, a rodent species recommended in the test guidelines.

Healthy young adult SPF bred Wistar rats, strain Hsd Cpb:WU(SPF), from the experimental animal breeder Harlan-Winkelmann GmbH, Borchon, Germany, were used. Animals of this strain have been used at Bayer AG in toxicological studies for years. Historical data on their physiology, diseases and spontaneous alterations are available. The state of health of the strain is randomly checked regularly at the instance of the Laboratory Animal Services, Bayer AG, for the most important specific infectious pathogens. The results of these examinations are archived.

Acclimatization: The animals were acclimatized to the animal room conditions for at least 5 days before use.

Identification: Animals were identified by both individual color-marking and cage-labels. All animals from this study were located on one cage-rack.

Randomization: Before the start of the study the health status of each animal was assessed. Animals were subsequently assigned to exposure groups at random (randomization procedure is described in section 7.17).

Health status: Only healthy rats free of signs were used for this study. The animals were not vaccinated or treated with anti-infective agents either before their arrival or during the acclimatization or study periods. The females were nulliparous and not pregnant.

Age and weight: At the study start the variation of individual weights did not exceed ± 10 per cent of the mean for each sex (see Appendix). Animals of the weight class used are 2 - 3 months old and hence fulfill the criterion for young adults (see Appendix).

Animal housing: During the acclimatization and study periods the animals were housed singly in conventional Makrolon® Type II cages (based on A. Spiegel and R. Gönnert, Zschr. Versuchstierkunde, 1, 38 (1961) and G. Meister, Zschr. Versuchstierkunde, 7, 144-153 (1965)). Cages and water bottles were changed twice a week while unconsumed feed was changed once per week. The legal requirements for housing experimental animals (86/609 EEC) were followed.

Bedding: Bedding consisted of type S 8/15 low-dust wood granulate from Ssniff, Soest/Westfalen, Germany. The wood granulate was randomly checked for harmful constituents at the request of the Laboratory Animal Services, Bayer AG.

Animal rooms: All animals were housed in a single room. For reasons of space availability rats from other acute toxicity studies were housed in the same room, however mistakes in animal assignments were excluded by adequate spatial separation, clear cage labeling, and appropriate organization of all work procedures. The housing of several studies in one animal room is not considered to be a deviation from current GLP-requirements since many acute studies comprise of 10 animals only (as required to perform a limit test).

Environmental Conditions in the Animal Room

The animal room environment was as follows:

Room temperature:	22 \pm 2 °C
Relative humidity:	approximately 50 %
Dark/light cycle:	12 h/12 h; artificial light from 6.00 a.m. to 6.00 p.m. Central European Time
Light intensity:	approximately 14 watt/m ² floor area
Ventilation:	approximately 10 air changes per hour

The room humidity and temperature were continuously monitored and documented using a calibrated thermohygrograph. Occasional deviations from these conditions occurred, e.g. as a result of animal room cleaning, but these had no detectable influence on the outcome of this study.

Cleaning, disinfection, and pest control: The animal room was regularly cleaned and disinfected once a week with an aqueous solution of TEGO® 2000. Contamination of the feed and contact with the test system were excluded. Pest control was not conducted in the animal room.

Feeding: Ration consisted of a standard fixed-formula diet (Altromin® 1324 pellets maintenance diet for rats and mice, Altromin GmbH, Lage) and tap water (drinking bottles). Both food and water were available *ad libitum*. The pelletized feed was contained in a rack in the stainless-steel wire cage cover. The nutritive composition and contaminant content of the standard diet was checked regularly by random sampling by the Laboratory Animal Services, Bayer AG. Details concerning general feed and water specifications are provided in the Appendix.

Water: Drinking quality tap-water (Drinking Water Decree of 05.12.1990, Bundesgesetzblatt [federal law gazette] part I, page 2612) was provided *ad libitum* in polycarbonate bottles containing approximately 300 ml (based on A. Spiegel and R. Gönnert, Zschr. Versuchstierkunde, 1, 38 (1961) and G. Meister, Zschr. Versuchstierkunde, 7, 144-153 (1965)). The results of feed and water analyses are retained by Bayer AG. The available data provided no evidence of an impact on the study objective.

7.3. Test Guidelines

The study described below was carried out in accordance with OECD Guideline No. 403. The study conditions were adjusted so as to fulfill both the EC Guideline 92/69/EEC and the TSCA § 798.1150 (1989) guidelines. Other recommendations (US EPA, 1984, 1988, 1989) and SOT (1992) were also considered so as to comply with internationally recognized and established procedures.

7.4. Exposure Conditions

Mode of exposure: Animals were exposed to the test substance in Plexiglas exposure tubes applying a *directed-flow* nose-only exposure principle. Tubes were

chosen that accommodated the animals size. These tubes were designed so that the rat's tail remained outside the tube, thus restrained-induced hyperthermia can be avoided. This type of exposure is preferable to whole-body exposure on scientific (Pauluhn, 1984) and technical reasons (rapid attainment of steady-state concentrations, no problems with regard to test atmosphere inhomogeneities, better capabilities to control all inhalation chamber parameters, easier cleaning of exhaust air, and lower consumption of test substance). Moreover, contamination of the fur can largely be avoided. The chambers used are commercially available (TSE, 61348 Bad Homburg) and the performance of this type of chamber has been published (Pauluhn, 1984; Pauluhn, 1988; Pauluhn, 1994).

Vehicle: The test substance was examined as without a carrier or vehicle.

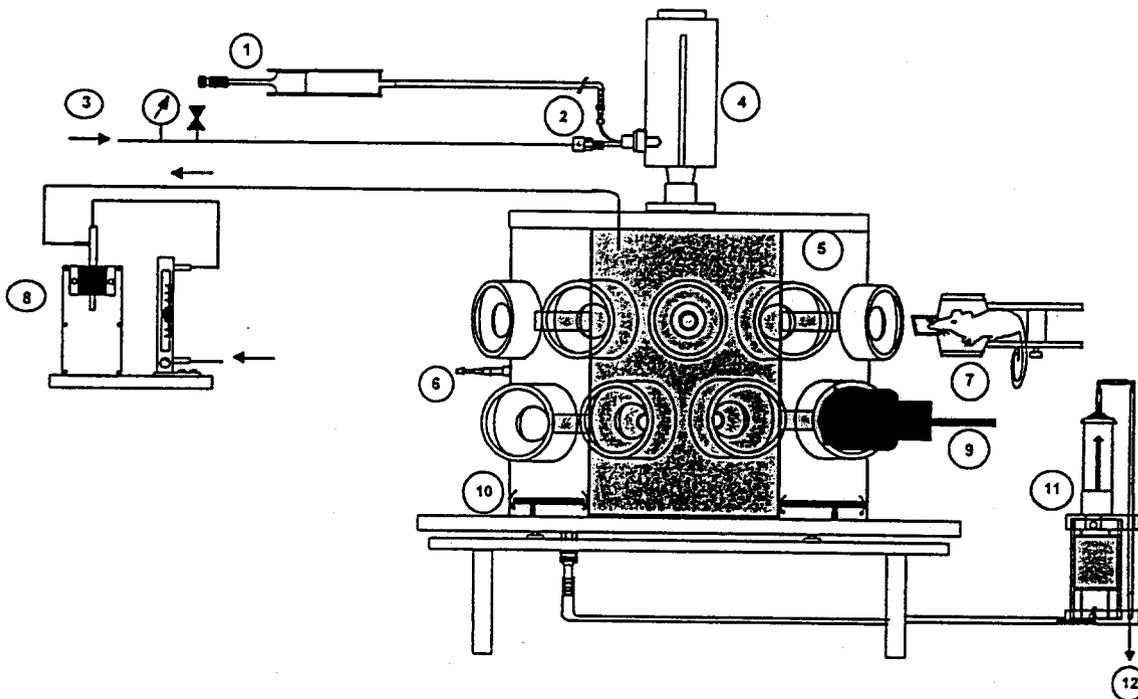
7.5. Generation of Atmosphere and Exposure Technique

Generation of atmosphere: Atmospheres of the test substance for nose-only inhalation exposures were generated under dynamic conditions using a Braun-infusion pump and a modified binary nozzle (in house modification of TSE-Nozzle; TSE, 61348 Bad Homburg). The test substance was nebulized using conditioned (dry, oil free) compressed air (dispersion pressure approximately 600 kPa). The respective concentration was achieved by spraying different volumes of liquid per unit of time. Further details are summarised in Figure 1 and Table 1 (see result section).

Description of apparatus: Dry conditioned air was used to aerosolize the test substance so as described above. After nebulization, the test substance was conveyed into the inner plenum of the inhalation chamber, the test atmosphere was then forced through openings in the inner concentric cylinder of the chamber, directly towards the rats' breathing zone. This *directed-flow* arrangement minimizes re-breathing of exhaled test atmosphere. The stability of the test atmosphere was monitored continuously using an aerosol photometer as real-time monitoring device (*vide infra*). The inhalation chamber used was suitable to accommodate 20 rats at the perimeter location. A slight positive balance between the air volume supplied and extracted ensured that no passive influx of air into the exposure chamber can occur. The slight positive balance provides also adequate dead-space ventilation of the exposure restrainers and prevents a bias-air flow through the restrainers. The pressure difference between the inner inhalation chamber and the exposure zone was 0.02 cm H₂O (Pauluhn, 1994). The exposure system was accommodated in an adequately ventilated enclosure. Temperature and humidity are measured by a

computer system using calibrated sensors. The sensors were located in the exposure zone of the inhalation chamber (cf. Fig. 1). Further technical details are provided in the ensuing sections.

Figure 1: Inhalation Chamber (schematic)



1. Metering pump with test substance	7. Animal in exposure tube
2. Binary nozzle	8. Real-time aerosol photometer
3. Conditioned pressured air	9. Sensor for measurement of humidity and temperature
4. Baffle / pre-separator	10. Exhaust air
5. Directed-flow nose only exposure port	11. Cotton-wool aerosol/HEPA filter (air make-up)
6. Sampling for analytical concentrations	12. Digitally controlled vacuum

Inhalation Chamber: The aluminum inhalation chamber has the following dimensions: inner diameter = 14 cm, outer diameter = 35 cm (two-chamber system), height = 25 cm (internal volume \approx 3.8 L). The construction of the inhalation chamber is shown schematically in Fig.1. Details of this modular chamber and its validation with

regard to spatial homogeneity of material distribution have been published (Pauluhn, 1994).

Inhalation chamber steady-state concentration: The test atmosphere generation conditions provide an adequate number of air exchanges per hour (> 200 x, continuous generation of test atmosphere). Under such test conditions steady state is attained within approximately one minute of exposure ($t_{99\%} = 4.6 \times$ chamber volume/flow rate; McFarland, 1976). The ratio between the air supplied and exhausted was chosen so that approximately 85% of the supplied air is removed from the chamber as exhaust. The remainder provides adequate dead-space ventilation for the exposure tubes. At each exposure port a minimal air flow rate of 0.75 l/min was provided. The test atmosphere can by no means be diluted by bias-air-flows. The inhalation chamber was operated in a well ventilated chemical fume hood.

Optimization of respirability: In order to increase the efficiency of the generation of respirable particles and to prevent larger particles from entering the chamber a PVC-pre-separator/baffle system was used (Tillery et al., 1976; Pauluhn, 1994).

Conditioning the compressed air: Compressed air was supplied by Boge compressors and was conditioned (i.e. freed from water, dust, and oil) automatically by a VIA compressed air dryer. Adequate control devices were employed to control supply pressure.

Air flows: Air flows are monitored and controlled continuously by flow-meters. The proper performance of the mass flow controllers is measured using precision flow meters of the Fisher & Porter company and soap bubble meters. For calibration purposes the "generic" scale of the tapered flow meter is derived mathematically taking into account the current ambient pressure and temperature (software supplied by Fisher & Porter, Göttingen, Germany). To ensure proper calibration the mathematically derived scale is confirmed by soap bubble meter measurements. Flow - meters are always used between 25% and 75% of their capacity.

Treatment of exhaust air: The exhaust air was purified via cotton-wool/HEPA filter cascades. These filters were disposed of by Bayer AG.

7.6. Inhalation chamber temperature and humidity

The temperature and humidity measurements were made using a computerized system (Leybold Heraeus). The values were recorded at intervals of 10 min (computerized recording). The test atmosphere temperature and humidity were

measured at the exposure location (*cf.* Fig. 1). Details of this monitoring system have been reported elsewhere (Pauluhn, 1986).

The relative humidity was measured with a humidity sensor (CCH capacitor). The humidity-sensor is protected from particles by a double sintered metal filter with an interposed Teflon membrane (pore size approximately .1 μm). This sensor was calibrated using saturated salt solutions according to Greenspan (1977). The temperature sensors were calibrated with a calibration thermometer. The measured values were recorded and evaluated with an Apple 2e computer and an MDP 8240/45 analogue-digital converter using an IEEE 488 interface.

7.7. Analysis of the test atmosphere

Nominal concentration: The nominal concentration was calculated from the ratio of the quantity of test substance sprayed into the baffle and the total throughput of air through the inhalation chamber. The lower analytical concentrations compared with the nominal concentrations are attributed to the efficient removal of larger particles in the baffle/preseparator system.

Gravimetric concentration: The test-substance concentration was determined by gravimetric analysis (filter: Glass Fiber-Filter, Sartorius, Göttingen, Germany). Gravimetric analyses were performed thrice during exposure to allow for direct comparisons with gravimetric cascade impactor analyses.

Analytical concentration: The test atmosphere was sampled by Florisil tubes. Following elution, the concentration of test substance was determined analytically. Further methodological details related to sampling as well as characterization of test atmosphere are provided in the Appendix. For reference/ calibration purposes the test compound was used.

Chamber samples were taken in the vicinity of the breathing zone (see Fig. 1). The number of samples taken was sufficient to characterize the test atmosphere and was adjusted so as to accommodate the sampling duration and/or the need to confirm specific concentration values. Optimally, samples were collected after the equilibrium concentration had been attained (for details of sampling frequency see Appendix). All analytical concentrations reported refer to mg DESMOPHEN PAC XP-7076/m³ air.

7.8. Collection Efficiency

The samples are taken from the inner cylinder (*cf.* Figure 1). Concentrations measured at the exposure locations (by using a modified exposure restrainer) were indistinguishable from those measured in the inner cylinder (Pauluhn, 1994). Each sampling activity is controlled by calibrated flow controllers and gas meters. In addition to soap bubble meter calibration the mass flow controllers used for analytical sampling of test atmosphere were also checked for correct volumetric performance.

The sampling equipment was adjusted with calibrated flow-meters to internationally recognized standards (ACGIH, 1978; Section I "Calibration of Air Sampling Instruments").

The conditions for generating the test atmosphere are optimized to provide maximum aerosol respirability to rats (Raabe, 1982; Snipes, 1989; SOT-Commentary, 1992). The absence of larger particles and high flow rates in the vicinity of the sampling ports make it possible to disregard potential anisokinetic sampling errors, thus ensuring a representative sampling even with different sampling probe orifice diameters and flow rates. The tolerance limits for the radius of the probe orifice are calculated using the following formula [ACGIH, 1978]. Calculations consider both a particle size distribution that encompasses aerodynamic diameters (D_{ae}) of 0.5 to 7.4 μm and sample flows ranging from 8 to 80 ml/sec.

$$5 \times 3 \sqrt{\frac{\text{flow} \times \tau}{4 \times \pi}} \leq r_p \leq \frac{1}{5} \times 2 \sqrt{\frac{\text{flow}}{g \times \tau \times \pi}}$$

r_p = radius of the sample probe in cm = $\frac{1}{2} \times D_p$
 τ = relaxation time ($D_{ae} 0.5 \mu\text{m} = 1 \times 10^{-6}$ sec; $D_{ae} 7.4 \mu\text{m} = 1.7 \times 10^{-4}$ sec)
 g = gravity constant = 980 cm/sec²

Tolerance limits calculations for the sample probe orifice (r_p) indicated that a representative sampling is assured when the orifice inner diameter is in the range of 1.0 to 1.6 cm. Orifices of the sampling instruments used here are in compliance with this criteria. Details of the D_p tolerance limit calculations are published elsewhere (Pauluhn, 1988; Pauluhn, 1994).

7.9. Stability of the Test Atmosphere

To monitor the integrity and stability of the aerosol generation and exposure system the stability of the exposure atmosphere was measured by using a RAS-2 real-time aerosol photometer (MIE, Bedford, Massachusetts, USA). Samples were taken continuously from the vicinity of the breathing zone.

This chamber monitoring allows for an overall survey of toxicologically relevant technical parameters (inlet and exhaust flows as well as atmosphere homogeneity, temporal stability, and generation performance). Interruptions in exposure (e.g. resulting from obstruction of orifices or other technical mishaps) are recorded and, if applicable, a commensurate interval is added to the exposure duration for compensation.

One example of this monitoring activity (copy of raw data) is provided in the Appendix.

7.10. Characterization of Aerodynamic Particle-Size Distribution

The samples for the analysis of the particle-size distribution were also taken in the vicinity of the breathing zone.

The particle-size distribution was analyzed using a BERNER-TYPE AERAS low-pressure critical orifice cascade impactor (Hauke, Gmunden, Austria). Specifications and evaluations are provided in the Appendix. The individual impactor stages had been covered by an aluminum foil and glass fiber filter which were subjected to gravimetric analysis. An adhesive stage coating (silicone spray) was not used to prevent particle bounce and re-entrainment accordingly. Gravimetric analyses were made using a digital balance.

Evaluation of particle-size distributions: For the evaluation of the cascade impactor analyses the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (GSD) are determined from the probit-transformed cumulative particle mass frequency distribution (y-axis) and the logarithmic effective cut-off diameters (ECD's) (x-axis) of the individual impactor stages by linear regression. The GSD is calculated from the regression line: percentile 84 / percentile 50. The relative mass with an aerodynamic diameter $\leq 3 \mu\text{m}$ ("respirable mass fraction") [Raabe, 1982; Snipes, 1989; SOT-Commentary, 1992] is calculated from the regression line. For probit transformation and linear regression FORTRAN algorithms published by Rosiello et al. (1977) are used. The MMAD was calculated using published following formulas [Marple and Rubow, 1980; Pauluhn, 1994].

To verify whether the aerosol distribution is in fact unimodal and log-normal the normalized mass per stage (f'_H) is evaluated as a histogram. $\Delta \log D_p$ is equal the difference $\log D_{p+1} - \log D_p$, whereas D_p is the lower (left) cut-size limit and D_{p+1} the higher (right) cut-size limit of the corresponding impactor stage. As demonstrated by the evaluations included in the Appendix, the impactor stage cut-off limit (D_{p+1}) to the right was used for all calculations.

$$f'_H = \frac{1}{N_f} \times \frac{\text{mass / stage}}{\Delta \log D_p}$$

The log-normal mass distribution $y'(D_{ae}) = 1/N_f \times y(D_{ae})$ as a function of the aerodynamic diameter (D_{ae}) is computed using the formula:

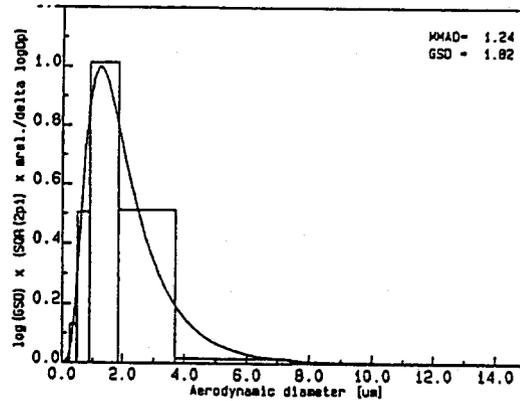
$$y'(D_{ae}) = \exp \left[-\frac{(\log D_{ae} - \log MMAD)^2}{2 \times \log^2 GSD} \right]$$

The normalization factor (N_f) is calculated as follows:

$$N_f = \frac{\Sigma \text{mass}}{\log GSD \times \sqrt{2\pi}}$$

Where Σmass is the total mass collected by the cascade impactor, where $m_{\text{relative}} = \text{mass per stage} / \Sigma \text{mass}$ (cf. Fig. 2).

Figure 2: Principle of characterization of aerosol atmosphere

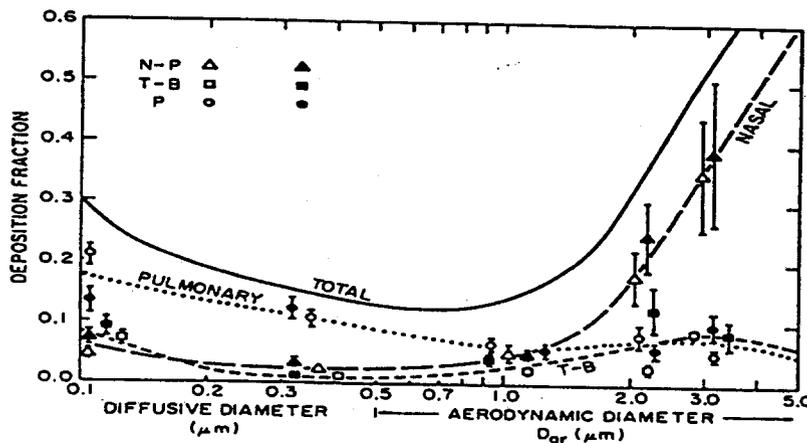


The algorithm for the calculation of particle size characteristics is taken from pertinent reference works on aerosol physics (Dennis, 1976; Marple and Rubow, 1980) and proves to be generally applicable (Pauluhn 1988; Pauluhn, 1994).

Respirability

Fig. 3, demonstrates that the particle size distribution achieved is adequate to reach all potential target structures of the respiratory tract.

Fig. 3 Respirability of Aerosols (Raabe, 1982)



7.11. Number of Animals per Group

Five male and five female rats were simultaneously exposed to each concentration under nose-only conditions for 4 h.

7.12. Control Animals

To identify exposure-related effects, comparisons with appropriate controls are conducted. Controls were exposed to conditioned air using almost similar exposure conditions as were used for the test substance (15 liters air/min; duration of exposure = 1 x 4 h; 5 males and females per group; 4 week observation period). Direct comparisons were made between the control and exposure groups.

Note: Control studies are performed under GLP-conditions but without assignment to a particular study. This allows use of control data for several studies that have been performed under similar experimental conditions within an applicable time frame. This procedure is in compliance with current testing guidelines as well as animal welfare regulations.

7.13. Body Weights and Duration of Observation Period

Body weights were measured before exposure, on days 3 and 7, and weekly thereafter. Individual weights are also recorded at death, if applicable. The period of observation was 2 weeks.

7.14. Clinical Signs

The appearance and behavior of each rat was examined carefully several times on the day of exposure and least once daily thereafter. Weekend assessments were made once a day (morning). Assessments from restraining tubes were made only if unequivocal signs occurred (e.g. spasms, abnormal movements, severe respiratory signs). Following exposure, observations are made and recorded systematically; individual records are maintained for each animal. Cage-side observations included, but were not limited to, changes in the skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system, and somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, lethargy, somnolence and prostration. The

time of death is recorded as precisely as possible, if applicable.

Since these signs can only be assessed adequately from freely moving animals, no specific assessment was performed during exposure while animals were restrained. Each rat was first observed in its home cage and then individually examined. The following reflexes were tested, based on recommendations made by Irwin (1968) and Moser et. al. (1988): visual placing response and grip strength on wire mesh, abdominal muscle tone, corneal and pupillary reflexes, pinnal reflex, righting reflex, tail-pinch response, startle reflex with respect to behavioral changes stimulated by sounds (finger snapping) and touch (back).

All signs exceeding the exposure day are reported in the form of incidence tables (see Appendix). The resolution of these tables is per one day, the maximum response is always displayed. The incidence of signs will reflect signs from surviving animals. Uncommon signs related to an agonal condition (if applicable) that may be observed on the day of death are recorded but may not be incorporated into the incidence tables. These signs are described in the results if they differ from previous observations.

7.15. Rectal Temperatures

The rectal temperatures were measured directly after cessation of exposure (approximately within ½hour after the end of exposure) using a Digimed H 11 digital thermometer with an rectal probe for rats.

7.16. Necropsy

All surviving rats were sacrificed at the end of the observation period using sodium pentobarbital (approximately 300 mg/kg body weight, intraperitoneal injection). All rats, irrespective of the day of death, were given a gross-pathological examination. Consideration was given to performing a gross necropsy on animals as indicated by the nature of toxic effects, with particular reference to changes related to the respiratory tract. All gross pathological changes were recorded and evaluated.

7.17. Statistical Evaluation of Data

Necropsy findings: If specific findings occur from the respiratory tract of surviving rats they are evaluated statistically using the pair-wise Fisher test after the R x C chi-squared test. The Fisher test was only performed if differences occurred between groups in the R x C chi-squared test or if a frequency value of < 5 was calculated.

This procedure was performed in accordance with Gad and Weil (1982). For calculation of the unilateral p value a symmetrical distribution was assumed ($p_{\text{unilateral}} = (p_{\text{bilateral}})/2$).

Body weights: Means and single standard deviations of body weights are calculated. Mean body weights are also depicted graphically as a function of time (see result section). Since in acute studies individual group means may differ prior to commencement of the first exposure, the body weight gain was statistically evaluated for each group. For these evaluations a one-way ANOVA (vide infra) is used.

Particle size analysis: The statistical methods used in the evaluation of the particle-size distribution were described in Section 7.10.

Physiological data: Data of rectal temperature measurements are statistically evaluated using the ANOVA procedure (vide infra).

Calculation of the LC_{50} : If calculation of a median lethal concentration (LC_{50}) is possible, it is performed by computer according to the method of Rosiello et al. (1977) as modified by Pauluhn (1983). This method is based on the maximum-likelihood method of C.I. Bliss (1938). If only 2 pairs of values with greater than 0% lethality and less than 100% are available then the first linear approximation is based on these values and a χ^2 -homogeneity test is not performed. The interpolated concentration at 50% lethality in this case is designated the approximate LC_{50} . Additionally, the moving average interpolation according to Schaper et al. (1994) is used for calculation.

Randomization: A computerized list of random numbers served the purpose to assign animals at random to the treatment groups.

Analysis of variance (ANOVA): This parametric method checks for normal distribution of data by comparing the median and mean. The groups are compared at a confidence level of $(1-\alpha) = 95\%$ ($p = 0.05$). The test for the between-group homogeneity of the variance employed Box's test if more than 2 study groups were compared with each other. If the above F-test shows that the intra-group variability is greater than the inter-group variability, this is shown in the Appendix as "*no statistical difference between the groups*". If a difference is found then a pairwise post-hoc comparison is conducted (1- and 2-sided) using the Games and Howell modification of the Tukey-Kramer significance test. This program was originally obtained from BCTIC.

7.18. Programming and Validating Software

Software code for the following purposes was written in Microsoft Fortran 77: particle-size analysis, ANOVA, and Fisher test. The computer programs were carefully validated. The validation was conducted using published text book data sets (e.g. BCTIC, Gad and Weil, 1982). However, it should be emphasized that the formal GLP-requirements required for software validation were not fulfilled. Wherever possible, raw data and calculated/derived values are displayed graphically to provide a versatile opportunity for data comparison.

7.19. Presentation of raw data

Raw data entered into, processed and/or stored by a computer system can be saved and printed out in various formats. The precision (number of decimal places) of the figures printed out and reproduced in this report reflects the toxicologically relevant precision in all cases. Deviations between manually calculated and computer-determined figures can thus arise due to rounding. A "zero" number of decimal places does not necessarily represent the pertinent measurement precision of the detection system.

7.20. Archiving the Raw Data and the Report

The protocol, raw data, and the final report are archived in locations specified by Bayer AG, in accordance with GLP requirements.

8. RESULTS

8.1. Generation and characterization of atmosphere

Technical information concerning generation of test atmospheres is provided in Table 1.

Table 1: Generation and characterization of chamber atmosphere

	Group 1	Group 2	Group 3	Group 4	Group 5
Target Conc. (mg/m ³)	0	500	1000	3000	5000
Nominal Conc. (µl/m ³)	Control	1667	4167	10000	25000
Gravimetric Conc. (mg/m ³)	--	583	1400	2727	4937
Analyt. Conc. (mg/m ³)	--	407	900	1942	3508
Inlet Air Flow (l/min)	15	15	15	15	15
Exhaust Air Flow (l/min)	13	13	13	13	13
Pump Rate (µl/min)	--	25	62.5	150	375
Temperature (mean, °C)	23.9	20.8	21.4	20.9	21.4
Rel. Humidity (mean, %)	12.7	4.8	4.1	4.1	6.5
MMAD (µm) ^a	--	1.10	1.15	1.29	1.48
GSD	--	1.85	1.86	1.83	1.89
Aerosol Mass < 3 µm (%)	--	94.9	93.8	92.0	86.5
Mass recovered (mg/m ³)	--	582	1430	2824	5367

MMAD = Mass Median Aerodynamic Diameters

GSD = Geometric Standard Deviation.

-- = not applicable, a) Mean of two analyses

For specific information concerning calculations of aerosol MMAD, GSD, and mass dependent size fraction below 3 µm, see Appendix.

Characterization of the test atmospheres: Analytical and real-time aerosol monitoring of the test atmosphere from the breathing zone (3 analytical determination and 3 filter samples/exposure) indicated that the exposure conditions were temporally stable over the exposure period. The comparison of concentrations obtained by gravimetric analysis (filter and cascade impactor analyses) and that one employing the analytical method described in the Appendix demonstrate that the gravimetric determinations provided higher concentrations. Due to the simplicity of the filter method, the results of this method are given preference for the toxicological assessment of results throughout this study. Experimental evidence suggests, that the particle-size distribution is adequate for acute inhalation toxicity studies (SOT,

1992). The results of characterization of test atmospheres are conclusive and no evidence of interstage wall-losses (cascade impactor) or significant sampling errors could be observed.

Temperature values in the inhalation chamber were in the range than suggested by the testing guidelines. Humidity values were lower; this is undoubtedly related to the use of dry air for generation to prevent hydrolysis of the test substance after aerosolization. However, this deviation from the guideline had no negative impact on the study results.

8.2. Clinical observations

The results obtained during and after exposures of rats for 4 hours to the test substance are summarized in Table 2.

Table 2: Summary of acute inhalation toxicity

N Group /sex	Actual Concentration (mg/m ³)	Toxicological Result	Onset and Duration of Signs	Onset and Duration of Mortality	Rectal Temperature (°C)
1 / m	0	0 / 0 / 5	--	--	38.2
2 / m	583	0 / 5 / 5	0d - 6d	--	28.3**
3 / m	1400	2 / 5 / 5	0d - 11d	2d	27.9**
4 / m	2727	5 / 1 / 5	0d	0d - 1d	24.8
5 / m	4937	5 / - ^a / 5	--	0d	--
1 / f	0	0 / 0 / 5	--	--	38.6
2 / f	583	0 / 5 / 5	0d - 10d	--	28.4**
3 / f	1400	0 / 5 / 5	0d - 12d	--	27.9**
4 / f	2727	4 / 5 / 5	0d - 13d	2d	26.6**
5 / f	4937	5 / - ^a / 5	--	0d	--

-- = not applicable, **) p < 0.01 (Tukey-Kramer *post-hoc* test), od: day of exposure, a) all animals died during or shortly after the exposure period

Values given in the 'Toxicological results' column are:

1st = number of dead animals.

2nd = number of animals with signs after cessation of exposure.

3rd = number of animals exposure

Mortality and LC₅₀-Calculation

Males:

LC₅₀ = 1276 mg/m³ air

Confidence interval (95%): 929 - 1752 mg/m³ air

Slope: 1.96

Females:

LC₅₀ = 2392 mg/m³ air

Confidence interval (95%): 1742 - 3283 mg/m³ air

Slope: 2.09

Males and females combined:

LC₅₀ = 1822 mg/m³ air

Confidence interval (95%): 1477 - 2249 mg/m³ air

Slope: 3.22

Calculation method: Bliss-Probit-Analysis according to Rosiello et al. (1977), modified by Pauluhn (1983).

The different mortality figures obtained in males and females demonstrate a gender specific difference in susceptibility, i.e., males were apparently more sensitive. Mortality occurred within the second postexposure days. No emphasize was made to calculate a more exact LC₅₀-value since the present results allow classification of the test substance (SOT, 1992, Pauluhn *et al.*, 1996).

Clinical signs

Details concerning signs and observations are provided in the Appendix in the form of various incidence tables. The following list of signs is focusing on toxicologically significant signs only.

Group 1: No clinical signs were observed.

Group 2: Bradypnea, laboured breathing pattern, sneezing, bristled and ungroomed hair-coat, limp, motility reduced, gait changes, nostrils: reddened and with red encrustations, nasal discharge, cyanosis, emaciation.

Group 3 and 4: Bradypnea, dyspnea, labored breathing pattern, sneezing, stridor, cyanosis, emaciation, bristled and ungroomed hair-coat, limp, motility reduced, gait

changes, nostrils: reddened and with red encrustations, nasal discharge.

Group 5: All rats died during or shortly after the exposure period

Reflex measurements

A battery of reflex measurements was made on day 1. Summaries of the reflex data are included in the Appendix. Comparison between the groups exposed to the test substance with those of the control group revealed a decreased righting response in group 2 and above and decreased tonus in group 4.

Body weights

Results of the evaluation of the body weights are included in the Appendix. Comparisons between control animals with those in the groups exposed to the test substance revealed statistically significant effects on body weight gains in all exposure groups. The overall change of mean body weights is depicted in Fig. 4.

Figure 4: Body Weights (means \pm standard deviation)

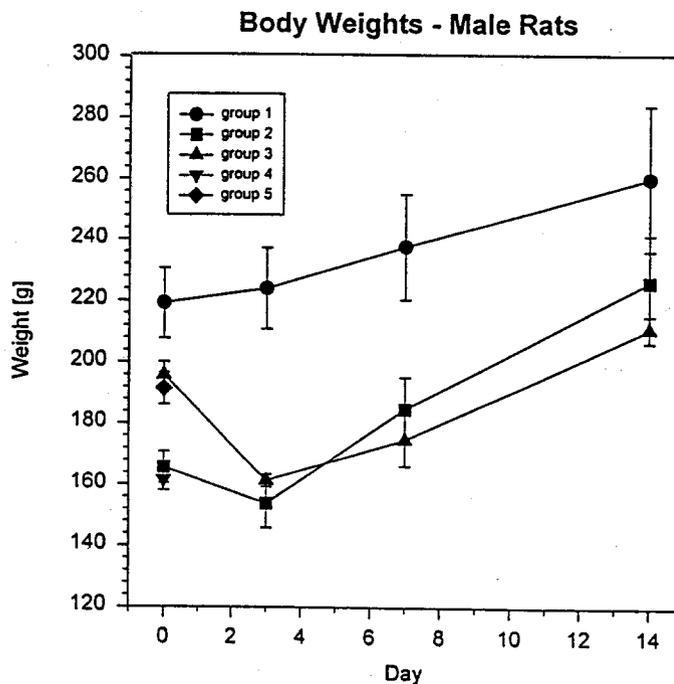
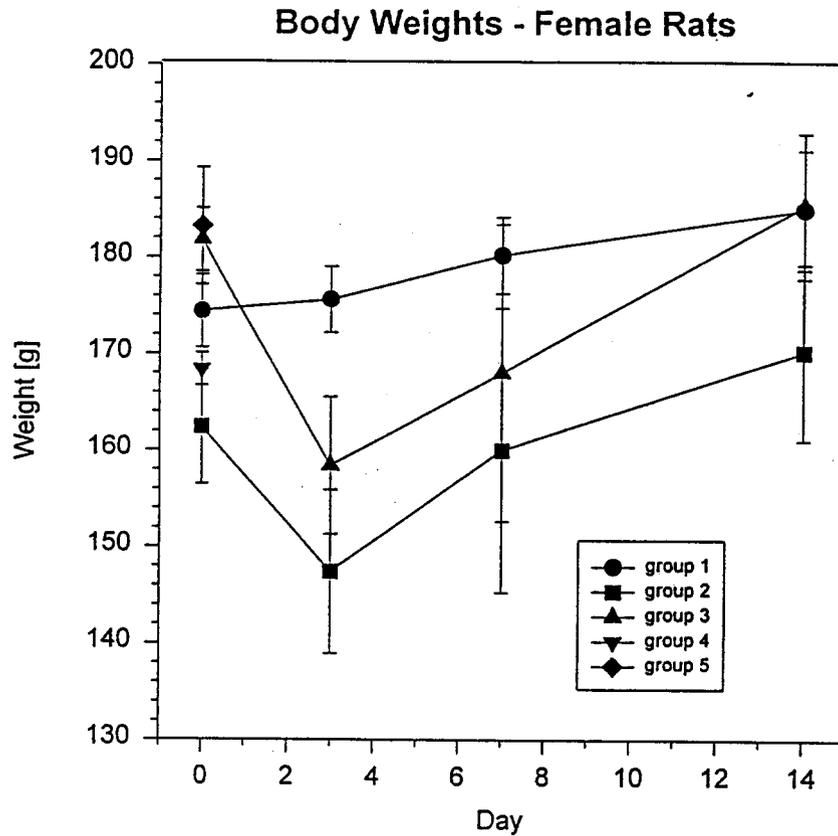
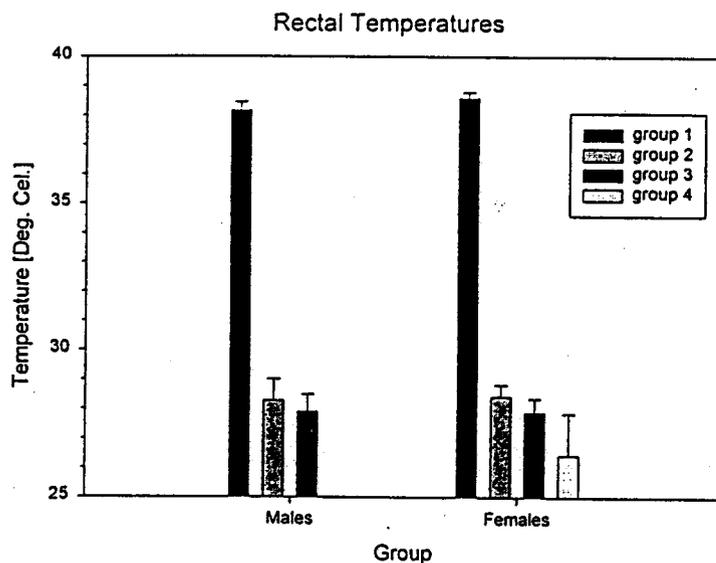


Figure 4: Body Weights (means \pm standard deviation) - continuation

Rectal temperature

Results of the evaluation of the rectal temperature are summarised in the Appendix. Mean values are shown in Table 2 and Fig. 5. Statistical comparisons between control animals with those in the exposure groups revealed statistically significant differences in all exposure groups, i.e., the rats exposed to the test substance experienced a concentration-dependent decrease in body temperature.

Figure 5: Body Temperatures (means \pm standard deviation)



Necropsy

Individual findings from the gross-pathological examinations - including the exact onset of mortality - are summarized in the Appendix. A qualitative description, only of findings of toxicological importance and for toxicological evaluation, is given below.

Animals sacrificed at the end of the observation period: In rats of group 2 a conclusive incidence of macroscopic findings could not be ascertained. Therefore, the discolorations of lungs as well as the enlarged lung-associated lymph nodes observed are not considered to be causally related to the exposure to the test substance. Such findings are often observed in control animals euthanized with a high dose of pentobarbital. From group 3 onwards the following findings are considered to be toxicologically significant: lung slightly collapsed and with gray-red, focal discolorations.

Animals that died intercurrently: From group 3 onwards the following findings are considered to be toxicologically significant: lung slightly collapsed, with red discolorations and edema, nose/muzzle area with red encrustations, pleural effusion, corneal opacity.

9. EVALUATION AND DISCUSSION

The exposure to a concentration of 583 mg/m³ air was tolerated without mortality whereas higher concentrations evoked mortalities. Signs were apparent in a concentration-dependent manner and persisted up the end of the 2-week postexposure period. The duration of signs was contingent upon respiratory changes. The major signs observed are as follows: bradypnea, dyspnea, labored breathing pattern, sneezing, stridor, cyanosis, emaciation, bristled and ungroomed hair-coat, limp, motility reduced, gait changes, nostrils/muzzle: reddened and with red encrustations, nasal discharge, decrease in body weights, hypothermia. Gross necropsy findings demonstrated lower respiratory tract damage ('bloated lung', edema, pleural effusions).

Experimental evidence suggests that the test substance is a potent respiratory tract irritant. Inhalation of respiratory irritants is known to induce reflex changes in the breathing pattern and cardiac output and are reported to be associated with the decline in the metabolic rate and body temperature of rodents (Jaeger and Gearhart, 1982; Mautz and Bufalino, 1989). The present observation in rats may reflect a more labile thermoregulatory physiology among rodents and may involve a complex set of physiological responses that may differ among mammalian species. Sensory irritation induces respiratory and concomitantly central distress in animals which appears to be the possible cause of hypothermia.

Thus, in summary, the aerosolized test substance proved to have a moderate acute inhalation toxicity to rats and experimental evidence suggests that mortality is causally related to lower respiratory tract irritation.

10. KEY TO ABBREVIATIONS

Konz.	Concentration
nomin.	Nominal
analyt.	Analytical
Expos.	Exposure
STAND, S, Std, s	Standard deviation
MW/MEANS	Means
F	F-test value (F-ratio)
DF	Degrees of freedom
PROB	Probability
SS	Total sum of squares
MS	Mean squares
TREATMENT	- between the groups
ERROR	- within the groups
TOTAL	- total

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12. APPENDIX

Atmosphere Characterization - Analytical Method

Group	Date of exposure (DD.MM.YY)	Sampling rate (l/min) / Total sampling volume (l)	Target Concentrations (mg/m ³ air)	Actual Concentrations (mg/m ³ air)	Mean Conc. (mg/m ³ air)
1	14.05.1998	n.a.	0	0 (air control)	n.a.
2	17.06.1998	1.0 / 10	500	405.3 327.3 489.0	407.2
3	10.06.1998	1.0 / 10	1000	629.0 998.1 1071.5	899.5
4	16.06.1998	1.0 / 10	3000	1996.5 1899.9 1929.0	1941.8
5	09.06.1998	1.0 / 10	5000	3417.6 4006.7 3099.4	3507.9

Atmosphere Characterization - Filter Analyses

Group	Date of exposure (DD.MM.YY)	Sampling rate (l/min) / Total sampling volume (l)	Target Concentrations (mg/m ³ air)	Actual Concentrations (mg/m ³ air)	Mean Conc. (mg/m ³ air)
1	14.05.1998	n.a.	0	0 (air control)	n.a.
2	17.06.1998	2 / 10	500	580 590 580	583
3	10.06.1998	2 / 10	1000	1520 1350 1330	1400
4	16.06.1998	2 / 10	3000	2730 2720 2730	2727
5	09.06.1998	2 / 10	5000	4860 4940 5010	4937

Particle-size Characterization of Test Atmosphere

Group	Date of exposure (DD.MM.YY)	Target Conc. (mg/m ³ air)	MMAD [μm]	GSD	Mass ≤ 3 μm [%]	Conc. (mg/m ³ air) Impactor
2	17.06.1998	500	1.09	1.85	95	582
			1.11	1.84	95	582
3	10.06.1998	1000	1.15	1.87	94	1435
			1.15	1.85	94	1426
4	16.06.1998	3000	1.28	1.83	92	2834
			1.29	1.83	92	2815
5	09.06.1998	5000	1.48	1.88	87	5349
			1.48	1.90	86	5386

Representative examples of evaluation of particle-size distributions for each group is provided on the next pages.

Characterization of Particle Size Distribution

ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Aerosol
Compound: Desmophen PAC XP-7076 (I)

Date of exposure: 17.06.98 Study-no.: T5067020
Nominal concentration: 500.0 mg/m³ air

N	Impactor stage (um - um)	Cut-Off diameter (um)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)
1	.06 - .12	.060	.000	.00	.00
2	.12 - .25	.120	.031	.16	.00
3	.25 - .49	.250	1.503	7.74	.16
4	.49 - .90	.490	6.672	34.37	7.90
5	.90 - 1.85	.900	7.969	41.05	42.28
6	1.85 - 3.69	1.850	2.615	13.47	83.33
7	3.69 - 7.42	3.690	.609	3.14	96.80
8	7.42 - 14.80	7.420	.012	.06	99.94
9	14.80 - 30.00	14.800	.000	.00	100.00

Mass Median Aerodynamic Diameter (MMAD): 1.09 um
Geometric standard deviation (GSD): 1.85
Number Median Aerodynamic Diameter (NMAD): .35 um
Surface Median Aerodynamic Diameter (SMAD): .75 um

System: BERNER-IMPACTOR I
Air flow: 5.56 liter/min.
Sampling time: 360.00 seconds
Concentration (computed): 581.86 mg/m³ air

Respirability (percent < 1.0 um):

1. Mass related: 44.5 % (measured)
2. Number related: 95.7 % (extrapolated)

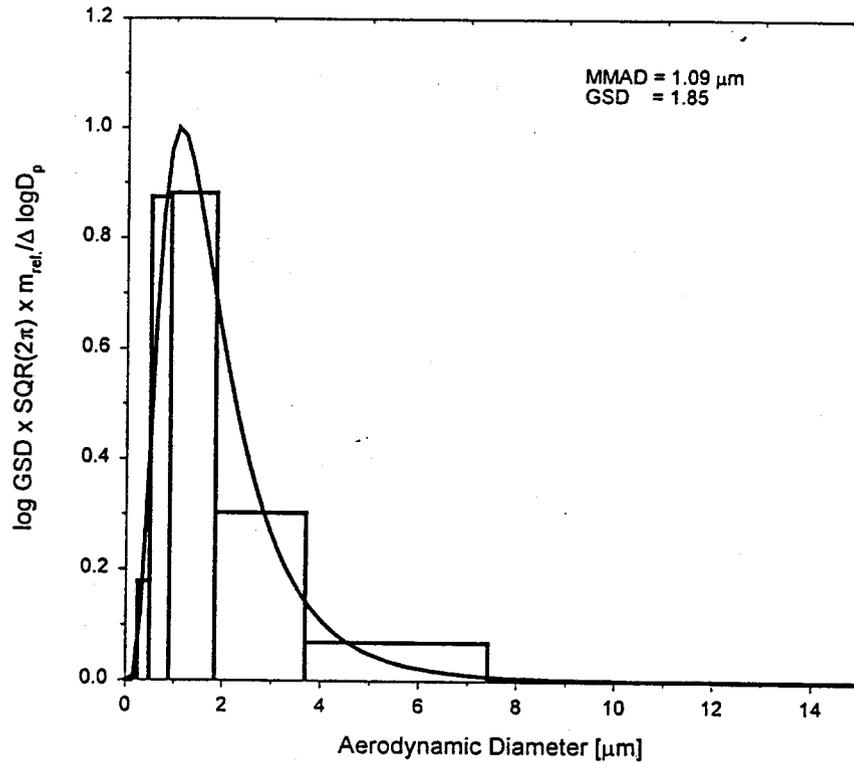
Respirability (percent < 3.0 um):

1. Mass related: 94.9 % (measured)
2. Number related: 99.1 % (extrapolated)

Respirability (percent < 5.0 um):

1. Mass related: 99.1 % (measured)
2. Number related: 99.1 % (extrapolated)
ECD-definition: right cut-size (Dp+1)

Particle-size Distribution
Target Concentration: 500 mg/m³ air



ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Aerosol
Compound: Desmophen PAC XP-7076 (I)

Date of exposure: 10.06.98 Study-no.: T5067020
Nominal concentration: 1000.0 mg/m3 air

N	Impactor stage (um - um)	Cut-Off diameter (um)	Mass/stage (mg)	Rel. mass (%)	Cumul. mass (%)
1	.06 - .12	.060	.000	.00	.00
2	.12 - .25	.120	.045	.19	.00
3	.25 - .49	.250	1.697	7.09	.19
4	.49 - .90	.490	7.544	31.51	7.28
5	.90 - 1.85	.900	9.983	41.70	38.79
6	1.85 - 3.69	1.850	3.733	15.59	80.50
7	3.69 - 7.42	3.690	.925	3.86	96.09
8	7.42 - 14.80	7.420	.011	.05	99.95
9	14.80 - 30.00	14.800	.000	.00	100.00

Mass Median Aerodynamic Diameter (MMAD): 1.15 um
Geometric standard deviation (GSD): 1.87
Number Median Aerodynamic Diameter (NMAD): .35 um
Surface Median Aerodynamic Diameter (SMAD): .78 um

System: BERNER-IMPACTOR I
Air flow: 5.56 liter/min.
Sampling time: 180.00 seconds
Concentration (computed): 1435.13 mg/m3 air

Respirability (percent < 1.0 um):

1. Mass related: 41.5 % (measured)
2. Number related: 95.1 % (extrapolated)

Respirability (percent < 3.0 um):

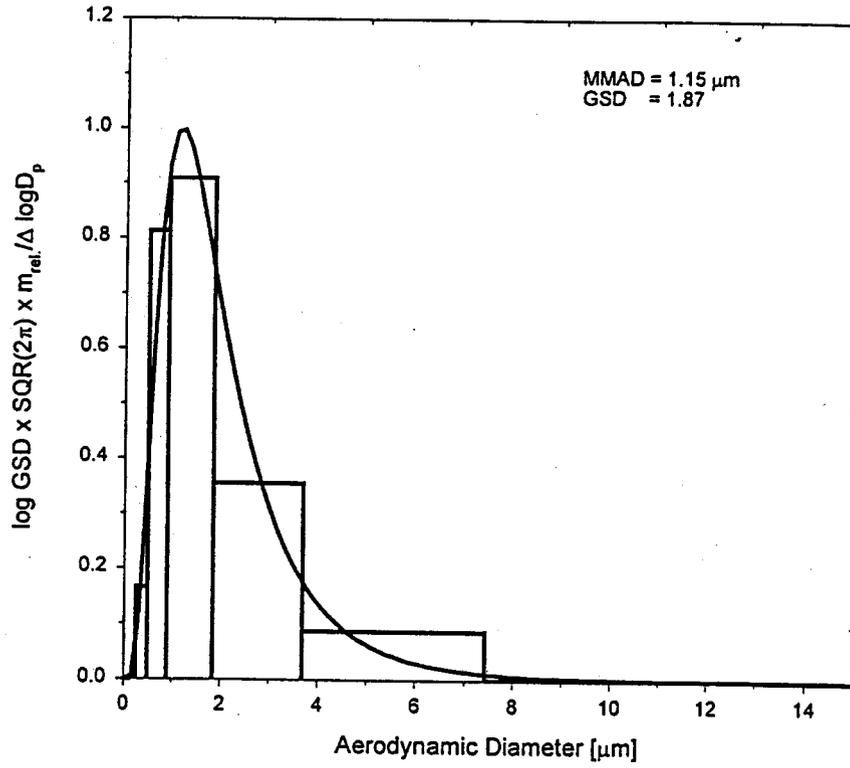
1. Mass related: 93.7 % (measured)
2. Number related: 99.1 % (extrapolated)

Respirability (percent < 5.0 um):

1. Mass related: 99.1 % (measured)
2. Number related: 99.1 % (extrapolated)

ECD-definition: right cut-size (Dp+1)

Particle-size Distribution
Target Concentration: 1000 mg/m³ air



ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Aerosol
 Compound: Desmophen PAC XP-7076 (I)

Date of exposure: 16.06.98 Study-no.: T5067020
 Nominal concentration: 3000.0 mg/m³ air

N	Impactor stage (um - um)	Cut-Off diameter (um)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)
1	.06 - .12	.060	.000	.00	.00
2	.12 - .25	.120	.056	.18	.00
3	.25 - .49	.250	1.441	4.57	.18
4	.49 - .90	.490	8.316	26.39	4.75
5	.90 - 1.85	.900	13.769	43.70	31.14
6	1.85 - 3.69	1.850	6.476	20.55	74.84
7	3.69 - 7.42	3.690	1.435	4.55	95.39
8	7.42 - 14.80	7.420	.016	.05	99.95
9	14.80 - 30.00	14.800	.000	.00	100.00

Mass Median Aerodynamic Diameter (MMAD): 1.28 um
 Geometric standard deviation (GSD): 1.83
 Number Median Aerodynamic Diameter (NMAD): .43 um
 Surface Median Aerodynamic Diameter (SMAD): .89 um

System: BERNER-IMPACTOR I
 Air flow: 5.56 liter/min.
 Sampling time: 120.00 seconds
 Concentration (computed): 2833.54 mg/m³ air

Respirability (percent < 1.0 um):

1. Mass related: 34.3 % (measured)
 2. Number related: 91.9 % (extrapolated)

Respirability (percent < 3.0 um):

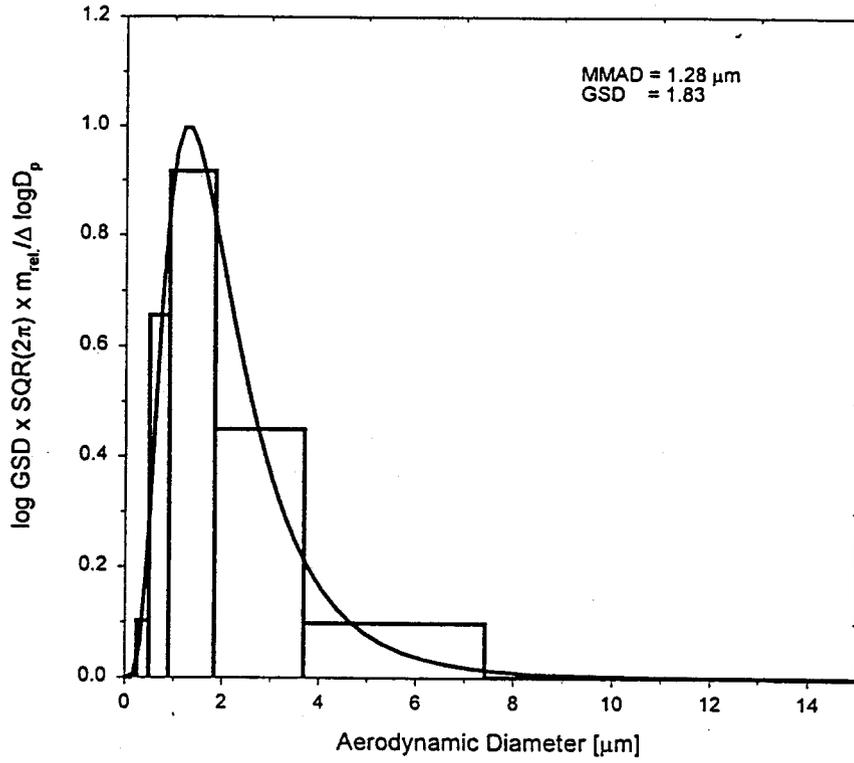
1. Mass related: 92.1 % (measured)
 2. Number related: 99.1 % (extrapolated)

Respirability (percent < 5.0 um):

1. Mass related: 98.9 % (measured)
 2. Number related: 99.1 % (extrapolated)

ECD-definition: right cut-size (Dp+1)

Particle-size Distribution
Target Concentration: 3000 mg/m³ air



ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Aerosol
Compound: Desmophen PAC XP-7076 (I)

Date of exposure: 09.06.98 Study-no.: T5067020
Nominal concentration 5000.0 mg/m3 air

N	Impactor stage (um - um)	Cut-Off diameter (um)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)
1	.06 - .12	.060	.001	.00	.00
2	.12 - .25	.120	.060	.10	.00
3	.25 - .49	.250	2.135	3.59	.10
4	.49 - .90	.490	11.354	19.09	3.69
5	.90 - 1.85	.900	25.382	42.68	22.78
6	1.85 - 3.69	1.850	15.683	26.37	65.46
7	3.69 - 7.42	3.690	4.723	7.94	91.83
8	7.42 - 14.80	7.420	.038	.06	99.77
9	14.80 - 30.00	14.800	.100	.17	99.83

Mass Median Aerodynamic Diameter (MMAD): 1.48 um
Geometric standard deviation (GSD): 1.88
Number Median Aerodynamic Diameter (NMAD): .45 um
Surface Median Aerodynamic Diameter (SMAD): .99 um

System: BERNER-IMPACTOR I
Air flow: 5.56 liter/min.
Sampling time: 120.00 seconds
Concentration (computed): 5348.56 mg/m3 air

Respirability (percent < 1.0 um):

1. Mass related: 26.9 % (measured)
2. Number related: 89.7 % (extrapolated)

Respirability (percent < 3.0 um):

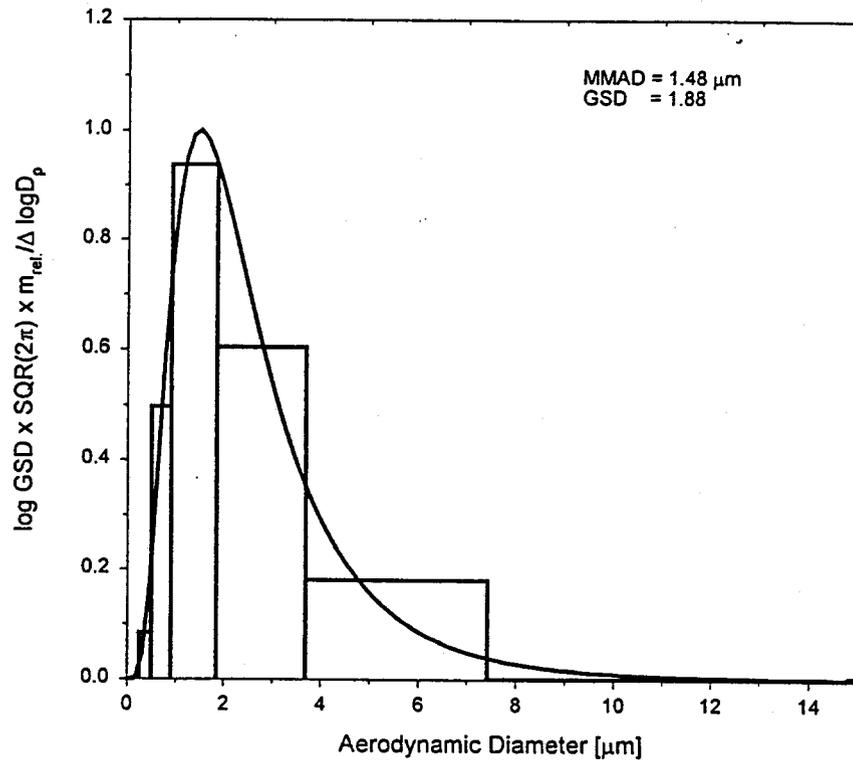
1. Mass related: 86.7 % (measured)
2. Number related: 99.1 % (extrapolated)

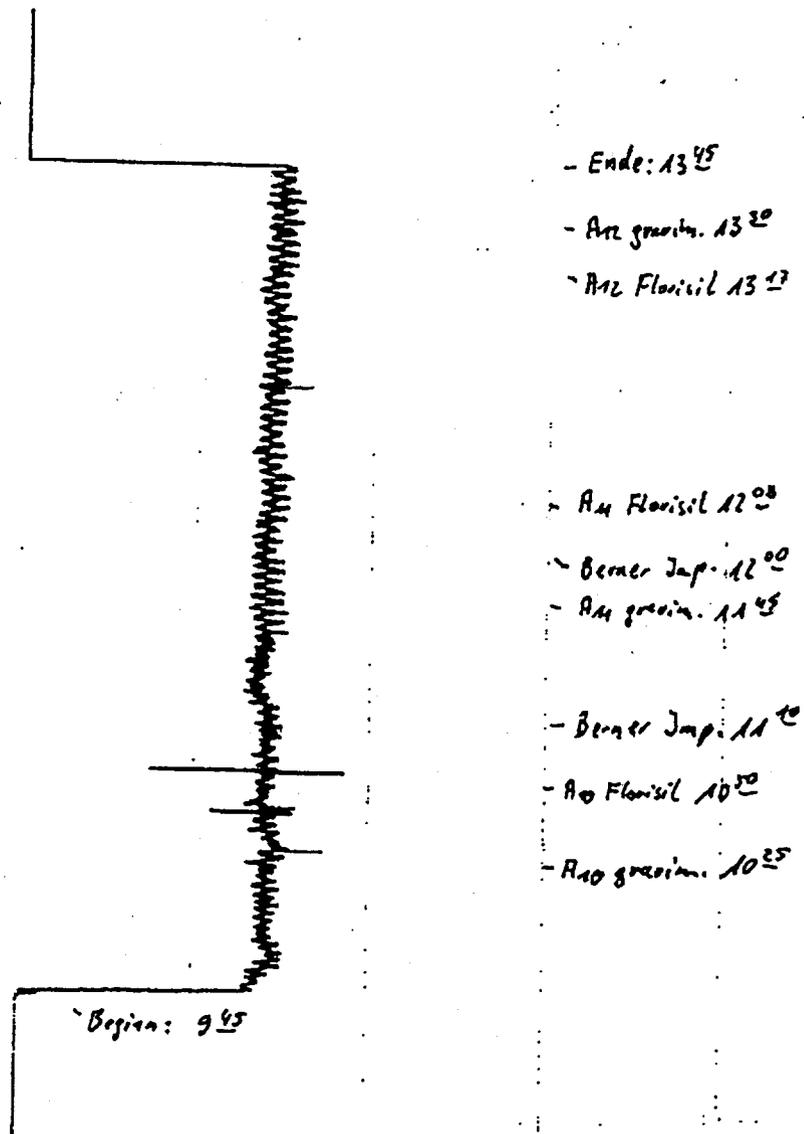
Respirability (percent < 5.0 um):

1. Mass related: 97.3 % (measured)
2. Number related: 99.1 % (extrapolated)

ECD-definition: right cut-size (Dp+1)

Particle-size Distribution
Target Concentration: 5000 mg/m³ air



Monitoring of Atmosphere (Example)Legend (copy of raw data):

Ai: i-th analytical sample, Florisil: analytical method, gravim: filter method, Berner-Imp.: cascade impactor sampling. Beginn: start, Ende: End, time: mm.hh

LC₅₀-Calculation

PROBIT - ANALYSIS

Desmophen PAC XP-7076

Study-no.: T5067020

Date: July 1998

Male Rats

Concentr. mg/m3 air	Probit obs.	Probit pred.	Mortality %	n/N
583.30	.01	3.67	.00	0/ 5
1400.00	4.75	4.75	40.00	2/ 5
2726.70	15.00	6.70	100.00	5/ 5
4936.70	15.00	7.73	100.00	5/ 5

LC50= 1275.76 mg/m3 air

Confidence interval(95%)= 928.98 - 1751.98 mg/m3 air

Slope= 1.96

MOVING AVERAGE INTERPOLATION

Desmophen PAC XP-7076

Male Rats

Number of animals in each dose level: 5
 Number of dose levels: 4
 Dose constant: 2.037894

No. of deaths	Calculated dose	Actual dose	Off by
0	583.300	583.300	.000
2	1188.704	1400.000	-211.296
5	2422.452	2726.699	-304.247
5	4936.702	4936.702	.000

LC50= 1276.41 mg/m3 air

Confidence interval(95%)= 900.58 - 1809.09 mg/m3 air

Print date: 05.08.1998

PROBIT - ANALYSIS

Desmophen PAC XP-7076

Study-no.: T5067020

Date: July 1998

Female Rats

Concentr. mg/m3 air	Probit obs.	Probit pred.	Mortality %	n/N
583.30	.01	2.55	.00	0/ 5
1400.00	.01	2.81	.00	0/ 5
2726.70	5.84	5.84	80.00	4/ 5
4936.70	15.00	6.52	100.00	5/ 5

LC50= 2391.65 mg/m3 air

Confidence interval(95%)= 1742.24 - 3283.13 mg/m3 air

Slope= 2.09

MOVING AVERAGE INTERPOLATION

Desmophen PAC XP-7076

Female Rats

Number of animals in each dose level: 5
 Number of dose levels: 4
 Dose constant: 2.037894

No. of deaths	Calculated dose	Actual dose	Off by
0	583.300	583.300	.000
0	1188.704	1400.000	-211.296
4	2422.452	2726.699	-304.247
5	4936.702	4936.702	.000

LC50= 1956.59 mg/m3 air

Confidence interval(95%)= 1471.73 - 2601.20 mg/m3 air

Print date: 05.08.1998

PROBIT - ANALYSIS

Desmophen PAC XP-7076

Study-no.: T5067020

Date: July 1998

Male and female Rats Combined

Concentr. mg/m3 air	Probit obs.	Probit pred.	Mortality %	n/N
583.30	.01	1.11	.00	0/10
1400.00	4.16	4.16	20.00	2/10
2726.70	6.28	6.28	90.00	9/10
4936.70	15.00	8.46	100.00	10/10

LC50= 1822.36 mg/m3 air
 Confidence interval(95%)= 1476.96 - 2248.53 mg/m3 air
 Slope= 3.22

MOVING AVERAGE INTERPOLATION

Desmophen PAC XP-7076

Male and female Rats Combined

Number of animals in each dose level: 10
 Number of dose levels: 4
 Dose constant: 2.037894

No. of deaths	Calculated dose	Actual dose	Off by
0	583.300	583.300	.000
2	1188.704	1400.000	-211.296
9	2422.452	2726.699	-304.247
10	4936.702	4936.702	.000

LC50= 1580.32 mg/m3 air
 Confidence interval(95%)= 1246.48 - 2003.58 mg/m3 air

Print date: 05.08.1998

ReflexesMeasurements on day:1 / MALES

Type of Reflex	Group 1	Group 2	Group 3	Group 4	Group 5
Number of animals investigated	5	5	5	0	0
Visual placing response	0	0	0	-	-
Grip strength (vertical)	0	0	0	-	-
Grip strength (horizontal)	0	0	0	-	-
Tonus	0	0	0	-	-
Cornea reflex	0	0	0	-	-
Light reflex	0	0	0	-	-
Pinna reflex	0	0	0	-	-
Startle reflex / sound	0	0	0	-	-
Startle reflex / touch	0	0	0	-	-
Tail-pinch response	0	0	0	-	-
Righting response (open field)	0	3 ^a	3 ^a	-	-
Righting response (drop method)	0	2 ^b	2 ^b	-	-

#: number of rats showing abnormal reflexes

group 2+ 3: ^a = impaired ^b = slightly uncoordinated

Measurements on day:1 / FEMALES

Type of Reflex	Group 1	Group 2	Group 3	Group 4	Group 5
Number of animals investigated	5	5	5	5	0
Visual placing response	0	0	0	0	-
Grip strength (vertical)	0	0	0	0	-
Grip strength (horizontal)	0	0	0	0	-
Tonus	0	0	0	3 ^a	-
Cornea reflex	0	0	0	0	-
Light reflex	0	0	0	0	-
Pinna reflex	0	0	0	0	-
Startle reflex / sound	0	0	0	0	-
Startle reflex / touch	0	0	0	0	-
Tail-pinch response	0	0	0	0	-
Righting response (open field)	0	0	0	2 ^b	-
Righting response (drop method)	0	0	0	2 ^c	-

#: number of rats showing abnormal reflexes

group 4 : ^a = reduced ^b = impaired ^c = slightly uncoordinated

Rectal Temperatures

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Rectal Temperature (centigrade) / MALES

Group-no.: 1 (1-5)
 38.300 38.000 38.000 38.600 37.900
 MEDIAN= 38.000 MEAN= 38.160 STD = .288

Group-no.: 2 (41-45)
 29.100 27.100 28.400 28.500 28.400
 MEDIAN= 28.400 MEAN= 28.300 STD = .731

Group-no.: 3 (21-25)
 28.700 27.100 27.800 27.800 28.200
 MEDIAN= 27.800 MEAN= 27.920 STD = .589

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
1.3904	2 & 324.	.2492

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	337.0	2	168.52	523.890	.000
ERROR	3.860	12	.32167		
TOTAL	340.9	14			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-39.66	5	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	39.66	5	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-49.38	6	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	49.38	6	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-1.28	8	.6526	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	1.28	8	.6526	NOT SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Rectal Temperature (centigrade) / FEMALES

Group-no.:	1 (6-10)				
	38.500	38.600	38.800	38.300	38.700
MEDIAN=	38.600	MEAN=	38.580	STD =	.192
Group-no.:	2 (46-50)				
	28.900	28.500	28.700	28.200	27.900
MEDIAN=	28.500	MEAN=	28.440	STD =	.397
Group-no.:	3 (26-30)				
	28.500	27.300	27.900	28.200	27.600
MEDIAN=	27.900	MEAN=	27.900	STD =	.474
Group-no.:	4 (36-40)				
	28.000	25.200	26.100	27.300	26.600
MEDIAN=	26.600	MEAN=	26.640	STD =	1.078

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
3.4042	3 & 461.	.0174

HETEROGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	455.7	3	151.90	383.833	.000
ERROR	6.332	16	.39575		
TOTAL	462.0	19			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-72.61	6	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	72.61	6	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-65.98	5	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	65.98	5	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 4	-34.47	4	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 4	34.47	4	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-2.76	8	.2812	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	2.76	8	.2812	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 4	-4.95	5	.0603	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 4	4.95	5	.0603	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
3 AND 4	-3.38	5	.1964	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
3 AND 4	3.38	5	.1964	NOT SIGNIFICANT

Body Weights

Analysis of Body Weights [all data in g]

Group 1: Control - MALES

	Postexposure Day			
	0	3	7	14
1	230.	238.	259.	291.
2	202.	206.	217.	236.
3	215.	218.	228.	246.
4	229.	236.	252.	280.
5	220.	222.	233.	249.
MEAN	219.2	224.0	237.8	260.4
STD	11.5	13.3	17.3	23.7

Group 2: 500 mg/m³ - MALES

	Postexposure Day			
	0	3	7	14
41	170.	166.	200.	249.
42	160.	146.	173.	209.
43	163.	148.	177.	221.
44	172.	157.	188.	219.
45	163.	152.	186.	234.
MEAN	165.6	153.8	184.8	226.4
STD	5.1	8.0	10.5	15.5

Group 3: 1000 mg/m³ - MALES

	Postexposure Day			
	0	3	7	14
21	203.	162.	166.	213.
22	191.			
23	195.	163.	183.	206.
24	195.	159.	175.	214.
25	195.			
MEAN	195.8	161.3	174.7	211.0
STD	4.4	2.1	8.5	4.4

Group 4: 3000 mg/m³ - MALES

	Postexposure Day			
	0	3	7	14
31	160.			
32	160.			
33	160.			
34	168.			
35	160.			
MEAN	161.6			
STD	3.6			

Group 5: 5000 mg/m³ - MALES

	Postexposure Day			
	0	3	7	14
11	186.			
12	189.			
13	198.			
14	196.			
15	188.			
MEAN	191.4			
STD	5.3			

Analysis of Body Weights [all data in g]

Group 1: Control - FEMALES

	Postexposure Day			
	0	3	7	14
6	180.	177.	183.	191.
7	175.	179.	185.	192.
8	175.	177.	180.	183.
9	170.	170.	175.	178.
10	172.	175.	178.	181.
MEAN	174.4	175.6	180.2	185.0
STD	3.8	3.4	4.0	6.2

Group 2: 500 mg/m³ - FEMALES

	Postexposure Day			
	0	3	7	14
46	170.	160.	185.	186.
47	161.	144.	153.	169.
48	167.	152.	160.	168.
49	158.	140.	155.	165.
50	156.	141.	147.	163.
MEAN	162.4	147.4	160.0	170.2
STD	5.9	8.5	14.7	9.1

Group 3: 1000 mg/m³ - FEMALES

	Postexposure Day			
	0	3	7	14
26	183.	151.	162.	182.
27	184.	165.	184.	196.
28	177.	154.	167.	182.
29	185.	167.	181.	190.
30	180.	155.	146.	177.
MEAN	181.8	158.4	168.0	185.4
STD	3.3	7.1	15.4	7.5

Group 4: 3000 mg/m³ - FEMALES

	Postexposure Day			
	0	3	7	14
36	167.			
37	167.			
38	171.			
39	168.	138.	136.	167.
40	169.			
MEAN	168.4			
STD	1.7			

Group 5: 5000 mg/m³ - FEMALES

	Postexposure Day			
	0	3	7	14
16	185.			
17	178.			
18	180.			
19	193.			
20	180.			
MEAN	183.2			
STD	6.1			

Analysis of Body Weight Gains [all data in g]

Group 1: Control - MALES

	Postexposure Day		
	3	7	14
1	8.00	21.00	32.00
2	4.00	11.00	19.00
3	3.00	10.00	18.00
4	7.00	16.00	28.00
5	2.00	11.00	16.00
MEAN	4.8	13.8	22.6
STD	2.6	4.7	7.0

Group 2: 500 mg/m³ - MALES

	Postexposure Day		
	3	7	14
41	-4.00	34.00	49.00
42	-14.00	27.00	36.00
43	-15.00	29.00	44.00
44	-15.00	31.00	31.00
45	-11.00	34.00	48.00
MEAN	-11.8	31.0	41.6
STD	4.7	3.1	7.8

Group 3: 1000 mg/m³ - MALES

	Postexposure Day		
	3	7	14
21	-41.00	4.00	47.00
22			
23	-32.00	20.00	23.00
24	-36.00	16.00	39.00
25			
MEAN	-36.3	13.3	36.3
STD	4.5	8.3	12.2

Analysis of Body Weight Gains [all data in g]

Group 1: Control - FEMALES

	Postexposure Day		
	3	7	14
6	-3.00	6.00	8.00
7	4.00	6.00	7.00
8	2.00	3.00	3.00
9	.00	5.00	3.00
10	3.00	3.00	3.00
MEAN	1.2	4.6	4.8
STD	2.8	1.5	2.5

Group 2: 500 mg/m³ - FEMALES

	Postexposure Day		
	3	7	14
46	-10.00	25.00	1.00
47	-17.00	9.00	16.00
48	-15.00	8.00	8.00
49	-18.00	15.00	10.00
50	-15.00	6.00	16.00
MEAN	-15.0	12.6	10.2
STD	3.1	7.7	6.3

Group 3: 1000 mg/m³ - FEMALES

	Postexposure Day		
	3	7	14
26	-32.00	11.00	20.00
27	-19.00	19.00	12.00
28	-23.00	13.00	15.00
29	-18.00	14.00	9.00
30	-25.00	-9.00	31.00
MEAN	-23.4	9.6	17.4
STD	5.6	10.8	8.6

Group 4: 3000 mg/m³ - FEMALES

	Postexposure Day		
	3	7	14
36			
37			
38			
39	-30.00	-2.00	31.00
40			
MEAN			
STD			

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 3 / MALES

```

Group-no.: 1
  8.000      4.000      3.000      7.000      2.000
MEDIAN=     4.000  MEAN=     4.800  STD =     2.588

Group-no.: 2
 -4.000     -14.000    -15.000    -15.000    -11.000
MEDIAN=    -14.000  MEAN=    -11.800  STD =     4.658

Group-no.: 3
 -41.000    -32.000    -36.000
MEDIAN=    -36.000  MEAN=    -36.333  STD =     4.509

```

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
.6152	2 & 178.	.5467

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	3177.	2	1588.3	102.960	.000
ERROR	154.3	10	15.427		
TOTAL	3331.	12			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
 TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
 (WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-9.85	6	.0009	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	9.85	6	.0009	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-20.42	3	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	20.42	3	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-10.41	4	.0029	SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	10.41	4	.0029	SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 7 / MALES

```

Group-no.: 1
  21.000    11.000    10.000    16.000    11.000
MEDIAN=    11.000  MEAN=    13.800  STD =    4.658

Group-no.: 2
  34.000    27.000    29.000    31.000    34.000
MEDIAN=    31.000  MEAN=    31.000  STD =    3.082

Group-no.: 3
   4.000    20.000    16.000
MEDIAN=    16.000  MEAN=    13.333  STD =    8.327

```

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
1.2760	2 & 178.	.2810

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	929.3	2	464.65	17.636	.001
ERROR	263.5	10	26.347		
TOTAL	1193.	12			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	9.74	7	.0005	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	9.74	7	.0005	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-.13	3	.9957	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	.13	3	.9957	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-5.00	2	.1276	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	5.00	2	.1276	NOT SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 14 / MALES

```

Group-no.: 1
  32.000    19.000    18.000    28.000    16.000
MEDIAN=    19.000  MEAN=    22.600  STD =    6.986

Group-no.: 2
  49.000    36.000    44.000    31.000    48.000
MEDIAN=    44.000  MEAN=    41.600  STD =    7.829

Group-no.: 3
  47.000    23.000    39.000
MEDIAN=    39.000  MEAN=    36.333  STD =    12.220

```

BOXS TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
.4334	2 & 178.	.6549

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	943.9	2	471.93	6.385	.016
ERROR	739.1	10	73.907		
TOTAL	1683.	12			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	5.73	8	.0092	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	5.73	8	.0092	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	2.52	3	.3153	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	2.52	3	.3153	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-.95	3	.7962	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	.95	3	.7962	NOT SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 3 / FEMALES

```

Group-no.: 1
  -3.000      4.000      2.000      .000      3.000
MEDIAN=      2.000  MEAN=      1.200  STD =      2.775

Group-no.: 2
  -10.000     -17.000     -15.000     -18.000     -15.000
MEDIAN=     -15.000  MEAN=     -15.000  STD =      3.082

Group-no.: 3
  -32.000     -19.000     -23.000     -18.000     -25.000
MEDIAN=     -23.000  MEAN=     -23.400  STD =      5.595

```

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
1.1043	2 & 324.	.3331

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	1564.	2	781.80	48.359	.000
ERROR	194.0	12	16.167		
TOTAL	1758.	14			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-12.35	8	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	12.35	8	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-12.46	6	.0001	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	12.46	6	.0001	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-4.16	6	.0586	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	4.16	6	.0586	NOT SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 7 / FEMALES

```

Group-no.: 1
  6.000      6.000      3.000      5.000      3.000
MEDIAN=     5.000  MEAN=     4.600  STD =     1.517

Group-no.: 2
 25.000      9.000      8.000      15.000     6.000
MEDIAN=     9.000  MEAN=    12.600  STD =     7.701

Group-no.: 3
 11.000     19.000     13.000     14.000    -9.000
MEDIAN=    13.000  MEAN=     9.600  STD =    10.807

```

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
4.7546	2 & 324.	.0093

HETEROGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	163.3	2	81.667	1.373	.290
ERROR	713.6	12	59.467		
TOTAL	876.9	14			

NO OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL
 NO STATISTICAL DIFFERENCE BETWEEN THE GROUPS

ONE-WAY ANALYSIS OF VARIANCE PROGRAM : ANOVA

Analysis of Day: 14 / FEMALES

```

Group-no.: 1
      8.000      7.000      3.000      3.000      3.000
MEDIAN= 3.000 MEAN= 4.800 STD = 2.490

Group-no.: 2
      1.000      16.000      8.000      10.000      16.000
MEDIAN= 10.000 MEAN= 10.200 STD = 6.261

Group-no.: 3
      20.000      12.000      15.000      9.000      31.000
MEDIAN= 15.000 MEAN= 17.400 STD = 8.620

```

BOXs TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.s	PROBABILITY
2.2833	2 & 324.	.1014

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	399.6	2	199.80	5.008	.026
ERROR	478.8	12	39.900		
TOTAL	878.4	14			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION

5. % ONE-TAILED TEST				

1 AND 2	2.53	5	.2637	NOT SIGNIFICANT
5. % TWO-TAILED TEST				

1 AND 2	2.53	5	.2637	NOT SIGNIFICANT
5. % ONE-TAILED TEST				

1 AND 3	4.44	5	.0565	NOT SIGNIFICANT
5. % TWO-TAILED TEST				

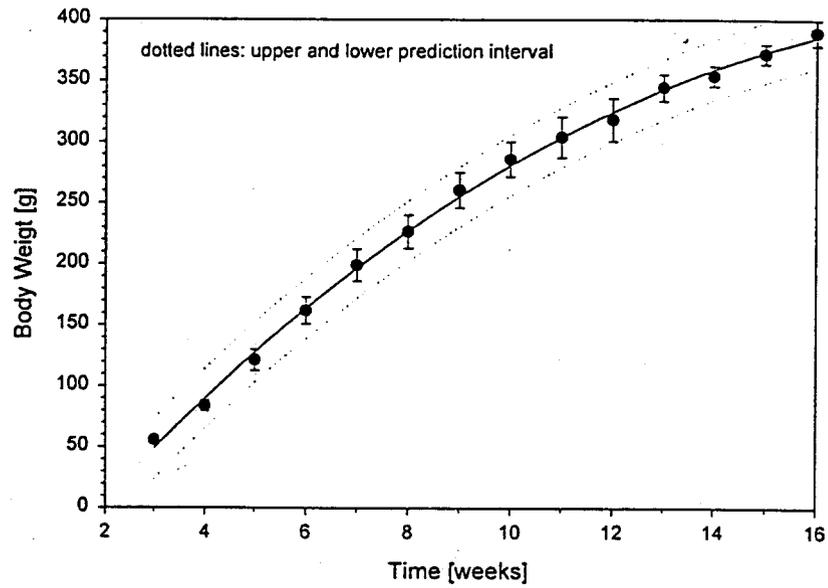
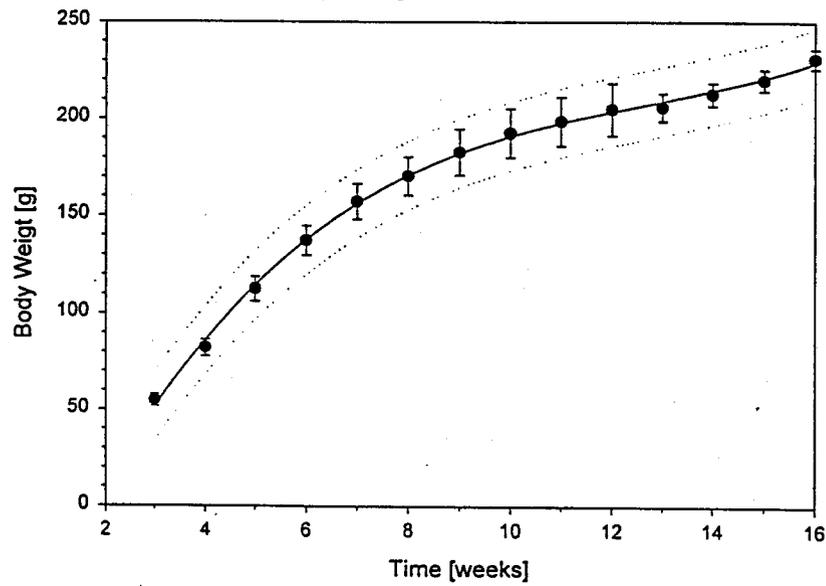
1 AND 3	4.44	5	.0565	NOT SIGNIFICANT
5. % ONE-TAILED TEST				

2 AND 3	2.14	7	.3425	NOT SIGNIFICANT
5. % TWO-TAILED TEST				

2 AND 3	2.14	7	.3425	NOT SIGNIFICANT

Body Weights / Age-Body Weight Reference Data

(data from Harlan-Winkelmann as of June 1998; n = 40 per sex)

Body Weights - Males Rats**Body Weights - Females Rats**

Clinical Observations²

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 500 mg/m3 air / Sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	5	5	2	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	5	5	3	0	0	0	0	0	0	0	0	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait changes (lurching)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	4	1	1	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Emaciation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ungroomed hair-coat	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	5	5	5	5	4	1	1	0	0	0	0	0	0	0	0
Nasal discharge (serous)	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

² Truncated characters: see next set of tables

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 1000 mg/m3 air / Sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	5	5	3	3	3	2	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	5	5	3	3	3	3	3	3	3	3	1	1	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0
Gait changes (lurching)	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	5	4	3	3	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	5	3	3	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0
Emaciation	0	0	0	3	3	2	2	1	1	1	0	0	0	0	0
Ungroomed hair-coat	0	5	2	2	2	1	0	0	0	0	0	0	0	0	0
Bristled hair-coat	5	5	3	3	3	3	3	2	2	1	1	0	0	0	0
Nasal discharge (serous)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	3	3	3	3	3	3	3	3	3	3	3	3	0

Legend: n = number of animals with signs

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 3000 mg/m3 air / Sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait changes (lurching)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Emaciation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ungroomed hair-coat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nasal discharge (serous)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: n = number of animals with signs

Test compound: Desmopren PAC XP-7076
 Study-no: T5067020

Concentration: 5000 mg/m3 air / Sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait changes (lurching)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Emaciation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ungroomed hair-coat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nasal discharge (serous)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: n = number of animals with signs

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 500 mg/m3 air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	5	4	3	2	2	1	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	5	4	3	1	1	1	1	1	1	1	1	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait changes (lurching)	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	0	1	1	2	2	1	1	1	1	0	0	0	0	0	0
Motility reduced	5	4	2	0	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	1	1	1	1	1	1	1	0	0	0	0	0
Emaciation	0	0	0	2	2	1	1	1	1	0	0	0	0	0	0
Ungroomed hair-coat	0	5	5	1	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	5	5	5	4	4	3	3	2	1	0	0	0	0	0	0
Nasal discharge (serous)	0	0	1	4	4	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	5	2	1	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 1000 mg/m3 air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	5	5	5	5	4	4	2	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	5	5	5	5	5	5	5	5	3	2	0	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0
Gait changes (lurching)	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	5	0	3	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	4	5	0	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
Emaciation	0	0	0	5	5	1	1	1	1	1	0	0	0	0	0
Ungroomed hair-coat	0	5	4	4	2	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	5	5	5	5	5	5	4	3	3	3	3	2	0	0	0
Nasal discharge (serous)	1	0	0	0	0	2	2	1	0	0	0	0	0	0	0
Nostrils: reddened	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	2	3	1	1	1	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	1	2	2	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Concentration: 3000 mg/m3 air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	5	5	1	1	1	1	1	1	1	1	1	0	0	0	0
Dyspnea	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	5	5	0	1	1	1	1	1	1	1	1	1	1	0	0
Stridor (rales)	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0
Gait changes (lurching)	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	5	5	1	1	1	1	1	1	1	1	1	1	0	0	0
Motility reduced	5	5	1	1	1	1	1	1	1	1	1	0	0	0	0
Cyanosis	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0
Emaciation	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0
Ungroomed hair-coat	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	5	5	1	1	1	1	1	1	1	1	1	1	1	1	0
Nasal discharge (serous)	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	4	4	1	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	1	1	1	1	1	1	1	1	1	1	1	1	0

Legend: n = number of animals with signs

Test compound: Desmopren PAC XP-7076
 Study-no: T5067020

Concentration: 5000 mg/m3 air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labored breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stridor (rales)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait changes (lurching)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Limp	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cyanosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Emaciation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ungroomed hair-coat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bristled hair-coat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nasal discharge (serous)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: reddened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nostrils/muzzle: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sneezing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: n = number of animals with signs

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Bradypnea

Day	Sex	Target Concentration - mg/m3 air																													
		500		1000		3000		5000		1000		3000		5000																	
		l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N										
0		5	0	0	5	0	5	0	1	1	0	0	0	0	5	0	0	5	1	4	0	5	0	3	2	5	0	0	0	0	
1		4	1	0	5	3	2	0	5	0	0	0	0	0	2	2	0	5	4	1	0	5	0	5	0	5	0	0	0	0	
2		2	0	0	5	2	1	0	3	0	0	0	0	0	3	0	0	5	3	2	0	5	0	0	1	1	0	0	0	0	
3		0	0	0	5	2	1	0	3	0	0	0	0	0	2	0	0	5	3	2	0	5	0	1	0	1	0	0	0	0	
4		0	0	0	5	3	0	0	3	0	0	0	0	0	2	0	0	5	3	1	0	5	0	1	0	1	0	0	0	0	
5		0	0	0	5	2	0	0	3	0	0	0	0	0	1	0	0	5	3	1	0	5	0	1	0	1	0	0	0	0	
6		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	3	1	0	5	0	1	0	1	0	0	0	0	
7		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	2	0	0	5	0	1	0	1	0	0	0	0	
8		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	1	0	1	0	0	0	0	
9		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	1	0	0	1	0	0	0	0
10		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	1	0	0	1	0	0	0	0
11		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	1	0	0	1	0	0	0	0
12		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0	0	0
13		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0	0	0
14		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Dyspnea

Day	Target Concentration - mg/m3 air																											
	500				1000				3000				5000				1000				3000				5000			
	Sex	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N			
0	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
1	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
2	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
3	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
4	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
5	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
6	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
7	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
8	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
9	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
10	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
11	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
12	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
13	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0		
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Labored breathing pattern

Day	Target Concentration - mg/m3 air																											
	500		1000		3000		5000		500		1000		3000		5000													
	Sex	M	M	M	M	M	M	M	F	F	F	F	F	F	F	F												
0	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N
1	5	0	0	5	0	5	0	5	0	1	0	1	0	0	0	0	0	0	0	0	5	0	0	5	2	3	0	5
2	5	0	0	5	3	2	0	5	0	0	0	0	0	0	0	0	4	0	0	5	2	3	0	5	1	4	0	5
3	3	0	0	5	2	1	0	3	0	0	0	0	0	0	0	0	3	0	0	5	1	4	0	5	0	0	0	0
4	0	0	0	5	2	1	0	3	0	0	0	0	0	0	0	0	1	0	0	5	2	3	0	5	0	1	0	1
5	0	0	0	5	1	2	0	3	0	0	0	0	0	0	0	0	0	1	0	5	3	2	0	5	0	1	0	1
6	0	0	0	5	1	2	0	3	0	0	0	0	0	0	0	0	0	1	0	5	4	1	0	5	0	1	0	1
7	0	0	0	5	1	2	0	3	0	0	0	0	0	0	0	0	1	0	0	5	4	1	0	5	0	1	0	1
8	0	0	0	5	2	1	0	3	0	0	0	0	0	0	0	0	1	0	0	5	4	1	0	5	0	1	0	1
9	0	0	0	5	3	0	0	3	0	0	0	0	0	0	0	0	1	0	0	5	5	0	0	5	0	1	0	1
10	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	0	1	0	0	5	3	0	0	5	1	0	0	1
11	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	0	1	0	0	5	2	0	0	5	1	0	0	1
12	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	1	0	0	1
13	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	1	0	0	1
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Stridor (rales)

Day	500		1000		3000		5000		500		1000		3000		5000					
	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N				
0	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	5	0	0	0	0
1	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	5	0	0	0	0
2	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	1	0	0
3	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	1	0	0
4	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	1	0	0	0
5	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	1	0	0	0
6	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	1	0	0	0
7	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	1	0	0	0
8	0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	5	1	0	0	0
9	0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	5	1	0	0	0
10	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	5	0	0	0	0
11	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	0
12	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	0
13	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Gait changes (lurching)

Day	Target Concentration - mg/m3 air																											
	500				1000				3000				5000				1000				3000				5000			
	Sex	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N			
0	1	0	0	5	2	3	0	5	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0			
1	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
2	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
3	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
4	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
5	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
6	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
7	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
8	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
9	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
10	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
11	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
12	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
13	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Motility reduced

Day	Sex	Target Concentration - mg/m3 air																												
		500		1000		3000		5000		1000		3000		5000																
		l	M	l	M	l	M	l	M	l	F	l	F	l	F															
0		1	4	0	5	0	1	4	5	0	1	1	0	0	0	0	0	5	0	5	0	1	4	5	0	0	0	0		
1		3	1	0	5	3	2	0	5	0	0	0	0	0	0	0	0	0	4	0	5	4	0	5	0	5	0	0	0	
2		1	0	0	5	1	2	0	3	0	0	0	0	0	0	0	0	0	4	1	0	5	4	1	0	5	0	1	0	0
3		1	0	0	5	3	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
4		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
5		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
6		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
7		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
8		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
9		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
10		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
11		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	1	0	1	0	0	0	
12		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	1	0	0	0	
13		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	1	0	0	0	
14		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Cyanosis

Day	Sex	Target Concentration - mg/m3 air																									
		500		1000		3000		5000		500		1000		3000		5000											
		l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N						
0		0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
1		0	0	0	5	0	0	0	5	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
2		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
3		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
4		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
5		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
6		0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	1	0	0
7		0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	1	0	0
8		0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	1	0	0
9		0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	0	0	0
10		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	0	0	0
11		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	1	0	5	0	1	0	0	0	0
12		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
13		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	0	0
14		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Bristled hair-coat

Day	Target Concentration - mg/m3 air																														
	500				1000				3000				5000				1000				3000				5000						
	Sex	M	F	N	M	F	N	M	F	N	M	F	N	M	F	N	M	F	N	M	F	N	M	F	N						
0	5	0	0	5	0	5	0	5	0	1	0	1	0	0	0	0	4	1	0	5	3	2	0	5	2	3	0	5	0	0	0
1	3	2	0	5	0	4	1	5	0	0	0	0	0	0	0	0	3	2	0	5	3	2	0	5	3	2	0	5	0	0	0
2	5	0	0	5	0	3	0	3	0	0	0	0	0	0	0	0	4	1	0	5	2	3	0	5	0	1	0	1	0	0	0
3	5	0	0	5	0	3	0	3	0	0	0	0	0	0	0	0	3	1	0	5	3	2	0	5	0	1	0	1	0	0	0
4	4	0	0	5	3	0	0	3	0	0	0	0	0	0	0	0	2	2	0	5	4	1	0	5	0	1	0	1	0	0	0
5	1	0	0	5	1	2	0	3	0	0	0	0	0	0	0	0	2	1	0	5	4	1	0	5	0	1	0	1	0	0	0
6	1	0	0	5	1	1	1	3	0	0	0	0	0	0	0	0	2	1	0	5	4	1	0	5	0	1	0	1	0	0	0
7	0	0	0	5	1	0	1	3	0	0	0	0	0	0	0	0	1	1	0	5	3	1	0	5	0	1	0	1	0	0	0
8	0	0	0	5	1	1	0	3	0	0	0	0	0	0	0	0	1	0	0	5	2	1	0	5	0	1	0	1	0	0	0
9	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	0	1	0	0	5	2	1	0	5	0	1	0	1	0	0	0
10	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	2	1	0	5	1	0	0	1	0	0	0
11	0	0	0	5	1	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	1	2	0	5	1	0	0	1	0	0	0
12	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	2	0	0	5	1	0	0	1	0	0	0
13	0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	1	0	0	1	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: 1 = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Nasal discharge (serous)

Day	500		1000		3000		5000		500		1000		3000		5000			
	M		M		M		M		F		F		F		F			
	l	s	N	l	s	N	l	s	N	l	s	N	l	s	N	l	s	N
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Nostrils: reddened

Day	500		1000		3000		5000		500		1000		3000		5000	
	Sex	M	M	M	M	M	M	M	F	F	F	F	F	F	F	F
0	l	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Nostrills: red encrustations

Day	Sex	Target Concentration - mg/m3 air																												
		500		1000		3000		5000		500		1000		3000		5000														
		l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N	l	m	s	N									
0		0	4	0	5	0	4	0	5	0	1	0	1	0	0	0	0	0	0	5	0	5	0	4	0	5	0	0	0	0
1		0	3	0	5	0	2	0	5	0	0	0	0	0	0	0	0	0	0	2	0	5	0	4	0	5	0	0	0	0
2		0	0	0	5	0	1	0	3	0	0	0	0	0	0	0	0	0	0	1	0	5	0	1	0	1	0	0	0	0
3		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
4		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
5		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
6		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
7		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
8		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
9		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
10		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
11		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
12		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
13		0	0	0	5	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0
14		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: Desmophen PAC XP-7076
 Study-no: T5067020

Sign: Bradypnea

Day	Sex	Target Concentration - mg/m3 air							
		500 M n/N	1000 M n/N	3000 M n/N	5000 M n/N	500 F n/N	1000 F n/N	3000 F n/N	5000 F n/N
0		5/ 5	5/ 5	1/ 1	0/ 0	5/ 5	5/ 5	5/ 5	0/ 0
1		5/ 5	5/ 5	0/ 0	0/ 0	4/ 5	5/ 5	5/ 5	0/ 0
2		2/ 5	3/ 3	0/ 0	0/ 0	3/ 5	5/ 5	1/ 1	0/ 0
3		0/ 5	3/ 3	0/ 0	0/ 0	2/ 5	5/ 5	1/ 1	0/ 0
4		0/ 5	3/ 3	0/ 0	0/ 0	2/ 5	4/ 5	1/ 1	0/ 0
5		0/ 5	2/ 3	0/ 0	0/ 0	1/ 5	4/ 5	1/ 1	0/ 0
6		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	2/ 5	1/ 1	0/ 0
7		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	1/ 1	0/ 0
8		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	1/ 1	0/ 0
9		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	1/ 1	0/ 0
10		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	1/ 1	0/ 0
11		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	0/ 1	0/ 0
12		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	0/ 1	0/ 0
13		0/ 5	0/ 3	0/ 0	0/ 0	0/ 5	0/ 5	0/ 1	0/ 0
14		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
 M = males, F = females