

Contract CDC-210-77-0048

FINAL REPORT

Toxicity Evaluation for
Establishing IDLH Values

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NOTICE

This report was prepared as an account of work sponsored by the National Institute for Occupational Safety and Health under Contract CDC-210-77-0048. It is not to be construed as a report, opinion, or recommendation of the National Institute for Occupational Safety and Health.

ABSTRACT

UBTL performed acute (30 minute) whole body inhalation toxicology exposures of animals to test atmospheres generated from each of ten industrial chemicals. The test and control animal groups consisted of 20 animals each, including 10 rats and 10 guinea pigs, with equal numbers of each sex.

Test animals were exposed simultaneously to a given test atmosphere by use of an inhalation chamber equipped with a drawer-type door which allowed rapid entry and exit of all animals concurrently. At the same time, control animals were exposed to air lacking the test compound in a similar, but separate, inhalation chamber. All animals were caged separately during and after the exposures.

Samples of the test atmospheres were collected with charcoal adsorption tubes, silica gel adsorption tubes, midget impingers or an inertial cascade impactor for subsequent chemical analysis. The chemical analyses were conducted using electron capture detector or flame ionization detector gas chromatography, colorimetric, or specific ion electrode methodology.

The industrial chemicals evaluated were: 2-aminoethanol (monoethanolamine), 2-diethylaminoethanol, diisopropylamine, ortho-toluidine, para-anisidine, ortho-anisidine, Aroclor 1254, phosgene, stibine and diazomethane.

Exposure of the test animals to the various test atmospheres resulted in manifestations ranging from minor irritation to ataxia, tremors, respiratory distress, and/or death during, or soon after, exposure. Irreversible pathological lesions were found in organs of some test animals, however, some of those lesions apparently were not related to the inhalation exposures.

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PROJECT SUMMARY

This project entailed the acute (30 minute) whole body inhalation chamber exposure of groups consisting of 10 rats and 10 guinea pigs, each animal individually caged, with equal numbers of both sexes, to various test compound concentrations in air. This work was performed by UBTL under contract to the National Institute for Occupational Safety and Health (NIOSH). The initial exposure concentration for each test compound (estimated IDLH level) was stipulated in the contract. However, subsequent test compound levels were determined on the basis of data collected from the initial exposure level of a given test compound.

This project was a study to determine test compound concentrations which will produce "no effect", a "minimal effect," and a "frank effect" in exposed test animals as defined in the contract and listed in Table 1. Visual observation of the test animals during the acute exposure and subsequently for 14 days was used to determine gross physiological effects such as: eye and nasal irritation, respiratory difficulties, central nervous system aberrations, incapacitation, and death. The body weight of each animal was monitored and on the 14th day after exposure, all surviving test and control animals were sacrificed. The weights of eight body organs in each test and control animal were determined and histopathological examination was performed on sections from these organs on 3 animals per sex per species for each exposure concentration.

A summary of experimental data collected from the animal exposures which were used to categorize the effect level of each experiment is given in Table 2.

The concentration of each test compound in the inhalation chamber test atmosphere was monitored by appropriate analytical methods at intervals during the exposure.

UBTL attempted to produce exposure vapor concentrations of several liquid test compounds which would produce the required effects in test animals, however, a "frank effect level" and/or a "minimal effect level" for some test compounds (2-aminoethanol, ortho-toluidine) appeared to be

Table 1

Definition of Effect Levels for Categorizing
Responses of Animals to Acute Inhalation Exposures

<u>Exposure Effect Terminology</u>	<u>Definition*</u>
No Effect	A "no-effect" concentration produces none of the following treatment-related effects in any animal: <ol style="list-style-type: none">1. Death2. Irreversible pathological lesions3. Impaired escape ability during the exposure.
Minimal Effect	A "minimal effect" concentration produces one or more of the following treatment-related effects in one (1) or two (2) [different]** animals regardless of sex or species: <ol style="list-style-type: none">1. Death2. Irreversible pathological lesions3. Impaired escape ability during the exposure.
Frank Effect	A "frank-effect" concentration produces one or more of the following treatment-related effects in three (3) or more [different]** animals regardless of sex or species: <ol style="list-style-type: none">1. Death2. Irreversible pathological lesions3. Impaired escape ability during the exposure.

* Letter dated August 22, 1978, to William G. Yates, UBTL, from Trent R. Lewis, NIOSH.

**Authors' insert per discussion with Richard W. Niemeier, NIOSH Project Officer, 15 February 1979. In determining the number of treatment-related effects, the different types of effects (i.e., death, irreversible lesions, or impaired escape ability) were added if they occurred in different animals; however, multiple effects found in the same animal were counted as only one effect.

Table 2
Summary of Data Collected from the Animal Exposures

Date	Experiment Number	Test Compound	Attempted Chamber Concentration*	Measured Chamber Concentration*	Exposure Observations	Post-Exposure Observations	Impaired Escape Ability	Booth Test Control	Irreversible Lesions Test Control	Type of effect	See Table Listed for Details
6-9-78	31-BA-4	2-Aminoethanol	** ppm 6.68 mg/l	** ppm 0.346 mg/l	Jerked movements by 4 guinea pigs, first noticed at 20 min.	1 rat had swollen, red eye.	No	0 0 0 0 0 0	No histopathology ²	No	8
12-21-77	1-BA-1	2-Aminoethanol	625 ppm 1.37 mg/l	170 ppm 0.377 mg/l	Generalized depressed activity.	Symptoms persisted 1 hr. 1 guinea pig ataxic 14 days post-exposure.	No	0 1 ¹ 0 0 0 2 ¹¹ 0 0 1 animal the same	0 0 0 0 0 0 0 0	Mild ¹¹	8
6-12-78	16-BA-3	2-Aminoethanol	400 ppm 0.842 mg/l	210 ppm 0.432 mg/l	No untoward effects.	Normal	No	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	No	0
6-16-78	23-BA-3	2-Aminoethanol	** ppm 2.10 mg/l	** ppm 0.511 mg/l	Generalized depressed activity immediately. Ataxia with jerking in guinea pigs by 15 min. 7 guinea pigs died.	Generalized depressed activity persisted 3 hr. 5 guinea pigs died by 1 hr. post-exposure	Yes (by 20 min. 5 guinea pigs died; remaining 3 were ataxic.)	0 0 ³ 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	Frank	0
1-6-78	2-BIA-1	Bisopropylamine	1000 ppm 3.49 mg/l	961 ppm 3.35 mg/l	Mesal/tearful irritation progressing to dyspnea. Generalized depressed activity. Eye closure in majority by 15 min.	Symptoms persisted 4 hr.	No	0 0 0 0 0 0 2 ⁰ 0 1 ⁰ 0	0 0 0 0 0 0 0 0	No	10
3-28-78	12-BIA-3	Bisopropylamine	2000 ppm 6.98 mg/l	1760 ppm 6.17 mg/l	Mesal/tearful irritation progressing to dyspnea. Generalized depressed activity up to 20 min., followed by ataxic dyspnea. Eye closure in majority of guinea pigs by 15 min. 2 animals died by 30 min.	Symptoms persisted 4 hr. 1 guinea pig died 10 min. post-exposure. Corneal opacity in 1 guinea pig at 14 days post-exposure.	Yes (2 died.)	1 2 0 0 0 1 0 0 0 0 same animal	0 0 0 0 0 0 0 0	Frank	10
5-15-78	10-BIA-2	Bisopropylamine	5000 ppm 17.5 mg/l	5120 ppm 17.9 mg/l	All animals died by 20 min. 5 guinea pigs died by 10 min. 5 rats died by 15 min. Death appeared to be respiratory.	Controls appeared normal	Yes (All died.)	10 ⁰ 10 ⁰ 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	Frank	10
1-11-78	3-BAE-1	2-Diethylaminoethanol	500 ppm 2.02 mg/l	542 ppm 2.32 mg/l	Mesal/tearful irritation progressing to dyspnea. Excitement, then depressed activity, then tremors, then shaking. Eye closure in majority by 20 min.	Symptoms persisted 2 hr.	No	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	No	20
6-5-78	17-BAE-3	2-Diethylaminoethanol	2000 ppm 8.07 mg/l	1650 ppm 5.56 mg/l	Mild mesal/tearful irritation. Generalized depressed activity by 20 min. Mild tremors. Eye closure in majority of animals by 20 min.	Corneal opacity in 2 rats by 5 days post-exposure. In 6 rats at 14 days post-exposure; seemed to be retreating at that time.	Yes (6 rats and 6 guinea pigs did not open eyes or move about in response to sharp auditory stimulus.)	0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 ⁰ 0 0 0 0 0 0 0 0	Frank ⁶	20
6-28-78	25-BAE-3	2-Diethylaminoethanol	** ppm 16.2 mg/l	** ppm 6.77 mg/l	Generalized depressed activity immediately. Mesal/tearful irritation by 5 min. severe eye irritation by 25 min. Labored breathing by 20 min. Rats non responsive to auditory stimulus, eyes did not open.	Generalized depressed activity and eye closure persisted 3 hr. Rats had swollen, bloody eyelids. Corneal opacity in 6 rats by 5 days post-exposure. In 5 rats at 14 days post-exposure.	Yes (9 rats did not open eyes or move about in response to sharp auditory stimulus.)	1 0 0 0 0 2 ⁰ 0 0 1 ¹	0 0 0 0 0 0 0 0	Frank ⁶	20



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Table 2
Summary of Data Collected from the Animal Exposures

Date	Experiment Number	Test Compound	Attempted Chamber Concentration*	Measured Chamber Concentration	Exposure Observations	Post-Exposure Observations	Impaired Escape Ability	Deaths Test Chamber	Irreversible Lesions Test Chamber	Type Effect	See Table Listed Details
1-18-78	4-07-1	Ortho-Toluidine	100 ppm 0.346 mg/l	133 ppm 0.480 mg/l	Mild/tearful irritation. Skin irritation with scratching. Eye closure in 2 guinea pigs by 25 min.	Normal	No	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	No	26
3-22-78	11-07-2	Ortho-Toluidine	500 ppm 2.10 mg/l	544 ppm 1.97 mg/l	Mild nasal/tearful irritation in guinea pigs. Generalized depressed activity. Eye closure in majority of guinea pigs by 10 min.	Normal	No	0 0 0 0 0 0 0 0	0 3 ¹ 0 1 ¹	No	26
7-5-78	26-07-3	Ortho-Toluidine	** ppm 3.49 mg/l	** ppm 2.78 mg/l	Generalized depressed activity in all animals by 10 min. Mild/tearful irritation primarily in guinea pigs; eye closure in majority of guinea pigs by 10 min.	Generalized depressed activity persisted 2 hr.	No	0 1 0 0 0 1 0 0	0 0 0 0 0 0 0 0	Minimal ²	26
									same animal		
1-25-78	5-08-1	Ortho-Anisidine	0.030 mg/l	0.0524 mg/l	Mild depressed activity. Mild irritation.	Symptoms persisted in guinea pigs 1 hr.	No	0 0 0 0 0 2 ¹ 0 0 0 0	0 0 0 0 0 0 0 0	No	32
4-26-78	16-08-2	Ortho-Anisidine	0.30 mg/l	0.286 mg/l	No untoward effects.	Normal	No	0 0 0 0 0 0 1 ¹ 0 0 0	0 1 ¹ 0 0 0	No	32
7-12-78	27-08-3	Ortho-Anisidine	>1 mg/l	0.846 mg/l	Initial hyperactivity in rats. Generalized depressed activity in all animals by 15 min. Mild nasal/tearful irritation in guinea pigs by 10 min. and in rats by 30 min.	Generalized depressed activity persisted 1 hr.	No	0 0 0 0 0 1 0 0 1 ¹	0 0 0 1 0 0 1 ¹	Minimal ²	32
5-3-78	17-08-1	Para-Anisidine	0.030 mg/l	0.0215 mg/l	No untoward effects.	Normal	No	0 0 0 0 0 0 0 0 1 ¹	0 0 0 0 0 0 0 0	No	38
8-2-78	30-08-3	Para-Anisidine	1 mg/l	0.128 mg/l	Initial hyperactivity in all animals. Generalized depressed activity in all animals by 15 min. Mild eye irritation in guinea pigs.	Normal	No	0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	No	38
7-26-78	28-08-2	Para-Anisidine	0.4 mg/l	0.246 mg/l	Initial hyperactivity in rats. Generalized depressed activity in all animals by 15 min. Eye irritation in guinea pigs by 15 min.	Normal	No	0 0 0 0 0 0 0 0 1 ¹	0 0 0 0 0 0 0 1 ¹	No	38

Table 2
Summary of Data Collected from the Animal Exposures

Date	Experiment Number	Test Compound	Accepted Chamber Concentration*		Measured Chamber Concentration	Exposure Observations	Post-Exposure Observations	Impaired Escape Ability	Deaths			Irreversible Lesions			Type of Effect	See Table Listed for Details
			ppm	µg/l					0	1	2	3	4	5		
3-1-78	8-5-1	Seibline	48 ppm 0.172 µg/l	29.1 ppm 0.125 µg/l	No untoward effects.	Normal	No	0	0	0	0	2	1	1	No	61
6-7-78	22-5-3	Seibline	225 ppm 0.864 µg/l	191 ppm 0.810 µg/l	Initial hyperactivity. Generalized depressed activity in rats by 15 min., in guinea pigs by 25 min., in guinea eye irritation in rats by 15 min., closure in mast rats by 25 min.	Generalized depressed activity. Persisted 4 hr.	No	0	1	0	0	2	3	0	Frank	64
5-24-78	28-5-3	Seibline	600 ppm 1.72 µg/l	513 ppm 1.43 µg/l	Generalized depressed activity. Shallow, rapid breathing in some guinea pigs by 15 min. Labored breathing in some rats by 20 min. Mild tremors in guinea pigs at 15 min.	Generalized depressed activity. Persisted 4 hr. 3 rats and 7 guinea pigs died in lateral recumbent position by 4 hr. Post-exposure re-attached within 18.5 rat cages.	Yes	7	0	10	0	3	1	1	Frank	64
5-31-78	21-P-3	Phosgene	0.5 ppm 1.7 µg/l	0.58 ppm 1.72 µg/l	No untoward effects.	Normal	No	0	0	0	0	2	0	1	No	58
3-8-78	8-P-1	Phosgene	2 ppm 6.81 µg/l	1.47 ppm 5.48 µg/l	Moderate depressed activity by 20 min.	Symptoms persisted in some rats 4 hr.	No	1	0	0	0	1	0	0	Minimal	58
5-18-78	19-P-2	Phosgene	20 ppm 66.1 µg/l	16.9 ppm 61.3 µg/l	Generalized depressed activity. rats in lateral recumbent position by 20 min. Head/neck/irritation. Labored breathing by 25 min. in rats.	Generalized depressed activity. Persisted more than 4 hr. 3 rats and 1 guinea pig died by 5 hr.	Yes	10	0	10	0	0	1	0	Frank	58
2-15-78	7-88-1	Dioxamethane (ethyl ether solvent)	10 ppm 14.3 µg/l	13.6 ppm 29.0 µg/l (4130 ppm)	No untoward effects.	Normal	No	0	0	0	0	0	0	0	No	54
5-18-78	18-88-2	Dioxamethane (ethyl ether solvent)	200 ppm 288 µg/l	27.3 ppm 38.5 µg/l (3400 ppm)	Generalized depressed activity, more so in rats.	Generalized depressed activity. Persisted 4 hr. in rats.	No	0	0	0	0	2	0	0	No	54
7-18-78	21-88-3	Dioxamethane (ethyl ether solvent)	200 ppm 288 µg/l	33.9 ppm 122 µg/l (2340 ppm)	Generalized depressed activity in all animals by 25 min. Mild eye irritation in rats by 25 min.	Generalized depressed activity. Persisted 1 hr.	No	0	0	0	0	2	1	0	Minimal ¹²	54
2-1-78	6-88-1	Arcleor 1254	5 µg/l	0.559 µg/l	No untoward effects.	Normal	No	0	0	0	0	0	1	0	No	63
4-18-78	15-88-2	Arcleor 1254	40 µg/l	44.4 µg/l	Generalized depressed activity by 20 min.	Normal	No	0	0	0	0	0	0	1	No	63
6-21-78	24-88-3	Arcleor 1254	600 µg/l	348 µg/l	Generalized depressed activity in rats by 15 min., in guinea pigs by 20 min. Explaining in rats by 20 min.	Normal	No	0	0	0	0	0	1	3	Minimal ¹³	63

Table 2
Summary of Data Collected from the Animal Exposures
(Footnotes)

- * The first level concentrations were specified in the contract; the second and third level attempted concentrations were chosen after consultation with the Project Officer and the Toxicology Consultant.
- ** The atmosphere was an aerosol-vapor mixture; therefore, the "ppm" designation is not applicable.
- 1 The effect(s) are probably not exposure-related; the reasons for this conclusion are detailed in the table indicated.
 - 2 Histopathology was not performed because only one possible significant finding was observed at the two, next-higher concentrations.
 - 3 No significant microscopic lesions were observed in the animals that died.
 - 4 The deaths were due to pulmonary edematous changes with degeneration of bronchial epithelium and degeneration of proximal tubular epithelium of the kidneys.
 - 5 The deaths were due to vacuolar degeneration of hepatocytes.
 - 6 Corneal opacity was present in several test rats at 14 days post-exposure, as noted in the Post-Exposure Observations. Most or all of these lesions were judged to be reversible by the pathologist. However, these lesions may have been sufficiently significant to justify a "Frank" effect classification in their own right.
 - 7 The conclusion should be verified by testing the compound at a higher concentration. However, a higher concentration was beyond the capabilities of UBTI equipment.
 - 8 Two animals were judged to have exposure-related irreversible lesions; the other finding is probably incidental.
 - 9 The deaths were due to pulmonary edema, disseminated intravascular congestion and coagulopathy, and renal infarction.
 - 10 The deaths were due to pulmonary edema, judged to be reversible.
 - 11 The effect may or may not be exposure-related; the results are inconclusive due to the small number of animals tested. However, a conservative approach was taken and the effect was, therefore, judged exposure-related in the animal that died. The other lesion is probably incidental.
 - 12 The conclusion should be verified by testing the compound at a higher dose as a pure material; however, this testing is necessarily precluded by the explosive nature of the pure chemical. Higher concentrations using ethyl ether solvent were attempted on pilot studies; see Results section.
 - 13 The effect may or may not be exposure-related; the results are inconclusive due to the small number of animals tested. However, a conservative approach was taken and the effect was, therefore, judged exposure-related.

unattainable because of their relatively low toxicity at concentrations approaching their vapor saturation levels in air. In these cases, a combination of vapor and aerosol was used to produce a higher concentration. With the combination of vapor and aerosol generation systems available at UBTL, a "frank" effect was produced with 2-aminoethanol and 2-diethylaminoethanol, but maximum generation capacity did not allow the production of a "frank" effect with ortho-toluidine.

Three test compounds (para-anisidine, ortho-anisidine, Aroclor 1254) were specified by the contract to be presented as aerosols. Two of these were produced at high enough concentrations to obtain "minimal" effect levels, but "frank" effect levels were not produced for any of them. This was due to the limitations of the aerosol generation apparatus available at UBTL and to the relatively low acute inhalation toxicity of those test compounds.

Of the three gaseous test compounds (stibine, phosgene, diazomethane), a "frank" effect was not produced for diazomethane due to its explosive nature when produced as an isolated compound. (See Results for more detailed discussion of this problem.)

The chemicals which were tested are listed in Table 3, along with each chemical formula, molecular weight, NIOSH Registry of Toxic Effects of Chemical Substances [1] (RTECS) reference number, some relevant toxicological data from the RTECS, the specified initial exposure concentration, and the threshold limit value. Aroclor 1254 was substituted by the Project Officer for the allyl propyl disulfide originally specified in the contract.

Table 3

Ten Industrial Compounds Tested

Test Compound	Chemical Formula	M.W.	NIOSH RTECS # [1]	TLV ppm	[6] ₃ mg/m ³	"Estimated" IDLH	Species	Acute Inhalation Exposure Toxicology		
								Exposure Conc. (ppm)	Mortality Interval	Death/Total Exposed
2-Aminoethanol	<chem>NH2CH2CH2OH</chem>	61.08	KJ57750	3	6	1000 ppm	rat	Sat. Vapor	4 hrs.	2/6
Diisopropylamine	<chem>[(CH3)2CH]2NH</chem>	101.19	IM40250	5	20	1000 ppm	rat	500 ppm 1000 ppm 2000 ppm	4 hrs. 4 hrs. 4 hrs.	0/6 2/6 5/6
2-Diethylethanol	<chem>(C2H5)2NCH2CH2OH</chem>	117.2	KK50750	10	50	500 ppm	rat	Sat. Vapor	8 hrs.	1/5
Ortho-Toluidine	<chem>Cc1ccc(N)cc1</chem>	107.2	XU29750	5	22	100 ppm	-*	-	-	-
Ortho-Anisidine	<chem>COc1ccc(N)cc1</chem>	123.15	BZ54250	-	0.5	30 mg/m ³	-	-	-	-
Para-Anisidine	<chem>COc1ccc(N)cc1</chem>	123.15	BZ54250	-	0.5	30 mg/m ³	-	-	-	-
Stibine	<chem>SbH3</chem>	124.78	NJ07000	0.1	0.5	40 ppm	-	-	-	-
Phosgene	<chem>Cl-C(=O)-Cl</chem>	98.92	SY56000	0.1	0.4	2 ppm	-	-	-	-
Diazomethane	<chem>CH2=N+=N-</chem>	42.04	PA70000	0.2	0.4	10 ppm	-	-	-	-
Aroclor 1254**	<chem>Xc1ccc(X)c(X)c1</chem>	mixture	CF61250	-	0.5	5 mg/m ³	-	-	-	-

x=variable degree of chlorine substitution

*Acute inhalation exposure data in rats or guinea pigs not available.

**Trade name of Monsanto Company for 54% chlorinated biphenyl compound mixture.

INTRODUCTION

The UBTL agreed to perform inhalation toxicity tests in animals of ten industrial compounds for NIOSH under Contract CDC-210-77-0048.

Background

The industrial chemicals tested at UBTL were reported to be immediately hazardous to a worker exposed to sufficiently high concentrations in air. This hazardous air concentration of a particular chemical is known as the "Immediately Dangerous to Life or Health" or "IDLH" level. This level is defined as the highest known concentration of the chemical which does not cause impairment of the ability to escape, nor irreversible adverse health effects, nor subsequent death, for up to 30 minutes of exposure. The logic behind this regulation is that if a worker were exposed to air concentrations up to the IDLH, for instance after failure of a respirator, he would have up to 30 minutes to escape. If a person were, however, temporarily required to work in an environment in which the ambient air concentration exceeded the IDLH level, it would be mandatory that he wear a respirator which had been tested and approved as "highly reliable."

Objective

The purpose of the animal experimentation was to generate heretofore unavailable acute inhalation toxicology data in laboratory animals on ten industrial chemicals. The resultant data will be useful in setting, or verifying, IDLH values for the compounds tested.

METHODS

Procurement of Test Compounds

The contract required that the test compounds used to generate the inhalation atmospheres be of "commercial technical grade." UBTL contacted various chemical manufacturers concerning the procurement of test compounds which they manufactured [2]. The manufacturers from which we received the technical grade test compounds are listed in Table 4. We acknowledge the cooperation of those companies in supplying test compounds and relevant product information.

Design and Operation of Inhalation Chambers

UBTL constructed two inhalation exposure chambers in 1976, and used them in performing the acute inhalation exposure studies for this project. These chambers were patterned after those developed by R. G. Hinners of the National Center for Air Pollution Control in Cincinnati, Ohio [3,4].

These chambers (see Figures 1, 2, 12 and 13) are constructed of stainless steel and glass, are essentially cubical in shape with conical top and bottom sections, with dimensions of approximately 1.0 m (3.3 feet) on a side, and contain a total volume of approximately 1260 liters (45 cubic feet). One chamber is equipped with a sliding-drawer system for rapid, concurrent insertion or removal of individually caged animals (10 rats and 10 guinea pigs). This chamber is used to expose the test animals to various test compound atmospheres. A second exposure chamber of similar construction is used to expose control animals to an atmosphere lacking the test compound. Visibility of the test animals is afforded by windows on all four sides of the exposure chambers. A windshield wiper inside the chamber aids visibility during exposures to atmospheres which condense on windows.

Gate valves on the bottom cones of the chambers facilitate the removal of residual test compound and animal waste material. The chambers are cleaned by scrubbing with hot water and detergent.

As shown schematically in Figure 2 prior to entering the chambers, the air supply passed through an absolute filter and then through an air

Table 4
Sources of Test Compounds

Lot #	Compound	Grade	Manufacturer
2972 TF-7314	2-Aminoethanol (Monoethanolamine) Diisopropylamine	Technical Technical	Union Carbide Corporation South Charleston, West Virginia
D6E	2-Diethylaminoethanol	Commercial	Eastman Organic Chemical Division Rochester, New York
100 1-H 28-H	Ortho-Toluidine Para-Anisidine Ortho-Anisidine	Technical Technical Technical	E. I. Dupont de Nemours Wilmington, Delaware
321	Phosgene	Commercial	Matheson Gas Products East Rutherford, New Jersey
032477	Diazomethane	Commercial	Prepared from Diazald obtained from Aldrich Chemical Company Milwaukee, Wisconsin
773268	Stibine	Fisher Certified	Prepared from antimony potassium tartrate obtained from Fisher Scientific Company Santa Clara, California
KE12-635	<u>Aroclor 1254</u>	Commercial	Monsanto Chemical St. Louis, Missouri

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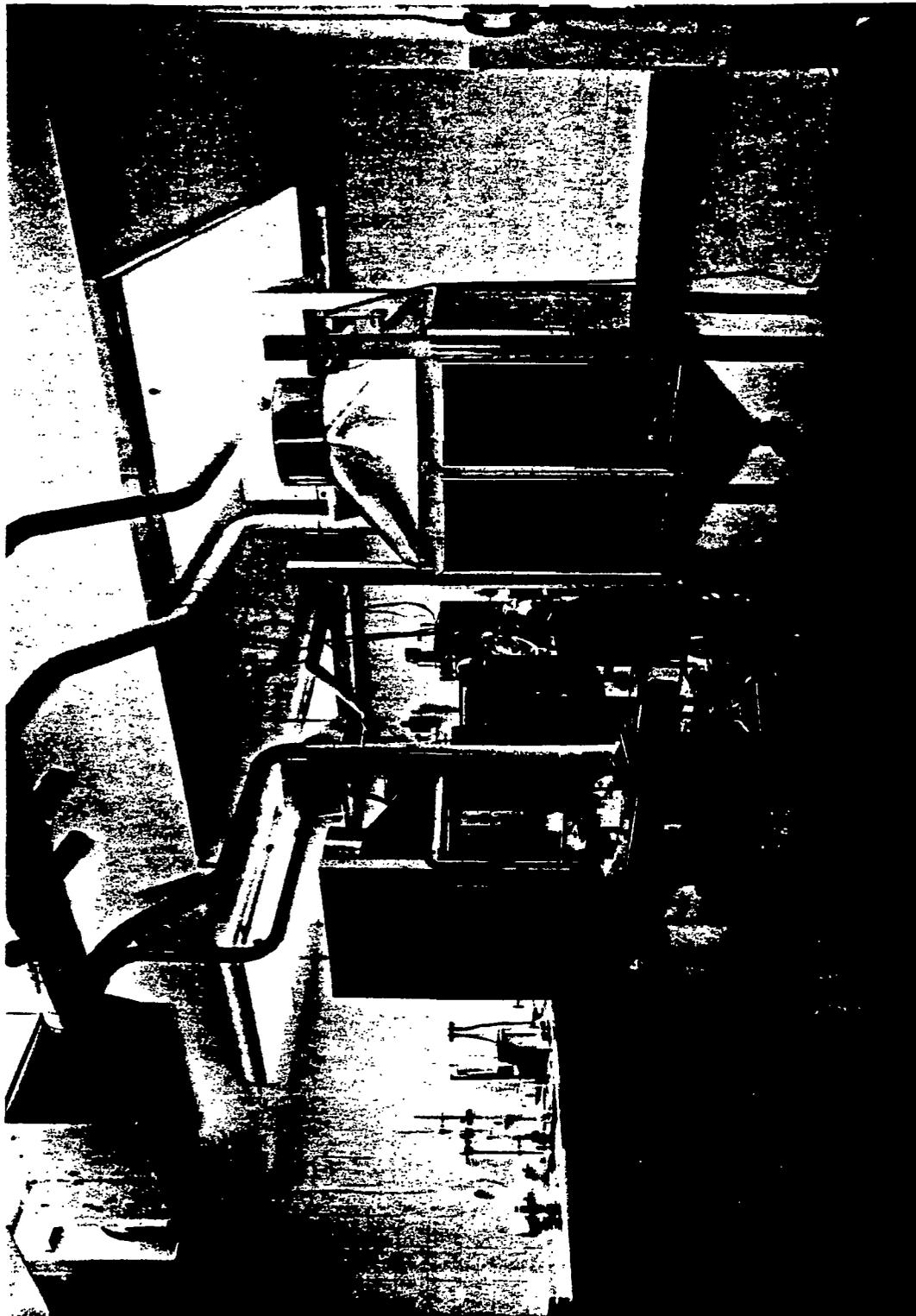


Figure 1. UBTL Inhalation Chamber Facility. The chamber on the left is used to expose animals to test compounds, while the similar chamber on the right is used as a control animal exposure chamber.

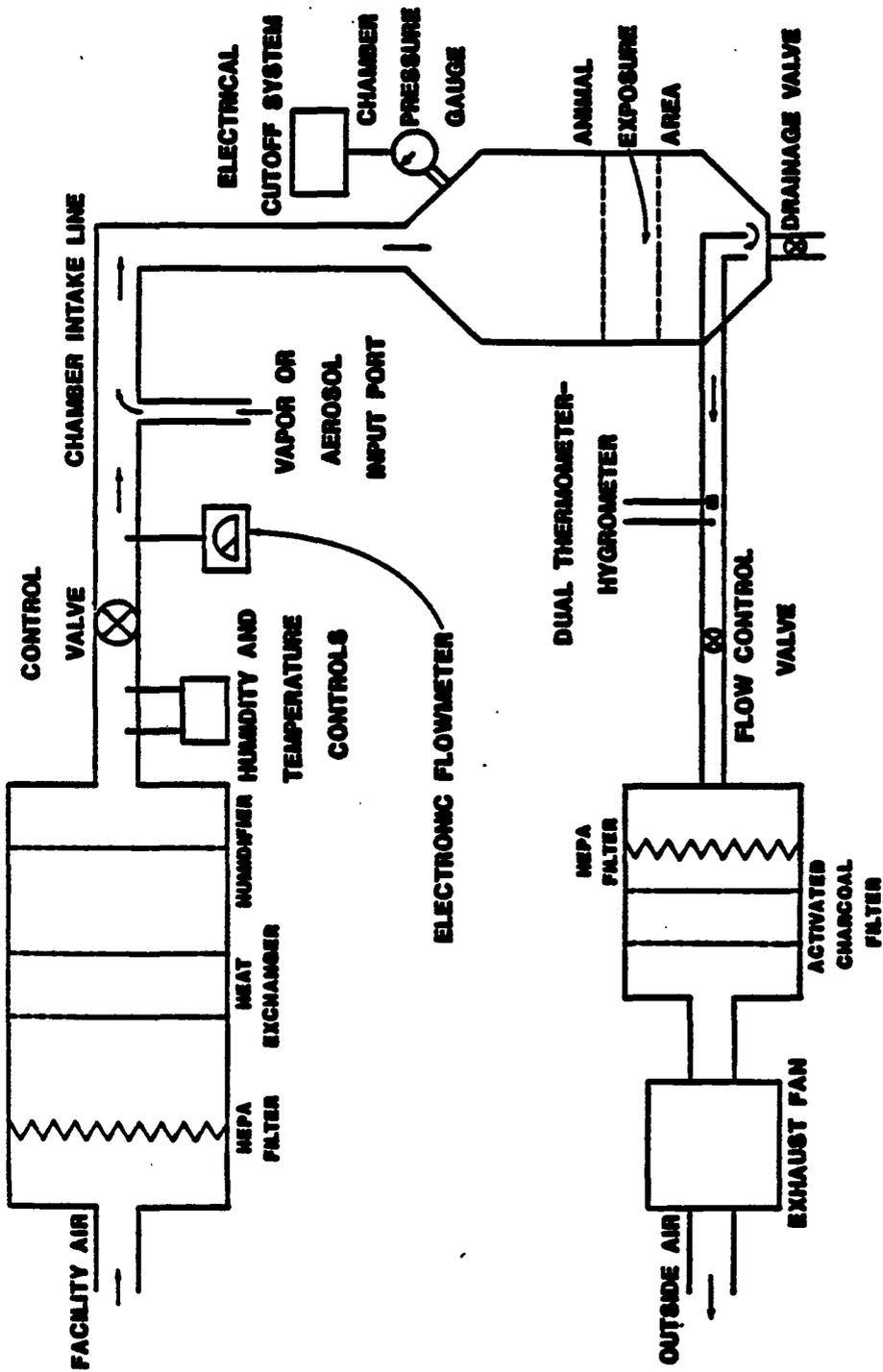


Figure 2. Schematic of UBTL Test Compound Inhalation Chamber. Although not shown in this diagram, the control inhalation chamber is supplied and exhausted by the same system except that no test compound is added.

conditioning system which maintained a mean temperature of 24.4°C and a mean relative humidity of 37%. Air flow is adjustable over a moderate range (20-900 liters/minute) and in this study was supplied at 600 liters/minute or less. The altitude of UBTL is 4838 feet and thus the mean barometric pressure for the exposures was 641 torr. All concentration computations in this report were based on ambient UBTL conditions of temperature and pressure [5,6].

An exhaust fan draws air through the inhalation chambers and into a filtering system consisting of an absolute particle filter (HEPA) and an activated charcoal bed filter (Westate Carbon) before exhausting to the outside. A negative pressure of approximately 8 to 19 mm of water is maintained within the chamber and exhaust system in order to reduce the possibility of contaminating the work area from system leaks.

Monitoring of the inhalation chamber intake air flow is performed by the use of an air mass velocity meter (Sierra Instruments, #441) with its sensing probe placed in the inhalation chamber intake duct upstream from the vapor generator dispersion nozzle. The air flow in the duct is calculated by multiplying the air mass velocity reading by the ratio of the density of air under standard factory calibration conditions (21.1°C, 760 torr) to nominal ambient UBTL conditions (25°C, 640 torr) and by the cross-sectional area of the intake duct [7]. Then, by addition of the gas flow from the vapor generator, the total flow into the chamber was estimated.

The inhalation chamber pressure is indicated by a dial pressure gauge (Dwyer, "Photohelic" #3302; 0 to ± 1 in H₂O) equipped with set point contacts connected to an alarm and an automatic electrical supply cutoff relay system. If the chamber pressure varied outside preselected limits, then the electrical supply to the vapor generator would be cut off and a bell alarm would sound.

Generation of Test Compound Atmospheres

The test compounds utilized in this study encompass all three states of matter at room temperature (See Table 5), and thus different methods of vaporization and/or dispersal were employed.

Table 5

Summary of Test Compound Data

Test Compound	UBTL Abbrev.	MW	BP (C)	Density (g/ml)	NIOSH Estimated IDLH (ppm)	mg/C/1*	Vapor Pressure (mm Hg)	Est. Max. Vapor Conc. ^a (ppm)	Est. Max. Vapor Conc. ^a (mg/l)
2-Aminoethanol	EA	61.06	170.5	1.0160	1000	2.104	0.4 @ 20°C	625	1.315
Diisopropylamine	DIA	101.19	83.5	0.722	1000	3.485	70 @ 20°C	109375	381
2-Diethylaminoethanol	DEAE	117.2	162	0.8851	500	2.018	1.4 @ 20°C	2190	8.831
Ortho-Toluidine	OT	107.2	199.7	1.004	100	0.3692	1 @ 44°C	<1563	<5.760
Ortho-Anisidine	OA	123.15	225 (5.2)	1.108	30 mg/m ³	0.030	<1 @ 20°C	Aerosol	Aerosol
Para-Anisidine	PA	123.15	246 (57)	1.071	30 mg/m ³	0.030	<1 @ 20°C	Aerosol	Aerosol
Stibine	S	124.78	-17	4.30 mg/ml	40	0.1719	>760 @ 20°C	10 ⁶	-
Phosgene	PG	98.92	8.3	3.41 mg/ml	2	0.006814	>760 @ 20°C	10 ⁶	-
Diazomethane	DM	42.04	-23	1.45 mg/ml	10	0.01448	>760 @ 20°C	10 ⁶	-
Aroclor 1254	ARO	**	**	1.44	5 gm/m ³	0.005	<<1 @ 20°C	Aerosol	Aerosol

* Calculated assuming nominal UBTL conditions of 25°C and 640 torr.

** Since this material consists of a mixture of several compounds, no discrete molecular weight nor boiling point is given.

Liquid Compound Atmosphere Generation

Three of the test compounds (diisopropylamine, 2-diethylamino-ethanol and ortho-toluidine) had sufficiently high vapor pressures to allow them to be vaporized to generate the initial low level concentrations required by the contract. However, 2-aminoethanol had a vapor saturation level below that for the estimated IDLH concentration (1000 ppm), and an atmosphere at that level was not generated.

The vapor generation system shown in Figure 3 consisted of a 1.9 m x 6 mm glass tube (Pyrex) wound in a helix. Stainless steel tees were connected to both ends of the glass tube with Teflon ferrules. The tee on the input end of the glass tube was connected through a rotameter with metering valve to a source of nitrogen for flushing and to the metering pump (Fluid Metering, Inc., #RPISY/CSC) with Teflon tubing. The Teflon tubing (0.8 mm ID x 1.5 mm OD, Altex #200-31) extended through the tee to distance of about 20 cm into the glass tube insuring delivery of liquid compound into the heated portion of the glass tubing for vaporization. The tee on the output end of the glass tube was connected through a rotameter with a metering valve to a source of compressed air for initial dilution of the compound vapor prior to entering into the chamber intake line [5,8,9,10,11].

The temperature of the glass vaporization tube was controlled by a proportional controller (RFL Industries #76RTD). That device indicated the temperature of the vaporization chamber on a meter display and provided the power for a heating tape wrapped around the glass vaporization tube. The vaporization tubing was maintained at a temperature several degrees above the boiling point of the test compound being vaporized.

When necessary, liquid test compound mass flow was determined by placing the test compound container on a top loading balance (Mettler, #P1210N) and measuring the weight loss over a known time interval.

The concentration range of each test compound was limited by the physical and chemical properties of that test compound and the operational characteristics of the UBTL vapor generation system. The rate of vapor-

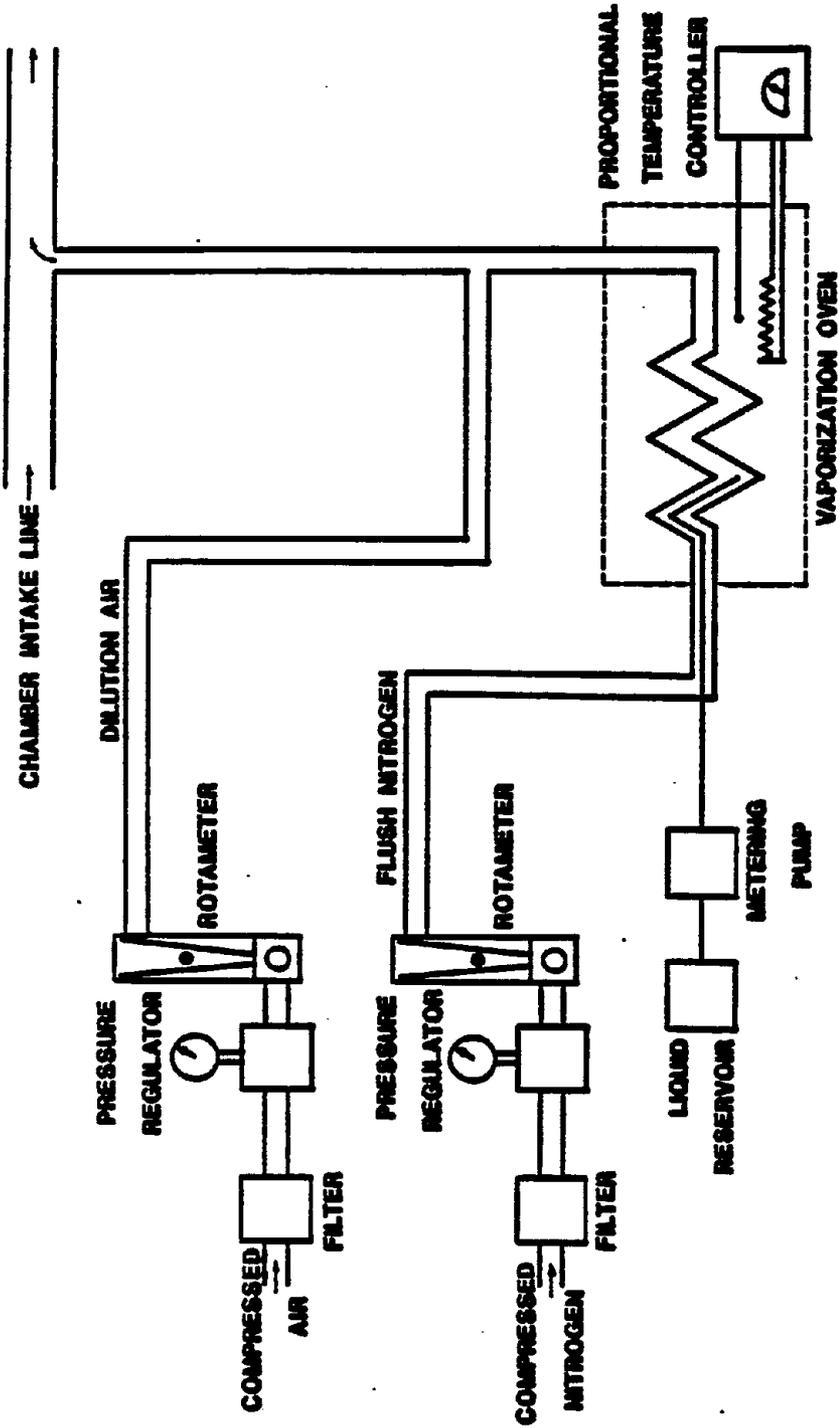


Figure 3. UBTL Vapor Generation System.

zation of a liquid test compound is dependent on the area of the contacting surface, the temperature of the contacting surface, the heat capacity of the liquid, and the flow of flush gas. For each test compound, there was a maximum concentration that could be produced, above which unvaporized liquid test compound would be present in the vaporizer output line. However, even with this limitation, this system allowed the production of test compound levels ranging from a few ppm to several thousand ppm, depending upon the compound.

A further limitation on the maximum test compound concentration generated was safety. It was mutually agreed by NIOSH and UBTL that generation of test compounds at concentrations within their known explosive limits would present undue hazard and should not be conducted.*

Gaseous Compound Atmosphere Generation

Phosgene was available commercially in cylinders, while both diazomethane and stibine were generated as needed for the exposures.

Phosgene was removed from the cylinder and accumulated as a liquid in a reservoir as shown in Figure 4. The liquid phosgene in the reservoir was maintained below room temperature (15-20°C) to prevent condensation of vaporized phosgene in the metering system [5,12].

The dilution air rotameter and chamber airflow were adjusted to the appropriate range and the phosgene supply rotameter was adjusted to produce the desired concentration.

Stibine is not commercially available as a compressed gas, thus it was necessary to generate the stibine as needed during the exposures. Stibine was initially generated by reacting two liquid solutions (A&B) in a glass reaction vessel as shown in Figure 5, and flushing the resulting gaseous stibine from the reaction mixture with compressed air [13,14].

Solution A consisted of the following reagent grade chemicals added to two liters of distilled water: 200 g potassium hydroxide, 20 g tartaric acid, 300 g potassium antimony tartrate [$K(SbO)C_4H_4O_6 \cdot \frac{1}{2}H_2O$] and 28 g sodium borohydride. The sodium borohydride was added to the other ingredients last because some decomposition of the mixture begins immediately after its addition. The sodium borohydride is a source of

*Letter dated April 26, 1977, addressed to A. U. Daniels, UBTL, from Trent R. Lewis, NIOSH.

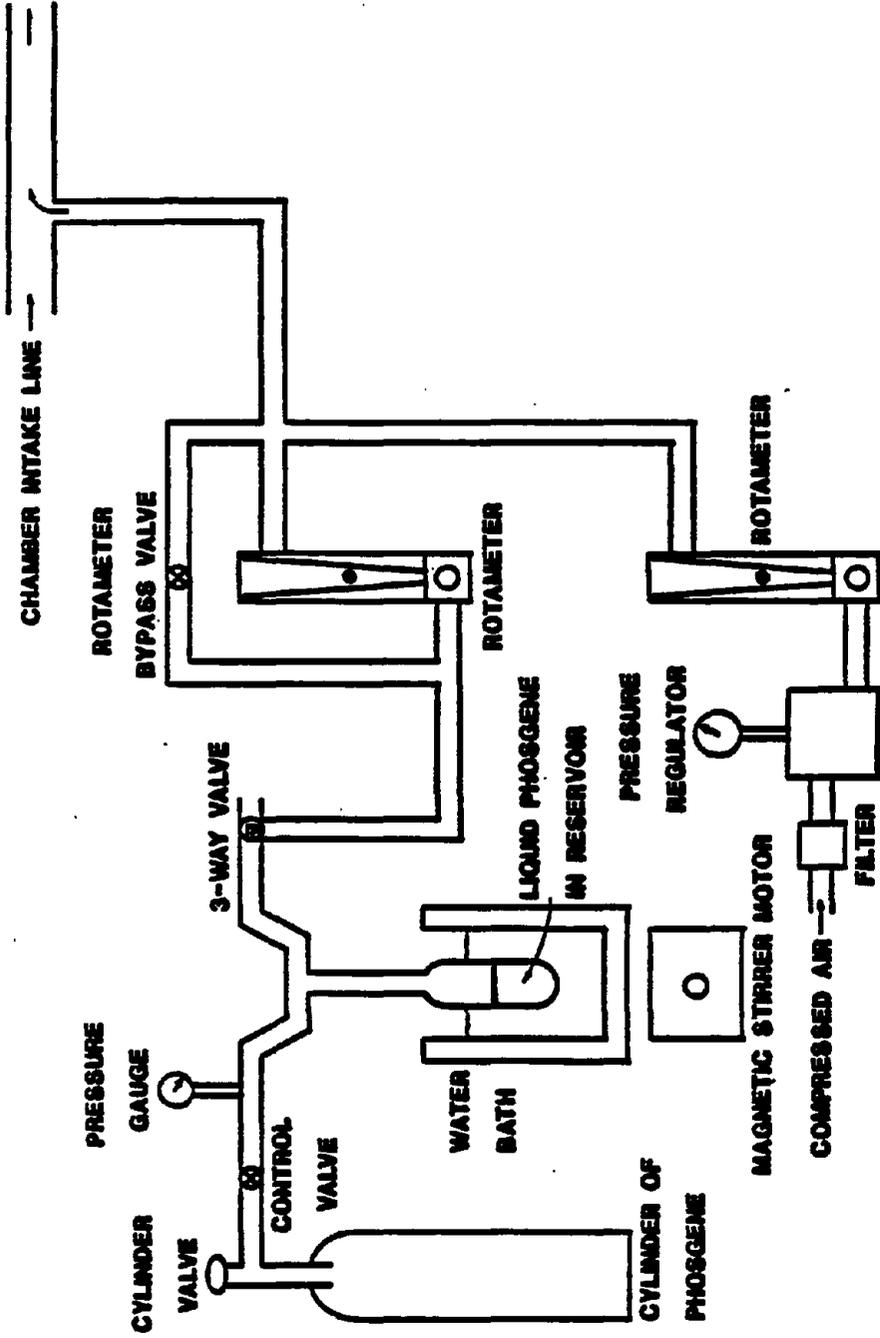


Figure 4. Phosgene Atmosphere Generation System.

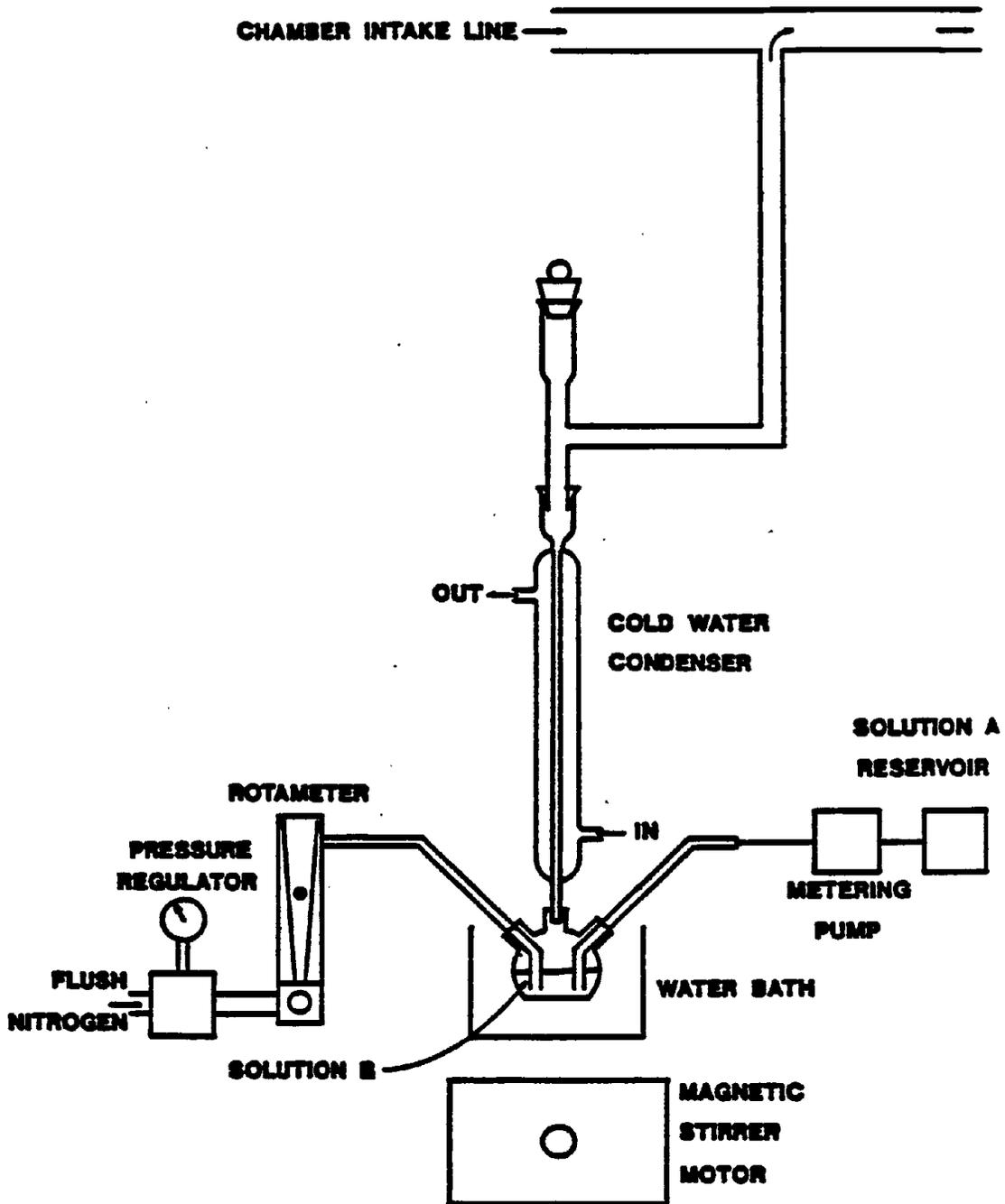


Figure 5. Stibine Atmosphere Generation System Used During First Exposure.

hydrogen for the subsequent reaction to produce stibine, but some hydrogen appears to be produced even in the highly basic solution since a darkening of the solution occurs. During and subsequent to the addition of the sodium borohydride, solution A is kept in a fume hood due to the potential for the evolution of stibine. Some particulate matter was present in solution A and this material was allowed to settle for a few minutes prior to using the solution for generation of stibine.

Solution B consisted of 8 molar sulfuric acid which was prepared by dilution of reagent grade concentrated sulfuric acid with distilled water.

The first stibine atmosphere was generated by placing an aliquot of the sulfuric acid solution in a 500 ml reaction flask, and adding solution A to that flask at a constant rate with a metering pump while a flow of 2 liters per minute nitrogen flush gas was maintained. The second and third exposure levels were generated in a different manner since they required the reaction of much larger quantities of the solutions A and B, the apparatus shown in Figure 6 was used. This apparatus allowed high flow rates of both solutions A and B (20-40 ml/min) without increasing the average reaction mixture volume nor the depth of the reaction mixture as did the initial generation system, thus a more uniform concentration was maintained with time.

Some potentially toxic impurities might have been present in the effluent from the stibine generation apparatus in addition to the stibine. Therefore, control animals were exposed to an atmosphere generated with that apparatus under the same conditions as the test animals, except the solution A did not contain potassium antimony tartrate. The control animals were exposed first, and then the test animals were exposed in the same chamber with a stibine test atmosphere.

Diazomethane is highly reactive and has explosive potential. Thus, this material is not available commercially as a compressed gas, and it must be generated as needed [15,16].

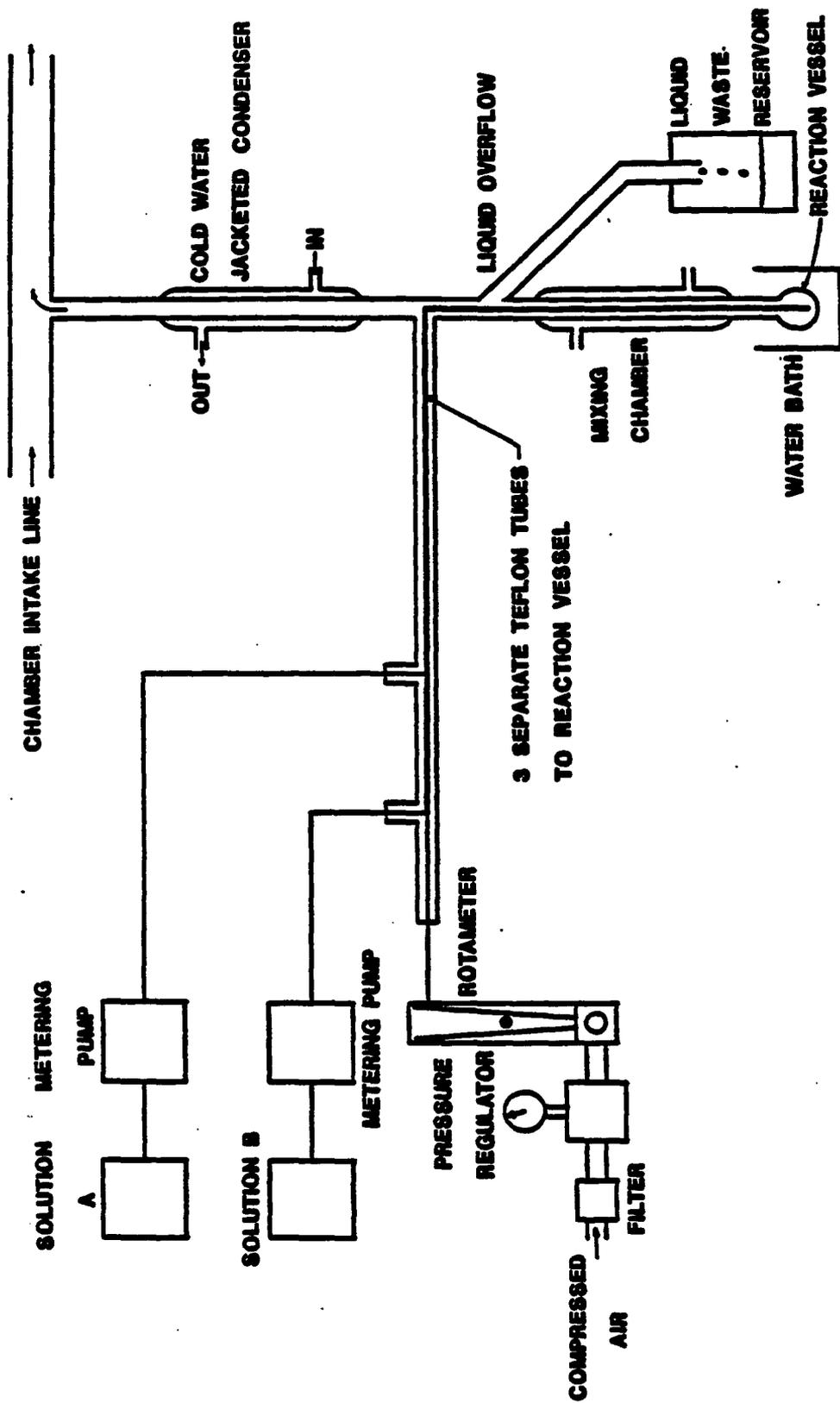


Figure 6. Stibine Atmosphere Generation System Used During Second and Third Exposures.

For generation of the first diazomethane atmosphere, two solutions were prepared. Solution A consisted of 21.5 g N-methyl-N-nitroso-p-toluene sulfonamide (Diazald, Aldrich Chemical Company) dissolved in 200 ml of anhydrous diethylether. Solution B consisted of 6 g potassium hydroxide, 10 ml distilled water, and 35 ml of 2-(2-ethoxyethoxy)-ethanol. Solution B was placed in the reaction flask of an apparatus of the same design as that used initially to generate stibine (see Figure 5). This apparatus was constructed with ground-glass-free parts (Clear-Seal, Wheaton Scientific Company) to reduce possibility of explosions that can be caused by contact of diazomethane with ground glass surfaces. Solution A was metered into the reaction flask with a syringe pump (Harvard Apparatus). The reaction vessel was maintained at 70°C and constantly flushed with a 2 l/min flow of nitrogen. The resulting diazomethane atmosphere contained a small amount of diethylether which was calculated to be well below the threshold limit values of 400 ppm.

The second and third diazomethane atmospheres were generated in a different manner in order to produce higher concentrations. A solution of diazomethane in ether was prepared by reacting solutions A and B in a glass reaction-distillation apparatus (Clear-Seal, Wheaton Scientific). The diazomethane generated was collected in 200 ml of anhydrous diethylether in an ice bath (~4°C). This solution of diazomethane in ether was maintained at 4°C until used. An aliquot of the solution was removed for analysis and the apparatus shown in Figure 7 was used to vaporize the solution to produce the diazomethane atmosphere.

A pressure of 100 torr was applied to the diazomethane/ether solution to reduce the formation of bubbles (diazomethane) in the metering pump system. During the second exposure, 4 l/min of compressed air was used to flush the vaporized component into the chamber intake line to be mixed with the chamber intake air flow. However, during the third exposure, the compressed air was used as the only source of dilution air for the atmosphere in order to produce a higher concentration of diazomethane in the test atmosphere.

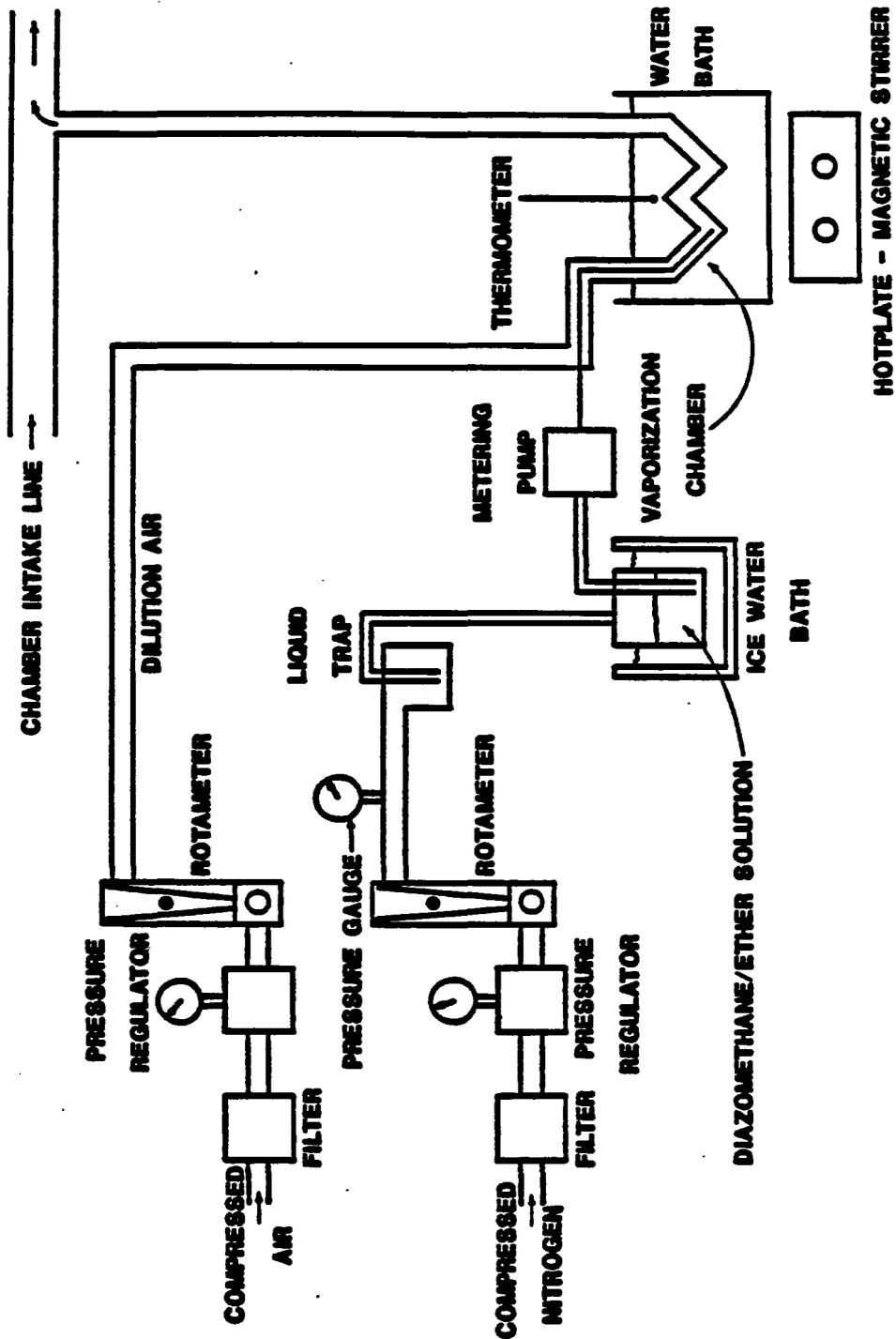


Figure 7. Diazomethane/Ether Vaporization System Used During Second And Third Exposures.

Since significant amounts of diethylether were present in these last two diazomethane atmospheres, the control animals were exposed to atmospheres with similar concentrations of diethylether without the diazomethane.

Aerosol Atmosphere Generation

Ortho-toluidine, 2-aminoethanol, and 2-diethylaminoethanol atmospheres at their maximum vapor phase concentrations did not produce sufficient toxicity. Therefore, higher mass concentrations of these compounds were produced by using the vapor generation system in combination with the ultrasonic nebulization system as shown in Figure 8. The vaporization system was operated under the conditions which had previously produced the highest vapor concentration of a given compound and the ultrasonic nebulizer operated at a pressure of 100 psig. Using the combination of vapor and aerosol generation systems, it was possible to generate atmospheres of sufficient concentration to produce "frank" effects in test animals with 2-aminoethanol and 2-diethylaminoethanol but not with ortho-toluidine.

Three of the test compounds were specified to be delivered as aerosols (ortho-anisidine, para-anisidine and Aroclor-1254) [10,17,18].

Both ortho-anisidine and Aroclor 1254 were aerosolized with a jet nebulizer (De Vilbiss #841) for the first exposure. A single stage inertial impactor was placed in series with the output of this nebulizer to insure that the majority of the aerosol particles would be within the respirable range ($\sim 0.1-10 \mu\text{m}$ equivalent aerodynamic diameter) [11,18]. Dilution air was mixed with the nebulizer output to produce a total flow sufficient to make the impactor function properly (Figure 9). The aerosol passed through an aerosol charge neutralizer (Heat-Systems Inc. #3054) prior to final dilution with the chamber intake line air.

The atmospheres for the second and third exposures of ortho-anisidine and Aroclor 1254 were produced using an ultrasonic nebulizer (Heat-Systems Ultrasonics #501) as shown in Figure 10. The ultrasonic nebulizer has a greater aerosol particle output than the previously used jet nebulizer. It was determined with the aid of a cascade inertial

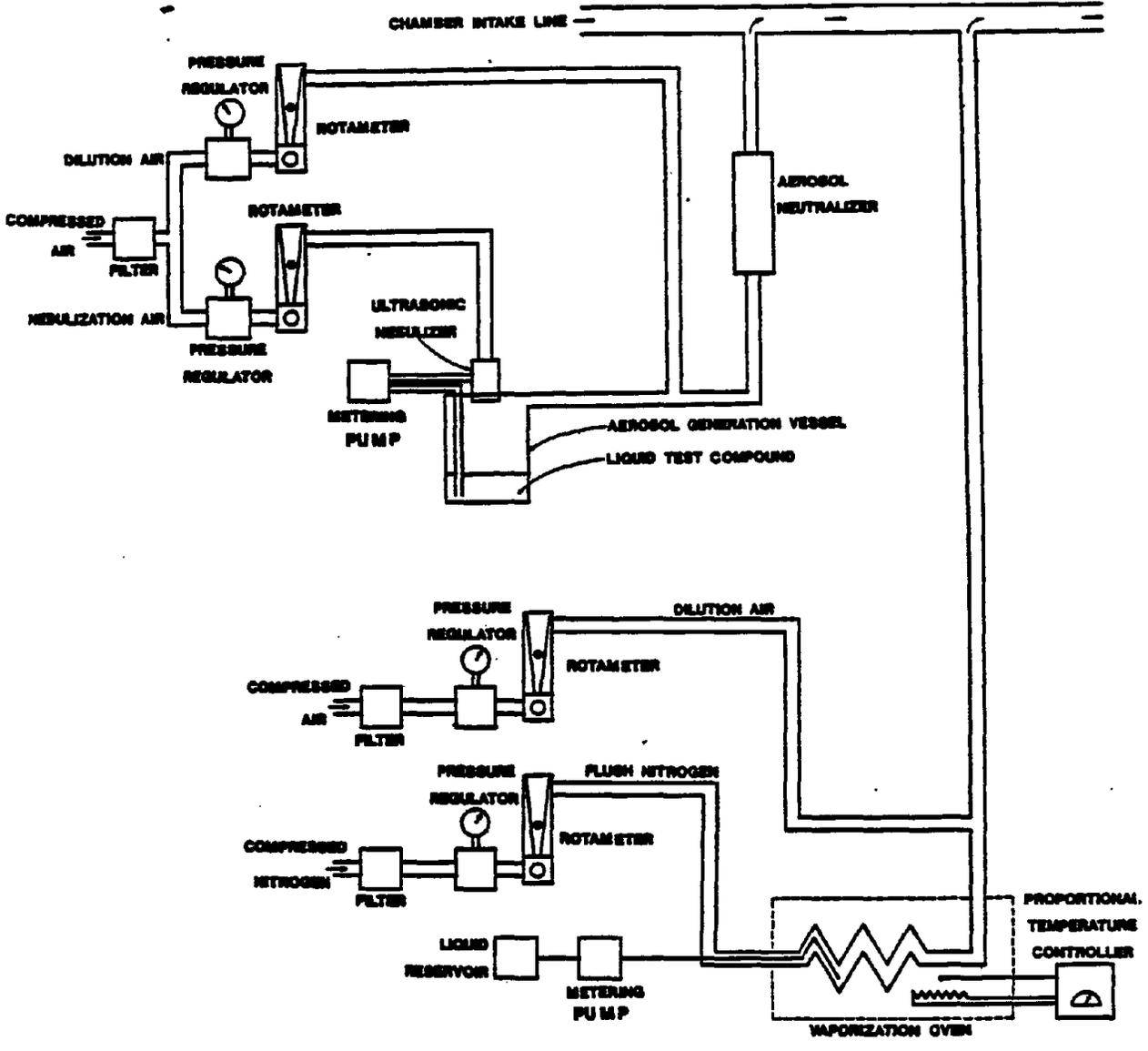


Figure 8. Combination Vapor and Aerosol Generation System. This system was used to produce the higher mass concentrations of 2-amino-ethanol, 2-diethylaminoethanol, ortho-toluidine and ortho-anisidine.

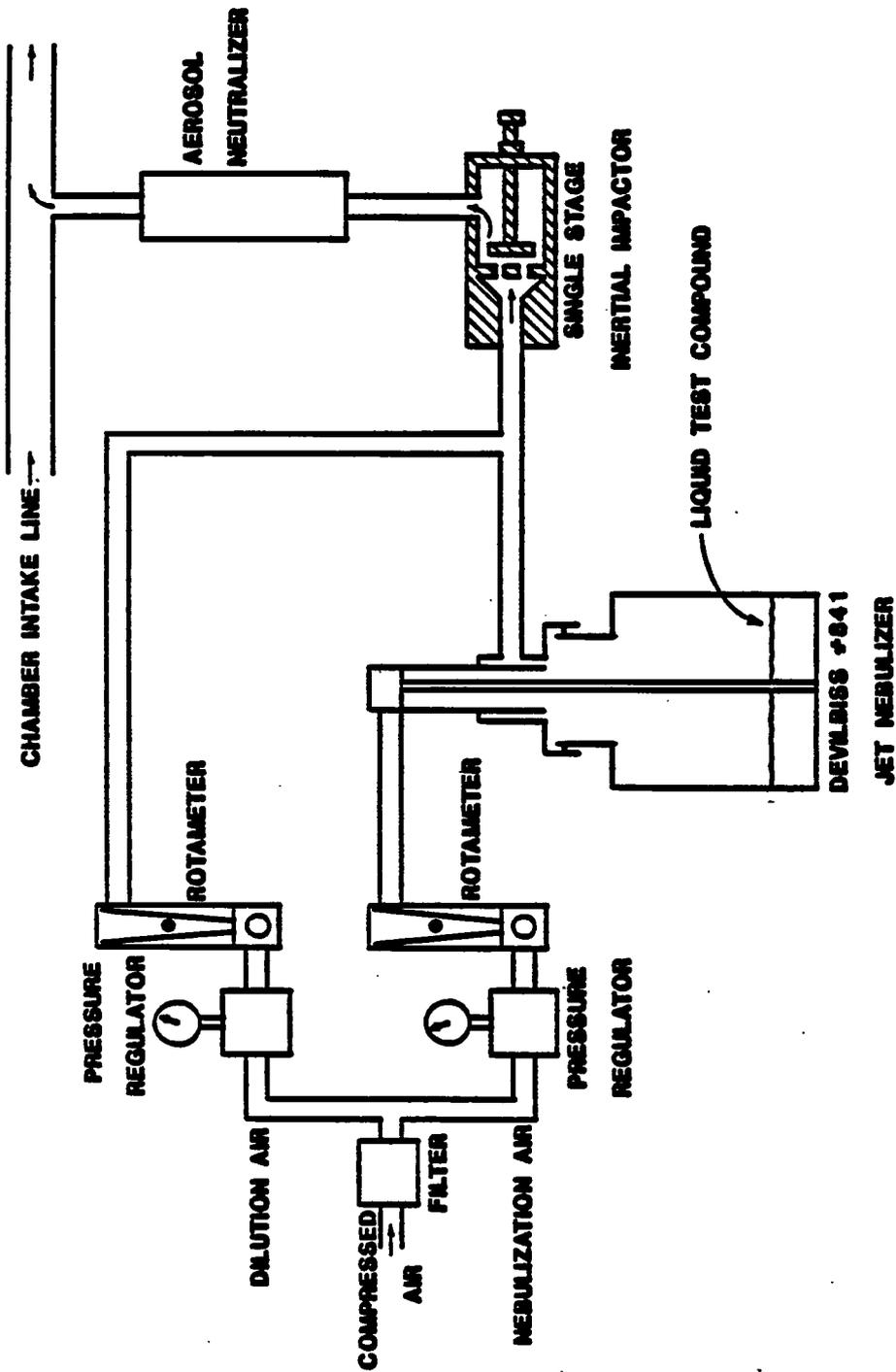


Figure 9. Jet Nebulizer Aerosol Generation System Used During First Exposures Of Ortho-Anisidine And Aroclor 1254.

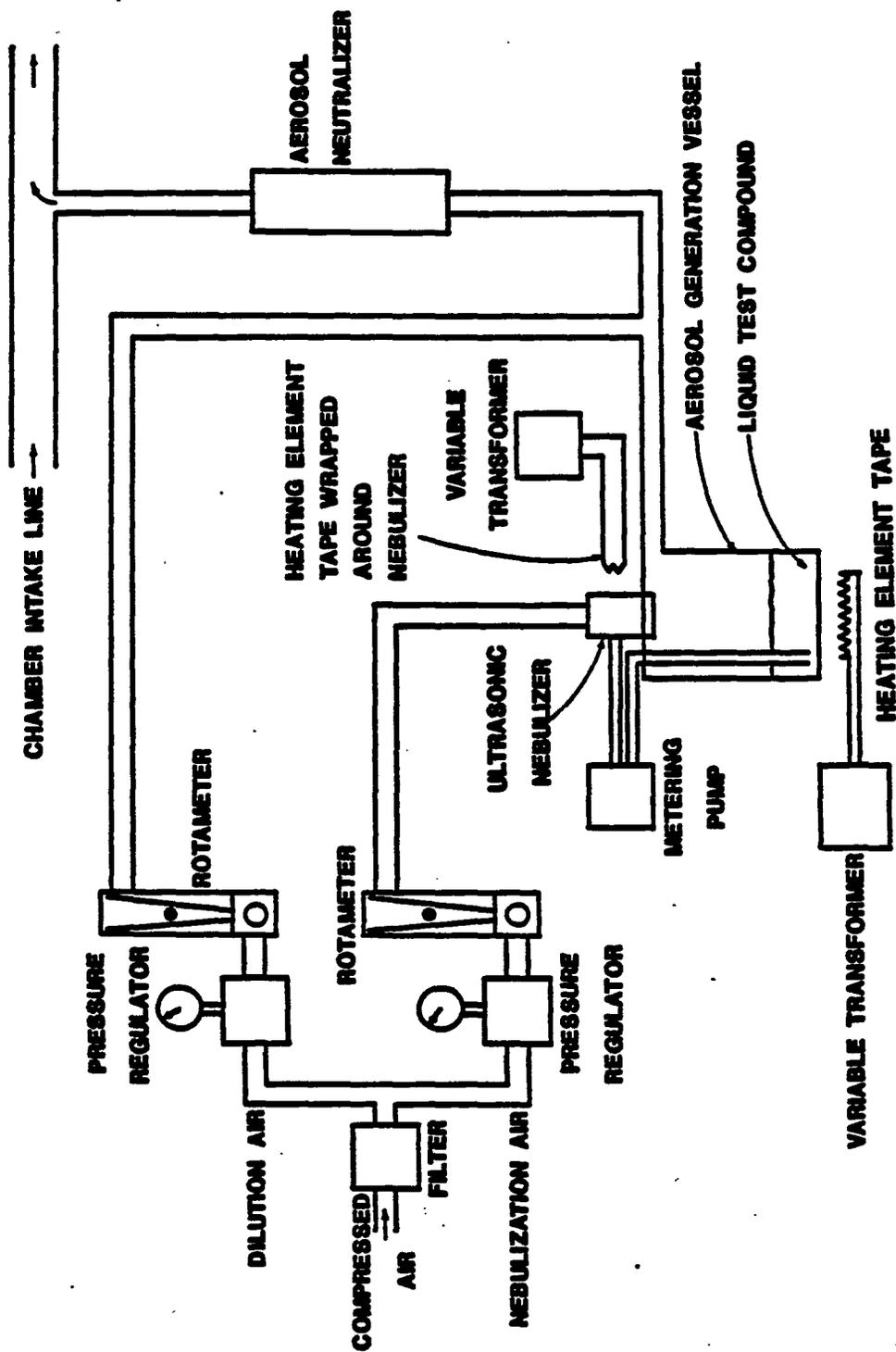


Figure 10. Ultrasonic Nebulizer Aerosol Generation System Used To Produce Second and Third Atmospheres Of Ortho-Anisidine and Aroclor 1254.

impactor that the inertial impactor was unnecessary because the ultrasonic nebulizer produced a majority of its particle output within the respirable size range. For the second and third exposures, the Aroclor 1254 was heated to 90°C in order to reduce its viscosity and allow it to be pumped for delivery to the ultrasonic nebulizer. It was not necessary to heat the ortho-anisidine for nebulization since it was not a viscous liquid at room temperature. In order to maximize the concentration of ortho-anisidine during the third exposure, a combination of the ultrasonic nebulization system and the vaporization system as shown in Figure 8 was used. Generation of a sufficiently high concentration of either Aroclor 1254 or ortho-anisidine to produce "frank" effects was not possible with the equipment available at UBTL.

Para-anisidine is a solid at room temperature (MP 57°C), and the first atmosphere of this compound was generated using a Wright dust feed apparatus (L. Adam, Ltd., #WDF-1) on loan from NIOSH in Cincinnati, Ohio. The solid material was initially pulverized using a mortar and pestle. Further reduction in particle size was accomplished with the use of a cryogenic vibration mill (Spex #6700) cooled with liquid nitrogen. This pulverized material was then sieved with a 250 µm mesh sieve (Tyler #60) and then placed in the Wright dust feed apparatus cylinder. The material was compressed with a force of ~600 psig. The cylinder containing the compressed para-anisidine was attached to the Wright dust feed apparatus and compressed air at 20 psig was used to disperse the material. The gears on the apparatus were arranged such that the cross shaft turned at 2 rpm (gears 72:36:72:36) [19,20]. The output from the dust feed apparatus was connected directly to the aerosol neutralizer as shown in Figure 11.

Due to the relatively low output of the Wright dust feed apparatus, the second and third exposure atmospheres were generated by a different procedure. Solid para-anisidine was placed in a cylindrical stainless steel pressure vessel. This pressure vessel was heated to 90°C by a heating element tape wrapped around the outside of the vessel and connected to a variable transformer. The melted para-anisidine was then fed from

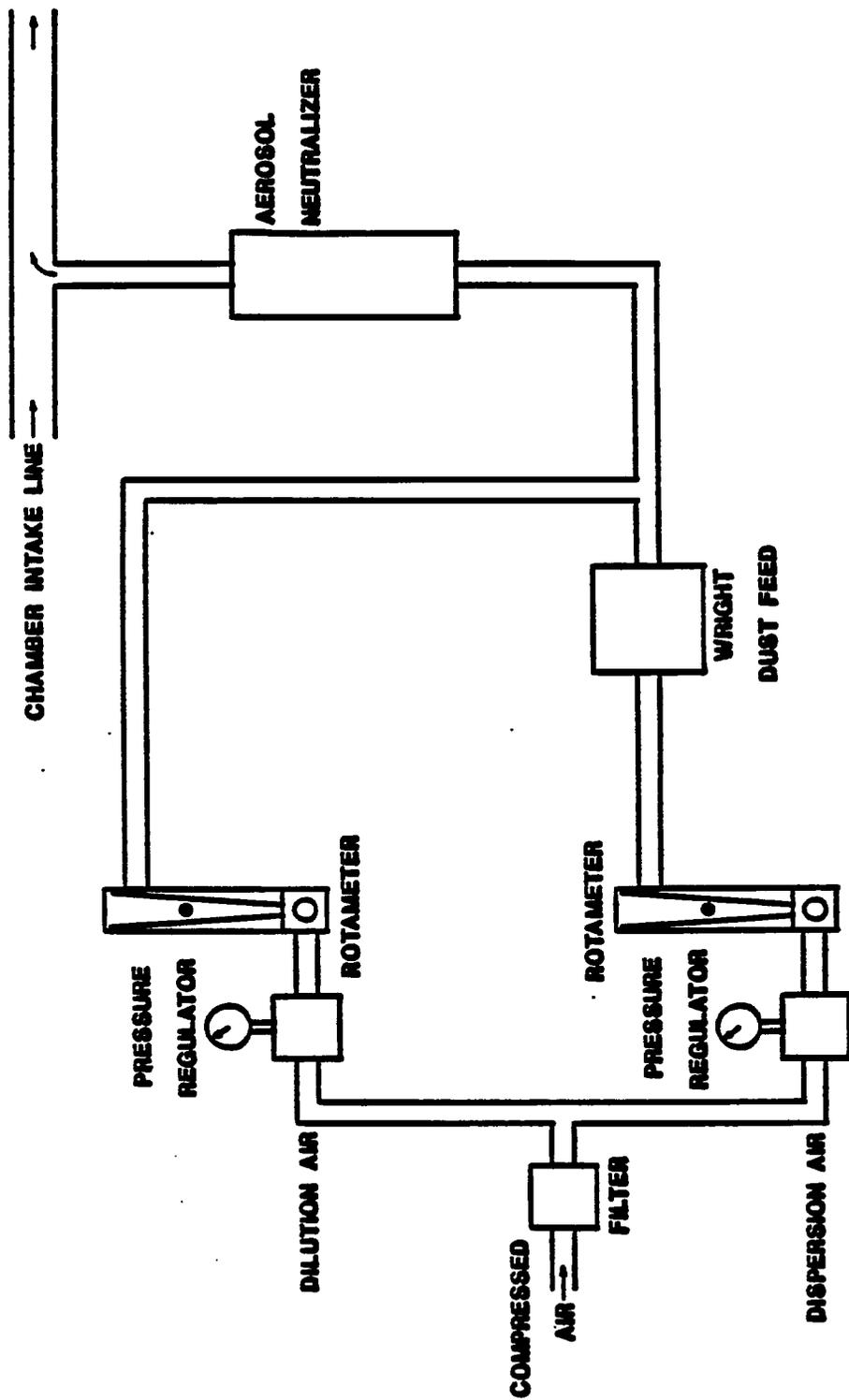


Figure 11. Wright Dust Feed System Used To Generate First Para-Anisidine Atmosphere.

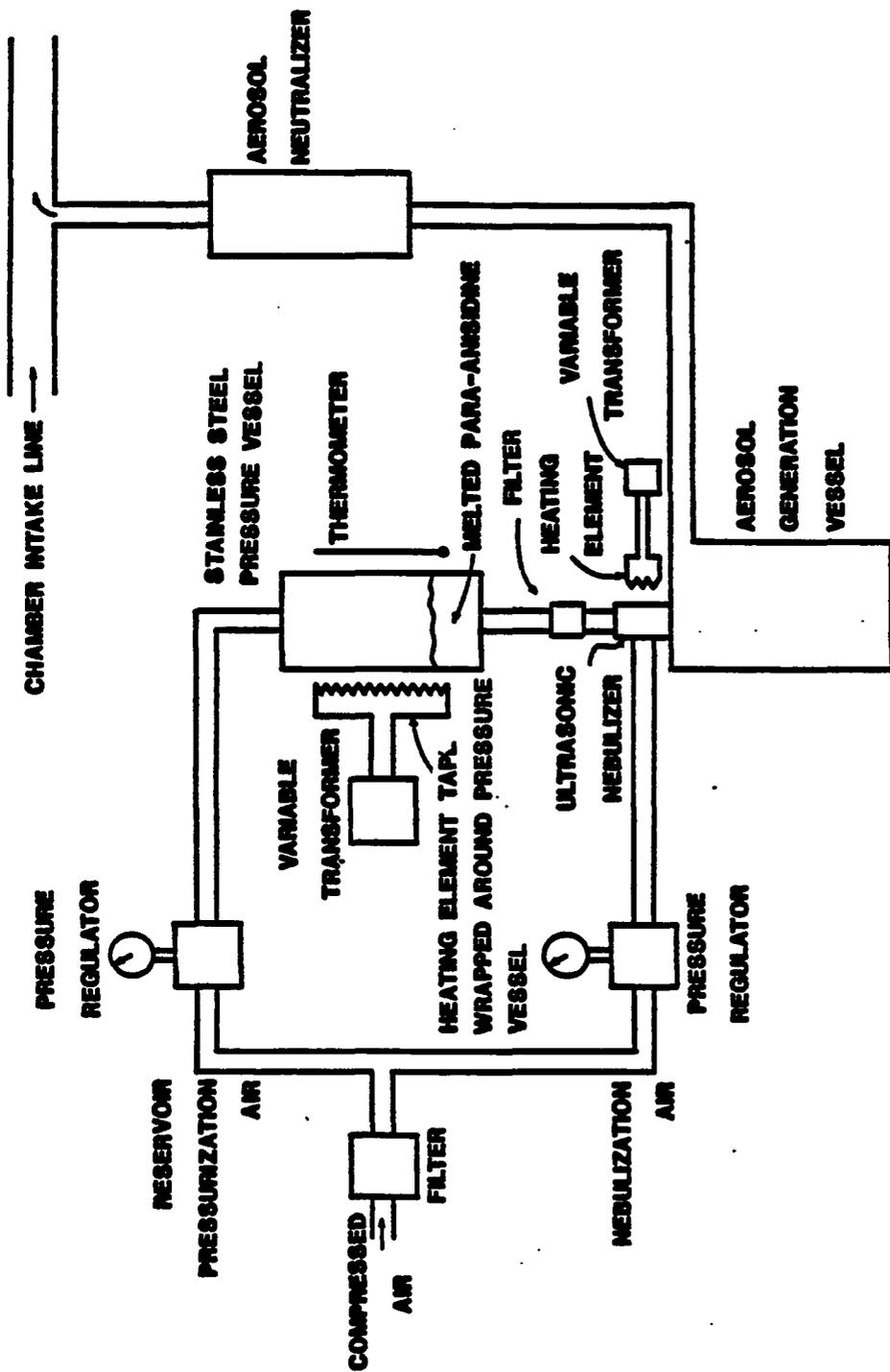


Figure 12. Ultrasonic Nebulizer Aerosol Generation System Used To Produce Second And Third Para-Ansidine Atmospheres.

the pressure vessel through a particle filter into the ultrasonic nebulizer apparatus (Figure 12) under a pressure of 60 psig. The temperature of the filter and nebulizer was maintained at 150°C with a heating tape element wrapped around them. This setup maintained the melted para-anisidine as a liquid until it was aerosolized by the ultrasonic nebulizer which was operated with a compressed air pressure of 100 psig. The comparison of gas chromatographic patterns of the original material and the material that had been nebulized as described did not indicate any change in the composition of the para-anisidine.

A "minimal" or a "frank" effect concentration for para-anisidine was not achievable due to limitations of the equipment available at UBTL. Also, experiment number 30-PA-3 was intended to produce a higher atmospheric concentration than number 29-PA-2, but a buildup of solidified para-anisidine around the nebulizer orifice reduced the efficiency of the nebulizer system thus causing the concentration to drop below that of the previous experiment (29-PA-2).

Sampling of Test Compound Atmospheres

The test compound atmospheres were sampled for subsequent chemical analysis by drawing known volumes of atmosphere through adsorption tubes (SKC Inc. #226-09 or #226-15) or midget impingers (Wheaton #75332) containing an appropriate collection medium (Table 6). The volume of atmosphere sampled was controlled by use of a vacuum sampling system (Figure 13) consisting of a rotameter equipped with a metering valve (Matheson #7632T-W/603), an activated charcoal and silica gel column, a vacuum pressure regulator (Matheson #49), and a laboratory vacuum pump (Sargent Welch #1400). The vacuum sampling system flow (l/min) was calibrated for a given rotameter setting by using a soap film flowmeter (Alltech Associates Inc. #4047) and an electric timer (Precision Scientific #69230). The total volume (l) sampled was calculated by multiplication of the sampling flow (l/min) by the sampling interval (min) [21,22,23].

Preliminary generation and sampling of test atmospheres were conducted prior to the days of formal exposure. During these preliminary experi-

Table 6

Summary of Analytical Methods for IDUJ Atmospheric Analysis

Test Compound	Collection Device*	Collection Medium	Sampling Rate	Amount Collection Medium	Description Solvent	Amount Solvent	Internal Standard	G.C. Column Temp.	Analytical Method**
2-Aminothanol	Impinger	95% Ethanol	0.046-1.18 l/min	15.0 ml	-	-	n-Octano	140°C	FID-DC with 1/4" x 6' glass column, 2% KOH + 10% Carbowax 20 M, 80/100 mesh Chromosorb W-AW or incubation of aliquot with 0.04% ninhydrin in pyridine 870°C for 10 min, then spectrophotometry: DU 417 nm
Nitropropylamine	Impinger	95% Ethanol	0.251-1.09 l/min	15.0 ml	-	-	n-Propanol	40°C	FID-DC with 1/4" x 4' glass column, 3.8 UC-89B, 80/100 mesh on Chromosorb W-HP
2-Diethylamino-ethanol	Impinger	95% Ethanol	0.515-1.20 l/min	15.0 ml	-	-	n-Octano	110°C	FID-DC with 1/4" x 4' glass column, 3.8 UC-89B, 80/100 mesh on Chromosorb W-HP
Ortho-Toluidine	Adsorption Tube	Silica Gel	0.513-1.23 l/min	520 mg	95% Ethanol	1.0 ml	n-Heptano	110°C	FID-DC with 1/4" x 6' glass column, 5% SE 30, 80/100 mesh Chromosorb W-AW-MS
Ortho-Anisidine	Adsorption Tube	Silica Gel	0.519-1.32 l/min	520 mg	95% Ethanol	1.0 ml	n-Octano	140°C	
Para-Anisidine	Adsorption Tube	Silica Gel	0.516-1.52 l/min	520 mg	95% Ethanol	1.0 ml	o-Toluidine	140°C	
Scitinin	Impinger	6% HCl ₂ in 6N HCl	0.058-0.084 l/min	15.0 ml	-	-	-	-	Oxidation with ceric sulfate, extraction with isopropyl ether, reaction with rhodamine B, then spectrophotometry: DU 545 nm
Phosgene	Impinger	Phosgene collection reagent**	0.518 l/min	15.0 ml	-	-	-	-	Transfer collection reagent to cassettes then spectrophotometry: DU 475 nm
Diazomethane	Impinger	0.1N NaOH	0.85-1.01 l/min	15.0 ml	-	-	-	-	Acidify with HNO ₃ and determine Cl ⁻ with chloride ion electrode
Diazomethane	Impinger	p-Nitrobenzoic acid in xylene	0.048-0.183 l/min	15.0 ml	-	-	Hexachlorobenzene	150°C	ECI-DC with 1/4" x 4' glass column, 3.8% UC-89B, 80/100 mesh Chromosorb W-HP
Ethyl ether	Adsorption Tube	Benzoic acid in xylene	0.516 l/min	15.0 ml	-	-	n-Octano	200°C	FID-DC with 1/8" x 6' S.S., 10% Carbowax 20M+2% KOH on 80/100 mesh Chromosorb W-AW with 1/8" x 6' S.S., 5% FFAM on 80/100 mesh Chromosorb W-AW
Arcelar 1254	Adsorption Tube	Activated charcoal	0.030-1.45 l/min	400 mg	Ethyl Acetate	2.0 ml	-	60°	FID-DC with 1/4" x 6' glass column, 5% SE 30, 80/100 mesh Chromosorb W-AW-MS
	Adsorption Tube	Pierisil	0.088-0.199 l/min	100 mg	Hexane	1.0 ml	Hexa-chlorobenzene	200°C	ECI-DC 1/4" x 4' glass column, 3.8% UC-89B, 80/100 mesh Chromosorb W-HP

*The impinger impingers connected in series, each containing 15.0 ml of collection medium or adsorption tubes with dual sections were used for collecting of all samples.

**0.25% 4(4'-nitrobenzyl) pyridine and 0.5% phenylbenzylamine in diethylphthalate.

***GC conditions: ECI @ 200°C, injection port @ 210°C and 5% IZL in argon carrier @ 90 ml/min. FID @ 260°C, injection port @ 210°C and boiling carrier @ 30 ml/min.

ments, small groups of animals were exposed to atmospheres to obtain an indication of what effects would occur during the formal exposures. Also, potential problems with generation, sampling and analysis of test atmospheres were determined and attempts were made to correct those problems prior to performing the formal exposures.

After the test animals had been placed in the chamber for a formal exposure, three approximately 10 minute samples of the atmosphere were collected with either adsorption tubes or midget impingers. When appropriate, a cascade impactor sample was also taken during the exposure.

Adsorption tube samples were collected by the following procedure. The ends of an adsorption tube were scored, removed and the back-up section end was connected to the hose of the vacuum sampling system (Figure 13). The rotameter was adjusted to a previously determined setting for each tube, as necessary, prior to inserting the adsorption tube into the chamber to a point just above the animal cages. Upon removal of an adsorption tube from the chamber, the end was sealed with a polyethylene cap and the sampling interval was noted [5,23].

Samples of the more volatile compounds (phosgene, diazomethane, stibine and diisopropylamine) were collected with two midget impingers in series connected to a glass tube extending into the chamber above the animal cages. However, to improve the sampling ability of the less volatile test compounds (2-aminoethanol, 2-diethylaminoethanol), the impingers were placed inside the chamber on a rack and connected to a vacuum sampling manifold. This arrangement allowed the impingers to sample the atmosphere directly and the test compound which condensed on the inside of the inlet tube to be readily rinsed into the impinger for analysis [23].

The collection efficiency for the first section of a given sampling system and compound was estimated by dividing the amount of material found in the first compartment by the total amount of compound found in both the first and second compartments. The overall collection efficiency was estimated by assuming the same collection efficiency for both collection compartments. Then the collection efficiency for the first compart-

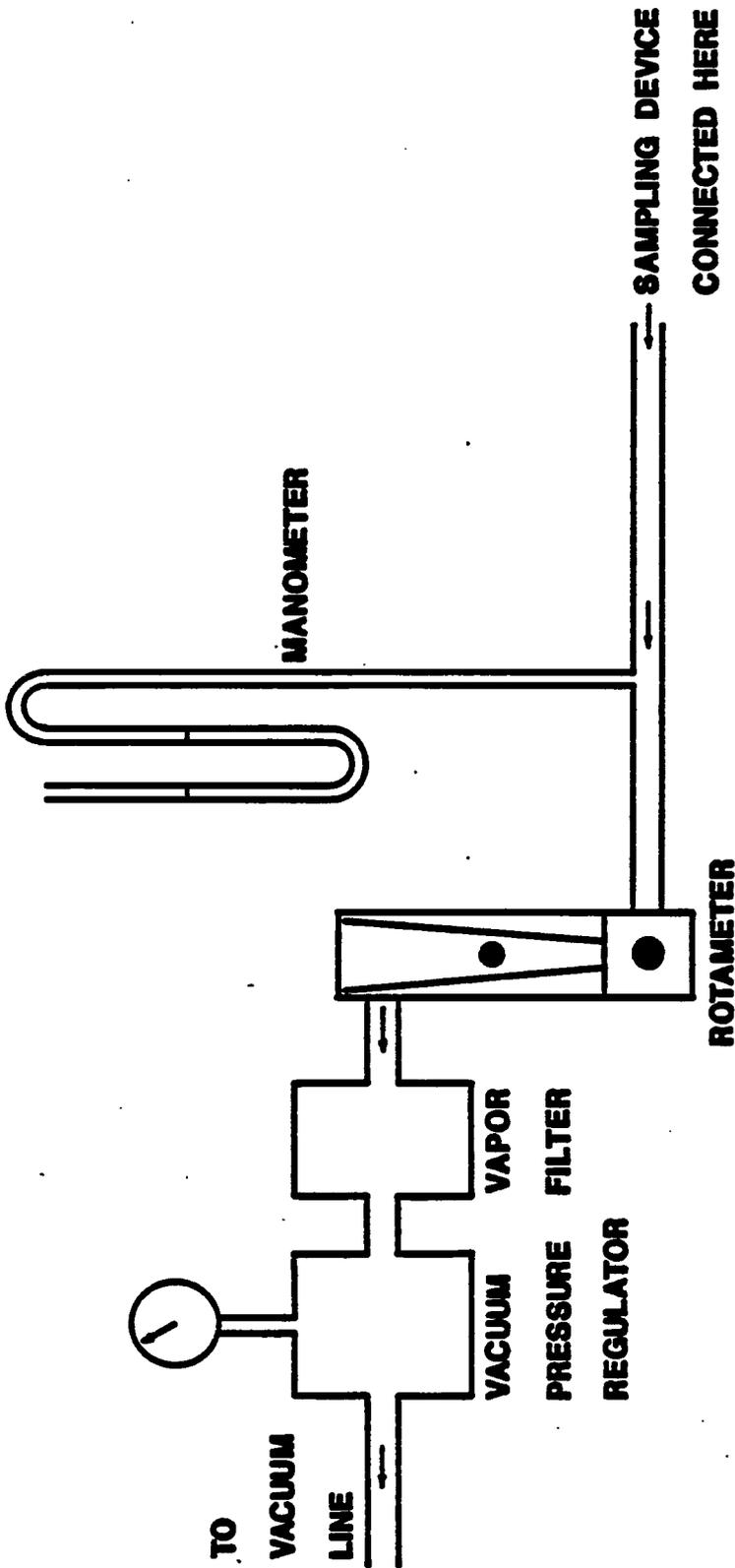


Figure 13. Vacuum Sampling System Used To Operate Test Atmosphere Sampling Devices.

ment was subtracted from 100%, and the difference was multiplied by the collection efficiency of the first compartment, and finally this product was added to the collection efficiency of the first compartment to yield the overall collection efficiency for that sampling system. The overall collection efficiency for the sampling system of all compounds was at least 99.5%, except for ethyl ether which was 98.3%.

When appropriate, a HNU #201 continuous gas monitor was used to monitor changes in the test atmosphere concentration before and during the animal exposures. However, the HNU #201 monitor was not a very satisfactory monitoring device for some compounds due to its lack of sensitivity for the compound, due to a prolonged response to residual test compound, or because an aerosol was present [24].

Those atmospheres which were produced as aerosols were sampled with a cascade impactor (Sandia Research Corporation, 5.0 l/min nominal sampling flow) in order to estimate the aerosol size distribution and verify that the majority of the particles were within the "respirable" size range. The cascade inertial impactor was a larger version of one designed by T. Mercer [25,26] and consisted of seven collection stages each designed to accept a glass coverslip (22 mm diameter) upon which the test material particles were collected. After a sample had been collected, the coverslip of each stage and the final filter were placed in a separate vial and eluted with an appropriate solvent. The amount of material collected on each stage was determined by the same chemical analysis that was used to determine the atmosphere concentration.

The aerodynamic resistance cutoff diameter for each impactor stage was estimated by use of the following equation [26,27]:

$$\text{ECD } (\mu\text{m}) = 1.257 \times 10^3 \sqrt{W^3/F}$$

where W = jet diameter in cm, F = volumetric flow in cm^3/min , and ECD = aerodynamic resistance cutoff diameter in μm . The cumulative percent of the amount of material found on each stage was plotted against the aerodynamic resistance cutoff diameter for each stage using logarithmic cumulative probability paper to determine if the aerosol particles were log-normally distributed. From this plot, the aerodynamic resistance

diameter value corresponding to the 50% cumulative probability value was taken as the mass median diameter. The geometric standard deviation of the aerosol particle distribution was estimated by dividing the aerodynamic resistance diameter at 84% cumulative probability by the aerodynamic resistance diameter at 50% cumulative probability (mass median diameter) [28,29].

Chemical Analysis of Atmospheres

As shown in Table 6, a variety of chemical analytical methods were employed to determine the concentrations of the test compound atmospheres. Gas chromatography was used for the majority of analyses, while colorimetry or a specific ion electrode was used for the other analyses.

Calibration Standards

High purity chemicals were used in the preparation of calibration standards for each analysis. When compounds were needed at low levels, were viscous liquids, or were solids, stock solutions were prepared by weighing out the compounds in volumetric flasks with subsequent dilution in an appropriate solvent. Standards of non-viscous liquid compounds at relatively high concentrations were prepared with microliter syringes rather than by weighing. Standards for the gaseous compounds were prepared from secondary analytes which were the resultant products of the reaction of the gaseous compound with materials present in the collection medium. Standards for the solid or liquid compounds were prepared by the addition of the analyte directly to the collection medium (activated charcoal, silica gel, ethanol) over a range such that atmosphere samples were bracketed by standards [30]. The calibration standard samples were treated in the same manner as the test atmosphere samples.

Diisopropylamine and 2-Diethylaminoethanol

Impinger samples of diisopropylamine on 2-diethylaminoethanol in ethanol were transferred to volumetric flasks, an aliquot of internal standard solution was added, and the samples were diluted to volume with 95% ethanol. The primary and back-up impingers were treated as separate samples to check for collection efficiency [31,32].

Duplicate 5.0 μ l aliquots of each sample or standard, along with 2.0 μ l flush solvent, were injected into a gas chromatograph equipped with a flame ionization detector (Hewlett-Packard #5750B). The gas chromatographic conditions are listed in Table 6 for each test compound along with other sampling and analysis information. The peak areas were quantitated by a digital electronic integration system (Hewlett-Packard #3351A). Comparison of the peak area ratios (test compound/internal standard) of the atmosphere samples with those of the calibration standards was used for quantitation of the test compound [33,34,35]. The total amount of test compound found per sample was divided by the total volume of atmosphere sampled to determine the concentration of test compound in the atmosphere.

2-Aminoethanol

Impinger samples from the first 2-aminoethanol exposure were analyzed by the similar method as described above for diisopropylamine and 2-diethylaminoethanol. However, due to intermittent problems with 2-aminoethanol interacting with components of the gas chromatograph, the method of analysis described below was used on subsequent analyses of 2-aminoethanol.

Impinger samples of 2-aminoethanol in 95% ethanol were transferred to volumetric flasks and diluted to 25.0 ml with 95% ethanol. An aliquot of each sample was then further diluted with 95% ethanol as necessary. Duplicate 5.00 ml aliquots of the diluted samples or standards containing a total of 0 to 100 μ g 2-aminoethanol were transferred into 25 x 150 mm test tubes, and 10.0 ml of 0.04% ninhydrin in anhydrous pyridine was added with thorough mixing. All samples and standards were simultaneously placed in a water bath at 75°C and incubated for 10 minutes. After the incubation, all samples and standards were immediately cooled to room temperature with a cold tap water bath and then transferred to cuvettes. The spectrophotometer (Coleman #54B) was set at 417 nm and adjusted to 0.000 absorbance with a cuvette containing a reagent blank. The absorbance of each sample and standard was then measured [36]. Comparison of the absorbance of samples with that of standards was used

to quantitate the amount of 2-aminoethanol present in each sample. The total 2-aminoethanol found per sample was divided by the total volume of atmosphere sampled to determine the concentration of 2-aminoethanol in the atmosphere.

Ortho-Toluidine, Para-Anisidine and Ortho-Anisidine

The contents of silica gel adsorption tubes which had been used to sample atmospheres containing ortho-toluidine, para-anisidine or ortho-anisidine were placed in septum capped vials (Wheaton Scientific #223713 and 224222). The primary and back-up sections were kept separate and collection efficiencies were determined to be 100% for ortho-toluidine, 99.7% for ortho-anisidine and 99.4% for para-anisidine. Standards for their analysis were prepared by adding various amounts of test compound to adsorption tubes. Atmosphere samples and standards were desorbed in 1.00 ml of 95% ethanol containing an internal standard [37,38,39,40,41].

Desorbed samples and standards were analyzed by gas chromatography procedures as described previously for diisopropylamine and 2-diethylaminoethanol. Since the desorption efficiency of these compounds in 95% ethanol is concentration dependent, a plot of standards prepared by addition of material to silica gel with subsequent desorption was used for quantitation of samples.

Aroclor-1254

The contents of florisil adsorption tubes provided by NIOSH which had been used to sample Aroclor-1254 atmospheres were separated into primary and back-up sections and transferred to separate vials. Iso-octane was added to desorb the Aroclor-1254, and after 30 minutes aliquots of the desorption solution were transferred to other vials and further diluted with iso-octane containing an internal standard. The mean desorption efficiency of Aroclor 1254 from the florisil into iso-octane was 96.6%. Calibration standards were prepared by addition of various amounts of stock solution of Aroclor-1254 in iso-octane to florisil adsorption tubes. After several hours, these standards were then processed in the same manner as the atmosphere samples [42,43].

Duplicate 5.0 μ l aliquots of each sample or standard along with 2.0 μ l of flush solvent were injected into a gas chromatograph equipped with an electron capture detector (Hewlett-Packard #5750B). The detector responses were quantitated by peak area or peak height ratios. Comparison of the responses of atmosphere samples with those of standards was used to determine the amount of Aroclor-1254 per sample. The concentration of Aroclor-1254 in each atmosphere sample was determined by dividing the total Aroclor-1254 per sample by the total volume of atmosphere sampled.

Stibine

After collection, the contents of each impinger were carefully transferred to 25.0 ml volumetric flasks with several rinsings. The samples were diluted to volume with 6% HgCl_2 in 6N HCl, and a 5.00 ml aliquot of this solution was placed in a 50 ml volumetric flask and diluted to volume with 6N HCl. Calibration standards were prepared in the same manner from a stock solution of potassium antimony tartrate in 6% HgCl_2 in 6N HCl such that 5.00 ml aliquots contained a range from 0 to 25 μ g antimony.

For analysis, duplicate 5.00 ml aliquots of each sample and each calibration standard were added to 25 x 150 mm culture tubes with Teflon lined screw caps. The following step required precise timing with a stopwatch and was performed individually on each sample. With an automatic pipette, 0.50 ml of 0.1N ceric sulfate was added to the sample, and the sample was vigorously stirred with a vortex mixer and allowed to stand for 1.0 minute, after which 0.2 ml of 1% aqueous hydroxylamine hydrochloride was added to quench the oxidation reaction. A small stream of compressed air was bubbled through the sample for about 15-20 seconds to expel any residual chlorine. Twenty milliliters of isopropyl ether was added to the sample and thoroughly shaken with a vortex mixer for 1.0 minute in order to extract the oxidized antimony into the ethereal phase. Each sample in a given analysis run was individually processed in this manner and allowed to stand until all other samples were processed.

Finally, 10 ml of 0.01% rhodamine B in 0.5N HCl was added to all samples, and each sample was thoroughly shaken for 15 seconds, and the

upper ethereal layer was poured into a cuvette. The absorbance relative to a reagent blank was then determined for each sample and calibration standard with a spectrophotometer (Coleman #54B) at 565 nm [13,44,45, 46,47,48].

The absorbance values for calibration standards for each sample were compared to determine the equivalent amount to stibine per 5.00 ml aliquot. The total amount of stibine collected was then found by multiplication by the appropriate dilution factor. The atmospheric concentration was determined by division of the total test compound found per sample by the total volume sampled.

Phosgene

Samples from the first exposure of phosgene were collected with impingers containing 15.0 ml of 0.25% 4(p-nitrobenzyl) pyridine and 0.5% phenylbenzylamine dissolved in diethylphthalate. The collection solution was transferred to a cuvette, and the absorbance of each sample was measured with a spectrophotometer (Coleman 54B) relative to a reagent blank at 475 nm within an hour after the exposure [47,48,49]. Calibration standards for this method were prepared by addition of aliquots of a stock solution of phosgene in diethylphthate to 15.0 ml aliquots of the collection reagent. The concentration of phosgene in the stock solution was determined by analysis of hydrolyzed aliquots of the stock solution for chloride with an argometric method [50].

Due to the complexity of calibrating the above analytical procedure, the second and third exposures were analyzed by a different method. Samples were collected with impingers containing 0.1N sodium hydroxide (aqueous). After collection, samples were diluted to a total volume of 15.0 ml and then adjusted to pH=4 with concentrated nitric acid. Standards were prepared with sodium chloride in 0.1N sodium hydroxide and adjusted to pH=4 with concentrated nitric acid. The potential difference between a chloride ion selective electrode (Orion #941700) and a double junction reference electrode (Orion #900200) was measured with a millivolt meter (Corning #130 pH meter) for each calibration standard and each atmospheric sample [51]. The chloride concentration

in atmospheric samples was determined by comparison of their potential difference with those of the standards. By use of a conversion factor and the volume of atmosphere sampled, the concentration of phosgene in the exposure atmosphere sample was calculated as with other compounds.

Diazomethane

Samples of diazomethane atmosphere were collected in a solution of either p-nitrobenzoic acid (10% saturated) or benzoic acid (5 mg/ml) dissolved in xylene. The benzoic acid was used for collection of high concentration samples and p-nitrobenzoic acid was used for collection of low concentration samples. In both cases, the methyl ester of the acid was formed by the reaction of the acid with diazomethane in the aliquot of the atmosphere sampled. The p-nitrobenzoate methyl ester was analyzed by electron capture detector gas chromatography, and the benzoate methyl ester was analyzed by flame ionization detector gas chromatography [52,53,54].

Impinger samples taken from test atmospheres were transferred to volumetric flasks, an internal standard solution was added and the samples were diluted to volume with xylene. Duplicate 5.0 μ l aliquots of samples and standards were injected into a gas chromatograph (Hewlett-Packard 5750B). Comparison of the peak area ratios of the samples with those of the calibration standards was used to quantitate the amount of methyl ester present. Multiplication of the amount of methyl ester found by the appropriate dilution factor and by a conversion factor gave the total amount of diazomethane collected. Division of the total amount of diazomethane collected by the total volume of atmosphere sampled gave the concentration of diazomethane in the atmosphere sampled.

As a preliminary check on the above-mentioned sampling and analysis methods for low levels of diazomethane, an ethereal solution of diazomethane was prepared from Diazald as prescribed by the Aldrich Chemical Company. Several sets of dual impingers connected in series containing 15.0 ml 10% saturated p-nitrobenzoic acid in xylene were set up with a sampling rate of 0.150 l/min. A 25.0 μ l aliquot of the diazomethane/ether solution was carefully added to the inlet port of each primary impinger,

and air was passed through the impinger sets for five minutes, thus total volume of 0.750 liters was swept over the diazomethane/ether solution and through the impinger sampling medium. To serve as control samples, 25.0 μ l aliquots of the diazomethane/ether solution were also added to each of several vials containing 15.0 ml of the collection medium. Analysis of the samples by Ni⁶³ electron capture detector gas chromatography revealed that the levels of methyl p-nitrobenzoate in the primary impinger samples were within 5% of those found in the vials to which the diazomethane/ether solution had been added directly. Also, no methyl p-nitrobenzoate was detectable in the backup impinger samples. Thus the analytical method appeared to be working satisfactorily, and an approximately 1000-fold increase in the sensitivity of the analysis for diazomethane was achieved by using the p-nitrobenzoic acid method over those employing benzoic acid or octonoic acid [52,53]. This method allowed the quantitation of low levels of diazomethane with a sampling time of approximately ten minutes as required by this contract.

Stibine, phosgene and diazomethane are gases, and the analytical techniques described were calibrated by weighing out aliquots of secondary standards rather than by weighing out aliquots of original gaseous compounds as was done with the solid and liquid compounds. These secondary standards were the compounds produced by the reaction of the test compound with the collection medium when a given gaseous atmosphere was sampled. As a check on the analytical methods for the atmospheres generated from the gases, the Project Officer requested the comparison spectrophotometric recordings of the absorbance versus wavelength for both test atmospheric samples and analytical calibration standards of stibine and phosgene be made under the same conditions. Gas chromatographic recordings of the diazomethane calibration standard and a diazomethane test atmosphere sample were also made under the same conditions for comparison. In all three cases, the responses of the analytical method to both calibration standards and test atmosphere samples were essentially the same. The phosgene concentration was also determined by collection in 0.1 N NaOH with subsequent analysis of the chloride hydrolysis product by ion selective

electrode methodology. In this case, the response of the electrode appeared to be the same for both calibration standards and test atmospheric samples.*

The chemical analyses provided the mass of material collected (mg or μg) from a given sample volume (l) of a test atmosphere. Thus, the primary analysis data are in mg/l or $\mu\text{g/l}$, and the parts per million ratio values (ppm) were calculated by multiplying the mg/l or $\mu\text{g/l}$ value by an appropriate conversion factor. All values of concentration were rounded to three significant figures and then the means, standard deviations, and coefficients of variation were calculated and rounded to three significant digits. Some differences in the coefficients of variation between the mg/l and ppm concentrations for some experiments were observed and are due to round off error.

The results of chemical analysis of each test compound atmosphere are listed in the Results section of this report.

Project Safety

Due to the potential hazards associated with the compounds studied, measures were taken to insure the safety of participating personnel [55,56,57].

When transfer of test compounds from shipping containers to smaller containers was necessary, such transfer was done in a fume hood. Safety glasses, rubber gloves and a plastic apron were worn by personnel during those transfer operations to reduce exposure to compounds.

A large rectangular plastic cabinet was constructed to house all apparatus needed to generate a given test atmosphere. The enclosure prevented the accumulation of test compound that might escape from the generation system.

When animals were inserted or removed from the exposure chamber, some test compound atmosphere would escape from the chamber. Thus, a plastic tent was constructed and placed around the drawer area of the chamber to prevent contamination of the room around the chamber.

*Letter #78E490 dated September 6, 1978, to Richard W. Niemeier, NIOSH, from William G. Yates and Neil H. Price, UBTL.

As additional precautions, hose-supplied compressed air respirators were worn during inhalation chamber operation and gloves were worn when handling the test animals after exposure.

Procurement and Handling of Test Animals

UBTL procured Hartley albino guinea pigs from Buckberg Lab Animals, Tomkins Cove, New York and Sprague-Dawley rats from Talonic Farms, German Town, New York. All animals were shipped by air carrier and checked upon arrival for normalcy before being appropriately caged. All incoming animals were isolated in a room separate from the exposed animals for a period of two weeks to check for latent health problems and to condition them to the UBTL environment.

The animal cages were cleaned and bedding was changed twice weekly. All animals were caged separately during and after exposure. Both food and water were available to all animals continually except during the inhalation exposure.

Extra animals were procured in each shipment to allow for animal deaths for use in preliminary exposures, and to increase the probability of having all animals within the weight range limits specified. The upper and lower weight range limits specified in the contract were expanded by ten grams after consultation with the Project Officer. The animal weight ranges used were: male rats 200-230 g, female rats 180-210 g, male and female guinea pigs 200-250 g.

Exposure of Animals to Test Compound Atmospheres

Four, multicompartement stainless steel wire mesh cages, having ten separate compartments each, were used to house the animals during an inhalation exposure. Twenty animals were test animals and twenty were controls. The animals exposed to a given atmosphere consisted of five male and five female rats placed alternately in one multicompartement cage, and five male and five female guinea pigs also placed alternately in a different multicompartement cage. The test chamber was equipped with a sliding drawer system which allowed all 20 test animals to be concurrently placed in the inhalation chamber (see Figures 14 and 15). A similar group of control animals was placed in an inhalation chamber having similar airflow, but without test compound atmosphere.

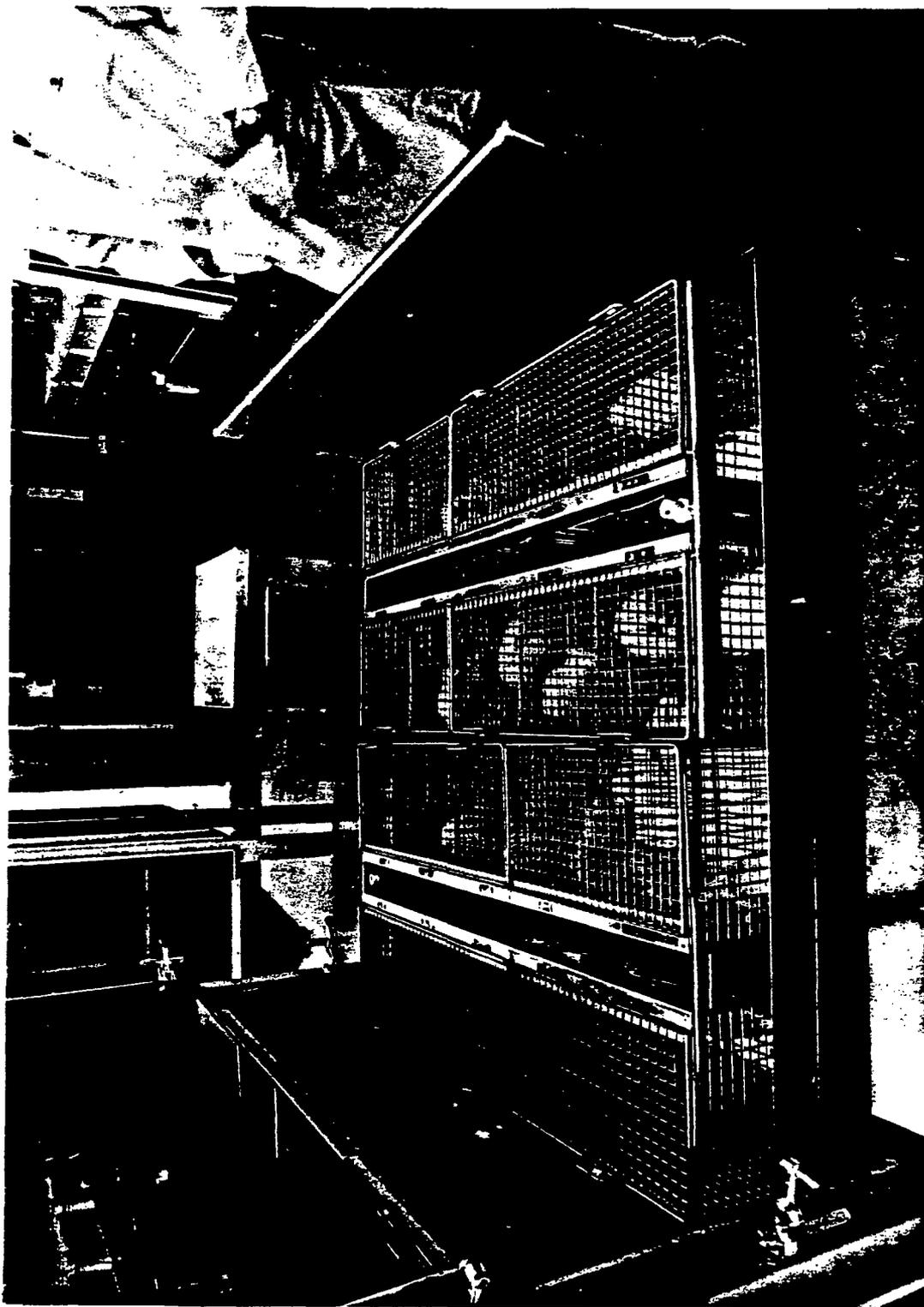


Figure 14. Test Compound Inhalation Chamber. The drawer is open and the test animals are in their individual exposure cages.

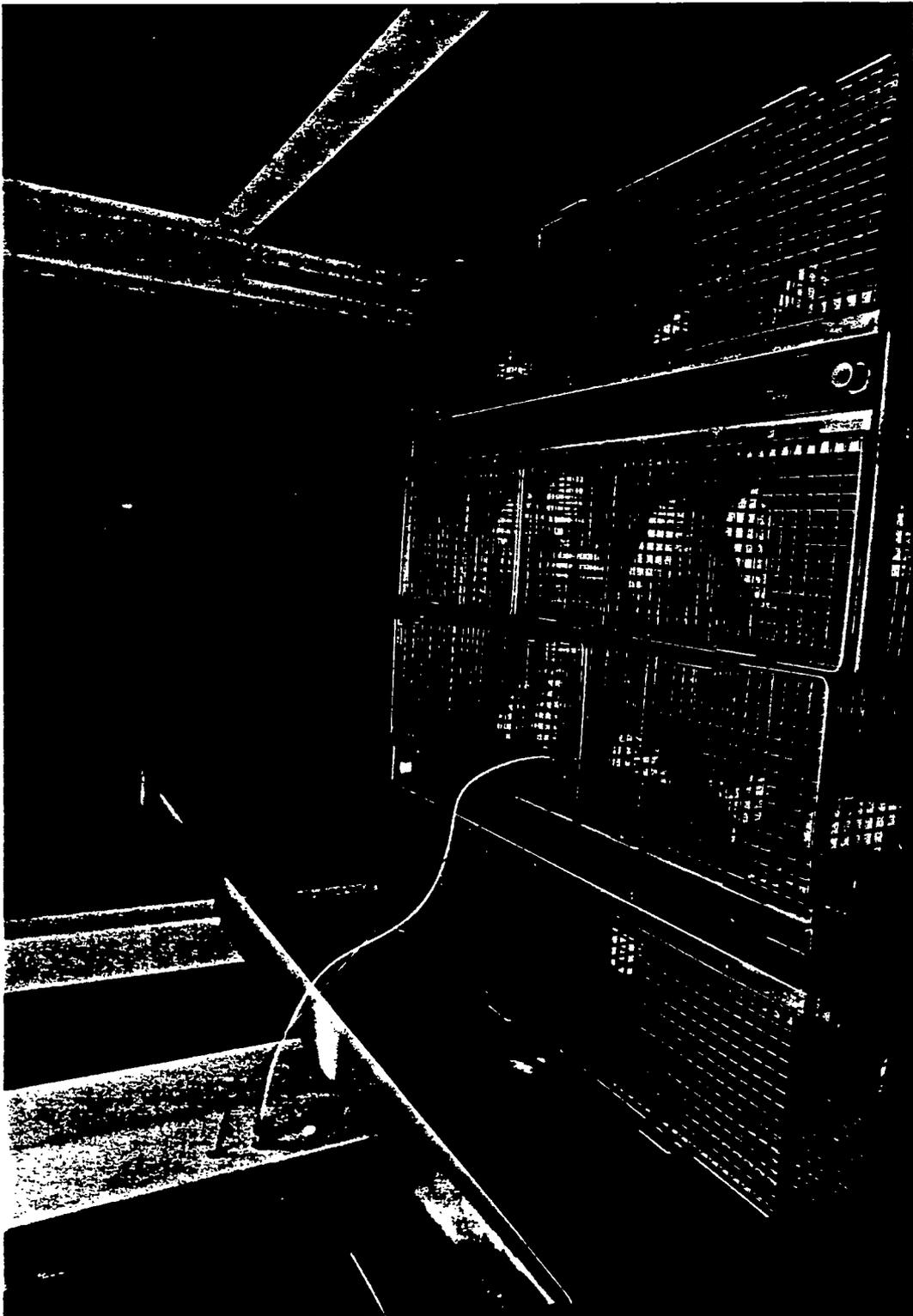


Figure 15. Test Compound Inhalation Chamber. The drawer is closed and the test animals are in individual cages within the test chamber.

After the animals had been placed in the exposure chambers, they were observed continuously during the 30 minute exposure interval and observation notes were recorded on data sheets. The animal observation data are summarized in Table 2 and are detailed in the Results section of this report.

At the end of the 30 minute exposure interval, the animals were immediately removed from the chambers and examined for signs of toxicity by observers. Later they were transferred to an animal holding room where they were observed and weighed before being placed in individual cages for the post-exposure observation period (see Figure 16).

The day of animal exposure was denoted as Day #1, and the day of animal necropsy was denoted as Day #15.

Weighing and Necropsy of Animals

In order to have an approximately even distribution of test animals between test and control groups with respect to weight, the following procedure, designed by John A. Burkart, Ph.D., UBTL Biostatistician, was used on the day prior to animal exposure. At least ten animals of a given species and sex were weighed (example, 13 male rats). Next, the body weights of those ten animals having body weights nearest the mean of the weight range were ranked in pairs by decreasing weight. One animal of each pair was randomly selected to serve as a control, and the other member of the pair served as a test animal. Thus, each test animal had a corresponding control animal of similar weight. The process was repeated until all four groups of animals had been randomized with respect to weight. At this time, each test animal was assigned a number which corresponded to the inhalation chamber multicompartiment cage section in which it would be exposed. This number also served as an identification number for a given animal throughout the remaining data gathering processes, as shown below:

Coding:	(Expt. #)	(Species)	(Usage)	(Animal Cage #) in Group	(Sex)
Example:	1	R	C	1	M
Explanation:	1st Expt.	Rat	Control	Rat #1 of Control Group	Male

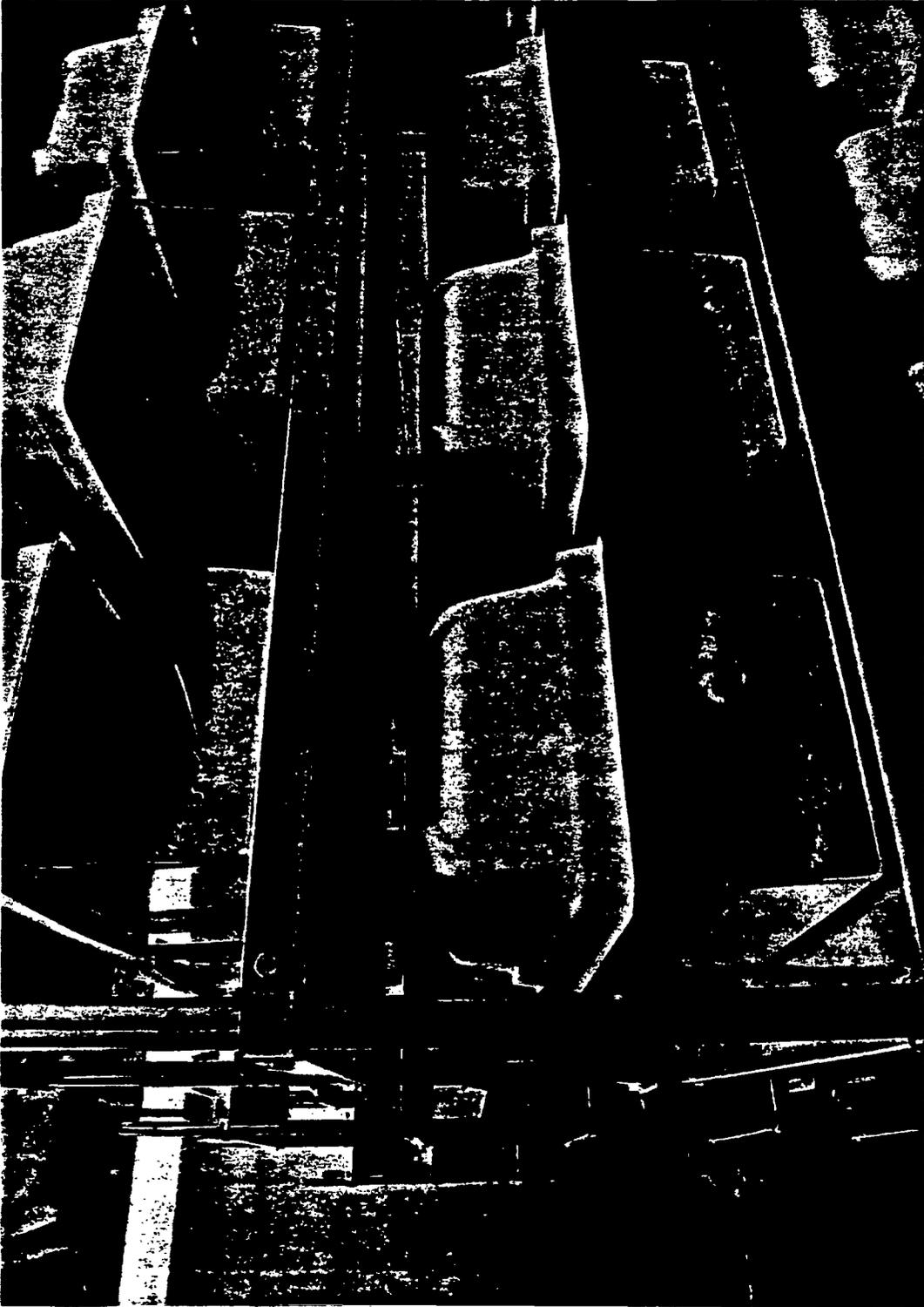


Figure 16. One Of The Rodent Holding Rooms At UBTL. Note that the animals are individually caged and that each cage is covered with a filter bonnet.

All animals were weighed on the day prior to their inhalation chamber exposure. Then, they were all weighed immediately after the exposure, and again 2 days, 5 days, 9 days, and 14 days after exposure.

All animals were observed daily for signs of toxicity, and those animals found dead were placed in a refrigerator until necropsy could be performed.

All surviving test and control animals were necropsied 14 days after exposure. On the day of necropsy, a given animal was sacrificed with an overdose of ethyl ether. Then, the animal was weighed, dissected, and examined grossly for pathological lesions. The following whole organs were removed and placed in 10% neutral buffered formalin: kidneys, adrenals, spleen, gonads, lungs, heart, liver, and brain. After at least 48 hours, the organs were trimmed and weighed. The paired organs were weighed together rather than separately. Also, gonads refer to both the testes and the epididymides in males and both ovaries and the uterus in females. The organ specimens of three test and three control animals per sex per species per exposure level were sent out for histopathological examination, and the remaining specimens were stored for possible future evaluation. Thus for a given experiment, 12 test animal specimens and 12 control animal specimens out of the total 40 animals per experiment were evaluated histopathologically.

Histopathology of Test Animal Organ Specimens

The histopathological preparation was done by a certified histologist at Intermountain Laboratories, Midvale, Utah; and the prepared slides were read by Kent R. Van Kampen, DVM, Ph.D, Veterinary Pathologist. Dr. Van Kampen has had several years of experience in evaluating histopathological lesions in rodents and he is board certified by the American College of Veterinary Pathologists. Dr. Van Kampen indicated on the histopathology report all lesions that he observed and he specifically stated those lesions that he judged to be "irreversible."

Statistical Evaluation of Body Weight and Organ Weight Data

After all the body weight, organ weight, and animal death data had been collected for a given experiment, the data were analyzed by John A. Burkart, Ph.D., UBTL Biostatistician. Dr. Burkart and his assistant made comparisons of organ-to-body weight ratios (at the time of necropsy) between control and test animal groups, using Student's t-test. In addition, weight changes during the post-exposure interval were computed by subtracting pre-exposure weight from each post-exposure weight on specific days, and those changes were analyzed using an analysis of variance for repeated measures design [58]. The differences between test and control animal data are shown in the summary tables in the Results Section of this report.

Project Schedule

During the first exposure of each test compound, we attempted to produce a concentration near the IDLH values estimated by NIOSH; but in some cases, actual exposure concentrations were either higher or lower. The second and third exposure concentration levels for a given compound were based on the effects observed in test animals and histopathology at the initial exposure concentration, on the toxicity data available from previous studies made by other investigators, and the exposure level categorization criteria. UBTL personnel discussed the results of each experiment with the Project Officer and followed his recommendations for subsequent exposures when possible.

Categorization of Exposures

The criteria for categorization of exposures with respect to "effect level" are listed in Table 1, while the assigned "effect level" for each exposure and the criteria upon which that assignment was made are shown in Table 2 and in the Results section.

Animal death during an exposure was sometimes difficult to determine conclusively, however, death was readily verified at the end of the exposure when the animals were removed from the chamber.

Not all of the irreversible lesions reported by the histopathologist appeared to be related to exposure of the test animals to a test atmosphere. In some cases, similar lesions were found in both test and control animals, and thus they were not considered to be exposure related. In other cases, lesions observed could be classified as processing artifacts or congenital defects and thus were not considered exposure related. Also, when all the histopathology results for a given test compound were available, it was possible to check for trends in various histopathological lesions with respect to increasing concentration. In dose related toxic effects, increasing incidence of a given lesion may correlate with an increase in concentration, however, due to the relatively small numbers of animals involved in these experiments, such trends were not always conclusively identifiable.

Deciding whether or not impairment of the ability of an animal to escape was present or not was sometimes difficult. During some exposures, the animals would appear not to move during the exposure, but upon removal from the chamber, they would immediately resume essentially normal activities. Thus in such cases, no impairment of the ability to escape was considered to be present. In other cases, the test animals would close their eyes for long periods of time presumably due to irritation caused by the test atmosphere. If they did not open their eyes and move about when given a sharp auditory stimulus created by striking the external sheet metal of the chamber with a hard, plastic rod, then an impairment of the ability to escape was considered to be present. Animals which were ataxic, narcotic, dead or otherwise unable to move in a normal manner immediately after the exposure were considered to have an impairment of the ability to escape.

RESULTS

A brief summary of the experimental results is shown in Table 2 of the Introductory Summary. This RESULTS section presents additional, more detailed data not shown in the Project Summary (Table 2) on chemical analyses, observations used to verify the impairment of ability to escape in test animals, animal deaths, irreversible histopathological lesions, and the differences between control and test animal organ and body weight data.

In order to facilitate comparison, experimental data for a given test compound are listed in increasing order of exposure concentration. The data for each compound are listed in tabular form in the following order: summary of chemical analyses, summary of exposure data used to categorize the type of effect, and summaries of the differences between test and control animal weight data.

2-Aminoethanol

Test animals were exposed to 2-aminoethanol at concentrations ranging from 0.346 to 0.887 mg/l either as a vapor or vapor-aerosol mixture in air (Table 7). Only a minor response was observed at the lowest and intermediate levels, while the highest level produced ataxia and death of seven guinea pigs during exposure and death of two guinea pigs within one hour post-exposure (Tables 2 and 8). No trend in the incidence of irreversible histopathological lesions was observed with increasing levels of exposure, however, probable irreversible damage to the adrenal medulla was found in a male guinea pig at an intermediate level.

A summary of the statistically significant differences ($\alpha=0.05$) between the test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 9) along with more detailed summaries of the results (Tables 10-12).

Table 7

2-Aminoethanol Atmosphere Analysis

Test Compound Concentration:

Experiment No.	31-EA-4		1-EA-1		14-EA-2		23-EA-3	
Date	8-9-78		12-21-77		4-12-78		6-14-78	
Attempted Chamber Conc.	>2.104 mg/l	*ppm	1.37 mg/l	625 ppm	0.842 mg/l	400 ppm	2.104 mg/l	*ppm
First Sample	0.301 mg/l	*ppm	0.447 mg/l	212 ppm	0.473 mg/l	225 ppm	0.826 mg/l	*ppm
Second Sample	0.298 mg/l	*ppm	0.392 mg/l	186 ppm	0.398 mg/l	189 ppm	0.947 mg/l	*ppm
Third Sample	0.438 mg/l	*ppm	0.293 mg/l	139 ppm	0.457 mg/l	217 ppm	1.080 mg/l	*ppm
Mean	0.346 mg/l	*ppm	0.377 mg/l	179 ppm	0.443 mg/l	210 ppm	0.951 mg/l	*ppm
Std. Dev.	0.080 mg/l	*ppm	0.0780 mg/l	37.0 ppm	0.0595 mg/l	18.9 ppm	0.127 mg/l	*ppm
Coef. Var.	23.1%		20.7%	20.7%	8.82%	8.96%	13.4%	*

Aerosol Size Distribution:**

Experiment No.	23-EA-3		31-EA-4	
	BCD(μm)	Cum. %	BCD(μm)	Cum. %
1	5.78	100.0	5.03	100.0
2	3.66	100.0	3.19	99.8
3	2.27	99.9	1.97	99.6
4	1.41	84.3	1.22	89.0
5	0.87	52.5	0.76	51.4
6	0.55	15.8	0.48	23.1
7	0.34	6.0	0.30	5.6
Median Aerodynamic Diameter (μm)	1.0		0.7	
Geometric Standard Deviation	1.4		1.5	

*Aerosol/vapor mixture, thus ppm definition not applicable.

**Aerosol size distribution analysis not performed on Experiment No. 1-EA-1 and 14-EA-2.

Table 8.
2-Aminoethanol

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability			Animal #	Time of Death	Irreversible Lesions Found	Type of Effect
			Rat	G. Pig	Rat				
8-8-78	31-BA-4	** ppm 0.346 mg/l	0	0	0	0	-	-	<p>† Histopathology not performed because only one possible significant finding was observed at the two next highest concentrations.</p>
12-21-78	1-BA-1	178 ppm 0.377 mg/l	0	0	0	0	1G76M 1G78P	9 days post-exp. ³	<p>Probable irreversible damage to adrenal Minimal³ medulla. Supportive meningoencephalomyelitis brain damage.³</p>
4-12-78	14-BA-2	210 ppm 0.443 mg/l	0	0	0	0	-	-	None found.
6-14-78	23-BA-3	** ppm 0.951 mg/l	0	10 ²	0	0	23G72M 23G74M 23G76M 23G78M 23G710M 23G73P 23G75P 23G77P 23G79P	<p>During exposure During exposure 1 day post-exp. During exposure 30 min. post-exp. During exposure During exposure During exposure During exposure</p>	<p>No irreversible lesions found in this group of animals. Frank</p>

* Sacrificed for necropsy 14 days post-exposure.

**Aerosol/vapor mixture, thus ppm definition not applicable.

¹ Death or lesion probably not related to exposure.

² Probably an infectious lesion

³ By 15 minutes G10 showed labored breathing. G2 was lying on side, G3 and G7 were static with uncontrolled movements. Rats appeared unaffected other than showing depressed activity. By 20 minutes all G had eyes open, G2 was lying on side, G7 had uncontrolled movements, G9 was gasping for breath. Ataxia was present in G2, 3, 4, 7, 8, 9, 10. Rats had eyes open and were very still. By 25 minutes G2, 3, 9 and 8 were lying on side. Rats remained motionless and upright except for occasional scratching. Immediately after exposure G2, 3, 4, 5, 7, 8 and 9 were dead; and G1, 6 and 10 were static with no righting reflex. However, rats were active and had righting reflex. (Due to aerosol nature of atmosphere, there was some difficulty in observing each animal closely at far side of chamber.)

⁴ The effect may or may not be exposure-related; the results are inconclusive due to the small number of animals tested. However, a conservative approach was taken and the effect was, therefore, judged to be exposure-related.

Table 9

2-Aminoethanol
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
8-9-78	31-EA-3	** ppm 0.346 mg/l	No significant difference found.	Liver (-)MG, (-)FG Kidney (-)MR Spleen (-)FR
12-21-78	1-EA-1	179 ppm 0.377 mg/l	No significant difference found.	Liver (-)MR, (-)FR Brain (-)FG Adrenal (-)MG Gonad (+)MR
4-12-78	14-EA-2	210 ppm 0.443 mg/l	No significant difference found.	Lung (+)MG Liver (+)MR
6-14-78	23-EA-3	** ppm 0.951 mg/l	BWA(-)MR	Lung (+)MG, (+)FG Liver (+)FG Kidney (+)FG Adrenal (-)FR Gonad (+)MR, (-)MG

* Abbreviations:

BWA = Body weight at autopsy
ABW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(±) = Variable differences between test and control groups observed

**Aerosol/vapor mixture, thus ppm definition does not apply.

TABLE 10A. EXPERIMENT 31-EA-4, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS
 MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	COLONS	SPLEEN		
RATS	MALE	CONTROL	293.0	6.67	36.99	7.37	3.17	6.41	.17	13.36	2.13		
		N	5	5	5	5	5	5	5	5	5		
		TEST	290.2	6.99	34.66	6.00	3.20	6.30	.10	13.19	2.26		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.34	.81	-1.01	-3.03	.83	-1.12	.33	-1.15	1.60		
P-VALUE	.7398	.4433	.3418	.0162	.4300	.9042	.7402	.0079	.1307				
RATS	FEMALE	CONTROL	217.0	0.65	35.41	6.70	3.61	0.46	.33	2.73	2.60		
		N	5	5	5	4	5	5	4	5	5		
		TEST	220.4	7.70	31.93	6.50	3.51	7.97	.26	2.54	2.27		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.36	-1.47	-1.65	-1.77	-.30	-1.49	-1.59	-.73	-4.13		
P-VALUE	.7311	.1005	.1370	.4659	.7147	.1750	.1554	.4050	.0033				
GUINEA PIG	MALE	CONTROL	289.6	10.43	45.47	0.55	4.52	11.74	.37	2.77	1.32		
		N	5	5	5	5	5	5	5	5	5		
		TEST	293.0	10.07	36.22	7.95	4.09	11.20	.35	3.30	1.15		
		N	5	5	5	5	5	5	5	4	5		
		T-TEST STATISTIC	.36	-.22	-2.35	-1.20	-2.09	-1.00	-1.03	1.47	-1.06		
P-VALUE	.7305	.0301	.0469	.2649	.0701	.3132	.3346	.1047	.1005				
GUINEA PIG	FEMALE	CONTROL	293.0	9.76	42.00	7.71	4.33	10.53	.45	4.73	1.07		
		N	5	5	5	5	5	5	5	5	5		
		TEST	289.2	0.70	36.52	7.39	4.15	10.79	.41	4.43	1.57		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.32	-1.70	-2.05	-.76	-.60	.52	-.02	-.27	-1.31		
P-VALUE	.7590	.1131	.0215	.4692	.5664	.6163	.4377	.7925	.2264				

* < .10 ** < .05 *** < .01 **** < .001

TABLE 10B. EXPERIMENT 31-EA-4, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	91.500	91.500	.11784	N.S.
SUBJECTS IN GROUPS	8	6212.0	776.50		
TIMES	5	61285.	12257.	569.12	P < .001
TIMES X GROUPS	5	12.500	2.50000	.10394	N.S.
TIMES X SUBJECTS IN GROUPS	40	963.00	24.075		
TOTAL	59	68564.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	203.200	206.600	226.000	249.200	264.800	293.000	240.600
TEST	5	202.200	205.000	222.400	246.000	262.200	290.200	238.133
TOTAL	10	202.700	205.800	224.200	248.000	263.500	292.000	239.367

TABLE 10C. EXPERIMENT 31-EA-4, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	54.000	54.000	.11462	N.S.
SUBJECTS IN GROUPS	8	3769.0	471.12		
TIMES	5	12480.	2496.0	60.583	p < .001
TIMES X GROUPS	5	19.000	3.8000	.92233E-01	N.S.
TIMES X SUBJECTS IN GROUPS	40	1648.0	41.200		
TOTAL	59	17970.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	177.000	178.200	185.200	198.000	200.400	217.000			192.767
TEST	2	5	178.000	178.800	186.000	199.400	203.800	220.400			194.667
TOTAL	10		178.300	179.500	186.000	198.700	202.100	210.700			193.717

TABLE 10D. EXPERIMENT 31-EA-4, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	13.888	13.888	.86537E-02	N.S.
SUBJECTS IN GROUPS	8	12018.	1502.2		
TIMES	5	68974.	13795.	87.809	P < .001
TIMES X GROUPS	5	626.00	125.20	.79694	N.S.
TIMES X SUBJECTS IN GROUPS	40	6284.0	157.10		
TOTAL	59	87915.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	199.800	196.200	196.800	222.400	228.800	255.200	289.600	231.867		
TEST	2	199.600	196.800	196.800	210.200	232.600	263.800	293.800	232.800		
TOTAL	10	199.300	196.500	196.500	216.300	230.700	259.500	291.700	232.333		

TABLE 10B. EXPERIMENT 31-EA-4, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	38.588	38.588	.57164E-01	N.S.
SUBJECTS IN GROUPS	8	5388.0	673.50		
TIMES	5	61193.	12239.	98.520	P < .001
TIMES X GROUPS	5	285.58	57.118	.45965	N.S.
TIMES X SUBJECTS IN GROUPS	40	4969.0	124.23		
TOTAL	59	71874.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL	
CONTROL	1	5	286.200	206.600	222.800	229.800	264.200	293.800	236.967
TEST	2	5	283.200	199.800	219.200	237.800	263.800	289.200	235.367
TOTAL	10		284.700	203.200	220.600	233.400	264.000	291.100	236.167

TABLE 11A. EXPERIMENT 1-EA-1, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)											
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	CANARDS	SPLEEN				
RATS	MALE	CONTROL	307.0	6.39	49.87	7.65	3.27	6.84	.14	12.12	2.00				
		N	5	5	5	5	5	4	5	5	5				
	FEMALE	TEST	301.2	7.25	39.11	6.99	3.56	9.63	.16	13.77	2.19				
		N	5	5	5	5	5	5	5	5	5				
		T-TEST STATISTIC	-.62	1.54	-3.11	+1.84	1.73	-.92	1.21	3.89	.56				
P-VALUE	.5545	.1618	.0145	.1033	.1217	.3961	.2544	.0149	.3665	*					
RATS	MALE	CONTROL	212.6	7.97	49.73	6.94	3.76	0.30	.21	2.70	2.00				
		N	5	5	5	5	5	5	5	5	5				
	FEMALE	TEST	212.6	8.25	33.48	6.63	3.80	0.86	.22	2.86	2.37				
		N	5	5	5	5	5	5	5	5	5				
		T-TEST STATISTIC	.88	.28	-4.81	-.63	.19	-.48	.44	-1.13	1.18				
P-VALUE	1.888	.7844	.0039	.5451	.8515	.7818	.6748	.2929	.3015	**					
GUINEA PIG	MALE	CONTROL	201.0	7.75	59.95	9.42	4.85	11.26	.42	3.42	1.31				
		N	5	5	5	5	5	5	5	5	5				
	FEMALE	TEST	317.5	7.87	43.48	9.48	4.85	10.85	.32	3.78	1.34				
		N	4	4	4	4	4	4	4	4	4				
		T-TEST STATISTIC	.66	.68	-2.89	-2.82	-.88	-.45	-2.55	.83	.26				
P-VALUE	.5332	.5158	.0752	.0633	1.088	.6684	.8388	.4461	.7992	#					
GUINEA PIG	MALE	CONTROL	254.8	8.89	43.14	9.21	4.27	13.98	.58	1.61	1.47				
		N	5	5	5	5	5	5	5	5	5				
	FEMALE	TEST	276.6	8.45	45.65	9.66	4.87	10.58	.62	2.58	1.67				
		N	5	5	5	5	5	5	5	5	5				
		T-TEST STATISTIC	.71	.39	.58	.64	-.43	-2.98	.82	1.32	.66				
P-VALUE	.4986	.7878	.5769	.5485	.6811	.0177	.4334	.2353	.5284	#					

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 11B. EXPERIMENT 1-EA-1, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	29.500	29.500	.46494E-01	N.S.
SUBJECTS IN GROUPS	8	5877.0	634.62		
TIMES	5	72776.	14555.	586.93	P < .001
TIMES X GROUPS	5	131.50	26.300	.91598	N.S.
TIMES X SUBJECTS IN GROUPS	40	1148.5	28.713		
TOTAL	59	79163.			

MEANS

TIMES:

GROUPS:	N	TIME						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	1	208.400	216.000	235.000	256.600	283.600	307.000	251.233
TEST	2	205.200	214.200	239.000	258.000	281.400	301.200	249.033
TOTAL	10	206.800	215.100	237.400	257.300	282.500	304.100	250.533

TABLE 11C. EXPERIMENT 1-EA-1, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	19.500	19.500	.70556E-01	N.S.
SUBJECTS IN GROUPS	8	2211.0	276.37		
TIMES	5	11828.	2365.6	119.02	P < .001
TIMES X GROUPS	5	85.500	17.100	.86038	N.S.
TIMES X SUBJECTS IN GROUPS	40	795.00	19.875		
TOTAL	59	14939.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11 DAY 12 DAY 13 DAY 14 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	176.000	177.400	183.200	192.000	203.400	212.600	190.900
TEST	5	175.800	176.000	182.800	198.000	207.000	212.600	192.033
TOTAL	10	175.900	176.700	183.000	195.400	205.200	212.600	191.467

TABLE 11D. EXPERIMENT 1-EA-1, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	546.00	546.00	.19587	N.S.
SUBJECTS IN GROUPS	7	19513.	2787.6		
TIMES	5	99558.	19912.	152.75	p <.001
TIMES X GROUPS	5	565.00	113.00	.06685	N.S.
TIMES X SUBJECTS IN GROUPS	35	4562.5	130.36		
TOTAL	53	.12474E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	5	178.400	192.200	213.600	222.600	249.000	301.800	226.267
TEST	4	179.500	193.750	211.500	234.000	259.750	317.500	232.667
TOTAL	9	178.889	192.889	212.667	227.667	253.778	308.778	229.111

TABLE 12A. EXPERIMENT 14-EA-2, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	COVADS	SPLEEN			
RATS	MALE	CONTROL	282.6	7.55	37.23	7.26	3.29	6.42	.20	14.42	2.32			
		N	5	5	5	5	5	5	5	5	5	5		
		TEST	281.4	7.59	40.74	6.81	3.55	6.77	.21	14.40	2.27			
		N	5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.17	-.89	3.53	-1.26	1.48	1.17	1.26	.17	-.19			
		P-VALUE	.8728	.9342	.0077	.2081	.2775	.2446	.6682	.6597				
RATS	FEMALE	CONTROL	192.2	0.77	33.22	6.35	3.05	0.81	.34	2.72	2.32			
		N	5	5	5	5	5	5	5	5	5			
		TEST	199.0	0.65	35.03	6.40	3.59	0.82	.35	2.42	2.30			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	.16	-.17	1.60	-.13	-.93	-1.03	.24	-.93	.30			
		P-VALUE	.8739	.8683	.1317	.8999	.3773	.3331	.8136	.3788	.7153			
GUINEA PIG	MALE	CONTROL	339.2	0.84	47.51	0.62	4.48	10.39	.34	2.70	1.28			
		N	5	5	5	5	5	5	5	5	5			
		TEST	329.2	0.76	54.34	0.62	4.98	10.59	.36	3.10	1.29			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.78	3.37	1.93	1.08	2.23	.61	.98	1.71	.28			
		P-VALUE	.4571	.0090	.0598	.8559	.5578	.3929	.1268	.6487				
GUINEA PIG	FEMALE	CONTROL	287.2	9.42	46.52	0.95	4.65	11.39	.42	3.35	1.70			
		N	5	5	5	5	5	5	5	5	5			
		TEST	277.0	9.98	56.09	0.82	4.43	11.68	.52	2.61	1.34			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.44	.55	1.34	-.44	-.92	.29	2.21	-.82	-1.88			
		P-VALUE	.6767	.5953	.2179	.6745	.3862	.7818	.6581	.4343	.3117			

(*) < .10 ** < .05 *** < .01 **** < .001

TABLE 12B. EXPERIMENT 14-EA-2, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	11.500	11.500	.3684E-01	N.S.
SUBJECTS IN GROUPS	8	2497.0	312.12		
TIMES	5	46689.	9337.8	591.80	P<.001
TIMES X GROUPS	5	53.500	10.700	.67722	N.S.
TIMES X SUBJECTS IN GROUPS	40	632.00	15.600		
TOTAL	59	49883.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	206.000	213.600	220.200	240.000	265.600	282.600			240.667
TEST	2	5	205.600	209.800	227.200	248.600	267.800	281.400			239.800
TOTAL	10		205.800	211.300	227.700	240.300	266.300	282.000			240.233

TABLE 12C. EXPERIMENT 14-EA-2, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	6.0000	6.0000	.36966E-01	N.S.
SUBJECTS IN GROUPS	8	1298.5	162.31		
TIMES	5	4657.5	931.50	62.569	P<.001
TIMES X GROUPS	5	25.750	5.1500	.34593	N.S.
TIMES X SUBJECTS IN GROUPS	40	595.50	14.888		
TOTAL	59	6503.2			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	5	174.600	176.400	176.400	183.000	188.000	188.000	192.000	199.200	199.200	185.567
TEST	5	174.000	176.400	176.400	179.600	188.200	188.200	191.600	199.600	199.600	184.933
TOTAL	10	174.400	176.400	176.400	181.300	188.100	188.100	191.800	199.500	199.500	185.250

TABLE 12D. EXPERIMENT 14-EA-2, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	588.00	588.00	.69813	N.S.
SUBJECTS IN GROUPS	8	6738.0	842.25		
TIMES	5	77752.	15550.	53.100	p < .001
TIMES X GROUPS	5	729.00	145.80	.49767	N.S.
TIMES X SUBJECTS IN GROUPS	40	11714.	292.85		
TOTAL	59	97521.			

MEANS

TIMES:

GROUPS	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	231.600	233.200	253.000	258.200	299.200	339.200	269.067
TREATMENT	5	231.400	237.200	247.800	249.600	281.600	329.200	262.800
TOTAL	10	231.500	235.200	250.400	253.900	290.400	334.200	265.933

TABLE 12E. EXPERIMENT 14-EA-2, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1269.5	1269.5	.46866	N.S.
SUBJECTS IN GROUPS	8	22846.	2755.8		
TIMES	5	56352.	11270.	37.676	p < .001
TIMES X GROUPS	5	632.50	126.50	.42288	N.S.
TIMES X SUBJECTS IN GROUPS	40	11965.	299.14		
TOTAL	59	92366.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	198.600	206.800	216.400	211.000	258.600	287.200	229.633		
TEST	2	5	194.200	193.800	213.600	206.400	236.800	277.800	228.433		
TOTAL	10	10	196.400	199.900	215.000	208.700	247.700	282.500	225.033		

TABLE 13A. EXPERIMENT 23-EA-3, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	EDWARDS	SPLEEN			
RATS	MALE	CONTROL	266.0	9.00	48.96	6.82	3.47	6.51	.17	12.79	2.31			
		M	5	5	5	5	5	5	5	5	5			
		TEST	266.0	9.03	38.68	7.11	3.71	6.00	.19	14.23	2.44			
		M	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-2.48	.83	-.62	.75	1.37	1.54	1.37	2.48	.68			
P-VALUE	.0435	.4328	.5547	.4745	.2076	.1612	.2065	.0435	.8127					
RATS	FEMALE	CONTROL	192.0	18.62	39.99	7.18	3.01	9.22	.39	3.01	2.00			
		M	5	5	5	5	5	5	5	5	5			
		TEST	202.0	9.65	48.34	6.58	3.71	8.69	.28	2.48	2.63			
		M	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.47	-1.17	.25	-.92	-.46	-1.58	-3.85	-1.67	-.68			
P-VALUE	.1881	.2763	.8852	.3835	.6688	.1336	.0159	.1338	.5157					
GUINEA PIG	MALE	CONTROL	280.6	12.21	82.54	18.01	5.16	15.73	.55	2.78	1.58			
		M	5	5	5	5	5	5	5	5	5			
		TEST	281.6	29.88	51.82	18.84	5.38	15.88	.53	2.19	1.67			
		M	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.36	18.69	-.15	.85	.84	.18	-.52	-2.69	.92			
P-VALUE	.7299	.0008	.9827	.3981	.4277	.9259	.6168	.0274	.3831					
GUINEA PIG	FEMALE	CONTROL	238.8	18.57	43.98	8.84	4.72	13.59	.55	2.97	1.43			
		M	5	5	5	5	5	5	5	5	5			
		TEST	218.8	25.84	56.82	18.13	5.21	14.69	.54	2.54	1.45			
		M	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.33	3.37	2.45	3.18	.85	.69	-.26	-.64	.15			
P-VALUE	.7458	.0097	.0481	.0138	.4288	.5118	.8848	.5487	.8815					

(*) <.10 * <.05 ** <.01 *** <.001

TABLE 13B. EXPERIMENT 23-EA-3, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	129.00	129.00	.55239E-01	N.S.
SUBJECTS IN GROUPS	9	18682.	2335.3		
TIMES	5	43934.	8786.9	61.350	P < .001
TIMES X GROUPS	5	298.00	59.600	.41613	N.S.
TOTAL	40	5729.0	143.23		
TOTAL	59	68773.			

MEANS

TIMES:

GROUPS:	N	1	2	3	4	5	6	TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	197.000	194.800	210.200	225.600	247.000	269.600	224.033
TEST	5	196.000	196.200	214.800	232.600	256.200	266.000	226.967
TOTAL	10	196.500	195.500	212.500	229.100	251.600	267.800	225.500

TABLE 13C. EXPERIMENT 23-EA-3, 2-AMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	614.50	614.50	.54022	N, S,
SUBJECTS IN GROUPS	0	9100.0	1137.5		
TIMES	5	10872.	2014.4	22.142	p < .001
TIMES X GROUPS	5	228.00	45.600	.50124	N, S,
TIMES X SUBJECTS IN GROUPS	40	3639.0	90.975		
TOTAL	59	23653.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	166.600	174.600	182.400	187.000	198.000	209.200	186.300
TEST	5	168.400	167.000	175.000	179.000	187.200	202.000	179.900
TOTAL	10	167.500	170.800	179.100	183.000	192.600	205.600	183.100

NOTE

Tables 13D and 13E are not presented here, since a majority of the test guinea pigs died during or after the exposure, and therefore the rate of growth analysis was not performed.

Diisopropylamine

Test animals were exposed to diisopropylamine vapor at concentrations ranging from 3.35 to 17.9 mg/l in air (Table 14). At the lowest level, nasal/lacrymal irritation, eye closure and dyspnea were present; but no deaths occurred and no irreversible lesions were observed (Table 2 and 15). During the intermediate level exposure, nasal/lacrymal irritations, eye closure and dyspnea were present; one rat died and one was found to have pulmonary congestion, inflammation hemorrhage and edema. A few minutes after the exposure, a guinea pig died. Corneal opacity was noted in one guinea pig 14 days post-exposure. At the highest level, all animals died during the exposure with apparent respiratory distress. The histopathology of the rats revealed degeneration of the proximal tubular epithelium and bronchial epithelium, while the guinea pigs showed vacuolar degeneration of the hepatocytes as a common lesion.

A summary of the statistically significant differences ($\alpha=0.05$) between the test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 16) along with more detailed summaries of the results (Tables 17-19).

Table 14

Diisopropylamine Atmosphere Analysis

Test Compound Concentration:

Experiment No.	2-DIA-1		12-DIA-3		10-DIA-2	
Date	1-4-78		3-29-78		3-15-78	
Attempted Chamber Conc.	3.49 mg/l	1000 ppm	6.99 mg/l	2000 ppm	17.4 mg/l	5000 ppm
First Sample	3.14 mg/l	902 ppm	6.06 mg/l	1730 ppm	18.0 mg/l	5150 ppm
Second Sample	3.38 mg/l	970 ppm	6.17 mg/l	1760 ppm	17.5 mg/l	4990 ppm
Third Sample	3.52 mg/l	1010 ppm	6.28 mg/l	1800 ppm	18.3 mg/l	5220 ppm
Mean	3.35 mg/l	961 ppm	6.17 mg/l	1760 ppm	17.9 mg/l	5120 ppm
Std. Dev.	0.192 mg/l	54.6 ppm	0.110 mg/l	35.1 ppm	0.404 mg/l	118 ppm
Coef. Var.	5.73%	5.68%	1.78%	1.99%	2.26%	2.30%

Table 15
Diisopropylamine

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Rat		G. Pig		Animal Deaths and Histopathological Specimens for Irreversible Lesions	Animal Deaths and Histopathological Evaluation of Organ Specimens for Irreversible Lesions	Type of Effect
			Test	Control	G. Pig	Rat			
1-4-78	2-DIA-1	961 ppm 3.35 mg/l	0	0	0	0	2RT2P 2RT1M	Spongiosis of white matter in brain ^{1a} Spongiosis of white matter in brain ^{1a} and focal microhemorrhages in cerebral white matter	No
3-29-78	12-DIA-3	1760 ppm 6.17 mg/l	1 ²	1 ²	0	0	12RT1M 12GT3M 12GT1M 12ECSM	Pulmonary lesions were fatal (congestion, inflammation, hemorrhage, edema). Congestion and exposure-related corneal erosion and edema. None found. Lung lesions may result in scarring ^{1c} (inflammation, hemorrhage).	Frank
3-15-78	10-DIA-2	5120 ppm 17.8 mg/l	10 ³	10 ³	0	0	10RT1M 10RT3M 10RT5M 10RT7M 10RT9M 10RT2F 10RT4F 10RT6F 10RT8F 10RT10F 10GT1M 10GT3M 10GT5M 10GT7M 10GT9M 10GT2F	Degeneration of proximal tubular epithelia and bronchial epithelium. Histopathology not performed. Necrosis of proximal tubular epithelium. Histopathology not performed. Necrosis of proximal tubular epithelium. Histopathology not performed. Necrosis of proximal convoluted tubular epithelium and bronchial epithelium. Histopathology not performed. Necrosis of proximal tubular epithelium. Necrosis of bronchial epithelium and proximal tubular epithelium. Histopathology not performed. Vacuolar degeneration of hepatocytes. Histopathology not performed. Vacuolar degeneration of hepatocytes. None found. Minimal vacuolar degeneration of hepatocytes. Histopathology not performed. Vacuolar degeneration of hepatocytes. Vacuolar degeneration of hepatocytes and fibrosis of liver. Histopathology not performed.	Frank

* Sacrificed for necropsy 14 days post-exposure.
¹ Death or lesion probably not related to exposure;
^{1a} Fixative artifact
^{1b} Congenital lesion
^{1c} Lesion only seen in control animals
^{1d} Lesion not seen at higher doses

² Deaths occurred at 25-30 minute portion of exposure and were preceded by labored breathing. Some eye closure observed, but animals opened eyes in response to auditory stimulus.

³ By 10 minutes GI, 5 and 10 appeared dead; G3, 4 and 8 were lying on sides; and R4 and 5 had labored breathing. By 15 minutes GI through 9 had labored breathing; and G2, 3, 4, 7 and 9 were static. Also R3, 4, 5, 6 and 7 were lying on sides. R5 appeared dead, and R7 had uncontrolled movements. By 20 minutes G7, 3, 5, 6, 8 and 10 and Rats 1, 2, 3, 4, 5, 7, 8 and 10 were lying on sides with little or no movement; and labored breathing was present in all animals. By 30 minutes all animals appeared dead, and all animals were confirmed dead immediately after exposure.

⁴ Although these lesions were judged to be reversible, they were considered to be significant.

Table 16

Diisopropylamine
 Summary of Statistically Significant Differences Between
 Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
1-4-78	2-DIA-1	961 ppm 3.35 mg/l	ΔBW(-)FR	Lung (+)MR, (+)FR, (+)MG, (+)FG
3-29-78	12-DIA-3	1760 ppm 6.16 mg/l	ΔBW(-)MR ΔBW(-)FR ΔBW(-)FG	Lung (-)FG Heart (-)MR
3-15-78	10-DIA-2	5130 ppm 17.9 mg/l	Not available since test animals died.	Not meaningful since control animals were not sacrificed until six days after the test animals had died.

* Abbreviations:

- BWA = Body weight at autopsy
- ΔBW = Change in body weight post-exposure
- M = Male
- F = Female
- R = Rat
- G = Guinea pig
- (-) = Test group less than control group
- (+) = Test group more than control group
- (±) = Variable differences between test and control groups observed

TABLE 17A. EXPERIMENT 2-DIA-1, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GNADS	SPLEEN			
RATS	MALE	CONTROL	309.0	4.09	46.64	7.50	3.72	6.16	.10	12.90	2.16			
		N	5	5	5	5	5	5	5	5	5			
		TEST	322.4	7.24	45.23	7.46	3.50	5.06	.16	12.97	2.35			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.67	4.03	-0.87	-0.85	-0.67	-2.05	-0.68	-0.00	1.19			
		P-VALUE	.1326	.0013	.4101	.9594	.5221	.0739	.5147	1.000	.2697			
				**				(*)						
RATS	FEMALE	CONTROL	220.6	5.59	41.74	6.90	3.72	0.16	.20	2.66	2.42			
		N	5	5	5	5	5	5	5	5	5			
		TEST	215.2	7.31	37.36	7.00	3.73	0.33	.31	2.07	2.32			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-2.26	3.00	-2.29	.49	.05	.65	.71	.61	-0.00			
		P-VALUE	.0541	.0047	.0512	.6379	.9629	.5344	.4900	.5614	.4484			
				**	(*)									
GUINEA PIG	MALE	CONTROL	331.0	6.52	49.02	0.55	3.95	10.64	.39	3.99	1.30			
		N	5	5	5	5	5	5	5	5	5			
		TEST	310.4	7.55	44.53	0.35	4.43	12.06	.37	3.76	1.64			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-2.24	2.50	-2.32	-0.50	2.20	3.05	-0.45	-0.96	1.27			
		P-VALUE	.0552	.0327	.0490	.6207	.0519	.0150	.6623	.3667	.2304			
				*	*		(*)	*						
GUINEA PIG	FEMALE	CONTROL	304.0	6.02	44.50	0.40	3.00	11.00	.51	4.50	1.40			
		N	5	5	5	5	5	5	5	5	5			
		TEST	289.6	7.46	44.75	0.47	4.22	12.00	.47	4.31	1.76			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.27	2.43	.09	.15	1.79	2.05	-0.99	-0.16	1.60			
		P-VALUE	.2411	.0414	.9307	.0051	.1115	.0745	.3524	.0000	.1323			
				*				(*)						

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 17B. EXPERIMENT 2-DIA-1, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	58.500	58.500	.36821	N.S.
SUBJECTS IN GROUPS	8	1271.0	158.87		
TIMES	5	66232.	13246.	337.81	P < .001
TIMES X GROUPS	5	348.00	69.600	1.7749	N.S.
TIMES X SUBJECTS IN GROUPS	40	1568.5	39.213		
TOTAL	59	69478.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						
		1	2	3	4	5	6	TOTAL
CONTROL	5	216.800	214.400	235.200	259.800	275.400	300.200	250.167
TEST	5	215.800	214.600	230.600	260.600	279.600	311.200	252.133
TOTAL	10	216.800	214.200	232.900	259.800	277.500	305.700	251.150

TABLE 17D. EXPERIMENT 2-DIA-1, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1622.5	1622.5	2.0507	N.S.
SUBJECTS IN GROUPS	0	6329.5	791.19		
TIMES	5	73171.	14634.	189.35	p < .001
TIMES X GROUPS	5	716.50	143.30	1.8541	N.S.
TIMES X SUBJECTS IN GROUPS	40	3091.5	77.288		
TOTAL	59	84931.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	221.000	225.400	250.000	259.000	291.000	327.600	264.133
TEST	2	5	219.800	224.400	232.200	255.200	280.400	310.400	253.733
TOTAL	10	10	220.400	224.900	241.100	262.100	286.100	319.000	258.933

TABLE 17E. EXPERIMENT 2-DIA-1, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1067.0	1067.0	1.0944	N. S.
SUBJECTS IN GROUPS	8	4506.0	563.25		
TIMES	5	53255.	10651.	137.92	P < .001
TIMES X GROUPS	5	629.00	125.80	1.6290	N. S.
TIMES X SUBJECTS IN GROUPS	40	3089.0	77.225		
TOTAL	59	62546.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						TOTAL		
		1	2	3	4	5	6			
CONTROL	5	215.000	217.400	237.800	259.200	276.000	290.200	298.600	250.600	
TEST	5	211.000	217.000	219.800	243.400	272.200	289.600	242.167		
TOTAL	10	213.000	217.200	228.800	251.300	274.100	293.900	246.383		

TABLE 18A. EXPERIMENT 12-DIA-3, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GANADS	SPLEEN		
RATS	MALE	CONTROL	301.0	7.99	40.32	7.33	3.56	6.16	.14	13.60	2.39		
		N	5	5	5	5	5	5	5	5	5		
		TEST	280.5	0.43	40.03	7.34	3.29	6.70	.17	14.36	2.35		
		N	4	4	4	4	4	4	4	4	4		
		T-TEST STATISTIC	-1.04	1.17	.24	.03	-2.53	2.12	1.98	1.46	-1.41		
P-VALUE	.1087	.2009	.0191	1.000	.0391	.0713	.0880	.1090	.6956				
							*						
RATS	FEMALE	CONTROL	280.0	0.04	36.35	6.77	3.09	0.76	.24	3.21	2.69		
		N	5	5	5	5	5	5	5	5	5		
		TEST	289.2	0.59	39.09	6.00	3.02	0.56	.20	2.01	2.55		
		N	15	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.19	-1.42	1.59	.26	-1.30	-1.53	1.68	-1.57			
P-VALUE	.6530	.0664	.1504	.0013	.7700	.5340	.1324	.5975	.5021				
GUINEA PIG	MALE	CONTROL	313.0	0.93	50.67	9.27	4.51	11.41	.41	3.29	1.31		
		N	5	5	5	5	5	5	5	5	5		
		TEST	300.7	10.06	61.49	10.36	4.62	11.40	.44	3.16	1.40		
		N	4	4	4	4	4	4	4	4	4		
		T-TEST STATISTIC	-.22	1.22	1.49	1.02	.32	-.02	.62	-.33	.97		
P-VALUE	.6200	.2619	.1003	.1116	.7611	1.000	.5524	.7404	.3655				
GUINEA PIG	FEMALE	CONTROL	279.6	11.74	43.62	0.53	4.50	12.01	.47	4.61	1.30		
		N	5	5	5	5	5	5	5	5	5		
		TEST	294.2	9.67	47.99	0.81	4.00	11.06	.40	3.02	1.53		
		N	4	4	4	4	4	4	4	4	4		
		T-TEST STATISTIC	1.75	-2.90	.93	.54	1.12	-.40	.35	-1.00	.00		
P-VALUE	.1241	.0231	.3053	.6076	.3010	.6465	.7395	.1024	.4094				
							*						

(*) <.10 * <.05 ** <.01 *** <.001

TABLE 18B. EXPERIMENT 12-DIA-3, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	7526.0	7526.0	10.023	p < .001
SUBJECTS IN GROUPS	7	5256.0	750.86		
TIMES	5	47284.	9456.8	424.07	p < .001
TIMES X GROUPS	5	2654.0	530.80	23.003	p < .001
TIMES X SUBJECTS IN GROUPS	35	700.50	22.300		
TOTAL	53	63500.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11 DAY 12 DAY 13 DAY 14 DAY 15						TOTAL	
		1	2	3	4	5	6		
CONTROL	5	210.200	210.000	231.000	253.000	270.000	301.000	301.000	247.467
TEST	4	205.250	205.000	195.000	223.250	252.750	261.000	223.700	236.987
TOTAL	9	208.000	207.770	215.000	240.222	266.770	283.667	236.987	

TABLE 18C. EXPERIMENT 12-DIA-3, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	88.750	88.750	.21173	N.S.
SUBJECTS IN GROUPS	8	3353.2	419.16		
TIMES	5	7577.8	1515.4	83.869	p<.001
TIMES X GROUPS	5	354.75	70.950	3.9267	p<.001
TIMES X SUBJECTS IN GROUPS	40	722.75	18.069		
TOTAL	59	12096.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	179.000	172.000	182.600	189.600	189.600	197.600	208.000	208.000	188.133
TEST	2	5	178.500	175.200	175.200	183.800	183.800	201.400	200.000	200.000	185.700
TOTAL	10	10	178.800	173.600	178.900	186.700	186.700	199.500	204.000	204.000	186.917

TABLE 18D. EXPERIMENT 12-DIA-3, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	187.50	187.50	.78959E-01	N.S.
SUBJECTS IN GROUPS	7	16622.	2374.6		
TIMES	5	54754.	10951.	34.440	P<.001
TIMES X GROUPS	5	2002.0	400.40	1.2592	N.S.
TIMES X SUBJECTS IN GROUPS	35	11129.	317.97		
TOTAL	53	84695.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11						TOTAL		
		1	2	3	4	5	6			
CONTROL	1	5	222.000	213.600	222.000	222.000	231.000	259.600	313.000	243.667
TEST	2	4	217.750	213.000	209.000	242.250	269.000	280.500	239.917	
TOTAL	9	220.111	213.333	216.222	236.444	263.778	302.111	242.000		

TABLE 18E. EXPERIMENT 12-DIA-3, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	191.00	191.00	.17734	N.S.
SUBJECTS IN GROUPS	7	7539.0	1077.0		
TIMES	5	44426.	8885.3	79.638	p<.001
TIMES X GROUPS	5	2480.0	496.00	4.4456	p<.001
TIMES X SUBJECTS IN GROUPS	35	3905.0	111.57		
TOTAL	53	58541.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	211.400	204.800	220.800	222.000	252.200	279.600	231.800
TEST	4	210.750	209.000	198.000	237.500	271.500	286.750	235.583
TOTAL	9	211.111	206.667	210.667	220.000	260.778	282.778	233.481

TABLE 19A. EXPERIMENT 10-DIA-2, DIISOPROPYLAMINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	COARDS	SPLEEN		
RATS	MALE	CONTROL	259.6	0.34	41.22	7.73	3.63	7.25	.15	14.21	2.74		
		H	5	5	5	5	5	5	5	5	5		
		TEST	218.2	15.76	64.00	0.56	5.24	0.60	.16	12.82	3.35		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-9.86	12.15	10.50	3.20	4.33	7.30	9.20	-2.39	2.83		
		P-VALUE	.0000	.0000	.0111	.0019	.0001	.0000	.0000	.0436	.0222		
RATS	FEMALE	CONTROL	199.0	9.77	37.00	7.17	3.04	0.64	.22	2.46	2.79		
		H	5	5	5	5	5	5	5	5	5		
		TEST	107.4	16.47	59.04	0.00	5.42	9.43	.26	2.45	2.90		
		H	5	5	5	5	5	4	5	5	5		
		T-TEST STATISTIC	-2.07	6.67	9.62	2.40	9.14	1.27	2.29	-0.03	.79		
		P-VALUE	.0725	.0002	.0000	.0300	.0009	.2365	.0554	.9072	.4503		
GUINEA PIG	MALE	CONTROL	246.2	12.10	42.75	10.47	8.39	14.02	.30	3.12	1.42		
		H	5	5	5	5	5	5	5	5	5		
		TEST	230.0	26.61	50.22	11.19	5.05	12.76	.39	2.23	1.66		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.75	14.01	3.01	.42	-.95	-7.79	.24	-4.30	1.02		
		P-VALUE	.4740	.0000	.0051	.6040	.3601	.4544	.0190	.0024	.3392		
GUINEA PIG	FEMALE	CONTROL	269.2	12.40	41.70	0.67	4.93	12.03	.35	3.42	1.71		
		H	5	5	5	5	5	5	5	5	5		
		TEST	214.0	26.75	55.04	11.23	5.11	13.06	.40	2.43	1.40		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-12.4	7.09	3.55	3.72	1.11	3.75	11.10	-2.56	-7.70		
		P-VALUE	.0000	.0000	.0075	.0059	.2904	.0057	.0000	.0337	.5047		

(*) < .10 ** < .05 *** < .01 **** < .001

NOTE

Tables 19B through 19E are not presented here, since all test animals died during the exposure, and therefore the rate of growth analysis was not obtainable.

2-Diethylaminoethanol

Test animals were exposed to concentrations of 2-diethylaminoethanol ranging from 2.27 to 8.77 mg/l as a vapor or vapor-aerosol mixture in air (Table 20). At the lowest level, nasal/lacrymal irritation, dyspnea and tremors were observed; but no irreversible histopathological lesions were found (Tables 2 and 21). The intermediate level also produced nasal/lacrymal irritation, dyspnea, tremors and eye closure. During the post-exposure interval, six rats developed corneal opacities, all of which were subsequently judged to be reversible by the histopathologist. At the highest level, nasal/lacrymal irritation, severe dyspnea and eye closure were observed during exposure. During the post-exposure observation period, some rats had swollen, bloody eyelids; and six rats developed corneal opacities. One rat died one day post-exposure and was found to have reversible congestion of the lungs and the heart which appeared to have caused death. Of those animals submitted for histopathology, one rat was found to have an irreversible ocular lesion, while another rat had a reversible ocular lesion. Also, one rat had nephritis which would cause scarring.

Although all of the corneal lesions found in the test rats at the intermediate level and all but one at the highest level were judged to be reversible by the histopathologist, the occurrence of such lesions in humans might be of sufficient consequence as to be considered a "frank effect" in its own right.

A summary of the statistically significant differences ($\alpha=0.05$) between the test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 22) along with more detailed summaries of the results (Tables 23-25).

Table 20
2-Diethylaminoethanol Atmosphere Analysis

Test Compound Concentration:

Experiment No.	<u>3-DEAE-1</u>		<u>13-DEAE-2</u>		<u>25-DEAE-3</u>	
Date	1-11-78		4-5-78		6-28-78	
Attempted Chamber Conc.	2.02 mg/l	500 ppm	8.07 mg/l	2000 ppm	16.2 mg/l	* ppm
First Sample	2.22 mg/l	549 ppm	5.57 mg/l	1380 ppm	9.42 mg/l	* ppm
Second Sample	2.28 mg/l	564 ppm	5.95 mg/l	1470 ppm	9.61 mg/l	* ppm
Third Sample	2.32 mg/l	573 ppm	6.07 mg/l	1500 ppm	7.27 mg/l	* ppm
Mean	2.27 mg/l	562 ppm	5.86 mg/l	1450 ppm	8.77 mg/l	* ppm
Std. Dev.	0.0503 mg/l	12.1 ppm	0.261 mg/l	62.5 ppm	1.30 mg/l	* ppm
Coef. Var.	2.22%	2.15%	4.45%	4.31%	14.8%	*

Aerosol Size Distribution:**

Experiment No.	<u>25-DEAE-3</u>	
Impactor Stage No.	ECD (μ m)	Cum. %
1	5.03	100.0
2	3.20	100.0
3	1.98	44.0
4	1.22	0.0
5	0.76	0.0
6	0.48	0.0
7	0.30	0.0
Median Aerodynamic Diameter (μ m)	2.1	
Geometric Standard Deviation	1.1	

*Aerosol/vapor mixture, thus ppm definition not applicable.

**Vapor atmosphere only, no aerosol analysis performed on Experiment No. 3-DEAE-1 and 13-DEAE-2.

Table 21
2-Diethylaminoethanol

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Rat		Cat		Control	G. Pig	Rat	Cat	G. Pig	Animal #	Time of Death	Irreversible Lesions Found	Type of Effect	
			Test	To Have Impaired Escape Ability	Control	Control										
1-11-78	3-DEAE-1	562 ppm 2.27 mg/l	0	0	0	0	0	0	0	0	0	-	-	None found	No	
4-5-78	13-DEAE-2	1450 ppm 5.86 mg/l	6 ³	8 ³	0	0	0	0	0	0	0	13RT1M *	1 day post-exp.	Diffuse granular keratitis ² mid cornea ² . Frank possible corneal ulceration ² . No irreversible ocular lesions. Marked congestion and keratitis of cornea. Marked vascular ingrowth into cornea. ²	Frank	
6-28-78	25-DEAE-3	** ppm 8.77 mg/l	9 ⁴	0 ⁴	0	0	0	0	0	0	0	25RT1M *	1 day post-exp.	Congestion of lungs and heart could have caused the death of this animal. Ocular lesions will cause scarring when healed. Acute ulcerative keratitis with diffuse fibrosis and focal calcifications. Ocular lesions could progress to an irreversible state. Iritis-mononuclear inflammatory cells infiltrating ciliary body with some exudate accumulating in the anterior chamber. Nephritis will cause scarring. Myocardial degeneration. ^{1a}		
												25RT5M *				
												25RT9M *				
												25RT10F *				
												25GL5M *				

* Sacrificed for necropsy 14 days post-exposure.

**Aerosol/vapor mixture, thus ppm definition not applicable.

¹ Death or lesion probably not related to exposure; lesion only seen in control animals.

² Although these lesions were judged to be reversible by the histopathologist, they are reported because these animals developed corneal opacities during the post-exposure observation period and this was considered significant.

³ By 5 minutes all animals were either squinting or had their eyes closed; and G1, 2, 3 and 4 had temporary head and body tremors. By 10 minutes R1, 2, 3, 5, 9 and 10 and G4, 8 and 9 had eyes closed, but they responded to an auditory stimulus by opening their eyes. By 15 minutes R2, 3, 4, 5, 6, 9 and 10 and G 2, 3, 5, 8, 9 and 10 had their eyes closed; and R3, 9 and 10 would not open their eyes in response to an auditory stimulus. By 25 minutes R3, 4, 5, 7, 8 and 10 and G 1, 2, 3, 4, 6, 7, 8 and 10 had eyes closed and would not open them in response to an auditory stimulus. By 30 minutes R1, 3, 4, 5, 6, 7, 8 and 10 and G1, 2, 3, 4, 5, 6, 7, 8 and 10 had eyes closed; and R3 and 10 and G1, 4 and 6 had head and body tremors. Immediately after completion of the exposure, all animals had normal righting reflex. During post-exposure observation period R1, 2, 5, 6 and 7 developed corneal opacity lesions. [Impairment of the ability to escape was judged to be present when animals failed to open their eyes in response to auditory stimulus.]

⁴ By 10 minutes R7 and 8 and G8 and 10 had mouths open and labored breathing (gasping); while R1, 2, 3, 4, 5, 6, 7 and 8 and G1 through 10 had eyes closed. By 15 minutes R2, 3, 4, 5, 6, 7, 8, 9 and 10 had mouths open and labored breathing (gasping); eyelids of R3, 7, 8 and 9 were swollen and purple. GB was trying to get out of the top of the cage. By 20 minutes R1, 3, 4, 6, 8, 9 and 10 and G1, 2, 3, 5, 7, 8, 9 and 10 had mouths open and labored breathing (gasping); R1, 3, 6, 8, 9 and 10 had swollen and purple eyelids. By 25 minutes R1 through 10 and G1, 2, 3, 5, 7, 8, 9 and 10 had labored breathing and rats made very little response to loud auditory stimulus. By 30 minutes only R3 opened eyes in response to auditory stimulus; while all G's opened eyes. Immediately after exposure, all animals exhibited normal righting reflex. During post-exposure observation period R2, 3, 4, 5, 6, 9 and 10 developed corneal opacity lesions. [Impairment of the ability to escape was judged to be present when animals failed to open their eyes in response to auditory stimulus.]

⁵ Lesions were judged to be reversible, but they appeared to cause death.

Table 22

2-Diethylaminoethanol
 Summary of Statistically Significant Differences Between
 Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
1-11-78	3-DEAE-1	562 ppm 2.27 mg/l	No significant difference found.	Adrenal (-)FR
4-5-78	13-DEAE-2	1450 ppm 5.86 mg/l	ΔBW(±)MG	Liver (-)FG Adrenal (-)MG
6-28-78	25-DEAE-3	** ppm 8.77 mg/l	ΔBW(-)MR	Kidney (-)MG Adrenal (-)MG Spleen (-)MR

* Abbreviations:

BWA = Body weight at autopsy
 ΔBW = Change in body weight post-exposure
 M = Male
 F = Female
 R = Rat
 G = Guinea pig
 (-) = Test group less than control group
 (+) = Test group more than control group
 (±) = Variable differences between test and control groups observed

**Aerosol/vapor mixture, thus ppm definition is not applicable.

TABLE 23A. EXPERIMENT 3-DEAE-1, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OVARIES	SPLEEN			
RATS	MALE	CONTROL	306.2	7.11	45.05	8.16	3.42	5.93	.17	14.01	2.44			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	292.4	7.01	41.37	7.61	3.41	5.00	.15	14.30	2.31			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.47		-1.29		-0.04		-1.13					
		P-VALUE	.1795	.0611	.2341	.3703	.9791	.0979	.5859	.7200	.5207			
RATS	MALE	CONTROL	203.0	0.10	45.30	7.45	3.60	0.06	.36	2.65	2.54			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	202.6	7.93	36.34	6.51	3.61	0.04	.26	3.30	2.30			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-0.29		-1.64		0.66		-3.22					
		P-VALUE	.7759	.6273	.1307	.2000	.9505	1.000	.0147	.1014	.3290			
GUINEA PIG	MALE	CONTROL	335.2	0.44	40.02	0.70	4.27	10.60	.30	3.71	1.41			
		H	6	6	6	6	6	6	6	6	6			
	FEMALE	CONTROL	319.6	9.07	49.01	0.63	4.35	10.97	.25	3.71	1.42			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.00		1.05		0.28		-1.30					
		P-VALUE	.3102	.3232	.7225	.7933	.7030	.6950	.2245	1.000	1.000			
GUINEA PIG	MALE	CONTROL	332.0	10.96	40.06	0.44	4.56	10.40	.34	4.51	1.30			
		H	4	4	4	4	4	4	4	4	4			
	FEMALE	CONTROL	311.4	0.69	40.04	0.53	4.06	11.35	.35	4.62	1.66			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.71		-1.30		-1.52		1.11					
		P-VALUE	.1307	.0917	.2350	.0977	.1723	.2535	.9149	.9101	.0959			

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 23B. EXPERIMENT 3-DEAE-1, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	81.500	81.500	.83392E-01	N.S.
SUBJECTS IN GROUPS	8	7818.5	977.31		
TINES	5	65837.	13167.	76.594	p < .001
TINES X GROUPS	5	644.50	128.90	.74980	N.S.
TINES X SUBJECTS IN GROUPS	40	6876.5	171.91		
TOTAL	59	81258.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL	
CONTROL	1	5	211.400	210.600	229.800	252.200	256.400	300.200	244.767
TEST	2	5	207.800	207.800	225.000	247.000	268.000	299.000	242.433
TOTAL	10		209.600	209.200	227.400	249.600	262.200	303.600	243.600

TABLE 23C. EXPERIMENT 3-DEAF-1, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	13.750	13.750	.74855E-01	N.S.
SUBJECTS IN GROUPS	6	1469.5	183.69		
TIMES	5	6213.5	1242.7	156.56	p < .001
TIMES X GROUPS	5	25.750	5.1500	.64802	N.S.
TIMES X SUBJECTS IN GROUPS	40	317.50	7.9375		
TOTAL	59	8040.0			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6				
CONTROL	5	177.200	176.400	181.800	191.200	193.800	203.800				187.367
TEST	5	176.400	173.400	182.000	188.800	193.400	204.400				186.400
TOTAL	10	176.800	174.900	181.900	190.000	193.600	204.100				186.883

TABLE 23D. EXPERIMENT 3-DEAE-1, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	694.00	694.00	.33532	N.S.
SUBJECTS IN GROUPS	9	18627.	2069.7		
TIMES	5	.12462E+06	24925.	292.09	p < .001
TIMES X GROUPS	5	554.50	110.90	1.2996	N.S.
TIMES X SUBJECTS IN GROUPS	45	3840.0	85.333		
TOTAL	65	.14034E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	1	202.000	192.500	223.000	235.500	271.667	318.667	240.556
TEST	2	203.000	201.000	223.400	247.600	297.000	320.400	247.067
TOTAL	11	202.455	196.364	223.182	241.000	278.636	319.455	243.515

TABLE 23E. EXPERIMENT 3-DEAE-1, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	13.800	13.800	.20031E-01	N.S.
SUBJECTS IN GROUPS	7	4543.0	649.00		
TIMES	5	76709.	15342.	304.23	p < .001
TIMES X GROUPS	5	80.500	16.100	.31926	N.S.
TIMES X SUBJECTS IN GROUPS	35	1765.0	50.429		
TOTAL	53	83110.			

MEANS

GROUPS:	N	TIMES:						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	4	213.250	208.500	234.000	248.750	285.250	311.750	250.250
TEST	2	5	213.400	208.000	237.000	246.600	290.000	311.600	251.233
TOTAL	9		213.333	208.222	236.111	247.556	287.889	311.667	250.796

TABLE 24A. EXPERIMENT 13-DEAE-2, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN		
RATS	MALE	CONTROL	294.2	7.43	36.46	6.78	3.31	6.36	.17	13.75	2.13		
		N	5	5	5	5	5	5	5	5	5		
	TEST	295.6	7.48	37.01	7.03	3.29	6.21	.16	14.40	2.04			
	N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	.22	.13	.46	.97	-.13	-.77	-.53	.94	-.54		
		P-VALUE	.8388	.8982	.6586	.6983	.4655	.6113	.3764	.6820			
RATS	FEMALE	CONTROL	269.8	8.82	34.68	6.91	3.79	8.18	.32	3.22	2.61		
		N	5	5	5	5	5	5	5	5	5		
	TEST	228.8	9.01	34.85	6.87	3.52	8.49	.31	2.47	2.49			
	N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	2.82	1.47	.18	-1.98	.05	-.17	-1.08	-.56			
		P-VALUE	.0785	.1792	.9226	.0836	.4226	.8718	.3473	.5924			
			(*)			(*)							
GUINEA PIG	MALE	CONTROL	237.6	9.27	58.65	18.98	4.68	14.29	.58	2.93	1.16		
		N	5	5	5	5	5	5	5	5	5		
	TEST	271.4	8.67	55.71	9.62	4.98	12.44	.41	3.22	1.24			
	N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.53	-.82	.74	-1.79	1.19	-1.45	-2.50	.73	1.33		
		P-VALUE	.1646	.4376	.4811	.1184	.2677	.1841	.0324	.4852	.2198		
									*				
GUINEA PIG	FEMALE	CONTROL	278.8	8.54	67.84	9.81	4.74	11.75	.45	3.48	1.37		
		N	5	5	5	5	5	5	5	5	5		
	TEST	255.8	8.77	46.48	8.16	4.71	12.63	.49	2.78	1.23			
	N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.69	.24	-3.31	-1.83	-.86	.78	.54	-1.16	-.82		
		P-VALUE	.3084	.8138	.0187	.3352	.9536	.4686	.6813	.2790	.4360		
					*								

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 24B. EXPERIMENT 13-DEAE-2, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	50.500	50.500	.30727E-01	N.S.
SUBJECTS IN GROUPS	0	13148.	1643.5		
TIMES	5	51210.	10244.	164.03	P<.001
TIMES X GROUPS	5	721.50	144.30	2.3106	N.S.
TIMES X SUBJECTS IN GROUPS	40	2498.0	62.450		
TOTAL	59	67636.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	212.600	210.000	229.000	240.000	265.200	282.200	239.967		
TEST	2	5	211.000	210.400	222.000	238.600	273.200	295.600	241.600		
TOTAL	10		211.800	210.200	225.900	239.300	269.200	288.900	240.803		

TABLE 24C. EXPERIMENT 13-DEAB-2, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	84.500	84.500	.64976E-01	N.S.
SUBJECTS IN GROUPS	8	10419.	1302.4		
TIMES	5	11881.	2376.3	23.590	P<.001
TIMES X GROUPS	5	61.000	12.200	.12115	N.S.
TIMES X SUBJECTS IN GROUPS	40	4028.0	100.70		
TOTAL	59	26474.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	184.600	184.800	191.600	196.600	212.800	221.000	198.567		
TEST	2	5	185.200	180.800	189.200	192.000	210.000	220.800	196.200		
TOTAL	10	184.900	182.400	190.400	194.300	211.400	220.900	197.383			

TABLE 24E. EXPERIMENT 1.3-DEAE-2, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3125.0	3125.0	2.4831	N.S.
SUBJECTS IN GROUPS	8	10068.	1258.5		
TIMES	5	33562.	6712.5	23.199	P<.001
TIMES X GROUPS	5	1471.0	294.20	1.0168	N.S.
TIMES X SUBJECTS IN GROUPS	40	11574.	289.35		
TOTAL	59	59800.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	219.200	216.000	233.600	260.200	205.000	270.000	240.000		240.000
TEST	2	5	219.600	214.400	213.400	230.000	265.000	255.000	234.367		234.367
TOTAL	10		219.400	215.200	223.500	249.100	275.400	266.900	241.583		241.583

TABLE 25A. EXPERIMENT 25-DEAE-3, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (% 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	CONVUS	SPLEEN		
RATS	MALE	CONTROL	295.6	0.13	30.62	7.05	3.67	6.33	.20	13.00	2.70		
		H	5	5	5	5	5	5	5	5	5		
	FEMALE	CONTROL	283.0	0.12	34.15	7.17	3.60	6.46	.20	14.09	2.25		
		H	4	4	4	4	4	4	4	4	4		
		T-TEST STATISTIC	-1.00	-0.03	-1.42	.35	-.25	.30	.02	.22	-3.04		
		P-VALUE	.1147	1.000	.1998	.7355	.8095	.7176	1.000	.0293	.0100	*	
RATS	MALE	CONTROL	203.6	10.10	34.51	6.73	3.67	0.70	.35	2.07	2.61		
		H	5	5	5	5	5	5	5	5	5		
	FEMALE	CONTROL	203.0	10.49	37.04	7.12	3.02	0.00	.32	2.94	2.99		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.03	.60	1.03	1.10	.33	-1.01	.71	.69			
		P-VALUE	1.000	.5652	.1030	.2526	.3035	.7501	.3401	.4976	.5093		
GUINEA PIG	MALE	CONTROL	279.4	11.72	46.14	9.06	4.32	11.07	.50	3.13	1.45		
		H	5	5	5	5	5	5	5	5	5		
	FEMALE	CONTROL	200.6	12.09	43.53	0.54	4.51	11.71	.36	2.05	1.30		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.41	.55	-.97	-2.45	1.11	-.30	-3.20	-.05	-3.30		
		P-VALUE	.6959	.5995	.3616	.0400	.2903	.7103	.0126	.4179	.7146		
GUINEA PIG	MALE	CONTROL	302.0	10.62	40.16	8.27	4.43	10.76	.40	4.59	1.02		
		H	5	5	5	5	5	5	5	5	5		
	FEMALE	CONTROL	291.0	12.10	39.01	0.01	4.29	11.19	.39	3.44	1.56		
		H	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.29	1.57	-.50	-.46	1.04	-2.06	-1.61	-1.10			
		P-VALUE	.2339	.1550	.5760	.4453	.6610	.3267	.0720	.1451	.2707		

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 25B. EXPERIMENT 25-DEAF-3, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2849.0	2849.0	13.932	p < .001
SUBJECTS IN GROUPS	7	1434.5	204.93		
TIMES	5	51531.	10306.	186.32	p < .001
TIMES X GROUPS	5	834.50	166.90	3.0173	p < .05
TIMES X SUBJECTS IN GROUPS	35	1936.0	55.314		
TOTAL	53	58585.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	209.800	211.400	228.800	251.600	274.000	295.600	245.200
TEST	4	207.750	202.500	204.500	227.750	250.000	283.000	230.583
TOTAL	9	208.889	207.444	218.000	241.000	266.889	290.000	238.704

TABLE 25C. EXPERIMENT 25-DEAE-3, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	510.00	510.00	.74893	N.S.
SUBJECTS IN GROUPS	8	5447.7	680.97		
TIMES	5	6167.2	1233.4	25.981	P. < .001
TIMES X GROUPS	5	396.75	79.350	1.6714	N.S.
TIMES X SUBJECTS IN GROUPS	40	1899.0	47.475		
TOTAL	59	14421.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	177.600	180.000	182.600	192.600	199.000	203.600	189.233
TEST	5	176.400	177.200	172.200	178.400	192.400	203.000	183.400
TOTAL	10	177.000	178.600	177.400	185.500	195.700	203.700	186.317

TABLE 25D. EXPERIMENT 25-DEAE-3, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	73.000	73.000	.14665E-01	N.S.
SUBJECTS IN GROUPS	8	39824.	4978.0		
TIMES	5	59617.	11923.	29.448	P < .001
TIMES X GROUPS	5	839.00	167.80	.41442	N.S.
TIMES X SUBJECTS IN GROUPS	40	16196.	404.90		
TOTAL	59	.11655E+06			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	210.200	183.600	202.800	222.000	226.800	279.400	220.800
TEST	2	5	210.600	180.600	193.400	217.800	239.000	208.600	223.000
TOTAL	10	10	210.400	186.100	198.100	219.900	232.900	284.000	221.900

TABLE 25E. EXPERIMENT 25-DEAE-3, 2-DIETHYLAMINOETHANOL, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1335.0	1335.0	1.4937	N.S.
SUBJECTS IN GROUPS	8	7150.0	893.75		
TIMES	5	70837.	14167.	147.31	P < .001
TIMES X GROUPS	5	691.50	138.30	1.4380	N.S.
TIMES X SUBJECTS IN GROUPS	40	3847.0	96.175		
TOTAL	59	83860.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	203.000	200.600	217.000	240.000	265.600	302.000	238.300		238.300
TEST	2	5	199.000	201.600	203.200	231.000	246.400	291.000	220.867		220.867
TOTAL	10	10	201.400	201.200	210.500	235.900	256.000	296.500	233.583		233.583

Ortho-Toluidine

Test animals were exposed to concentrations of ortho-toluidine ranging from 0.490 to 2.27 mg/l in air as a vapor or vapor-aerosol mixture (Table 26). The lowest level produced nasal/lacrymal irritation and apparent skin irritation since test animals were scratching more than control animals (Tables 2 and 27). The intermediate level produced nasal/lacrymal irritation and eye closure in the majority of guinea pigs within ten minutes. At the highest level, nasal/lacrymal irritation was present primarily in guinea pigs along with eye closure. The only irreversible lesion and death apparently related to exposure occurred in a guinea pig at the highest level; the lesion was acute pulmonary congestion. Due to limitations of the atmosphere generation equipment available at UBTL, no higher levels could be produced.

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 28) along with more detailed summaries of the results (Tables 29-31).

Table 26
Ortho-Toluidine Atmosphere Analysis Summary

<u>Test Compound Concentration</u>						
Experiment No.	<u>4-OT-1</u>		<u>11-OT-2</u>		<u>26-OT-3</u>	
Date	1-18-7		3-22-78		7-5-78	
Attempted Chamber Conc.	0.369 mg/1	100 ppm	2.10 mg/1	500 ppm	3.69 mg/1	ppm
First Sample	0.456 mg/1	124 ppm	1.45 mg/1	414 ppm	2.56 mg/1	*
Second Sample	0.497 mg/1	135 ppm	0.960 mg/1	275 ppm	2.92 mg/1	*
Third Sample	0.516 mg/1	140 ppm	1.41 mg/1	404 ppm	2.88 mg/1	*
Mean	0.490 mg/1	133 ppm	1.27 mg/1	364 ppm	2.79 mg/1	*
Std. Dev.	0.0307 mg/1	8.19 ppm	0.272 mg/1	77.5 ppm	0.197 mg/1	*
Coef. Var.	6.27%	6.16%	21.4%	21.3%	7.06%	*

Aerosol Size Distribution:**

Experiment No.	<u>26-OT-3</u>	
Impactor Stage No.	ECD (μ m)	Cum. %
1	5.18	100.0
2	3.80	72.8
3	2.03	36.2
4	1.26	4.7
5	0.78	0.9
6	0.49	0.9
7	0.31	0.9
Median Aerodynamic Diameter (μ m)	2.5	
Geometric Standard Deviation	1.5	

*Aerosol/vapor mixture, thus definition of ppm not applicable.

**Vapor atmosphere only, no aerosol distribution analysis performed on Experiments 4-OT-1 and 11-OT-2.

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Table 27
Ortho-Toluidine

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability		Animal #	Time of Death	Irreversible Lesions Found	Type of Effect
			Rat	G. Pig				
1-18-78	4-OT-1	133 ppm 0.490 mg/l	0	0	0	-	None found	No
3-22-78	11-OT-2	364 ppm 1.27 mg/l	0	0	0	11GT1M *	Hydrocephalus - probably not exposure related. Pneumonitis may result in scarring of lungs. Focal and diffuse nonsuppurative pneumonia may result in scarring ^{1a,c} .	No
7-7-78	26-OT-3	** 11 ppm 2.75 mg/l	0	0	0	11GT3M * 11GT5M * 11EC6F *	Focal granulomatous pneumonia will cause scarring in lungs ¹ .	Minimal

* Sacrificed for necropsy 14 days post-exposure.

**Vapor/aerosol mixture, thus ppm definition not applicable.

¹ Death or lesion probably not related to exposure;

1a probably an infectious lesion

1b congenital lesion

1c also seen in control animals

Ortho-Toluidine
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
1-18-78	4-OT-1	133 ppm 0.490 mg/l	No significant difference found.	Brain (-)MG Adrenal (+)MR, (+)FR, (-)MG
3-22-78	11-OT-2	364 ppm 1.21 Mg/l	No significant difference found.	Adrenal (+)MR Spleen (+)FR
7-5-78	26-OT-3	** ppm 2.78 mg/l	ΔBW (-)MR ΔBW (-)MG	Kidney (-)FR Heart (+)MG Adrenal (-)MR, (-)FR, (-)MG, (-)FG

* Abbreviations:

BWA = Body weight at autopsy
ΔBW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(±) = Variable differences between test and control groups observed

**Aerosol/vapor mixture, thus ppm definition not applicable.

TABLE 29A. EXPERIMENT 4-OT-1, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
			MEAN WEIGHT (GRAMS)	LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GOVADS	SPLEEN		
RATS	MALE	CONTROL	297.6	5.13	49.01	7.70	3.49	5.73	.26	12.93	2.22		
		N	5	5	5	5	5	5	5	5	5		
		TEST	291.6	5.10	44.05	8.06	3.30	6.42	.34	13.11	2.34		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.51	.17	-1.40	.80	-.07	2.20	3.02	.40	.97		
P-VALUE	.6240	.8675	.2004	.4066	.4007	.0590	.0051	.7010	.3602				
						(*)	**						
RATS	FEMALE	CONTROL	213.0	6.12	30.62	7.27	3.71	0.13	.36	2.99	2.43		
		N	5	5	5	5	5	5	5	5	5		
		TEST	200.4	6.11	37.46	7.00	3.04	7.90	.56	3.02	2.43		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.67	-.02	-.71	-.63	.44	-.40	5.95	1.67	.03		
P-VALUE	.1336	1.000	.4991	.5493	.6683	.6983	.0003	.1320	1.000				

GUINEA PIG	MALE	CONTROL	346.0	7.67	44.76	9.43	4.67	11.12	.41	3.50	1.75		
		N	5	5	5	5	5	5	5	5	5		
		TEST	347.2	7.30	47.07	9.02	4.30	9.95	.31	3.56	1.40		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.04	-.36	1.00	-.01	-.71	-2.34	-2.75	.20	-1.21		
P-VALUE	.9724	.7200	.1009	.4434	.4959	.0473	.0249	.8430	.2611				
												*	
GUINEA PIG	FEMALE	CONTROL	303.0	7.29	40.72	9.35	4.62	11.00	.50	5.10	1.07		
		N	5	5	5	5	5	5	5	5	5		
		TEST	303.2	6.90	40.67	9.04	4.66	11.62	.45	5.52	1.35		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.03	-.89	-.02	1.17	.16	-.20	-.79	.21	-1.54		
P-VALUE	.9917	.3993	1.000	.2730	.0762	.7032	.4090	.0371	.1616				

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 29B. EXPERIMENT 4-OT-1, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS											
SOURCE OF VARIATION		DEGREES OF FREEDOM		SUM OF SQUARES		MEAN SQUARE		F-RATIO		SIGNIFICANCE	
GROUPS		1		294.50		294.50		.34019			N.S.
SUBJECTS IN GROUPS		8		6925.5		865.69					
TIMES		5		60482.		12096.		443.89			P < .001
TIMES X GROUPS		5		80.500		17.700		.64835			N.S.
TIMES X SUBJECTS IN GROUPS		40		1092.0		27.300					
TOTAL		59		68882.							

MEANS		TIMES:					
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15
GROUPS:	N	1	2	3	4	5	6
CONTROL	1	205.400	200.200	223.800	244.800	265.800	293.800
TEST	2	203.200	203.400	220.800	235.400	260.800	291.600
TOTAL	10	204.300	205.800	221.900	240.100	262.900	292.700
						240.167	235.733
							237.950

FIGURE 29C. EXPERIMENT 4-OT-1, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	295.00	295.00	1.2570	N.S.
SUBJECTS IN GROUPS	8	1877.5	234.69		
TIMES	5	7329.0	1465.8	108.08	p < .001
TIMES X GROUPS	5	138.00	27.600	2.0350	N.S.
TIMES X SUBJECTS IN GROUPS	40	542.50	13.562		
TOTAL	59	10182.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	5	182.200	177.200	183.200	183.200	193.200	199.600	199.600	213.600	191.500	
TEST	5	181.200	174.800	182.200	186.600	192.000	192.000	205.600	187.067		
TOTAL	10	181.700	176.000	182.700	189.900	195.800	209.600	189.283			

TABLE 29D. EXPERIMENT 4-OT-1, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	380.00	380.00	.45632	N.S.
SUBJECTS IN GROUPS	8	6662.0	832.75		
TIMES	5	.12419E+06	24838.	624.08	P < .001
TIMES X GROUPS	5	247.00	49.400	1.2412	N.S.
TIMES X SUBJECTS IN GROUPS	40	1592.0	39.800		
TOTAL	59	.13307E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11 DAY 12 DAY 13 DAY 14 DAY 15						TOTAL								
		1	2	3	4	5	6									
CONTROL	1	5	222.000	219.400	243.000	268.400	300.800	346.800	300.800	346.800	300.800	268.400	243.000	219.400	222.000	266.733
TEST	2	5	222.200	226.200	246.400	276.600	312.000	347.200	276.600	312.000	347.200	276.600	246.400	226.200	222.200	271.767
TOTAL	10	10	222.100	222.800	244.700	272.500	306.400	347.000	272.500	306.400	347.000	272.500	244.700	222.800	222.100	269.250

TABLE 29E. EXPERIMENT 4-CT-1, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	14.000	14.000	.15630E-01	N.S.
SUBJECTS IN GROUPS	8	7165.5	895.69		
TIMES	5	67294.	13459.	134.27	p < .001
TIMES X GROUPS	5	128.00	25.600	.25539	N.S.
TIMES X SUBJECTS IN GROUPS	40	4009.5	100.24		
TOTAL	59	78611.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	211.000	212.000	229.800	249.400	279.000	303.000	247.500		247.500
TEST	2	5	212.600	212.400	231.200	247.800	272.000	303.200	246.533		246.533
TOTAL	10		211.800	212.200	230.500	248.600	275.500	303.500	247.017		247.017

TABLE 30A. EXPERIMENT 11-OT-2, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OWARDS	SPLEEN			
RATS	MALE	CONTROL	308.0	7.15	42.42	6.96	3.42	6.06	.14	14.12	2.33			
		H	5	5	5	5	5	5	5	5	5			
		TEST	285.2	7.29	51.68	8.84	3.82	6.88	.10	14.89	2.33			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.48	.21	2.89	1.93	1.28	1.58	2.74	.48	-.81			
		P-VALUE	.1762	.8419	.0781	.8896	.2348	.1523	.8253	.6488	1.088			
				(*)		(*)			*					
RATS	FEMALE	CONTROL	286.4	8.53	37.76	6.82	4.28	8.58	.23	2.87	2.34			
		H	5	5	5	4	5	5	4	5	5			
		TEST	286.2	8.27	39.38	7.28	3.94	8.98	.29	3.27	2.63			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.83	-.43	.83	.65	-1.13	1.88	2.01	.68	1.91			
		P-VALUE	1.088	.6786	.4322	.5351	.2983	.3117	.8843	.5166	.8925	(*)		
									(*)					
GUINEA PIG	MALE	CONTROL	307.8	8.82	54.88	9.53	4.92	11.72	.37	3.67	1.36			
		H	5	5	5	5	5	5	5	5	5			
		TEST	287.8	9.46	58.13	10.12	5.25	12.77	.37	4.15	1.52			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.81	.72	-.76	.84	.94	.85	.81	.86	1.17			
		P-VALUE	.4485	.4892	.4665	.4254	.3769	.4192	1.888	.4173	.2762			
GUINEA PIG	FEMALE	CONTROL	278.8	9.49	49.84	9.33	4.61	12.88	.44	3.31	1.31			
		H	5	5	5	5	5	5	5	5	5			
		TEST	296.8	9.26	48.34	8.92	4.63	11.68	.43	3.37	1.76			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	.71	-.33	-2.30	-.56	.85	-.32	-.34	.86	2.32			
		P-VALUE	.4988	.7535	.8582	.5926	.9641	.7681	.7444	.9526	.8498	*		

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 30B. EXPERIMENT 11-OT-2, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	121.00	121.00	.21694	N.S.
SUBJECTS IN GROUPS	8	4462.0	557.75		
TIMES	5	61828.	12366.	1224.3	P < .001
TIMES X GROUPS	5	12.000	2.4000	.23762	N.S.
TIMES X SUBJECTS IN GROUPS	40	404.00	10.100		
TOTAL	59	66827.			

MEANS

TIMES:

GROUPS:	N	1	2	3	4	5	6	TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	215.000	213.400	233.400	251.600	282.400	299.200	249.167
TEST	5	214.000	210.400	230.400	249.000	278.000	295.400	246.333
TOTAL	10	214.500	211.900	231.900	250.300	280.600	297.300	247.750

TABLE 30C. EXPERIMENT 11-OT-2, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	6.0000	6.0000	.27634E-01	N.S.
SUBJECTS IN GROUPS	0	1737.0	217.12		
TIMES	5	4912.0	902.40	63.075	p < .001
TIMES X GROUPS	5	107.00	21.400	1.3740	N.S.
TIMES X SUBJECTS IN GROUPS	40	623.00	15.575		
TOTAL	59	7385.0			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	183.000	177.400	182.000	187.200	195.600	204.000	180.200	
TEST	2	182.000	175.000	184.400	192.000	197.800	201.000	180.833	
TOTAL	10	182.500	176.200	183.200	189.600	196.700	202.900	180.517	

TABLE 30D. EXPERIMENT 11-OT-2, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	570.00	570.00	.64663	N.S.
SUBJECTS IN GROUPS	8	7052.0	881.50		
TIMES	5	57795.	11559.	45.341	P<.001
TIMES X GROUPS	5	2670.0	534.00	2.0946	N.S.
TIMES X SUBJECTS IN GROUPS	40	10197.	254.94		
TOTAL	59	78284.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	215.600	211.000	222.400	232.800	265.400	307.000	242.367		
TEST	2	5	216.000	215.000	236.400	251.200	284.800	287.800	248.533		
TOTAL	10		215.800	213.800	229.400	242.800	275.100	297.400	245.450		

TABLE 30E. EXPERIMENT 11-OT-2, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2220.5	2220.5	.68014	N.S.
SUBJECTS IN GROUPS	8	26118.	3264.7		
TIMES	5	32348.	6469.7	20.915	P<.001
TIMES X GROUPS	5	2140.5	428.10	1.3039	N.S.
TIMES X SUBJECTS IN GROUPS	40	12373.	309.34		
TOTAL	59	75201.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL	
		1	2	3	4	5	6		
CONTROL	1	5	229.600	226.600	222.800	218.200	255.200	278.000	238.400
TEST	2	5	227.600	223.800	233.200	249.200	272.800	296.800	250.567
TOTAL	10		228.600	225.200	228.000	233.700	264.000	287.400	244.403

TABLE 31A. EXPERIMENT 26-OT-3, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GOVADS	SPLEEN		
RATS	MALE	CONTROL	384.8	0.24	48.48	7.58	3.48	6.25	.23	12.84	2.36		
		N	5	5	5	5	5	5	5	5	5		
	TEST	N	294.6	0.63	48.88	7.34	3.31	6.11	.16	12.83	2.29		
		5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.37	.72	-.17	-.31	-1.81	-.74	-3.39	-.88	-.34		
		P-VALUE	.2883	.4936	.8687	.7668	.3422	.4832	.8895	1.888	.7417	**	
RATS	FEMALE	CONTROL	218.4	9.54	36.51	7.14	3.71	8.44	.39	4.98	2.66		
		N	5	5	5	5	5	5	5	5	5		
	TEST	N	287.6	8.65	36.24	6.83	3.39	8.56	.26	4.81	2.51		
		5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.48	-1.48	-.18	-2.87	-1.82	.26	-2.46	-.44	-.99		
		P-VALUE	.6436	.1988	.8582	.8289	.3371	.7992	.8395	.6684	.3489	*	
GUINEA PIG	MALE	CONTROL	277.2	14.21	45.28	8.49	4.84	11.11	.53	3.64	1.43		
		N	5	5	5	5	5	5	5	5	5		
	TEST	N	264.5	14.88	42.93	8.97	5.18	12.36	.38	3.18	1.43		
		4	4	4	4	4	4	4	4	3	4		
		T-TEST STATISTIC	-.98	-.13	-.74	1.86	2.97	1.59	-2.88	-1.88	.81		
		P-VALUE	.3583	.8965	.4836	.3253	.0289	.1554	.8267	.3285	1.888	*	
GUINEA PIG	FEMALE	CONTROL	267.6	13.98	39.76	8.88	4.41	18.99	.55	4.25	1.62		
		N	5	5	5	5	5	5	4	5	5		
	TEST	N	271.4	12.85	38.86	8.22	4.11	11.57	.45	5.38	1.54		
		5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.25	-.71	-.79	.33	-1.36	.65	-2.33	1.89	-.58		
		P-VALUE	.8889	.4984	.4589	.7588	.2182	.5361	.8528	.3888	.6282	(*)	

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 31B. EXPERIMENT 26-OT-3, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	426.50	426.50	1.1515	N.S.
SUBJECTS IN GROUPS	8	2963.0	370.37		
TIMES	4	55913.	13978.	1406.1	p < .001
TIMES X GROUPS	4	232.00	58.000	6.1661	p < .001
TIMES X SUBJECTS IN GROUPS	32	301.00	9.4062		
TOTAL	49	59836.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	TOTAL
CONTROL	5	220.800	208.600	256.200	277.400	304.600	253.520	
TEST	5	220.600	207.600	247.600	268.000	294.600	247.680	
TOTAL	10	220.700	208.100	251.900	272.700	299.600	250.600	

TABLE 31C. EXPERIMENT 26-OT-3, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	82.000	82.000	.47927	N.S.
SUBJECTS IN GROUPS	8	1368.7	171.09		
TIMES	4	6864.7	1716.2	95.137	P < .001
TIMES X GROUPS	4	29.250	7.3125	.40537	N.S.
TIMES X SUBJECTS IN GROUPS	32	577.25	18.039		
TOTAL	49	8922.0			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 5	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	
CONTROL	5	185.200	176.000	197.600	202.400	210.400	194.320
TEST	5	184.600	175.000	193.600	198.000	207.600	191.760
TOTAL	10	184.900	175.500	195.600	200.200	209.000	193.040

TABLE 31D. EXPERIMENT 26-OT-3, ORTHIO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2.0000	2.0000	.14414E-02	N.S.
SUBJECTS IN GROUPS	7	9712.7	1387.5		
TIMES	4	67038.	16760.	513.56	p < .001
TIMES X GROUPS	4	410.00	102.50	3.1409	p < .05
TIMES X SUBJECTS IN GROUPS	28	913.75	32.634		
TOTAL	44	78077.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	TOTAL
CONTROL	1	171.600	169.600	210.000	246.400	274.200	214.360	
TEST	2	175.750	174.500	214.250	240.750	264.500	213.950	
TOTAL	9	173.444	171.778	211.889	243.889	269.889	214.178	

TABLE 31E. EXPERIMENT 26-OT-3, ORTHO-TOLUIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	128.00	128.00	.90360E-01	N.S.
SUBJECTS IN GROUPS	8	11332.	1416.6		
TIMES	4	46603.	11651.	133.20	p. < .001
TIMES X GROUPS	4	55.000	13.750	.15720	N.S.
TIMES X SUBJECTS IN GROUPS	32	2799.0	87.469		
TOTAL	49	60918.			

MEANS

TIMES:

GROUPS:	N	TIMES					TOTAL
		DAY 0	DAY 1	DAY 6	DAY 10	DAY 15	
CONTROL	5	193.400	190.800	226.000	251.200	270.600	226.400
TEST	5	198.000	197.200	227.200	254.200	271.400	229.600
TOTAL	10	195.700	194.000	226.600	252.700	271.000	228.000

Ortho-Anisidine

Test animals were exposed to concentrations of ortho-anisidine aerosol ranging from 0.0524 to 0.946 mg/l in air (Table 32). Little effect was observed at the lowest and intermediate levels other than nasal/lacrymal irritation (Tables 2 and 33). At the highest level, nasal/lacrymal irritation was observed in both rats and guinea pigs and focal emphysema was present in one of the rats at necropsy. Due to limitations of the atmosphere generation equipment available at UBTL, no higher levels could be produced.

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 34) along with more detailed summaries of the results (Tables 35-37).

Table 32

Ortho-Anisidine Atmosphere Analysis

Test Compound Concentration:

Experiment No.	<u>5-OA-1</u>	<u>16-OA-2</u>	<u>27-OA-3</u>
Date	1-25-78	4-26-78	7-12-78
Attempted Chamber Conc.	0.030 mg/l	0.300 mg/l	1.00 mg/l
First Sample	0.0472 mg/l	0.273 mg/l	0.946 mg/l
Second Sample	0.0548 mg/l	0.299 mg/l	0.917 mg/l
Third Sample	0.0552 mg/l	0.286 mg/l	0.972 mg/l
Mean	0.0524 mg/l	0.286 mg/l	0.946 mg/l
Std. Dev.	0.00451 mg/l	0.0130 mg/l	0.0276 mg/l
Coef. Var.	8.60%	4.55%	2.92%

Aerosol Size Distribution:*

Experiment No.	<u>16-OA-2</u>		<u>27-OA-3</u>		
	Impactor Stage No.	ECD(μ m)	Cum. %	ECD(μ m)	Cum. %
1		5.64	100.0	5.18	100.0
2		3.57	99.4	3.28	98.7
3		2.21	80.7	2.03	87.9
4		1.37	43.5	1.26	11.0
5		0.85	15.4	0.78	1.2
6		0.53	3.7	0.49	1.1
7		0.33	0.3	0.31	1.1
Median Aerodynamic Diameter (μ m)		1.4		1.6	
Geometric Standard Deviation		1.8		1.4	

*Aerosol size distribution analysis not performed on Experiment No. 5-OA-1, but an inline single stage impactor was used to remove larger particles prior to mixing aerosol with the inhalation chamber intake air.

Table 33
Ortho-Amsidine

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability			Animal #	Time of Death	Irreversible Lesions Found	Type of Effect
			Rat	G. Pig	Rat				
1-25-78	5-0A-1	0.0524 mg/l	0	0	0	0	5NT7M 5NT6F	Osseous metaplasia of the lung. ^{1b} Infarct in kidney - will repair by scarring.	No
4-26-78	16-0A-2	0.286 mg/l	0	0	0	0	16RT4P	Granulomatous pneumonitis may cause scarring.	No
7-12-78	27-0A-3	0.946 mg/l	0	0	0	0	27RT2P 27GC4P	Focal emphysema. ² Focal myocardial fiber degeneration. ^{1d}	Minimal ²

* Sacrificed for necropsy 14 days post-exposure.

¹ Death or lesion probably not related to exposure;

^{1a} probably an infectious lesion

^{1b} a congenital lesion

^{1c} lesion not seen at higher doses

^{1d} lesion only seen in control animals.

² The conclusion should be verified by testing the compound at a higher concentration; however, a higher concentration was beyond the capabilities of WTL equipment.



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Table 34

Ortho-Anisidine
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
1-25-78	5-0A-1	0.0524 mg/l	ΔBW(+) ^{FR}	Brain (-)MR
4-26-78	16-0A-2	0.286 gm/l	No significant difference found.	Lung (+)FG** Adrenal (+)MR**
7-12-78	27-0A-3	0.946 mg/l	No significant difference found.	No significant difference found.

* Abbreviations:

BWA = Body weight at autopsy
 ΔBW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(±) = Variable differences between test and control groups observed

**Control group terminated 24 hours later than test group.

TABLE 35A. EXPERIMENT 5-OA-1, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GWARDS	SPLEEN		
RATS	MALE	CONTROL	277.4	4.76	40.38	7.11	3.48	6.08	.22	14.58	2.86		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	295.4	4.99	45.68	7.10	3.27	5.97	.24	13.95	2.36		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.82	.64	1.36	-.01	-.72	-1.44	.54	-.81	1.67		
		P-VALUE	.4343	.5387	.2188	1.888	.4938	.1877	.6834	.4488	.1344		
RATS	FEMALE	CONTROL	211.6	5.81	36.97	7.12	3.66	8.67	.32	2.86	2.79		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	219.2	5.63	36.94	6.93	3.69	7.81	.35	3.09	2.48		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	1.39	-.75	-.83	-.48	.12	-3.24	.44	.45	-1.19		
		P-VALUE	.2828	.4742	.9863	.6988	.9849	.8118	.6749	.6633	.2681		
GUINEA PIG	MALE	CONTROL	345.8	6.66	58.49	8.76	3.95	18.17	.25	3.54	1.27		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	285.6	6.73	45.88	18.91	4.54	12.77	.36	3.38	1.18		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.48	.18	-1.17	1.42	1.14	.98	1.58	-.61	-1.38		
		P-VALUE	.1996	.9243	.2769	.1923	.2857	.3932	.1738	.5562	.2868		
GUINEA PIG	FEMALE	CONTROL	385.2	6.72	38.71	8.33	4.27	11.58	.29	4.68	1.63		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	387.2	6.95	43.82	8.38	4.88	11.44	.31	4.55	1.45		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.25	.56	1.78	-.87	-1.03	-.13	.79	-.87	-.76		
		P-VALUE	.8854	.5885	.1269	.9473	.3324	.8976	.4541	.9489	.4698		

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 35C. EXPERIMENT 5-OA-1, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	180.00	180.00	.57727	N.S.
SUBJECTS IN GROUPS	8	2494.5	311.81		
TIMES	5	11154.	2230.9	167.89	p < .001
TIMES X GROUPS	5	328.00	65.600	4.9370	p < .01
TIMES X SUBJECTS IN GROUPS	40	531.50	13.288		
TOTAL	59	14688.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	180.600	176.000	186.600	191.200	197.400	211.600	190.567
TEST	5	179.600	174.800	187.000	194.800	208.000	219.200	194.033
TOTAL	10	180.100	175.400	186.800	193.000	203.100	215.400	192.300

TABLE 35D. EXPERIMENT 5-OA-1, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3588.0	3588.0	1.0429	N.S.
SUBJECTS IN GROUPS	8	27524.	3440.5		
TIMES	5	71134.	14227.	20.583	P <.001
TIMES X GROUPS	5	6800.0	1360.0	1.9676	N.S.
TIMES X SUBJECTS IN GROUPS	40	27640.	691.20		
TOTAL	59	.13669E+06			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	222.000	223.000	254.400	275.000	304.400	345.600	271.033
TEST	2	5	224.000	220.000	252.000	268.000	283.000	285.000	255.567
TOTAL	10	10	223.000	221.900	253.200	271.500	293.700	315.700	263.300

TABLE 35E. EXPERIMENT 5-0A-1, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1.5000	1.5000	.25820E-02	N.S.
SUBJECTS IN GROUPS	8	4647.5	580.94		
TIMES	5	72314.	14463.	304.24	p < .001
TIMES X GROUPS	5	70.500	14.100	.29661	N.S.
TIMES X SUBJECTS IN GROUPS	40	1901.5	47.537		
TOTAL	59	78935.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	216.400	205.400	233.000	250.800	274.000	305.200	247.467
TEST	2	5	213.800	206.000	232.400	247.400	276.400	307.200	247.200
TOTAL	10		215.100	205.700	232.700	249.100	275.200	306.200	247.333

TABLE 36A. EXPERIMENT 16-OA-2, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OVARIES	SPLEEN			
RATS	MALE	CONTROL	297.2	9.02	33.30	7.44	3.50	6.43	.16	14.46	2.10			
		N	5	5	5	5	5	5	5	5	5	5		
		TEST	292.4	8.59	34.94	7.41	3.73	6.57	.21	13.69	2.17			
		N	5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.58	.66	.53	-.18	.87	.88	2.95	-1.17	-.10			
P-VALUE	.5752	.6100	.9241	.4688	.4037	.0184	.2760	.9265						
RATS	FEMALE	CONTROL	211.0	9.37	40.20	6.22	3.60	0.17	.27	2.03	2.41			
		N	5	5	4	5	5	4	5	5	5	5		
		TEST	207.6	9.56	37.50	6.14	3.95	0.30	.33	2.60	2.54			
		N	5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-.93	.20	-1.36	-.41	.76	.35	1.88	.09	.52			
P-VALUE	.3818	.0450	.2189	.6978	.4677	.7308	.1027	.9283	.6164					
GUINEA PIG	MALE	CONTROL	301.0	11.74	51.61	9.06	4.92	11.75	.42	3.00	1.36			
		N	5	5	5	5	5	5	5	5	5	5		
		TEST	311.2	11.92	59.69	9.21	4.75	11.77	.43	3.61	1.67			
		N	5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.41	.22	1.73	.20	-.30	.82	.35	1.16	2.84			
P-VALUE	.6896	.8385	.1210	.8475	.7739	1.009	.7305	.2814	.0762					
GUINEA PIG	FEMALE	CONTROL	293.6	11.14	40.51	0.25	4.28	11.29	.51	3.54	1.62			
		N	5	5	5	5	5	5	5	5	5	5		
		TEST	297.0	12.07	52.05	0.30	4.21	11.49	.57	2.00	1.33			
		N	5	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.21	2.60	.69	-.40	-.27	.35	1.46	-1.17	-1.78			
P-VALUE	.8390	.0277	.5117	.6990	.7927	.7304	.1024	.2762	.1126					

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 36B. EXPERIMENT 16-0A-2, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	595.50	595.50	.62577	N.S.
SUBJECTS IN GROUPS	8	7613.0	951.62		
TIMES	5	60842.	12168.	405.45	p < .001
TIMES X GROUPS	5	156.50	31.300	1.0429	N.S.
TIMES X SUBJECTS IN GROUPS	40	1200.5	30.013		
TOTAL	59	70400.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11						TOTAL
		0	1	2	3	4	5	
CONTROL	5	211.400	217.800	230.400	264.800	283.600	301.600	252.933
TEST	5	210.200	213.600	232.800	257.600	272.600	293.600	246.633
TOTAL	10	210.800	215.700	235.600	261.200	277.600	297.600	249.783

TABLE 36C. EXPERIMENT 16-OA-2, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	37.000	37.000	.91295E-01	N.S.
SUBJECTS IN GROUPS	8	3242.2	405.28		
TIMES	5	5120.5	1024.1	67.906	p < .001
TIMES X GROUPS	5	45.250	9.0500	.60008	N.S.
TIMES X SUBJECTS IN GROUPS	40	603.25	15.081		
TOTAL	59	9048.2			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	176.800	176.400	182.800	192.800	193.800	199.800	187.067	
TEST	2	176.000	174.200	180.200	188.600	192.800	201.200	185.500	
TOTAL	10	176.400	175.300	181.500	190.700	193.300	200.500	186.283	

TABLE 36D. EXPERIMENT 16-OA-2, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3713.0	3713.0	2.6260	N.S.
SUBJECTS IN GROUPS	8	11311.	1413.9		
TIMES	5	83216.	16643.	98.024	P < .001
TIMES X GROUPS	5	966.50	193.30	1.1385	N.S.
TIMES X SUBJECTS IN GROUPS	40	6791.5	169.79		
TOTAL	59	.10500E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	1	203.200	205.000	215.600	224.000	253.000	300.600	233.033
TEST	2	207.600	210.600	231.600	245.600	279.400	322.400	249.567
TOTAL	10	205.500	207.800	223.600	235.200	266.600	311.500	241.700

TABLE 36E. EXPERIMENT 16-OA-2, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	23.000	23.000	.20916E-01	N.S.
SUBJECTS IN GROUPS	8	8797.0	1099.6		
TIMES	5	56995.	11399.	229.19	P < .001
TIMES X GROUPS	5	384.50	76.900	1.5461	N.S.
TIMES X SUBJECTS IN GROUPS	40	1969.5	49.738		
TOTAL	59	68189.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL	
CONTROL	1	5	213.200	213.400	233.400	244.600	259.200	301.000	244.133
TEST	2	5	212.000	212.800	235.000	240.800	271.200	300.400	245.367
TOTAL	10		212.600	213.100	234.200	242.700	265.200	300.700	244.750

TABLE 37A. EXPERIMENT 27-OA-3, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GOVADS	SPLEEN			
RATS	MALE	CONTROL	286.4	8.25	43.58	7.13	3.57	6.42	.15	13.58	2.19			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	294.8	7.98	43.83	7.29	3.48	6.19	.10	13.89	2.27			
		H	5	5	5	5	5	5	5	5	5			
			T-TEST STATISTIC	1.19	-.89	.15	.57	-.75	-.89	1.87	.53	.68		
		P-VALUE	.2667	.4889	.8836	.4748	.4812	.8990	.6137	.5166				
									(*)					
RATS	MALE	CONTROL	287.4	9.22	37.45	6.43	3.64	7.88	.23	2.56	2.44			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	218.8	9.44	36.51	6.58	3.58	8.34	.25	3.37	2.19			
		H	5	5	5	5	5	5	5	5	5			
			T-TEST STATISTIC	.47	.34	-.29	.17	-.62	1.22	.97	1.94	-.62		
		P-VALUE	.6517	.7416	.7881	.8698	.5529	.2578	.3684	.8886	.5513			
														(*)
JUNEA PIG	MALE	CONTROL	287.2	14.68	43.45	7.94	4.34	12.35	.37	3.87	1.22			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	278.6	12.88	38.57	7.84	4.21	12.38	.44	3.88	1.28			
		H	5	5	5	5	5	5	5	5	5			
			T-TEST STATISTIC	-.46	-1.62	-1.29	-.25	-.63	.83	1.25	-.25	-.24		
		P-VALUE	.6552	.1447	.2348	.8188	.5454	1.888	.2468	.8122	.8148			
JUNEA PIG	MALE	CONTROL	287.8	13.91	38.87	7.57	4.84	11.68	.43	3.84	1.24			
		H	5	5	5	5	5	5	5	5	5			
	FEMALE	CONTROL	286.4	12.52	36.89	7.68	4.21	11.96	.42	4.88	1.45			
		H	5	5	5	5	5	5	5	5	5			
			T-TEST STATISTIC	-1.11	-1.18	-1.12	.11	1.84	.65	-.23	.26	2.81		
		P-VALUE	.9134	.3814	.2957	.9121	.3271	.5343	.8246	.7981	.8796			
														(*)

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 37B. EXPERIMENT 27-OA-3, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	400.50	400.50	.51084	N, S.
SUBJECTS IN GROUPS	8	6272.0	784.00		
TIMES	5	57978.	11596.	1153.8	P < .001
TIMES X GROUPS	5	54.500	10.900	1.0846	N, S.
TIMES X SUBJECTS IN GROUPS	40	402.00	10.050		
TOTAL	59	65107.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6						TOTAL
		1	2	3	4	5	6	
CONTROL	5	202.400	205.200	219.200	230.200	260.200	286.400	235.267
TEST	5	206.000	208.000	225.000	242.200	266.600	294.800	240.433
TOTAL	10	204.200	206.600	222.100	240.200	263.400	290.600	237.850

TABLE 37C. EXPERIMENT 27-OA-3, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	15.500	15.500	.58066E-01	N.S.
SUBJECTS IN GROUPS	8	2135.5	266.94		
TIMES	5	6796.0	1359.2	146.35	P < .001
TIMES X GROUPS	5	56.500	11.300	1.2167	N.S.
TIMES X SUBJECTS IN GROUPS	40	371.50	9.2875		
TOTAL	59	9375.0			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	178.600	178.400	183.600	188.800	188.800	192.800	207.400		188.267
TEST	2	5	177.400	179.600	182.400	189.200	189.200	197.000	210.000		189.267
TOTAL	10		178.000	179.000	183.000	189.000	189.000	194.900	208.700		188.767

TABLE 37D. EXPERIMENT 27-OA-3, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	209.50	209.50	.89583E-01	N.S.
SUBJECTS IN GROUPS	8	18709.	2338.6		
TIMES	5	68914.	13783.	130.86	p < .001
TIMES X GROUPS	5	177.00	35.400	.33610	N.S.
TIMES X SUBJECTS IN GROUPS	40	4213.0	105.32		
TOTAL	59	92222.			

MEANS

TIMES:

GROUPS:	N	TIMES:					
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15
		1	2	3	4	5	6
CONTROL	5	193.000	192.200	209.600	231.200	261.000	287.200
TEST	5	192.400	191.000	203.800	231.000	254.200	278.600
TOTAL	10	192.700	192.000	206.700	231.100	257.600	282.900

TABLE 37E. EXPERIMENT 27-OA-3, ORTHO-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	16.000	16.000	.14049E-01	N, S,
SUBJECTS IN GROUPS	8	9111.0	1138.9		
TIMES	5	52096.	10419.	93.846	P < .001
TIMES X GROUPS	5	581.50	116.30	1.0475	N, S,
TIMES X SUBJECTS IN GROUPS	40	4441.0	111.02		
TOTAL	59	66245.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	209.000	208.400	212.600	242.400	268.600	287.800	236.133
EST	2	209.600	208.400	226.400	242.400	261.800	286.400	239.167
TOTAL	10	209.300	208.400	219.500	242.400	265.200	287.100	236.650

Para-Anisidine

Test animals were exposed to concentrations of para-anisidine aerosol ranging from 0.0215 to 0.246 mg/l in air (Table 38). Little effect was noted for the lowest, intermediate and highest levels of exposure other than eye irritation in guinea pigs and generalized depressed activity in all animals (Tables 2 and 39). No exposure related irreversible lesions were found. Due to limitations of the atmosphere generation equipment available at UBTL, no higher level could be produced.

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 40) along with more detailed summaries of the results (Tables 41-43).

Table 38

Para-Anisidine Atmosphere Analysis

Test Compound Concentration:

Experiment No.	<u>17-PA-1</u>	<u>30-PA-3</u>	<u>29-PA-2</u>
Date	5-3-78	8-9-78	7-26-78
Attempted Chamber Conc.	0.030 mg/l	1.00 mg/l	0.40 mg/l
First Sample	0.0121 mg/l	0.156 mg/l	0.143 mg/l
Second Sample	0.0291 mg/l	0.131 mg/l	0.297 mg/l
Third Sample	0.0234 mg/l	0.0998 mg/l	0.298 mg/l
Mean	0.0215 mg/l	0.129 mg/l	0.246 mg/l
Std. Dev.	0.00865 mg/l	0.0282 mg/l	0.0892 mg/l
Coef. Var.	40.2%	21.9%	36.3%

Aerosol Size Distribution:*

Experiment No.	<u>30-PA-3</u>		<u>29-PA-2</u>		
	Impactor Stage No.	ECD(μ m)	Cum. %	ECD(μ m)	Cum. %
	1	5.03	100.0	5.03	100.0
	2	3.19	74.7	3.19	89.9
	3	1.97	59.3	1.97	77.4
	4	1.22	33.2	1.22	50.0
	5	0.76	16.3	0.76	35.5
	6	0.48	9.7	0.48	30.0
	7	0.30	8.5	0.30	28.5
Median Aerodynamic Diameter (μ m)		1.8		1.2	
Geometric Standard Deviation		2.3		2.1	

*Aerosol size distribution analysis performed on Experiment No. 17-PA-1 indicated that 80% of the collected material at stage #7 and 27% of the collected material at stage #1, thus a log normal distribution of particle size was not present, but the majority of the particles appeared to be in the submicron size range.

Table 39
Para-Amsidine

Exposure Effects Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability			Animal #	Time of Death	Irreversible Lesions Found	Type of Effect
			Rat	G. Pig	Rat				
5-3-78	17-PA-1	0.0215 mg/l	0	0	0	0	178C10P *	Hydronephrosis ^{1a} .	No
8-2-78	30-PA-3	0.129 mg/l	0	0	0	0	308T1M *	Reversible pulmonary congestion and bilateral renal necrosis and congestion.	No
7-26-78	29-PA-2	0.246 mg/l	0	0	0	0	298C6P *	May have pulmonary scarring from nonsuppurative pneumonitis ^{1b} .	No

* Sacrificed for necropsy 14 days post-exposure.

¹ Death or lesion probably not related to exposure;

^{1a} congenital lesion

^{1b} lesion only seen in control animals.

² The lesions were judged to be reversible but would have caused death if exposure had been longer.

Table 40

Para-Anisidine
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
5-3-78	17-PA-1	0.0215 mg/l	No significant difference found.	Spleen (-)FR
8-2-78	30-PA-3	0.129 mg/l	No significant difference found.	Liver (+)FR Kidney (+)FR Heart (-)MG
7-26-78	29-PA-2	0.246 mg/l	BWA(+)FG Δ BW(+)FG	Adrenal (+)FR, (-)FG

* Abbreviations:

BWA = Body weight at autopsy
 Δ BW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(\pm) = Variable differences between test and control groups observed

TABLE 41A. EXPERIMENT 17-PA-1, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO ($\times 1000$)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GNONDS	SPLEEN			
RATS	MALE	CONTROL	299.0	0.53	30.02	7.12	3.37	6.15	.16	13.20	1.94			
		N	5	5	5	5	5	5	5	5	5			
	TEST	CONTROL	296.2	0.74	37.00	7.10	3.29	6.17	.16	13.05	2.04			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.64	.33	-1.00	.16	-.56	.11	-.26	1.17	.62			
		P-VALUE	.5403	.7400	.3449	.0760	.9081	.9159	.7994	.2745	.5529			
RATS	FEMALE	CONTROL	212.6	11.00	37.21	6.49	3.07	0.43	.20	3.20	2.61			
		N	5	5	5	5	5	5	5	5	5			
	TEST	CONTROL	211.0	10.42	37.00	6.25	3.90	0.45	.27	3.27	2.13			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.15	-1.02	.43	-.68	.46	.05	-.27	.13	-2.55			
		P-VALUE	.0002	.3350	.6754	.5144	.6573	.9503	.7949	.9017	.0342			*
GUINEA PIG	MALE	CONTROL	317.2	9.73	40.99	0.13	4.41	10.60	.32	3.11	1.13			
		N	5	5	5	5	5	5	5	5	5			
	TEST	CONTROL	307.6	9.99	41.20	0.66	4.06	11.39	.35	3.23	1.19			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.02	.20	.06	1.13	-1.02	1.40	.46	.30	.52			
		P-VALUE	.3397	.7057	.9531	.2907	.3355	.1772	.6543	.7126	.6185			
GUINEA PIG	FEMALE	CONTROL	286.0	11.70	43.31	0.16	4.72	11.50	.41	2.69	1.21			
		N	5	5	5	5	5	5	5	5	5			
	TEST	CONTROL	286.0	10.95	42.99	7.91	4.20	11.64	.43	3.15	1.11			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.07	-.03	-.11	-.46	-1.45	.25	.55	.85	-.91			
		P-VALUE	.9495	.4316	.9162	.6591	.1062	.8119	.5953	.4225	.3910			

(*) < .10 ** < .05 *** < .001

TABLE 41B. EXPERIMENT 17-PA-1, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	35.500	35.500	.32328	N.S.
SUBJECTS IN GROUPS	8	878.50	109.81		
TIMES	5	60139.	12028.	1099.7	P < .001
TIMES X GROUPS	5	63.000	12.600	1.1520	N.S.
TIMES X SUBJECTS IN GROUPS	40	437.50	10.937		
TOTAL	59	61553.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	208.600	212.400	227.600	251.200	270.600	293.000	243.900
TEST	5	209.200	212.600	227.200	251.400	274.000	298.200	245.433
TOTAL	10	208.900	212.500	227.400	251.300	272.300	295.600	244.667

TABLE 41C. EXPERIMENT 17-PA-1, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	32.000	32.000	.74941E-01	N.S.
SUBJECTS IN GROUPS	8	3416.0	427.00		
TIMES	5	5776.5	1155.3	37.464	p < .001
TIMES X GROUPS	5	35.500	7.1000	.23024	N.S.
TIMES X SUBJECTS IN GROUPS	40	1233.5	30.838		
TOTAL	59	10493.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	180.600	179.800	184.400	191.600	199.800	206.600	190.467
TEST	5	179.600	177.000	183.800	192.800	196.400	204.400	189.000
TOTAL	10	180.100	178.400	184.100	192.200	198.100	205.500	189.733

TABLE 41D. EXPERIMENT 17-PA-1, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	107.00	107.00	.13750	N.S.
SUBJECTS IN GROUPS	8	6225.5	778.19		
TIMES	5	61278.	12256.	188.44	P < .001
TIMES X GROUPS	5	758.50	151.70	2.3325	N.S.
TIMES X SUBJECTS IN GROUPS	40	2601.5	65.038		
TOTAL	59	70971.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	224.600	220.400	246.800	248.800	248.800	305.200	302.800	302.800	258.100
TEST	2	5	227.200	223.400	235.600	255.400	255.400	293.800	297.200	297.200	255.433
TOTAL	10		225.900	221.900	241.200	252.100	252.100	299.500	300.000	300.000	256.767

TABLE 41E. EXPERIMENT 17-PA-1, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	341.00	341.00	.18244	N.S.
SUBJECTS IN GROUPS	8	14952.	1869.1		
TIMES	5	59385.	11877.		
TIMES X GROUPS	5	438.50	87.700	187.82	p < .001
TIMES X SUBJECTS IN GROUPS	40	2529.5	63.238	1.3868	N.S.
TOTAL	59	77647.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	198.200	192.800	215.800	223.400	274.000	278.200	230.400
TEST	2	198.800	191.200	211.600	224.800	263.200	265.000	225.633
TOTAL	10	198.500	192.000	213.700	223.700	268.600	271.600	228.017

TABLE 42A. EXPERIMENT 30-PA-3, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	CONVUS	SPLEEN			
RATS	MALE	CONTROL	292.0	0.45	41.03	7.17	3.67	6.60	.16	13.00	2.57			
		H	5	5	5	5	5	5	5	5	5			
	TEST	295.0	0.19	44.06	7.50	3.71	6.47	.10	13.41	2.29				
	H	5	5	5	5	5	5	5	5	5				
FEMALE	T-TEST STATISTIC	.21		.64	.63	.11	-.50	1.49	-.69	-1.07				
	P-VALUE	.8377	.6861	.5375	.9141	.6296	.1747	.5896	.3167					
RATS	MALE	CONTROL	204.2	9.22	31.92	6.11	3.53	0.33	.26	2.54	2.24			
		H	5	5	5	5	5	5	5	5	5			
	TEST	204.0	0.00	36.04	6.79	3.76	9.06	.29	2.72	2.40				
	H	5	5	5	5	5	5	5	5	5				
FEMALE	T-TEST STATISTIC	.09	-.01	2.30	2.56	.01	1.90	1.35	1.27	.74				
	P-VALUE	.9339	.4414	.0447	.9334	.4439	.0029	.2126	.2307	.4031				
GUINEA PIG	MALE	CONTROL	300.6	11.26	40.40	0.61	4.79	11.36	.33	2.09	1.41			
		H	5	5	5	5	5	5	5	5	5			
	TEST	294.4	11.55	42.02	7.06	4.17	11.62	.30	2.92	1.55				
	H	5	5	5	5	5	5	5	5	5				
FEMALE	T-TEST STATISTIC	-.33	.24	-2.13	-2.00	-.34	1.90	.11	.56					
	P-VALUE	.7501	.0196	.0661	.0407	.7433	.0942	.9139	.5926					
GUINEA PIG	MALE	CONTROL	281.0	11.64	41.06	7.00	4.71	11.97	.45	4.70	1.57			
		H	5	5	5	5	5	5	5	5	5			
	TEST	272.0	12.71	34.67	7.26	4.70	12.10	.43	4.13	1.74				
	H	5	5	5	5	5	5	5	5	5				
FEMALE	T-TEST STATISTIC	-.60	.60	-1.49	-.91	-.04	-.26	-.29	-.59	.70				
	P-VALUE	.5651	.5624	.1745	.3916	.9007	.0013	.7770	.5712	.4509				

(*) <.10 * <.05 ** <.01 *** <.001

TABLE 42B. EXPERIMENT 30-PA-3, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2.0000	2.0000	.29641E-02	N.S.
SUBJECTS IN GROUPS	8	5398.0	674.75		
TIMES	5	62923.	12585.	608.69	P < .001
TIMES X GROUPS	5	68.500	12.100	.58525	N.S.
TIMES X SUBJECTS IN GROUPS	40	827.00	20.675		
TOTAL	59	69210.			

MEANS

TIMES:

GROUPS:	N	1	2	3	4	5	6	TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	224.000	204.000	222.200	242.000	263.600	292.800	230.233
TEST	2	5	206.800	203.400	222.000	239.200	265.200	295.000	238.600
TOTAL	10		205.400	204.100	222.100	240.600	264.400	293.900	238.417

TABLE 42C. EXPERIMENT 30-PA-3, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	103.75	103.75	.32031	N.S.
SUBJECTS IN GROUPS	8	2591.2	323.91		
TIMES	5	7057.0	1411.4	82.508	P < .001
TIMES X GROUPS	5	62.500	12.500	.73073	N.S.
TIMES X SUBJECTS IN GROUPS	40	684.25	17.106		
TOTAL	59	10499.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	176.600	174.600	180.200	187.800	194.400	204.200	186.300		
TEST	2	5	176.000	170.400	177.600	182.600	190.600	204.000	183.667		
TOTAL	10		176.300	172.500	178.900	185.200	192.500	204.500	184.983		

TABLE 42D. EXPERIMENT 30-PA-3, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	96.500	96.500	.34447E-01	N.S.
SUBJECTS IN GROUPS	8	22411.	2801.4		
TIMES	5	68262.	13652.	189.91	p < .001
TIMES X GROUPS	5	177.00	35.400	.28500	N.S.
TIMES X SUBJECTS IN GROUPS	40	4968.5	124.21		
TOTAL	59	95915.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11 DAY 12 DAY 13 DAY 14 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	206.200	203.800	219.600	243.000	268.800	300.600	240.333
TEST	5	207.200	202.800	221.800	236.600	264.800	294.400	237.800
TOTAL	10	206.700	203.300	220.700	239.800	266.400	297.500	239.067

TABLE 42E. EXPERIMENT 30-PA-3, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	482.00	482.00	.26578	N.S.
SUBJECTS IN GROUPS	8	14588.	1813.6		
TIMES	5	46866.	9213.2	87.164	P < .001
TIMES X GROUPS	5	316.00	63.200	.59792	N.S.
TIMES X SUBJECTS IN GROUPS	40	4228.0	105.70		
TOTAL	59	65600.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL	
CONTROL	1	5	205.600	199.600	219.800	234.000	262.200	281.800	234.000
TEST	2	5	202.600	200.400	213.800	231.600	240.800	272.800	228.333
TOTAL	10	10	204.600	200.000	216.800	232.800	255.500	277.300	231.167

TABLE 43A. EXPERIMENT 29-PA-2, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN			
RATS	MALE	CONTROL	288.8	7.89	34.28	6.92	3.32	5.26	.14	13.64	2.21			
		N	5	5	5	5	5	2	5	5	5			
		TEST	294.6	7.24	38.87	6.98	3.36	5.79	.22	13.38	2.35			
		N	5	5	5	5	5	2	5	5	5			
		T-TEST STATISTIC	.97	-1.13	1.63	-.86	.29	.98	4.82	-.61	1.11			
		P-VALUE	.3595	.2926	.1487	.9516	.7886	.3954	.8566	.5563	.2984			
RATS	FEMALE	CONTROL	288.8	8.82	34.58	6.65	3.62	7.54	.24	2.82	2.34			
		N	5	5	5	5	5	4	5	5	5			
		TEST	289.6	8.74	35.83	6.32	3.48	7.54	.38	2.75	2.55			
		N	5	5	5	5	5	3	4	4	4			
		T-TEST STATISTIC	1.38	-.12	-.27	-1.84	-.88	-.88	2.63	-.23	.89			
		P-VALUE	.2848	.9872	.7922	.2114	1.888	.8463	.8265	.4885				
GUINEA PIG	MALE	CONTROL	284.8	12.56	41.51	8.98	4.48	12.22	.45	2.95	1.28			
		N	5	5	5	5	5	5	5	5	5			
		TEST	281.8	11.71	48.52	8.35	4.18	11.91	.43	3.86	1.34			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.18	-.51	-.27	-1.86	-.78	-.58	-.26	.38	.47			
		P-VALUE	.9248	.6264	.7967	.4551	.6278	.8839	.7787	.6516				
GUINEA PIG	FEMALE	CONTROL	278.4	11.85	38.54	7.88	4.44	11.75	.59	3.96	1.66			
		N	5	5	5	5	5	5	5	5	5			
		TEST	294.8	8.85	34.88	7.19	3.92	10.93	.39	4.54	1.36			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	2.62	-2.23	-1.38	-1.45	-1.84	-1.16	-3.89	.68	-1.25			
		P-VALUE	.8387	.0566	.2285	.1838	.3291	.2792	.8148	.5647	.2458			

(*) <.10 * <.05 ** <.01 *** <.001

TABLE 43B. EXPERIMENT 29-PA-2, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN OF BODY WEIGHT ON MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	4.5000	4.5000	.14566E-01	N, S,
SUBJECTS IN GROUPS	8	2471.5	308.94		
TIMES	5	59782.	11956.	1189.7	P < .001
TIMES X GROUPS	5	92.000	18.400	1.8300	N, S,
TIMES X SUBJECTS IN GROUPS	40	482.00	10.050		
TOTAL	59	62752.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	283.200	285.600	225.800	237.200	261.600	288.800	236.900		236.900
TEST	2	5	282.800	284.400	223.800	237.600	262.200	294.600	237.433		237.433
TOTAL	10		282.600	285.000	224.400	237.400	261.900	291.700	237.167		237.167

TABLE 43C. EXPERIMENT 29-PA-2, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	493.00	493.00	1.9336	N.S.
SUBJECTS IN GROUPS	8	2039.7	254.97		
TINES	5	7859.7	1571.9	60.484	p < .001
TINES X GROUPS	5	248.00	49.600	2.5395	p < .05
TINES X SUBJECTS IN GROUPS	40	781.25	19.531		
TOTAL	59	11422.			

MEANS

TINES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	174.000	170.600	176.800	180.200	186.800	200.000	181.400		
TEST	2	5	174.400	172.600	181.000	186.400	198.800	209.600	187.133		
TOTAL	10		174.200	171.600	178.900	183.300	192.800	204.800	184.267		

TABLE 43D. EXPERIMENT 29-PA-2, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS									
SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE				
GROUPS	1	9.0000	3.0000	.15340E-02	N.S.				
SUBJECTS IN GROUPS	8	46936.	5867.0						
TIMES	5	64460.	12892.	115.35	P < .001				
TIMES X GROUPS	5	466.50	93.300	.83401	N.S.				
TIMES X SUBJECTS IN GROUPS	40	4470.5	111.76						
TOTAL	59	.11634E+06							

MEANS		TIMES:						
GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	1	5	195.400	190.600	199.600	234.000	254.200	284.000
TEST	2	5	193.800	193.600	209.400	227.200	256.200	281.000
TOTAL	10		194.600	196.100	204.500	231.000	255.200	282.900

TABLE 43E. EXPERIMENT 29-PA-2, PARA-ANISIDINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1197.5	1197.5	1.7360	N.S.
SUBJECTS IN GROUPS	8	5518.5	689.81		
TIMES	5	54673.	10935.	396.36	$p < .001$
TIMES X GROUPS	5	357.50	71.500	2.5918	$p < .05$
TIMES X SUBJECTS IN GROUPS	40	1103.5	27.588		
TOTAL	59	62850.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	204.000	200.800	214.200	234.000	252.800	278.400	230.700
TEST	2	206.400	204.800	223.000	242.600	266.200	294.800	239.633
TOTAL	10	205.200	202.800	218.600	238.300	259.500	286.600	235.167

Stibine

Test animals were exposed to concentrations of gaseous stibine ranging from 0.125 to 1.43 mg/l in air (Table 44). The lowest level did not produce any untoward effects (Tables 2 and 45). At the intermediate level, eye irritation and closure were present in rats and generalized depressed activity was present in all animals. One guinea pig died one day post-exposure, and four other animals had renal tubular dilation and/or pulmonary inflammation lesions at necropsy. At the highest level, generalized depressed activity was present in all animals, tremors were present in guinea pigs and some rats exhibited dyspnea. Post-exposure, seven rats and eight guinea pigs died; and several had lesions such as pulmonary edema, intravascular congestion, coagulopathy, and pulmonary congestion. In this case, there appeared to be an increase in lesions with an increase in exposure level.

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 46) along with more detailed summaries of the results (Tables 47-49).

Table 44

Stibine Atmosphere Analysis

Test Compound Concentration:

Experiment No.	8-S-1	22-S-3	20-S-2
Date	3-1-78	6-7-78	5-24-78
Attempted Chamber Conc.	0.172 mg/l 40 ppm	0.966 mg/l 225 ppm	1.718 mg/l 400 ppm
First Sample	0.135 mg/l 31.5 ppm	0.815 mg/l 190 ppm	1.25 mg/l 291 ppm
Second Sample	0.126 mg/l 29.4 ppm	0.877 mg/l 204 ppm	1.28 mg/l 298 ppm
Third Sample	0.114 mg/l 26.4 ppm	0.764 mg/l 178 ppm	1.49 mg/l 346 ppm
Fourth Sample	-	-	1.71 mg/l 398 ppm
Mean	0.125 mg/l 29.1 ppm	0.819 mg/l 191 ppm	1.43 mg/l 333 ppm
Std. Dev.	0.0105 mg/l 2.56 ppm	0.0566 mg/l 13.0 ppm	0.214 mg/l 49.6 ppm
Coef. Var.	8.40%	6.91%	15.0%
		6.81%	14.9%

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Inquired Escape Ability				Animal #	Time of Death	Irreversible Lesions Found	Type of Effect
			Test	Control	Rat	G. Pig				
3-1-78	8-S-1	29.1 ppm 0.125 mg/l	0	0	0	0	8671M	•	Granuloma will cause scarring in lungs ^{1a,c} . No Adrenal cortical adenoma.	Frank
			0	0	0	0	8674F	•		
			0	0	0	0	86C8F	•	Hydronephrosis of one kidney ^b .	
			0	0	0	0	86C4F	•	Resolution of granuloma will cause scarring in lungs.	
6-7-78	22-S-3	191 ppm 0.819 mg/l	0	0	0	0	22RT1M	•	Renal tubular dilation and calcification will result in scarring.	Frank
			0	0	0	0	22RT5M	•	Renal tubular dilation will result in scarring.	
			0	0	0	0	22GT5M	•	Renal tubular dilation, calcific debris in renal pelvis and pulmonary inflammation will cause permanent scarring.	
			0	0	0	0	22GT7M	•	Pulmonary focal granulomatous inflammation will result in fibrosis.	
5-24-78	20-S-2	330 ppm 1.43 mg/l	0 ²	1 ²	0 ³	0 ³	20RT1M	2 hr. post-exp.	Histopathology not performed. ⁴	Frank
			0	0	0	0	20RT3M	2 hr. post-exp.	Fatal (acute) pulmonary edema.	
			0	0	0	0	20RT5M	1 hr. post-exp.	Pulmonary edema and intravascular congestion and coagulopathy.	
			0	0	0	0	20RT7M	3 hr. post-exp.	Fatal pulmonary edema and generalized intravascular congestion.	
			0	0	0	0	20RT9M	1 hr. post-exp.	Histopathology not performed.	
			0	0	0	0	20RT2F	9 hr. post-exp.	Histopathology not performed.	
			0	0	0	0	20RT4F	4 days post-exp.	Disseminated intravascular congestion and coagulopathy.	
			0	0	0	0	20RT8F	•	Pulmonary fibrosis.	
			0	0	0	0	20RT10F	•	Renal infarcts.	
			0	0	0	0	26GT1M	9.5 hr. post-exp.	Acute pulmonary congestion, hemorrhage and edema.	
			0	0	0	0	26GT2M	4 hr. post-exp.	Histopathology not performed.	
			0	0	0	0	26GT3M	1 hr. post-exp.	Acute pulmonary congestion and edema caused death.	
			0	0	0	0	26GT5M	1 hr. post-exp.	Histopathology not performed.	
			0	0	0	0	26GT5M	•	Pulmonary scarring and fibrosis.	
0	0	0	0	26GT2F	4 hr. post-exp.	Death due to pulmonary congestion and edema.				
0	0	0	0	26GT4F	3 hr. post-exp.	Acute pulmonary congestion, hemorrhage and edema.				
0	0	0	0	26GT6F	2 hr. post-exp.	Histopathology not performed.				
0	0	0	0	26GT10F	1 hr. post-exp.	Acute pulmonary edema, congestion and hemorrhage.				
0	0	0	0	26RC3M	•	Gaseous metaplasia of the lung ^b .				

¹ Animal sacrificed for necropsy 14 days post-exposure.

² Death or lesion probably not related to exposure;

³ In probably an infectious lesion

⁴ In a congenital lesion

⁵ Also seen in control animals

⁶ Lesion not seen at higher doses.

⁷ By 10 minutes GB and 4 had uncontrolled movements (jumping), while rats were relatively normal. By 15 minutes GB was lying on its side, and no eye irritation was noted in either species. By 20 minutes GB and 3 were lying down with breathing difficulty; R2, 3, 5, 8 and 9 were showing breathing difficulty. By 30 minutes R1, 4, 6, 7 and 10 had labored breathing; and G3 had tremors.

⁸ Control animals were exposed to atmosphere generated without antimony present, and only a slight apparent skin irritation in rats was observed.

⁹ The lesions were judged to be reversible, but they appeared to have caused death.



Stibine
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
3-1-78	8-S-1	29.1 ppm 0.129 mg/l	No significant difference found.	Adrenal (-)MR Gonad (+)FG
6-7-78	22-S-3	191 ppm 0.819 mg/l	Δ BW(\pm)MR Δ BW(-)MG	Adrenal (+)FR Liver (+)MG Kidney (+)FG Heart (+)MR
5-24-78	20-S-2	333 ppm 1.43 mg/l	Not available since most test animals died during or shortly after exposure.	Probably not meaningful since control animals were not sacrificed until six days after test animals had died.

* Abbreviations:

BWA = Body weight at autopsy
 Δ BW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(\pm) = Variable differences between test and control groups observed

TABLE 47A. EXPERIMENT 8-S-1, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OVARIS	SPLEEN			
RATS	MALE	CONTROL	387.0	9.06	39.03	7.69	3.45	6.09	.21	14.32	2.33			
		N	5	5	5	5	5	5	5	5	5			
	FEMALE	TEST	309.0	9.22	42.86	7.98	3.34	5.48	.16	14.34	2.36			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	.23	.22	1.98	.46	-.86	-1.13	-2.61	.84	.29			
P-VALUE	.0216	.0347	.0832	.6586	.4166	.2914	.0312	.9842	.7776					
			(*)				*							
RATS	MALE	CONTROL	216.0	10.02	37.55	7.36	3.97	8.31	.36	2.63	2.07			
		N	5	5	5	5	5	5	5	5	5			
	FEMALE	TEST	211.2	10.08	39.57	6.06	3.67	8.12	.30	2.37	2.96			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.78	-.03	1.00	-1.08	-1.53	-.24	-1.69	-1.02	.42			
P-VALUE	.4555	1.000	.3110	.3104	.1635	.0162	.1301	.3425	.6067					
GUINEA PIG	MALE	CONTROL	291.6	10.25	43.77	0.86	4.79	11.56	.42	3.30	1.25			
		N	5	5	5	5	5	5	5	5	5			
	FEMALE	TEST	315.2	10.35	45.02	0.30	4.44	11.16	.35	3.49	1.27			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.12	.17	.39	-.75	-1.49	-.47	-1.56	.42	.15			
P-VALUE	.2955	.0673	.7075	.4774	.1735	.6402	.1566	.6845	.0017					
GUINEA PIG	MALE	CONTROL	310.0	10.00	43.71	0.35	4.30	11.29	.46	3.36	1.40			
		N	5	5	5	5	5	5	5	5	5			
	FEMALE	TEST	304.0	11.37	45.30	9.02	4.77	11.61	.43	4.64	1.63			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.24	.76	.36	.67	.71	.22	-.52	2.67	1.34			
P-VALUE	.0185	.4700	.7304	.5246	.4969	.0200	.6195	.0285	.2170					

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 47B. EXPERIMENT 8-S-1, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	1.5000	1.5000	.13940E-02	N.S.
SUBJECTS IN GROUPS	8	8608.5	1076.1		P < .001
TIMES	4	66906.	16727.	759.22	N.S.
TIMES X GROUPS	4	31.500	7.8750	.35745	
TIMES X SUBJECTS IN GROUPS	32	705.00	22.031		
TOTAL	49	76253.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	217.200	219.000	250.000	258.000	286.000	307.000	257.600
TEST	2	5	216.000	217.400	258.800	287.600	309.800		257.920
TOTAL	10		216.600	218.200	258.400	287.200	308.400		257.760

TABLE 47C. EXPERIMENT 8-S-1, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	7.2500	7.2500	.20433E-01	N.S.
SUBJECTS IN GROUPS	8	2838.5	354.81		
TIMES	4	7255.5	1813.9	151.06	p < .001
TIMES X GROUPS	4	83.750	20.937	1.7437	N.S.
TIMES X SUBJECTS IN GROUPS	32	384.25	12.008		
TOTAL	49	10569.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	TOTAL
CONTROL	5	185.800	182.600	199.200	208.400	216.800	198.560	
TEST	5	185.400	184.800	199.000	208.600	211.200	197.800	
TOTAL	10	185.600	183.700	199.100	208.500	214.000	198.180	

TABLE 47D. EXPERIMENT 8-S-1, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	462.50	462.50	.33649	N.S.
SUBJECTS IN GROUPS	8	18996.	1374.5		
TIMES	4	69522.	17381.	156.89	P < .001
TIMES X GROUPS	4	277.00	69.250	.62511	N.S.
TIMES X SUBJECTS IN GROUPS	32	3545.0	110.78		
TOTAL	49	84803.			

MEANS

TIMES:

GROUPS:	N	TIMES					TOTAL	
		DAY 0	DAY 1	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	217.400	214.800	244.000	275.800	311.600	252.720
TEST	2	5	218.800	217.200	257.800	285.000	315.200	258.800
TOTAL	10	10	218.100	216.000	250.900	280.400	313.400	255.760

TABLE 47E. EXPERIMENT 8-S-1, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	16.000	16.000	.76958E-02	N.S.
SUBJECTS IN GROUPS	8	16632.	2079.1		P < .001
TIMES	4	54293.	13573.	40.635	N.S.
TIMES X GROUPS	4	245.00	61.250	.18337	
TIMES X SUBJECTS IN GROUPS	32	10689.	334.03		
TOTAL	49	81875.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	TOTAL
		1	2	3	4	5		
CONTROL	5	227.200	221.400	257.000	287.600	312.800	261.200	
TEST	5	227.800	225.200	258.800	284.600	304.000	260.000	
TOTAL	10	227.500	223.300	257.900	286.100	308.400	260.640	

TABLE 48A. EXPERIMENT 22-S-3, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN			
RATS	MALE	CONTROL	260.2	0.71	33.25	7.23	3.72	7.24	.17	13.64	2.27			
		N	5	5	5	5	5	5	5	5	5			
	TEST	H	245.6	0.23	33.43	0.23	4.32	7.41	.20	14.96	2.60			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.53		.05	1.27	2.43	.30	1.40	1.43	1.11			
		P-VALUE	.1636	.4227	.9630	.2402	.0412	.7113	.1991	.1916	.3010			
RATS	FEMALE	CONTROL	211.4	9.05	37.29	6.70	3.61	0.65	.23	3.04	2.56			
		N	5	5	5	5	5	5	5	5	5			
	TEST	H	200.6	10.24	34.44	7.16	3.07	0.92	.31	2.61	2.07			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.16	.91	-1.11	.75	1.40	.56	2.67	-0.84	1.05			
		P-VALUE	.2004	.3005	.2990	.4739	.1990	.5913	.0202	.4261	.1021			
GUINEA PIG	MALE	CONTROL	290.2	12.34	39.00	0.50	4.74	11.94	.34	3.15	1.39			
		N	5	5	5	5	5	5	5	5	5			
	TEST	H	255.2	11.01	49.90	11.34	4.70	13.14	.46	2.61	1.76			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.70	-.36	2.67	1.32	.10	1.26	2.19	-1.51	1.11			
		P-VALUE	.1120	.7202	.0203	.2221	.9200	.2437	.0599	.1706	.3001			
GUINEA PIG	FEMALE	CONTROL	293.2	11.50	37.73	7.07	4.16	11.62	.42	5.31	1.62			
		N	5	5	5	5	5	5	5	5	5			
	TEST	H	277.0	11.39	40.75	0.46	4.29	11.00	.44	4.19	1.96			
		N	4	4	4	4	4	4	4	4	4			
		T-TEST STATISTIC	-1.44	-.13	.93	2.46	.40	.30	.35	-1.05	1.60			
		P-VALUE	.1939	.9007	.3015	.0432	.6452	.7133	.7360	.3207	.1371			

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 48B. EXPERIMENT 22-S-3, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	453.50	453.50	3.6926	N.S.
SUBJECTS IN GROUPS	8	982.50	122.81		
TIMES	5	20700.	4140.0	56.538	$p < .001$
TIMES X GROUPS	5	1118.5	223.70	3.0550	$p < .05$
TIMES X SUBJECTS IN GROUPS	40	2929.0	73.225		
TOTAL	59	26183.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						TOTAL		
		1	2	3	4	5	6			
CONTROL	5	208.800	209.400	225.800	218.600	259.600	260.200	230.400		
TEST	5	211.200	213.000	209.600	221.600	248.400	245.600	224.900		
TOTAL	10	210.000	211.200	217.700	220.100	254.000	252.900	227.650		

TABLE 48C. EXPERIMENT 22-S-3, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	326.50	326.50	.69663	N.S.
SUBJECTS IN GROUPS	8	3749.5	468.69		
TIMES	5	7636.0	1527.2	66.005	p < .001
TIMES X GROUPS	5	274.00	54.800	2.3684	N.S.
TIMES X SUBJECTS IN GROUPS	40	925.50	23.138		
TOTAL	59	12911.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	178.600	177.200	184.200	194.000	201.400	211.400	191.133
TEST	5	178.600	177.000	174.000	188.400	199.400	200.600	186.467
TOTAL	10	178.600	177.100	179.500	191.200	200.400	206.000	188.800

TABLE 48D. EXPERIMENT 22-S-3, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3024.0	3024.0	1.9974	N.S.
SUBJECTS IN GROUPS	8	12112.	1514.0		
TIMES	5	37177.	7435.4	30.514	p < .001
TIMES X GROUPS	5	4041.5	808.30	3.3171	p < .05
TIMES X SUBJECTS IN GROUPS	40	9747.0	243.67		
TOTAL	59	66101.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	206.800	205.800	207.800	239.800	266.200	290.200	236.100		
TEST	2	5	211.800	205.200	205.800	223.200	230.200	255.200	221.900		
TOTAL	10		209.300	205.500	206.800	231.500	248.200	272.700	229.000		

TABLE 48E. EXPERIMENT 22-S-3, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	900.00	900.00	.49665	N.S.
SUBJECTS IN GROUPS	7	12685.	1812.1		
TIMES	5	41628.	8325.6	122.69	p < .001
TIMES X GROUPS	5	462.50	92.500	1.3632	N.S.
TIMES X SUBJECTS IN GROUPS	35	2375.0	67.857		
TOTAL	53	58050.			

MEANS

TIMES:

GROUPS:	N	TIME						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	214.800	209.000	221.600	243.400	268.000	293.200	241.800
TEST	2	4	212.000	210.250	215.000	233.250	254.000	277.000	233.583
TOTAL	9		213.556	210.000	210.667	230.889	261.778	286.000	238.148

TABLE 49A. EXPERIMENT 20-S-2, STIBINE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GNADNS	SPLEEN			
RATS	MALE	CONTROL	249.4	9.60	41.00	7.85	3.66	7.14	.14	12.32	2.20			
		H	5	5	5	5	5	5	5	5	5			
		TEST	201.6	15.43	47.47	9.60	5.40	8.94	.21	12.55	3.11			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-5.26	7.40	1.02	6.71	7.41	4.99	4.10	.29	2.95			
		P-VALUE	.0000	.0001	.1069	.0001	.0001	.0011	.0031	.7007	.0185	*		
			***	***	***	***	**	**	**	*	*			
RATS	FEMALE	CONTROL	201.0	10.29	40.63	7.30	3.54	9.26	.25	2.51	2.57			
		H	5	5	5	5	5	5	5	5	5			
		TEST	197.4	12.02	43.50	9.46	4.55	9.26	.41	3.07	2.70			
		H	5	5	4	5	5	4	5	5	5			
		T-TEST STATISTIC	-.46	1.36	1.64	4.03	2.49	-.01	2.21	1.56	.39			
		P-VALUE	.6551	.2114	.1403	.0376	1.000	.0625	.1563	.7044				
					**	*		(*)						
GUINEA PIG	MALE	CONTROL	250.0	12.94	30.01	0.60	4.23	12.05	.30	2.05	1.27			
		H	5	5	5	5	5	5	5	5	5			
		TEST	215.0	24.73	50.30	11.04	6.23	16.56	.43	2.13	2.27			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.76	2.07	2.96	2.93	2.24	2.59	1.19	.25	3.41			
		P-VALUE	.1160	.0200	.0103	.0190	.0321	.2696	.0101	.0093	**			
			*	*	*	(*)	*			**				
GUINEA PIG	FEMALE	CONTROL	245.0	12.00	40.41	9.13	4.70	13.12	.43	3.45	1.05			
		H	5	5	5	5	5	5	5	5	5			
		TEST	210.2	24.62	54.60	10.40	5.75	15.63	.52	2.55	2.37			
		H	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.27	4.60	3.20	1.51	2.20	2.25	1.15	-1.43	3.07			
		P-VALUE	.2303	.0016	.1701	.0524	.0549	.2847	.1903	.0154	*			
			**	**		(*)	(*)			*				

(*) <.10 * <.05 ** <.01 *** <.001

NOTE

Tables 49B through 49E are not presented here, since a majority of the test animals died shortly after the exposure, and therefore the rate of growth analysis was not performed.

Phosgene

Test animals were exposed to concentrations of gaseous phosgene ranging from 1.72 to 64.2 $\mu\text{g}/\text{l}$ in air (Table 50). At the lowest level, no untoward effects were observed except that one guinea pig had pulmonary scarring which may have been exposure-related (Tables 2 and 51). The intermediate level produced depressed activity in all animals. One rat died two days post-exposure and had pulmonary edema, while one guinea pig had pulmonary inflammation which could cause scarring. At the highest level, generalized depressed activity was present in all animals. The rats showed nasal/lacrymal irritation and five rats were in the lateral recumbent position by the end of exposure. Ten rats and five guinea pigs died within two days post-exposure and the following lesions were commonly found in those animals: pulmonary edema, congestion and inflammation.

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 52) along with more detailed summaries of the results (Tables 53-55).

Table 50

Phosgene Atmosphere Analysis

Test Compound Concentration:

Experiment No.	21-PG-3	9-PG-1	19-PG-2
Date	5-31-78	3-8-78	5-17-78
Attempted Chamber Conc.	1.70 µg/l 0.50 ppm	6.81 µg/l 2 ppm	68.1 µg/l 20 ppm
First Sample	1.68 µg/l 0.490 ppm	7.26 µg/l 2.13 ppm	55.3 µg/l 16.2 ppm
Second Sample	1.55 µg/l 0.455 ppm	4.97 µg/l 1.46 ppm	62.5 µg/l 18.4 ppm
Third Sample	1.92 µg/l 0.564 ppm	4.80 µg/l 1.41 ppm	74.8 µg/l 22.0 ppm
Mean	1.72 µg/l 0.503 ppm	5.68 µg/l 1.67 ppm	64.2 µg/l 18.9 ppm
Std. Dev.	0.188 µg/l 0.0557 ppm	1.37 µg/l 0.402 ppm	9.86 µg/l 2.93 ppm
Coef. Var.	10.9%	24.1%	15.4%
	11.1%	24.1%	15.5%

Table 51
Phosgene

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Rat		G. Pig		Animal Deaths and Histopathological Evaluation of Organ Specimens for Irreversible Lesions	Type of Effect
			Test	Control	Test	Control		
5-31-78	21-P-3	0.50 ppm 1.72 µg/l	0	0	0	0	21G75M *	Focal encephalitis will cause irreparable No damage.
			0	0	0	0	21G77M *	Focal pulmonary granulomas with scarring.
			0	0	0	0	21G71M *	Myocardial lesion ^{1b} .
3-8-78	9-P-1	1.67 ppm 5.68 µg/l	0	0	0	0	9K77M	Pulmonary edema ³ .
			0	0	0	0	9G77M *	Resolution of pulmonary inflammation may cause scarring.
5-19-67	19-P-2	18.9 ppm 64.2 µg/l	5 ²	0 ²	0 ²	0 ²	19RT1M	4 hrs. post-exp. Histopathology not performed. ³
							19RT3M	7 hrs. post-exp. Pulmonary congestion and edema.
							19RT5M	7 hrs. post-exp. Histopathology not performed.
							19RT7M	4 hrs. post-exp. Pulmonary edema ³ .
							19RT9M	4.5 hrs. post-exp. Pulmonary edema.
							19RT2P	1 day post-exp. Pulmonary congestion and edema ³ .
							19RT4F	1 day post-exp. Pulmonary inflammation and edema.
							19RT6F	1 day post-exp. Histopathology not performed. ³
							19RT8F	7 hrs. post-exp. Pulmonary inflammation and edema.
							19RT10F	7 hrs. post-exp. Histopathology not performed.
							19G71M	7 hrs. post-exp. Pulmonary congestion and edema.
							19G75M	7 hrs. post-exp. Pulmonary inflammation may cause scarring.
							19G79M	2 days post-exp. Histopathology not performed. ³
				19G76F	1 day post-exp. Pulmonary congestion and edema.			
				19G78F	4 hrs post-exp. None found.			
				19G710F	1 day post-exp. Pulmonary congestion and edema. ³			

* Sacrificed for necropsy 14 days post-exposure.

¹ Lesion or death probably not related to exposure;

^{1a} probably an infectious lesion

^{1b} lesion only seen in control animals.

² By 10 minutes RI and 4 were squinting, but G did not show eye irritation. By 15 minutes RI, 2, 3, 4, 6, 7, 10 and G6 were squinting; but all G's opened their eyes in response to an auditory stimulus. By 25 minutes RI had labored jerky breathing, RI0 was lying on side, and all other rats were lying with little or no movement. By 30 minutes RI, 2, 3, 6, and 10 were lying with head sideways; RI, 5, 6, and 7 had very labored breathing; and all G's appeared normal but with depressed activity. Immediately after removal from chamber, all animals showed depressed activity.

³ The lesions were judged to be reversible, but they appeared to have caused death.

Table 52

Phosgene
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
5-31-78	21-P-3	0.50 ppm	ΔBW(+) FG	Brain (-)FG
		1.72 μg/l		Spleen (-)MR
3-8-78	9-P-1	1.67 ppm	ΔBW(±) MR	Kidney (+)MG
		5.68 μg/l		Spleen (+)MG
5-19-78	19-P-2	18.9 ppm	BWA(-)FR**	Lung (+)MR, (+)FR**
		64.2 μg/l		Liver (+)MR, (+)FR, (-)FG**
			BWA(+) FG**	Kidney (+)FR, (-)FG**
				Heart (+)MR, (+)FR**
		Brain (+)FR, (-)FG**		
			Adrenal (+)FR, (-)FG**	
			Spleen (+)FR, (-)FG**	

* Abbreviations:

BWA = Body weight at autopsy

ΔBW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(±) = Variable differences between test and control groups observed

**Possibly not meaningful since control animals were not sacrificed until three days after exposed animals had died.

TABLE 53A. EXPERIMENT 21-P-3, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OVARIES	SPLEEN			
RATS	MALE	CONTROL	277.2	0.34	40.60	7.55	3.60	6.03	.15	14.40	2.24			
		N	5	5	5	5	5	5	5	5	5			
	TEST	TEST	292.0	0.29	37.07	6.72	3.34	6.33	.14	12.93	1.87			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	.71	-1.40	-1.41	-1.46	-1.46	-1.46	-1.46	-1.46	-1.46	-1.46	-1.46	-1.46
		P-VALUE	.4989	.9597	.1759	.1965	.1830	.4550	.4180	.2375	.0097	**		
RATS	FEMALE	CONTROL	229.0	0.29	36.27	6.30	3.34	7.02	.21	3.39	2.07			
		N	5	5	5	5	5	5	5	5	5			
	TEST	TEST	200.0	9.33	36.24	6.00	3.70	0.51	.20	3.02	2.43			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.37	1.00	-.01	.02	1.16	1.02	-.33	-.36	1.54			
		P-VALUE	.2005	.0971	1.000	.4375	.2789	.3395	.7463	.7254	.1631			
				(*)										
GUINEA PIG	MALE	CONTROL	310.0	11.40	45.50	0.90	4.10	11.30	.34	2.00	1.64			
		N	5	5	5	5	5	5	5	5	5			
	TEST	TEST	307.0	11.74	43.73	0.31	4.04	10.97	.40	3.26	1.65			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-.21	.39	-.42	-1.10	-.11	-.52	1.45	1.17	.03			
		P-VALUE	.8393	.7000	.6874	.2737	.9165	.6142	.1053	.2771	1.000			
GUINEA PIG	FEMALE	CONTROL	289.0	10.59	42.05	7.53	4.05	11.09	.41	4.14	1.39			
		N	5	5	5	5	5	5	5	5	5			
	TEST	TEST	305.2	9.63	36.92	7.20	3.99	9.30	.34	4.27	1.41			
		N	5	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.20	-.59	-1.01	-.52	-.12	-3.94	-1.91	-.14	.09			
		P-VALUE	.2352	.5743	.3430	.6150	.9049	.0043	.0931	.6940	.9335			
								**						
				(*)										

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 53B. EXPERIMENT 21-P-3, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	43.500	43.500	.52158E-01	N.S.
SUBJECTS IN GROUPS	8	6672.0	834.00		
TIMES	5	68922.	13784.	271.15	P < .001
TIMES X GROUPS	5	73.500	14.700	.28916	N.S.
TIMES X SUBJECTS IN GROUPS	40	2033.5	50.838		
TOTAL	59	77744.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 7 DAY 8 DAY 9 DAY 10 DAY 11 DAY 12 DAY 13 DAY 14 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	200.200	202.200	227.200	248.400	265.800	298.600	240.267
TEST	5	200.000	202.800	225.000	245.400	263.800	292.800	238.567
TOTAL	10	200.500	202.500	226.500	246.900	264.800	295.700	239.417

TABLE 53C. EXPERIMENT 21-P-3, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	166.50	166.50	.94956	N.S.
SUBJECTS IN GROUPS	8	1482.7	175.34		
TIMES	5	7913.5	1582.7	105.65	p < .001
TIMES X GROUPS	5	91.500	18.300	1.2215	N.S.
TIMES X SUBJECTS IN GROUPS	40	599.25	14.981		
TOTAL	59	10173.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	172.200	172.400	182.000	187.200	192.200	200.400	185.867
TEST	2	5	170.600	169.000	181.000	185.400	188.400	200.000	182.533
TOTAL	10	10	171.400	170.700	182.300	186.300	190.300	204.200	184.200

TABLE 53D. EXPERIMENT 21-P-3, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	99.000	99.000	.11535	N.S.
SUBJECTS IN GROUPS	8	6866.0	858.25		
TIMES	5	96613.	19323.	103.36	P < .001
TIMES X GROUPS	5	318.00	63.600	.34020	N.S.
TIMES X SUBJECTS IN GROUPS	40	7478.8	186.95		
TOTAL	59	.11137E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	200.000	197.600	215.600	246.200	271.200	310.800	240.367		
TEST	2	5	200.200	200.400	213.200	234.200	271.000	307.000	237.800		
TOTAL	10	10	200.500	199.000	214.400	240.200	271.100	309.300	239.083		

TABLE 53E. EXPERIMENT 21-P-3, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	131.50	131.50	.72639E-01	N.S.
SUBJECTS IN GROUPS	0	14480.	1811.1		
TIMES	5	77480.	15496.	177.84	p < .001
TIMES X GROUPS	5	1132.5	226.50	2.5993	p < .05
TIMES X SUBJECTS IN GROUPS	40	3485.5	87.137		
TOTAL	59	96710.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	204.800	197.200	221.200	245.000	266.800	289.000	237.333
TEST	5	201.800	203.200	213.200	240.800	277.600	305.200	240.300
TOTAL	10	203.300	200.200	217.200	242.900	272.200	297.100	238.817

TABLE 54A. EXPERIMENT 9-P-1, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)											
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	OVARIES	SPLEEN				
RATS	MALE	CONTROL	310.6	7.78	37.15	7.26	3.51	5.09	.15	14.25	2.52				
		N	5	5	5	5	5	5	5	5	5				
	TEST	309.7	0.41	41.05	7.75	3.93	5.09	.16	14.36	2.35					
	N	4	4	4	4	4	4	4	4	4					
		T-TEST STATISTIC	-.07	1.23	1.50	1.45	1.49	-.01	.44	.33	-1.03				
		P-VALUE	.9424	.2595	.1771	.1893	.1790	1.000	.6598	.7503	.3359				
RATS	FEMALE	CONTROL	195.6	9.06	30.56	6.91	3.75	9.16	.26	3.67	2.46				
		N	5	5	5	5	5	5	5	5	5				
	TEST	191.2	9.54	34.21	6.54	3.00	9.25	.24	2.90	2.20					
	N	5	5	5	5	5	5	5	5	5					
		T-TEST STATISTIC	-1.14	.72	-.71	-1.34	.50	.42	-.65	-1.11	-.94				
		P-VALUE	.2800	.4910	.5005	.5751	.6806	.5327	.2986	.3763					
GUINEA PIG	MALE	CONTROL	206.0	9.30	44.15	0.26	5.01	11.96	.41	3.02	1.10				
		N	5	5	5	5	5	5	5	5	5				
	TEST	306.2	9.35	47.11	9.43	4.66	11.51	.37	3.30	1.46					
	N	5	5	5	5	5	5	5	5	5					
		T-TEST STATISTIC	1.33	-.04	1.55	2.35	-2.09	-.46	-1.03	1.33	2.61				
		P-VALUE	.2215	.9756	.1595	.0469	.0697	.6604	.3352	.2199	.0309				*
							(*)								
GUINEA PIG	FEMALE	CONTROL	317.6	9.07	40.20	0.43	4.93	10.67	.39	3.05	1.67				
		N	5	5	5	5	5	5	5	5	5				
	TEST	323.4	8.90	42.22	0.06	4.02	10.55	.43	5.46	1.00					
	N	5	5	5	5	5	5	5	5	5					
		T-TEST STATISTIC	.27	-.23	-.52	-.71	-.35	-.19	.89	2.23	.48				
		P-VALUE	.7910	.0272	.6162	.4991	.7347	.0517	.3992	.0560	.6420				(*)

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 54B. EXPERIMENT 9-P-1, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS									
SOURCE OF VARIATION		DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE			
GROUPS		1	113.50	113.50	.22134	N.S.			
SUBJECTS IN GROUPS		7	3589.5	512.79		P < .001			
TIMES		5	61398.	12280.	398.14	P < .05			
TIMES X GROUPS		5	437.50	87.500	2.8370				
TIMES X SUBJECTS IN GROUPS		35	1079.5	30.843					
TOTAL		53	66618.						

MEANS		TIMES:						
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
GROUPS:	N	1	2	3	4	5	6	
CONTROL	1	5	220.200	216.800	241.200	264.600	286.600	310.600
TEST	2	4	220.750	222.500	228.500	250.750	282.250	309.750
TOTAL	9	220.444	219.333	235.556	262.000	284.667	310.222	255.370

TABLE 54C. EXPERIMENT 9-P-1, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	26.750	26.750	.41533	N.S.
SUBJECTS IN GROUPS	8	515.25	64.406		
TIMES	5	3884.7	760.95	61.491	P < .001
TIMES X GROUPS	5	59.500	11.900	.96162	N.S.
TIMES X SUBJECTS IN GROUPS	40	495.00	12.375		
TOTAL	59	4901.2			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	174.200	169.800	177.200	185.000	187.000	195.600	181.333		
TEST	2	5	174.800	169.800	176.200	184.600	183.400	191.200	180.000		
TOTAL	10	10	174.500	169.400	176.700	184.800	185.200	193.400	180.667		

TABLE 54D. EXPERIMENT 9-P-1, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	216.50	216.50	.20391	N.S.
SUBJECTS IN GROUPS	8	8494.0	1061.7		
TIMES	5	84043.	16809.	114.46	P < .001
TIMES X GROUPS	5	1018.0	203.60	1.3864	N.S.
TIMES X SUBJECTS IN GROUPS	40	5874.0	146.85		
TOTAL	59	99646.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	195.600	192.000	216.600	227.600	250.400	286.800	229.500		229.500
TEST	2	5	193.000	191.000	210.600	233.400	264.800	306.200	233.300		233.300
TOTAL	10		194.300	191.900	213.600	230.500	261.600	296.500	231.400		231.400

TABLE 54E. EXPERIMENT 9-P-1, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	374.50	374.50	.20228	N.S.
SUBJECTS IN GROUPS	8	14811.	1851.4		p < .001
TIMES	5	79166.	15833.	103.84	N.S.
TIMES X GROUPS	5	869.00	173.80	1.1399	
TIMES X SUBJECTS IN GROUPS	40	6099.0	152.48		
TOTAL	59	.10132E+06			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL	
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15		
CONTROL	1	5	226.200	220.000	244.200	260.000	293.400	317.600	260.233
TEST	2	5	225.600	219.600	226.400	250.600	285.800	323.400	255.233
TOTAL	10	10	225.900	219.800	235.300	255.300	289.600	320.500	257.733

TABLE 55A. EXPERIMENT 19-P-2, PHOSGENE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GNADS	SPLEEN		
RATS	MALE	CONTROL	259.0	0.05	35.17	7.29	3.37	7.02	.19	13.14	2.35		
		N	5	5	5	5	5	5	5	5	5		
		TEST	211.2	21.74	49.02	0.89	5.94	0.10	.24	13.30	2.51		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.93	7.92	2.91	1.46	4.33	1.51	1.16	.14	.51		
P-VALUE	.0094	.0000	.0195	.1026	.0025	.1606	.2795	.0095	.6223				
			(*)	***	*	***	***						
RATS	FEMALE	CONTROL	251.0	7.13	26.11	5.00	2.01	6.97	.22	2.46	1.69		
		N	5	5	5	5	5	5	5	5	5		
		TEST	169.0	27.79	40.64	0.46	6.54	10.07	.34	3.00	2.32		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-3.79	9.68	5.92	7.35	9.80	4.07	6.56	.95	2.32		
P-VALUE	.0053	.0000	.0004	.0001	.0000	.0012	.0002	.3696	.0492				
			***	***	***	***	***	***	***	*			
GUINEA PIG	MALE	CONTROL	234.0	16.11	50.97	10.63	5.41	14.39	.49	3.14	1.93		
		N	5	5	5	5	5	5	5	5	5		
		TEST	213.5	23.64	61.70	11.66	7.32	16.14	.64	3.67	1.92		
		N	4	4	4	4	4	4	4	4	4		
		T-TEST STATISTIC	-1.40	2.13	1.35	1.10	2.15	1.03	1.59	.61	-.03		
P-VALUE	.2050	.0709	.2195	.3004	.0690	.1106	.1549	.5600	.9853				
			(*)			(*)							
GUINEA PIG	FEMALE	CONTROL	181.0	18.00	65.29	12.36	6.29	17.25	.77	4.25	2.37		
		N	5	5	5	5	5	5	5	5	5		
		TEST	243.0	21.40	50.56	9.06	5.76	13.77	.52	3.40	1.63		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	2.75	.01	-3.91	-3.40	-.63	-3.45	-3.90	-.64	-2.35		
P-VALUE	.0250	.4417	.0045	.0094	.5439	.0006	.0041	.5403	.0470				
			*	***	***	***	***	***	***	*			

(*) < .10 * < .05 ** < .01 *** < .001

NOTE

Tables 55B through 55E are not presented here, since a majority of test animals died within a few hours after exposure, and therefore the rate of growth analysis was not performed.

Diazomethane

The animals were exposed to concentrations of gaseous diazomethane (with ethyl ether) ranging from 20.0 to 122 $\mu\text{g}/\text{l}$ in air (Table 56). At the lowest level, no untoward effects were observed, while some depressed activity was observed at the intermediate level (Tables 2 and 57). The depressed activity could have been due mainly to the effect of the ethyl ether present along with the diazomethane. The highest level produced generalized depressed activity in all animals and some eye irritation in rats. One guinea pig was found to have pulmonary edema, congestion and hemorrhage at necropsy. Once again, the depressed activity was probably due mainly to the presence of ethyl ether along with the diazomethane.

To obtain additional information about the acute toxicity of diazomethane/ether atmospheres at higher levels, a pilot series of static exposures was performed. Glass jars of one gallon capacity were used as exposure chambers. For exposure, an animal was placed in the jar, the lid was securely fastened, and an aliquot of diazomethane/ethyl ether solution was immediately injected through a septum in the lid. All exposures lasted 15 minutes. Five groups of four animals each (two guinea pigs and two rats) were used in this series of experiments as shown in Table 58.

At the end of 15 minutes, Groups I and II appeared normal, while Groups III, IV and V all showed some ataxia or narcosis. However, the narcosis and ataxia appeared to be due to the ethyl ether, and all groups appeared normal during the following 14 days.

This small pilot study was not intended to be definitive; however, it suggested that much higher levels of diazomethane than those produced thus far would be needed to produce acute toxicity. These higher levels could not be achieved without concomitantly achieving levels of ether which would possibly mask the effect of the diazomethane during exposure. Also, the level of ethyl ether would be in the explosive range in air and thus not appropriate for our exposure chamber system.

Thus, it was concluded that further attempts to produce toxic manifestations with diazomethane/ether solutions should not be made in our dynamic inhalation chamber system. An alternative would have been to isolate the diazomethane as a gas and dilute it with air in a manner similar to that used for phosgene. However, the potential danger of explosion from isolated diazomethane precluded this approach.

A summary of the statistically significant ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 59) along with more detailed summaries of the results (Tables 60-62).

Table 56

Diazomethane Atmosphere Analysis

Diazomethane Concentration:

Experiment No.	7-DM-1		18-DM-2		28-DM-3	
Date	2-15-78		5-10-78		7-19-78	
Attempted Chamber Conc.	14.5 µg/l	10 ppm	290 µg/l	200 ppm	290 µg/l	200 ppm
First Sample	7.26 µg/l	5.01 ppm	21.5 µg/l	14.8 ppm	116 µg/l	79.6 ppm
Second Sample	15.1 µg/l	10.4 ppm	61.2 µg/l	42.3 ppm	144 µg/l	98.8 ppm
Third Sample	37.7 µg/l	26.0 ppm	28.1 µg/l	19.4 ppm	107 µg/l	73.4 ppm
Fourth Sample	-	-	47.1 µg/l	32.5 ppm	-	-
Mean	20.0 µg/l	13.8 ppm	39.5 µg/l	27.3 ppm	122 µg/l	83.9 ppm
Std. Dev.	15.8 µg/l	10.9 ppm	18.1 µg/l	12.5 ppm	19.3 µg/l	13.2 ppm
Coef. Var.	79.0%	79.0%	45.8%	45.8%	15.8%	15.8%

Ethyl Ether Concentration:*

Experiment No.	7-DM-1		18-DM-2		28-DM-3	
First Sample	-	-	7.87 mg/l	3080 ppm	7.21 mg/l	2830 ppm
Second Sample	-	-	10.5 mg/l	4110 ppm	4.80 mg/l	1880 ppm
Third Sample	-	-	8.30 mg/l	3250 ppm	-	-
Mean	0.357 mg/l	~120 ppm	8.89 mg/l	3480 ppm	6.01 mg/l	2360 ppm
Std. Dev.	-	-	1.41 mg/l	552 ppm	1.70 mg/l	672 ppm
Coef. Var.	-	-	15.9%	15.9%	28.4%	28.5%

*Ethyl ether was used as a solvent for the diazomethane.

Table 57
Diazomethane

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability			Animal Deaths and Histopathological Evaluation of Organ Specimens for Irreversible Lesions	Type of Effect		
			Rat	G. Pig	Control				
2-15-76	7-DM-1	12.6 ppm 20.0 µg/l	0	0	0	0	None found	No	
5-10-76	18-DM-2	27.3 ppm 39.5 µg/l	0	0	0	0	18GT9M 18GT10F	Spongiosis in brain ^{1b} Spongiosis in brain	No
7-19-76	28-DM-3	83.9 ppm 122 µg/l	0	0	0	0	28RT8F 28RT10F	Regression of mass in fallopian tube ^{1c} may cause scarring and obstruction. Regression of mass in fallopian tube ^{1c} may cause scarring and obstruction. Pulmonary edema, congestion and hemorrhage could cause death.	Minimal ²
							28GT7N	Pulmonary inflammation and hemorrhage will cause scarring. ^{1d} Pulmonary disseminated granuloma and inflammation will cause scarring.	
							28CC3M		
							28CC5M		

* Sacrificed for necropsy 14 days post-exposure.

¹ Death or lesion probably not related to exposure;

^{1a} probably an infectious lesion

^{1b} fixative artifact

^{1c} congenital lesion

^{1d} lesion only seen in control animals.

² The conclusion should be verified by testing the compound at a higher concentration; however, this testing was necessarily precluded by the explosive nature of the isolated chemical. Higher concentrations using ethyl ether as a solvent were attempted in pilot studies (see Table 58).

Table 58

Pilot Study of Diazomethane Acute Toxicity in Static Exposure Chambers

Group	Calculated Initial Concentration in Chambers*			Effects During 15 min. Exposures
	$\frac{\text{mg/l}}{\text{Ethyl Ether}}$ ppm	$\frac{\text{mg/l}}{\text{Diazomethane}}$ ppm	ppm	
I	0	0	0	Normal
II	177	69,100	0	Ataxia** Narcosis
III	17.7	6,900	0.235	Normal
IV	88.4	34,500	1.50	Slight Ataxia**
V	177	69,100	3.04	Ataxia** Narcosis

* Since the change in diazomethane concentration with time is not known in these exposures, caution must be used in the interpretation of the data obtained. A total volume of 4.0 liters, a pressure of 641 torr and a temperature of 25°C were used in making these calculations.

**All animals appeared normal within ten minutes after being removed from exposure chambers.

Table 59

Diazomethane
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
2-15-78	7-DM-1	13.8 ppm 20.0 µg/l	ΔBW(-)MR	Lung (-)MR Kidney (+)MG
5-10-78	18-DM-2	27.3 ppm 39.5 µg/l	Due to an error in randomization, control animals were lighter than test animals.	Differences found would be biased due to initial body weight difference between control and test animals.
7-19-78	28-DM-3	83.9 ppm 122 µg/l	ΔBW(-)MR ΔBW(+)FR	Lung (+)MR Brain (-)FG Adrenal (+)FG

* Abbreviations:

BWA = Body weight at autopsy
 ΔBW = Change in body weight post-exposure
 M = Male
 F = Female
 R = Rat
 G = Guinea pig
 (-) = Test group less than control group
 (+) = Test group more than control group
 (±) = Variable differences between test and control groups observed

TABLE 60A. EXPERIMENT 7-DM-1, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN		
RATS	MALE	CONTROL	295.2	7.11	37.30	7.37	3.55	6.11	.20	13.31	2.13		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	308.6	5.49	42.94	7.24	3.39	6.48	.10	12.09	2.34		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	1.88	-3.46	1.98	-.27	-.66	1.49	-.49	-.67	.85		
P-VALUE	.0969	.0085	.0946	.7967	.5306	.1739	.6385	.5229	.4222				
			(*)	**									
RATS	FEMALE	CONTROL	214.0	7.53	35.02	6.04	3.53	7.75	.26	2.90	2.64		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	219.6	7.37	37.30	6.94	3.66	8.42	-.20	2.03	2.46		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	.01	-.36	1.69	.25	.55	1.51	.61	-.76	-.92		
P-VALUE	.4488	.7268	.1298	.8685	.5964	.1784	.5559	.4683	.3856				
GUINEA PIG	MALE	CONTROL	319.0	6.46	50.03	0.39	4.23	10.97	.31	3.77	1.26		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	297.2	7.36	47.52	9.20	4.59	12.60	.35	3.92	1.25		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	-1.17	1.90	-.81	3.26	1.73	2.22	.65	.55	-.12		
P-VALUE	.2771	.0827	.4399	.0116	.1214	.0576	.5317	.8955	.9861				
			(*)		#			(*)					
GUINEA PIG	FEMALE	CONTROL	203.0	6.90	40.36	0.65	4.92	12.07	.35	4.55	1.35		
		N	5	5	5	5	5	5	5	5	5		
	FEMALE	TEST	312.0	6.90	41.24	0.10	4.45	11.00	.40	4.71	1.45		
		N	5	5	5	5	5	5	5	5	5		
		T-TEST STATISTIC	1.40	-.02	.47	-.77	-1.12	-.78	.77	.16	.50		
P-VALUE	.1990	1.868	.6534	.4662	.2966	.4583	.4657	.8083	.5885				

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 60B. EXPERIMENT 7-DM-1, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	564.50	564.50	1.1541	N.S.
SUBJECTS IN GROUPS	8	3913.0	489.12		
TIMES	5	66155.	13231.	1052.2	p <.001
TIMES X GROUPS	5	327.00	65.400	5.2000	p <.001
TIMES X SUBJECTS IN GROUPS	40	503.00	12.575		
TOTAL	59	71463.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	5	211.000	209.400	220.600	243.600	260.400	295.200	242.700
TEST	5	211.600	211.600	231.600	250.400	279.200	300.600	248.633
TOTAL	10	211.300	210.500	230.100	247.000	273.800	301.900	245.767

TABLE 60C. EXPERIMENT 7-DM-1, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	7.5000	7.5000	.74212E-01	N.S.
SUBJECTS IN GROUPS	8	888.50	101.06		P < .001
TIMES	5	10350.	2070.1	58.292	N.S.
TIMES X GROUPS	5	113.50	22.700	.63921	
TIMES X SUBJECTS IN GROUPS	40	1420.5	35.512		
TOTAL	59	12700.			

MEANS

TIMES:

GROUPS:	N	1	2	3	4	5	6	TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	180.800	180.800	191.600	196.800	206.400	214.800	195.067
TEST	5	183.400	181.200	188.000	195.000	207.400	219.600	195.767
TOTAL	10	182.100	180.600	189.800	195.900	206.900	217.200	195.417

TABLE 60D. EXPERIMENT 7-DM-1, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	370.50	370.50	.31184	N.S.
SUBJECTS IN GROUPS	8	9585.0	1198.1		P < .001
TIMES	5	70431.	14086.	82.665	N.S.
TIMES X GROUPS	5	1242.5	248.50	1.4583	
TIMES X SUBJECTS IN GROUPS	40	6816.0	170.40		
TOTAL	59	88365.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL.
CONTROL	1	5	224.400	218.600	237.200	268.800	296.800	319.800	268.933		
TEST	2	5	224.800	219.800	241.200	258.800	295.600	297.200	255.967		
TOTAL	10	10	224.600	218.800	239.200	263.400	296.200	308.500	258.450		

TABLE 60E. EXPERIMENT 7-DM-1, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	985.00	985.00	1.2104	N.S.
SUBJECTS IN GROUPS	8	5981.5	747.69		
TIMES	5	57491.	11498.	60.521	P < .001
TIMES X GROUPS	5	1385.5	277.10	1.4585	N.S.
TIMES X SUBJECTS IN GROUPS	40	7599.5	189.99		
TOTAL	59	73363.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	5	215.000	208.200	227.600	249.400	267.600	283.800	241.933
TEST	5	216.600	213.800	229.600	254.600	270.800	312.800	249.700
TOTAL	10	215.800	211.000	228.600	252.000	269.200	298.300	245.817

TABLE 61A. EXPERIMENT 18-DM-2, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GOVADS	SPLEEN		
RATS	MALE	CONTROL	302.2	0.58	30.44	7.49	3.30	6.30	.22	12.92	2.35		
		N	5	5	5	5	5	5	5	5			
		TEST	299.2	9.09	30.06	7.30	3.21	6.17	.19	13.71	2.62		
		N	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	-1.40	4.02	.19	-.54	-.74	-1.15	-1.07	1.72	2.63		
P-VALUE	.6982	.0039	.0570	.6843	.4705	.2017	.0900	.1242	.0300				
			**					(*)		*			
RATS	FEMALE	CONTROL	207.2	0.92	34.22	6.66	3.54	0.77	.35	3.22	2.47		
		N	5	5	5	5	5	5	5	5			
		TEST	215.0	11.50	36.47	6.29	3.60	0.34	.30	3.15	2.43		
		N	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	1.37	5.75	1.53	-1.45	.32	-1.05	-3.53	-.69	-.40		
P-VALUE	.2070	.0004	.1652	.1590	.7564	.0070	.0070	.9273	.6972				
			***					(*)		**			
GUINEA PIG	MALE	CONTROL	269.6	12.12	53.42	9.77	4.05	12.65	.46	2.52	1.00		
		N	5	5	5	5	5	5	5	5			
		TEST	310.0	14.57	57.06	9.20	4.04	10.90	.30	3.32	1.66		
		N	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	3.16	3.62	.72	-.70	-.95	-2.61	-4.37	4.92	-.64		
P-VALUE	.0134	.0000	.4902	.4573	.9000	.0309	.0024	.0012	.5375				
			**				**	**	**	**			
GUINEA PIG	FEMALE	CONTROL	274.4	12.93	40.05	0.25	4.75	11.93	.43	4.74	2.13		
		N	5	5	5	5	5	5	5	5			
		TEST	295.0	15.05	49.79	0.42	4.40	11.12	.41	4.26	2.21		
		N	5	5	5	5	5	5	5	5			
		T-TEST STATISTIC	2.57	1.35	.20	-1.14	-2.56	-.30	-.30	-.40	.05		
P-VALUE	.0330	.2126	.7037	.7050	.2067	.0336	.7112	.6437	.9061				
			*				*	*	*	*			

(*) <.10 ** <.05 *** <.01 **** <.001

TABLE 61B. EXPERIMENT 18-DM-2, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	459.00	459.00	1.1283	N.S.
SUBJECTS IN GROUPS	8	3254.5	406.81		
TIMES	5	63938.	12788.	478.94	P < .001
TIMES X GROUPS	5	2929.0	585.80	21.948	P < .001
TIMES X SUBJECTS IN GROUPS	40	1868.0	26.700		
TOTAL	59	71649.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 3 DAY 6 DAY 10 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	210.400	209.000	220.000	258.600	281.600	302.200	248.433
TEST	5	221.000	222.000	209.600	235.000	269.000	299.200	242.900
TOTAL	10	216.100	215.500	219.200	247.200	275.300	300.700	245.667

TABLE 61C. EXPERIMENT 18-DM-2, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	43.000	43.000	.16600	N.S.
SUBJECTS IN GROUPS	8	1849.5	231.19		
TIMES	5	18967.	2193.4	184.95	$p < .001$
TIMES X GROUPS	5	1156.5	231.30	11.067	$p < .001$
TIMES X SUBJECTS IN GROUPS	40	836.00	20.900		
TOTAL	59	14852.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	176.000	172.400	181.600	192.800	201.200	207.200	188.533	
TEST	2	184.000	182.400	170.800	182.600	205.800	215.800	190.233	
TOTAL	10	180.000	177.400	176.200	187.700	203.500	211.500	189.383	

TABLE 61D. EXPERIMENT 18-DM-2, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	14414.	14414.	11.251	p < .005
SUBJECTS IN GROUPS	8	10249.	1281.1		
TINES	5	51578.	10316.	49.594	p < .001
TINES X GROUPS	5	658.00	131.60	.63269	N.S.
TINES X SUBJECTS IN GROUPS	40	8320.0	208.00		
TOTAL	59	85219.			

MEANS

TINES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	199.000	193.000	202.000	223.000	235.200	269.600	220.433		
TEST	2	5	230.600	216.200	225.200	254.800	271.800	310.800	251.433		
TOTAL	10		214.800	204.600	214.000	238.900	253.100	290.200	235.933		

TABLE 61E. EXPERIMENT 18-DM-2, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3776.0	3776.0	4.0808	p < .05
SUBJECTS IN GROUPS	8	7462.5	925.31		
TIMES	5	49715.	9943.1	53.504	p < .001
TIMES X GROUPS	5	1501.5	300.30	1.6159	N.S.
TIMES X SUBJECTS IN GROUPS	40	7433.5	185.84		
TOTAL	59	69829.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	200.000	192.800	200.800	206.800	226.500	243.800	274.400		224.400
TEST	2	5	226.000	215.400	204.200	242.200	258.000	295.800			240.267
TOTAL	10		213.000	204.100	206.500	234.400	250.900	285.100			232.333

TABLE 62A. EXPERIMENT 28-DM-3, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN			
RATS	MALE	CONTROL	276.0	0.11	37.06	7.62	3.36	6.75	.10	13.32	2.35			
		H	5	5	5	5	5	5	5	5	5			
	TEST	H	261.6	10.62	39.20	7.72	3.52	6.75	.22	14.83	2.34			
		H	5	5	5	5	5	5	5	5	5			
		H	-2.11	2.49	.98	.22	1.21	-.08	.93	.70	-.09			
P-VALUE	.0681	.0376	.3550	.0347	.2611	1.000	.3706	.4566	.9343					
			(*)											
RATS	FEMALE	CONTROL	205.0	9.92	36.76	6.64	3.92	0.51	.27	3.01	2.50			
		H	5	5	5	5	5	5	5	5	5			
	TEST	H	200.6	11.51	35.36	6.00	3.00	7.61	.30	3.52	2.45			
		H	5	5	5	5	5	5	5	5	5			
		H	.59	1.51	-.45	.60	-.47	-2.28	.46	.67	-.25			
P-VALUE	.5770	.1694	.6629	.5103	.6530	.0510	.6551	.5210	.0056					
							(*)							
GUINEA PIG	MALE	CONTROL	206.6	12.91	44.23	0.06	3.97	11.63	.34	3.41	1.17			
		H	5	5	5	5	5	5	5	5	5			
	TEST	H	202.4	15.97	45.43	0.59	4.55	10.33	.39	2.00	1.35			
		H	5	5	5	5	5	5	5	5	5			
		H	-.29	.93	.25	.90	1.40	-1.04	.95	-2.15	2.23			
P-VALUE	.7793	.3701	.0084	.3959	.1902	.1037	.3714	.0633	.0567					
								(*)						
GUINEA PIG	FEMALE	CONTROL	265.2	12.25	30.15	7.05	4.10	12.31	.30	4.02	1.47			
		H	5	5	5	5	5	5	5	5	5			
	TEST	H	265.0	13.56	41.17	7.03	4.45	10.34	.55	3.15	1.44			
		H	5	5	5	5	5	5	5	5	5			
		H	.07	1.04	1.02	-.07	1.11	-4.13	3.65	-.09	-.10			
P-VALUE	.9492	.3267	.3377	.9463	.2993	.0033	.0065	.0065	.3900	.9210				
								**						

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 62B. EXPERIMENT 28-DM-3, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	3465.5	3465.5	8.1136	$P < .01$
SUBJECTS IN GROUPS	8	3417.0	427.12		
TIMES	5	45812.	9162.4	791.57	$p < .001$
TIMES X GROUPS	5	2825.0	565.00	48.812	$p < .001$
TIMES X SUBJECTS IN GROUPS	40	463.00	11.575		
TOTAL	59	55982.			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	5	197.200	199.000	212.800	233.000	258.600	276.000	229.433
TEST	5	199.200	201.800	180.200	204.400	230.200	261.600	214.233
TOTAL	10	198.200	200.400	196.500	218.700	248.400	268.800	221.833

TABLE 62C. EXPERIMENT 28-DM-3, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	442.75	442.75	1.1679	N, S,
SUBJECTS IN GROUPS	8	3832.7	379.89		
TIMES	5	18982.	2196.5	146.13	p < .001
TIMES X GROUPS	5	990.25	198.05	13.176	p < .001
TIMES X SUBJECTS IN GROUPS	40	601.25	15.031		
TOTAL	59	16849.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	177.488	175.688	181.888	188.488	199.888	205.888	187.867		187.867
TEST	2	5	175.888	173.688	161.888	176.888	200.488	208.688	182.433		182.433
TOTAL	10		176.200	174.600	171.800	182.200	199.700	207.200	185.150		185.150

TABLE 62D. EXPERIMENT 28-DM-3, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	589.00	589.00	.13229	N.S.
SUBJECTS IN GROUPS	0	35610.	4452.2		
TIMES	5	91236.	18247.	448.06	p < .001
TIMES X GROUPS	5	353.00	70.600	1.7336	N.S.
TIMES X SUBJECTS IN GROUPS	40	1629.0	40.725		
TOTAL	59	.12943E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	177.400	177.200	203.600	223.000	254.600	286.600	220.400
TEST	2	5	176.400	176.200	191.800	216.800	241.200	282.400	214.133
TOTAL	10	10	176.900	176.700	197.700	219.900	247.900	284.500	217.267

TABLE 62E. EXPERIMENT 28-DM-3, DIAZOMETHANE, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	7.0000	7.0000	.65169E-02	N.S.
SUBJECTS IN GROUPS	8	8593.0	1074.1		
TIMES	5	67245.	13449.	452.45	P < .001
TIMES X GROUPS	5	103.50	20.700	.69630	N.S.
TIMES X SUBJECTS IN GROUPS	40	1189.0	29.725		
TOTAL	59	77130.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	173.000	172.000	191.600	216.000	239.200	265.200	289.633		
TEST	2	5	175.200	177.200	193.200	213.000	237.400	265.800	210.300		
TOTAL	10	10	174.500	174.600	192.400	214.500	238.300	265.500	289.967		

Aroclor 1254

Test animals were exposed to concentrations of Aroclor 1254 aerosol ranging from 0.559 to 348 µg/l in air (Table 63). The lowest level produced no untoward effects, while the intermediate and highest level produced some generalized depressed activity in all animals and some squinting in rats (Tables 2 and 64). At the highest level, an apparently exposure-related lesion of focal myocardial degeneration was found in a male guinea pig. Due to limitations of the atmosphere generation equipment available at UBTL, higher levels could not be produced; however, the highest level produced was (348 µg/l), approximately seventy times the IDLH level estimated by NIOSH (5 µg/l).

A summary of the statistically significant differences ($\alpha=0.05$) between test and control groups with respect to total body weight and organ-to-body weight ratios is included (Table 65) along with more detailed summaries of results (Tables 66-68).

Table 63

Aroclor 1254 Atmosphere Analysis Summary

Test Compound Concentration:

Experiment No.	<u>6-ARO-1</u>	<u>15-ARO-2</u>	<u>24-ARO-3</u>
Date	2-1-78	4-19-78	6-21-78
Attempted Chamber Conc.	5 µg/l	40 µg/l	400 µg/l
First Sample	0.500 µg/l	54.6 µg/l	346 µg/l
Second Sample	0.661 µg/l	33.4 µg/l	331 µg/l
Third Sample	0.516 µg/l	45.2 µg/l	366 µg/l
Mean	0.559 µg/l	44.4 µg/l	348 µg/l
Std. Dev.	0.0887 µg/l	10.6 µg/l	17.6 µg/l
Coef. Var.	15.9%	23.9%	5.06%

Aerosol Size Distribution:*

Experiment No.	<u>15-ARO-2</u>		<u>24-ARO-3</u>		
	Impactor Stage No.	ECD(µm)	Cum. %	ECD(µm)	Cum. %
1		5.64	100.0	5.78	100.0
2		3.58	97.8	3.66	76.3
3		2.22	82.3	2.27	53.2
4		1.37	43.4	1.41	28.1
5		0.84	24.3	0.87	13.2
6		0.53	11.2	0.55	3.5
7		0.33	4.8	0.34	0.7
Median Aerodynamic Diameter (µm)		1.6		2.2	
Geometric Standard Deviation		1.4		2.1	

Table 64
Aroclor 1254

Exposure Data Used to Categorize Type of Effect

Date	Experiment #	Concentration	Number of Test Animals Judged To Have Impaired Escape Ability			Animal Deaths and Histopathological Evaluation of Organ Specimens for Irreversible Lesions	Animal #	Time of Death	Irreversible Lesions Found	Type of Effect	
			Rat	G. Pig	Rat					G. Pig	No
2-1-78	6-ARO-1	0.599 µg/l	0	0	0	0	66T2F *	Focally diffuse granulomatous pneumonia may cause scarring.		No	
4-19-78	15-ARO-2	44.4 µg/l	0	0	0	0	15CC9M *	Focal malacia of the brain. ^b		No	
6-21-78	24-ARO-3	348 µg/l	0	0	0	0	24GT7M *	Focal myocardial degeneration. ²		Minimal ²	
							24CC1M *	Nonsuppurative interstitial pneumonia will scar during the healing phase.			
							24CC2F *	Nonsuppurative interstitial pneumonia may cause scarring.			

* Sacrificed for necropsy 14 days post-exposure.

¹ Death or lesion probably not related to exposure;

^{1a} probably an infectious lesion

^{1b} lesion only seen in control animals.

² The effect may or may not be exposure related. The results are inconclusive due to the small number of animals tested. However, a conservative approach was taken and the effect was, therefore, judged to be exposure related.

Table 65

Aroclor-1254
Summary of Statistically Significant Differences Between
Test and Control Groups

Date	Experiment #	Concentration	Total Body Weight*	Organ-to-Body Weight Ratios*
2-1-78	6-ARO-1	0.559 µg/l	No significant difference found.	Adrenal (-)MR, (-)FR, (-)MG, (-)PG Spleen (-)MR
4-19-78	15-ARO-1	44.4 µg/l	ΔBW(+)MR ΔBW(+)MG	Liver (+)MG** Kidney (-)FR** Brain (-)MG**
6-21-78	24-ARO-3	348 µg/l	No significant difference found.	Heart (-)MR Adrenal (+)MG Spleen (-)MR

* Abbreviations:

BWA = Body weight at autopsy
 ΔBW = Change in body weight post-exposure

M = Male

F = Female

R = Rat

G = Guinea pig

(-) = Test group less than control group

(+) = Test group more than control group

(±) = Variable differences between test and control groups observed

**Some of the difference may have been due to half of controls sacrificed one day later than remainder.

TABLE 66A. EXPERIMENT 6-ARO-1, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (x 1000)									
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN		
RATS	MALE	CONTROL	289.2	5.46	43.82	7.85	3.47	6.45	.28	13.97	2.51		
		TEST	296.8	4.92	41.59	7.62	3.47	6.11	.17	14.19	2.15		
	FEMALE	T-TEST STATISTIC	.01	-1.69	-.55	-.69	.01	-.83	-4.85	.47	-2.31		
		P-VALUE	.4482	.1287	.5943	.5884	1.068	.4294	.6818	.6589	.8494	*	
RATS	FEMALE	CONTROL	214.0	6.89	39.85	6.71	3.75	7.99	.44	2.94	2.59		
		TEST	210.6	5.88	40.68	6.61	3.79	7.54	.26	3.07	2.62		
	MALE	T-TEST STATISTIC	-.97	-.61	.35	-.24	.22	-.91	-4.33	.50	.25		
		P-VALUE	.3587	.5561	.7325	.9135	.9348	.3098	.6825	.6326	.8124	**	
GUINEA PIG	MALE	CONTROL	301.2	6.88	46.48	8.91	4.18	10.96	.42	3.19	1.34		
		TEST	304.4	8.09	45.61	9.48	4.53	11.89	.29	3.48	1.41		
	FEMALE	T-TEST STATISTIC	.17	1.58	-.17	.75	1.10	1.13	-2.52	.87	.34		
		P-VALUE	.8576	.1789	.8706	.4739	.3853	.2916	.8357	.4118	.7442	*	
GUINEA PIG	FEMALE	CONTROL	304.8	7.34	42.47	8.29	4.51	11.33	.42	4.89	1.65		
		TEST	313.6	7.88	44.76	8.46	4.55	10.79	.31	5.29	1.68		
	MALE	T-TEST STATISTIC	.71	-.38	.62	.39	.10	-.96	-2.93	.47	-.29		
		P-VALUE	.4976	.7139	.5532	.7848	.9225	.3653	.8191	.6518	.7822	*	

(*) < .10 ** < .01 *** < .001

TABLE 66B. EXPERIMENT 6-ARO-1, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	620.50	620.50	1.7656	N.S.
SUBJECTS IN GROUPS	8	2811.5	351.44		
TIMES	5	75818.	15164.	398.80	p < .001
TIMES X GROUPS	5	162.00	32.400	.85839	N.S.
TIMES X SUBJECTS IN GROUPS	40	1524.0	38.100		
TOTAL	59	80936.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 6 DAY 10 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	195.800	199.800	220.800	240.800	258.800	289.200	235.600
TEST	5	194.200	207.600	228.400	247.600	276.200	297.600	242.833
TOTAL	10	194.600	203.300	224.600	244.200	272.800	293.400	238.817

TABLE 66C. EXPERIMENT 6-ARO-1, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	540.00	540.00	3.0769	N.S.
SUBJECTS IN GROUPS	8	1404.8	175.50		
TIMES	5	10901.	2180.2	87.252	p < .001
TIMES X GROUPS	5	102.00	36.400	1.4567	N.S.
TIMES X SUBJECTS IN GROUPS	40	999.50	24.987		
TOTAL	53	14026.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
		1	2	3	4	5	6	
CONTROL	1	173.800	175.200	191.800	194.000	205.800	214.800	192.700
TEST	2	172.200	174.600	183.200	186.800	197.400	206.800	186.700
TOTAL	10	173.000	174.900	187.500	190.400	201.600	210.600	189.700

TABLE 66D. EXPERIMENT 6-ARO-1, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS											
SOURCE OF VARIATION		DEGREES OF FREEDOM		SUM OF SQUARES		MEAN SQUARE		F-RATIO		SIGNIFICANCE	
GROUPS		1		35.500		35.500		.19089E-01		N.S.	
SUBJECTS IN GROUPS		0		14070.		1059.7					
TIMES		5		78741.		15748.		68.777		P < .001	
TIMES X GROUPS		5		194.00		38.800		.16945		N.S.	
TIMES X SUBJECTS IN GROUPS		40		9159.0		228.90					
TOTAL		59		.10301E+06							

MEANS		TIMES:						
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
GROUPS:	N	1	2	3	4	5	6	
CONTROL	1	5	205.600	203.400	219.800	238.200	270.000	301.200
TEST	2	5	205.600	206.000	227.000	239.800	273.600	304.400
TOTAL	10		205.100	204.700	223.400	239.600	275.800	302.800

TABLE 66E. EXPERIMENT 6-ARO-1, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	350.50	350.50	.42767	N.S.
SUBJECTS IN GROUPS	8	6556.5	819.56		
TINES	5	83968.	16794.	99.533	p < .001
TINES X GROUPS	5	177.50	35.500	.21040	N.S.
TINES X SUBJECTS IN GROUPS	40	6749.0	168.73		
TOTAL	59	97802.			

MEANS

TINES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	203.000	202.400	225.800	247.200	265.600	304.800	241.467
TEST	2	206.200	206.800	226.600	249.800	275.600	313.600	246.300
TOTAL	10	204.600	204.600	226.200	248.100	270.600	309.200	243.883

TABLE 67B. EXPERIMENT 15-ARO-2, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	101.00	101.00	.26605	N.S.
SUBJECTS IN GROUPS	8	3037.0	379.62		
TIMES	5	65045.	13009.	900.28	p < .001
TIMES X GROUPS	5	259.00	51.800	3.5848	p < .01
TIMES X SUBJECTS IN GROUPS	40	570.00	14.450		
TOTAL	59	69020.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 3 DAY 6 DAY 10 DAY 15						TOTAL
		1	2	3	4	5	6	
CONTROL	5	205.600	200.000	227.400	249.600	266.400	290.800	241.300
TEST	5	204.400	204.800	228.800	252.800	273.200	299.400	243.900
TOTAL	10	205.000	206.400	228.100	251.200	269.800	295.100	242.600

TABLE 67C. EXPERIMENT 15-ARO-2, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	10.500	10.500	.48951E-01	N.S.
SUBJECTS IN GROUPS	8	1716.0	214.50		
TIMES	5	14830.	2966.1	219.91	P < .001
TIMES X GROUPS	5	134.50	26.900	1.9944	N.S.
TIMES X SUBJECTS IN GROUPS	40	539.50	13.487		
TOTAL	59	17231.			

MEANS

TIMES:

GROUPS:	N	DAY 0 DAY 1 DAY 2 DAY 3 DAY 4 DAY 5 DAY 6 DAY 10 DAY 15						TOTAL	
		1	2	3	4	5	6		
CONTROL	5	170.000	171.000	177.600	177.600	193.600	201.400	211.800	187.467
TEST	5	169.400	169.600	181.000	187.600	198.200	214.000	186.633	
TOTAL	10	169.700	170.300	179.300	190.300	199.800	212.900	187.050	

TABLE 67D. EXPERIMENT 15-ARO-2, AROCIOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2829.5	2829.5	.78696	N.S.
SUBJECTS IN GROUPS	9	32359.	3595.5		
TIMES	5	72517.	14503.	100.25	p < .001
TIMES X GROUPS	5	2880.5	576.10	3.9820	p < .01
TIMES X SUBJECTS IN GROUPS	45	6510.5	144.68		
TOTAL	65	.11710E+06			

MEANS

TIMES:

GROUPS:	N	TIMES						TOTAL
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
CONTROL	1	209.200	203.200	220.800	241.000	255.400	278.000	234.600
TEST	2	207.500	207.167	228.000	247.667	284.667	311.500	247.750
TOTAL	11	208.273	205.364	224.727	244.636	271.364	296.273	241.773

TABLE 67E. EXPERIMENT 15-ARO-2, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	480.50	480.50	.20299	N.S.
SUBJECTS IN GROUPS	7	16569.	2367.1		
TIMES	5	67156.	13431.	112.72	p < 001
TIMES X GROUPS	5	375.50	75.100	.63026	N.S.
TIMES X SUBJECTS IN GROUPS	35	4170.5	119.16		
TOTAL	53	88752.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	198.400	197.000	213.200	235.200	270.000	296.200	235.000	270.000	296.200	235.000
TEST	2	191.000	194.250	214.500	232.500	260.500	281.250	229.000	260.500	281.250	229.000
TOTAL	9	195.111	195.770	213.770	234.000	265.770	289.556	232.333	265.770	289.556	232.333

TABLE 68A. EXPERIMENT 24-ARO-3, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANIMAL	SEX	GROUP	MEAN WEIGHT (GRAMS)	MEAN ORGAN-TO-BODY WEIGHT RATIO (* 1000)										
				LUNGS	LIVER	KIDNEYS	HEART	BRAIN	ADRENALS	GONADS	SPLEEN			
RATS	MALE	CONTROL	302.4	0.83	37.15	6.87	3.76	6.17	.25	13.04	2.29			
		N	5	5	5	5	5	5	5	5	5			
		TEST	310.0	0.10	35.45	6.84	3.10	5.80	.22	13.01	1.90			
		N	5	5	5	5	5	5	5	5	5			
		P	1.46	-.88	-.56	-.87	-3.18	-1.27	-.77	-.87	-2.52			
		T-TEST STATISTIC	.1036	.4033	.5917	.9462	.8130	.2381	.4619	.9430	.8359			
		P-VALUE												
RATS	FEMALE	CONTROL	213.4	9.52	33.57	6.90	3.73	0.80	.39	3.41	2.65			
		N	5	5	5	5	5	5	5	5	5			
		TEST	209.6	9.56	30.00	6.61	3.79	0.56	.37	4.14	2.39			
		N	5	5	5	5	5	5	5	5	5			
		P	-.52	-.06	1.61	-.74	.32	-.83	-.47	.70	-1.44			
		T-TEST STATISTIC	.6284	.9578	.1456	.4780	.7553	.4326	.6540	.4596	.1098			
		P-VALUE												
GUINEA PIG	MALE	CONTROL	306.0	12.87	44.67	8.49	4.62	11.56	.37	3.50	1.36			
		N	5	5	5	5	5	5	5	5	5			
		TEST	295.0	13.68	40.12	8.50	4.32	11.67	.46	3.31	1.32			
		N	5	5	5	5	5	5	5	5	5			
		P	-.91	.56	1.20	.02	-.94	.19	2.90	-.92	-.34			
		T-TEST STATISTIC	.3095	.5902	.2351	1.000	.3750	.0560	.0190	.3869	.7440			
		P-VALUE												
GUINEA PIG	FEMALE	CONTROL	293.2	11.33	35.70	8.25	4.29	11.41	.53	4.66	1.56			
		N	5	5	5	5	5	5	5	5	5			
		TEST	295.2	12.91	42.50	7.68	4.02	10.99	.50	3.99	1.47			
		N	5	5	5	5	5	5	5	5	5			
		P	.26	1.10	2.05	-1.06	-.62	-1.10	-.77	-.77	-.40			
		T-TEST STATISTIC	.8010	.2724	.0749	.3203	.5536	.2710	.4680	.4647	.6454			
		P-VALUE												

(*) < .10 * < .05 ** < .01 *** < .001

TABLE 68B. EXPERIMENT 24-ARO-3, AROCIOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE RATS											
SOURCE OF VARIATION		DEGREES OF FREEDOM		SUM OF SQUARES		MEAN SQUARE		F-RATIO		SIGNIFICANCE	
GROUPS		1		390.00		390.00		.91751		N, S,	
SUBJECTS IN GROUPS		8		3400.5		425.06					
TIMES		5		48325.		9665.0		57.560		P < .001	
TIMES X GROUPS		5		1095.5		219.10		1.3040		N, S,	
TIMES X SUBJECTS IN GROUPS		40		6716.5		167.91					
TOTAL		59		59927.							

MEANS		TIMES:						
		DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	
GROUPS:	N	1	2	3	4	5	6	
CONTROL	1	5	226.000	218.000	235.000	260.000	257.400	295.600
TEST	2	5	227.800	214.600	234.600	262.400	279.800	304.200
TOTAL	10		227.300	216.300	234.800	261.200	268.600	299.900
								248.000
								253.900
								251.350

TABLE 68C. EXPERIMENT 24-ARO-3, AROCIOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE RATS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	73.000	73.000	.70289E-01	N.S.
SUBJECTS IN GROUPS	8	8308.5	1038.6		
TIMES	5	5867.0	1013.4	38.260	P < .001
TIMES X GROUPS	5	63.000	12.600	.47570	N.S.
TIMES X SUBJECTS IN GROUPS	40	1059.5	26.487		
TOTAL	59	14571.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	191.600	185.200	190.600	196.800	196.800	204.000	211.800	211.800	196.667
TEST	2	5	186.800	182.200	187.800	190.800	190.800	201.800	209.400	209.400	194.467
TOTAL	10	10	189.200	183.700	189.200	197.800	197.800	202.900	210.600	210.600	195.567

TABLE 68D. EXPERIMENT 24-ARO-3, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF MALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	2042.0	2042.0	1.2021	N.S.
SUBJECTS IN GROUPS	8	13589.	1698.7		
TIMES	5	82174.	16435.	116.85	P < .001
TIMES X GROUPS	5	1667.0	333.40	2.3784	N.S.
TIMES X SUBJECTS IN GROUPS	40	5626.0	140.65		
TOTAL	59	.10510E+06			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 3	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	5	198.800	196.400	218.000	239.600	272.000	305.400	238.367
TEST	5	202.200	195.600	203.400	216.800	247.400	295.600	226.700
TOTAL	10	200.500	196.000	210.700	227.800	259.700	300.500	232.533

TABLE 68E. EXPERIMENT 24-ARO-3, AROCLOR 1254, DETAILED SUMMARY OF ANIMAL WEIGHT ANALYSIS

ANALYSIS OF VARIANCE TABLE FOR REPEATED MEASURES DESIGN ON BODY WEIGHT OF FEMALE GUINEA PIGS

SOURCE OF VARIATION	DEGREES OF FREEDOM	SUM OF SQUARES	MEAN SQUARE	F-RATIO	SIGNIFICANCE
GROUPS	1	180.50	180.50	.20050	N.S.
SUBJECTS IN GROUPS	8	7202.0	900.25		
TIMES	5	63680.	12736.	126.68	$p < .001$
TIMES X GROUPS	5	529.00	105.80	1.0523	N.S.
TIMES X SUBJECTS IN GROUPS	40	4021.5	100.54		
TOTAL	59	75613.			

MEANS

TIMES:

GROUPS:	N	DAY 0	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 10	DAY 15	TOTAL
CONTROL	1	5	204.600	198.800	216.600	240.000	253.800	294.000	236.300		
TEST	2	5	207.800	201.600	214.000	228.000	253.200	292.400	232.833		
TOTAL	10		206.200	200.200	215.300	234.000	250.500	293.200	234.567		

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