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Attn: 8(e) Coordinator

Re: DIETHYLDISULFIDE
CAP Agreement No. CAP-0111
Dow Reference No. CAP00789

Dear Sir/Madam:

The Dow Chemical Co. submits the enclosed document titled:

A 10-DAY REPEATED INHALATION TOXICITY STUDY OF DIETHYLDISULFIDE IN RATS

pursuant to TSCA Section 8(e) Compliance Audit Program.

The document contains information which may reasonably support the conclusion that the referenced chemical may present a substantial risk of injury to human health or the environment, as indicated in the Reporting Guide provided by EPA in connection with the CAP. Dow has not, however, determined that any risk actually exists. The information is summarized below:

THE MALES HAD SLIGHTLY SWOLLEN SCROTAL SACS. HEMATOLOGY REVEALED EFFECTS SUGGESTIVE OF A HEMOLYTIC ANEMIA IN MALES AND FEMALES IN THE 450 PPM EXPOSURE GROUP.

Dow requests guidance from EPA whether the Agency believes the information contained in this document satisfies the criteria in the CAP Reporting Guide. Any correspondence relating to this submission should reference document number CAP00789.

Where appropriate, three types of information have been removed from the document: the term "Dow Confidential", individual employee/researcher names (due to privacy considerations); and Dow internal number systems. This is done with prior agreement from EPA. The original documents containing this information are retained by Dow according to a document retention policy.

Sincerely,

Paul A. Wright

Paul A. Wright
Attorney
517/636-1853

COMPANY SANITIZED

A 10-DAY REPEATED INHALATION TOXICITY STUDY OF DIETHYLDISULFIDE IN RATS

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CONFIDENTIAL SUBMISSION

March 26, 1979

Toxicology Research Laboratory
Health and Environmental Sciences, USA
Dow Chemical, U.S.A.
Midland, Michigan 48640

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SUMMARY

A repeated inhalation toxicity study of diethyldisulfide in rats was conducted at mean exposure concentrations of 53, 150 and 437 ppm (will be called 50, 150 and 450 ppm throughout this report). The duration of exposure was 6 hours daily for 10 consecutive days. Body weights were recorded every other day and the rats were observed daily for signs of toxicity. Hematological and clinical chemistry, including thyroxine, data were obtained. A measure of iodine uptake by the thyroid was obtained using ^{125}I on a separate group of male rats which were added to the study for this purpose. Gross and microscopic pathological examinations were conducted at the termination of the experiment. Weights of various organs were recorded and organ/body weight ratios were calculated.

Slightly decreased body weight gain was the only effect attributed to inhalation of diethyldisulfide at 50 ppm in both male and female rats. Eye irritation was observed in male and female rats exposed to 150 ppm diethyldisulfide. This was accompanied by body weight and relative organ weight effects in both sexes. The female rats of this exposure group exhibited darkened spleens upon gross pathologic examination.

Inhalation of 450 ppm diethyldisulfide produced extensive body weight and organ weight effects in male and female rats. Eye irritation and slight urine staining were observed in both sexes during and after

exposure. The males also had slightly swollen scrotal sacs. Hematology revealed effects suggestive of hemolytic anemia in males and females in the 450 ppm exposure group. This phenomenon could account for effects on bilirubin level, PCV, RBC and the histological and weight changes of the spleens. The liver was also effected in both sexes and thyroxine levels were decreased in males.

There was no effect on iodine uptake by the thyroid in male rats at any concentration tested.

Based on the results of this study, it is not possible to predict the results of repeated inhalation of diethyldisulfide at concentrations below 50 ppm. It is certain that concentrations sustained at or above 50 ppm are too high for humans both from an odor/comfort standpoint and for toxicity reasons. The clinical signs suggestive of a hemolytic anemia which were observed at 450 ppm have not been characterized as to time of onset nor as to reversibility.

An Industrial Hygiene Guide (IHG) may be chosen using these data if at least a 100 fold safety factor below 50 ppm is used bringing the IHG to 0.5 ppm. This could be done because the effects at 50 ppm were only on body weight and are not considered serious. It is recommended that this IHG be for total mono- and disulfides in light of the similar toxic effects attributed to dimethylsulfoxide (DMSO) and DEDS's likelihood of being the same or similar to metabolites of various mono- and disulfides.

INTRODUCTION

Diethyldisulfide (DEDS), $H_3C-CH_2-S-S-CH_2-CH_3$, is a decomposition product of Dursban*. Its formation is promoted by the presence of the [redacted] DEDS is an oily liquid with a high vapor pressure and a strong "rotten cabbage" odor which is noticeable in the ppb range.

Diethyldisulfide is low in acute oral toxicity with an LD50 in rats of 2030 mg/kg.[1] Disulfides, including DEDS, have been shown to inhibit thyroid function in the rat after oral doses of ~600 mg/kg.[2,3] In a study by Gage[4] rats were exposed to 250 ppm dimethyldisulfide for 13 x 6 hours. The rats were lethargic, had respiratory difficulty and reduced weight gain. Their organs were "congested". Twenty 6-hour exposures to 100 ppm had no adverse effects upon four rats. An acute inhalation study ([redacted][5] using a "saturated" atmosphere of DEDS (4390 ppm - nominal) at room temperature caused the death of all six rats exposed. A "half-saturated" atmosphere of DEDS (2156 ppm - nominal) resulted in the death of one of six exposed rats. In a Dow report (HET [redacted])[6] the oral LD50 for rats was reported to be approximately 2000 mg/kg, and DEDS was shown to be slightly irritating to the eyes and skin.

The purpose of this study was to determine what the target organ(s) are and to define a no-adverse effect level in rats to facilitate selection of an Industrial Hygiene Guide.

*Trademark of The Dow Chemical Company.

METHODS

Test Material

Diethyldisulfide is an oily liquid with a boiling point of 150°C and a high vapor pressure. The DEDS used in this study was purchased from Eastman Organic Chemicals and included 1.5 kg of Lot No. A6 and 1.0 kg of Lot No. 5B, both at least 98.9% pure by gas chromatography.[7]

Exposure Chambers, Vapor Generation and Analysis

The exposure chambers used in this study were made of stainless steel and glass and were 1 cubic meter in size with pyramidal shaped tops and bottoms. The chambers were operated under dynamic airflow conditions. Diethyldisulfide vapor was generated by metering the liquid compound at a controlled rate into a glass flask maintained at a temperature high enough to vaporize the liquid but not so high as to cause charring or decomposition (approximately 130°C). The vapor was swept into the air inlet of the exposure chamber where it was further diluted by the main chamber air to the desired concentration. Chamber airflow was regulated to provide 4 to 8 air changes per hour. The nominal concentration of diethyldisulfide in each exposure chamber was calculated as the ratio of the weight of DEDS used to the rate of airflow through the chamber. Analytical concentrations of DEDS vapor in the exposure chambers were determined by gas chromatography using manual injection. The chromatographic conditions were as follows:

Instrument:	Varian Aerograph Model 2440
Column:	6' x 2 mm glass packed with 10% OV-17 on CWHP (80/100 mesh)
Detector:	Hydrogen flame ionization
Temperatures:	Injector: 160°C Detector: 160°C Column: 150°C
Gas Flow Rates:	Helium: 20.7 ml/min Air: 300 ml/min Hydrogen: 30 ml/min
Gas Sample Volume:	0.5 ml (injected by hand)

Standards for the analysis were prepared by injecting known volumes of DEDS into 100 liter Saran bags containing filtered air. Samples of the chamber atmosphere were collected three times each day for each chamber in Saran bags, and 0.5 ml aliquots were manually injected into the GC immediately after collection.

Animal Exposure

Four groups of Fischer 344 (Charles River) rats 10 weeks of age consisting of 10 rats/sex/group were used. Females were put on test one day later than males. The groups were exposed to 0 (room air), 50, 150 and 450 ppm diethyldisulfide vapor 6 hours per day for 10 consecutive days. Another 5 male rats were added to each exposure group (plus 10 for control) at the beginning of the study for use in the iodine-125 experiment described later in this report.

Rats were randomly assigned to treatment groups from a single lot of animals by use of the computer program GRAND. CLIST (Computations

Research Laboratory, Dow Chemical, U.S.A.) which generates random numbers. Rats were housed two or three per cage and controls were kept in cages in an animal holding room for the duration of the experiment. Food and water were removed during the exposure period (including controls), but were available ad libitum at all other times. Due to an oversight, food was not removed from control rats on the first exposure day.

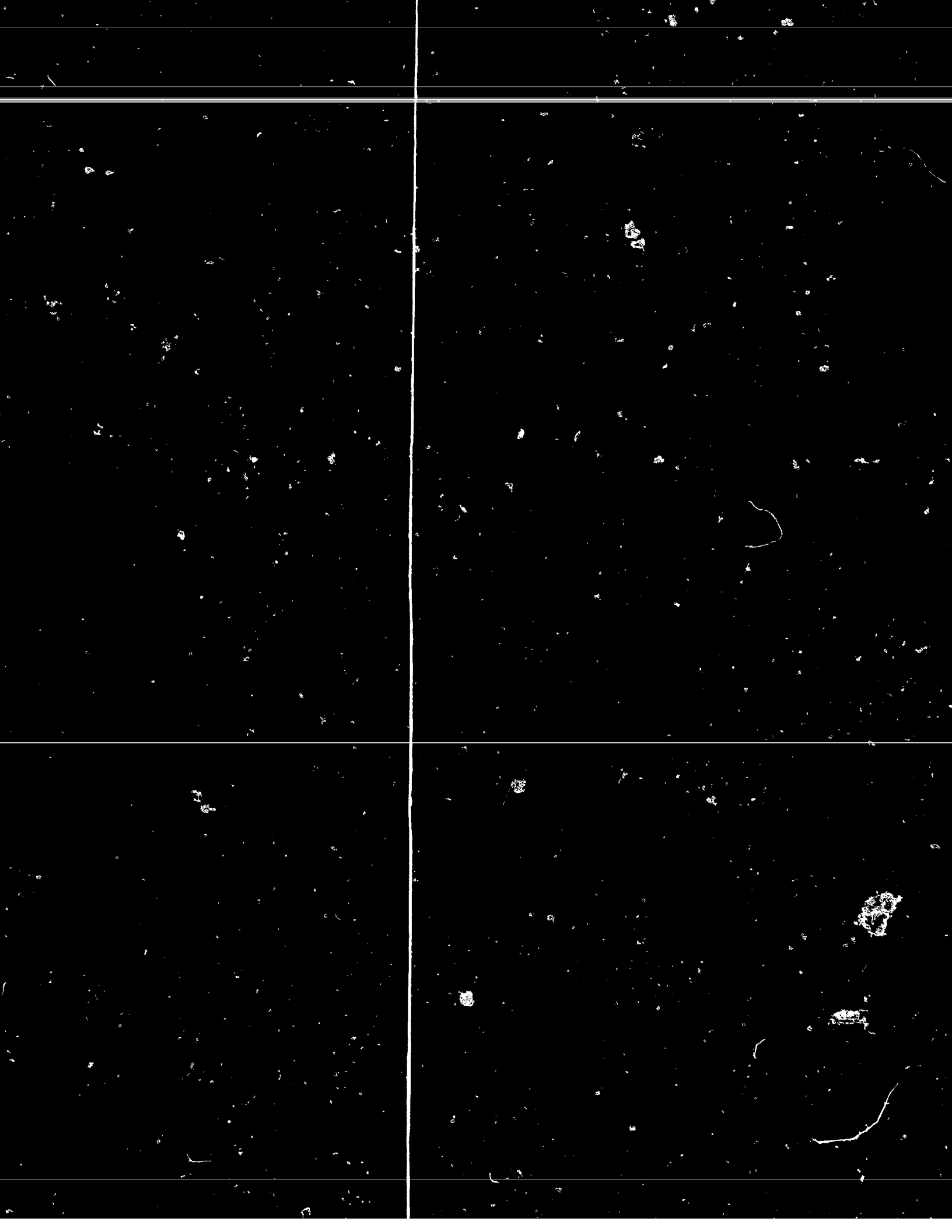
Animal Observation and Body Weights

All rats were weighed prior to exposure on exposure days 0, 2, 4, 6, 8 and 10. All rats were observed during each exposure day for changes in appearance or demeanor. Two rats from the ^{125}I group (1-50 ppm, 1-negative control) were found in a moribund state at the end of the seventh exposure day and were sent for pathologic examination at that time.

Clinical Studies

Hematological parameters, including red cell count, hemoglobin concentration, packed cell volume, total and differential white cell counts[a] and reticulocyte count (females only) were determined on blood from 5 rats/sex/group prior to necropsy. Blood for hematology was obtained from the tail veins. At necropsy, clinical chemistry determinations

[a]PCV: Microhematocrit Centrifuge*, Clay-Adams Co., New York; RBC, WBC Counts, Hgb: Coulter Counter Model 2BI and Hemoglobinometer, Coulter Electronics, Hialeah, FL.



of blood urea nitrogen (BUN), alkaline phosphatase activity (AP), bilirubin and serum glutamic pyruvic transaminase activity (SGPT)[b] were performed on serum from 10 rats/sex/group. A portion of each clinical chemistry serum sample was sent to Bioscience Laboratory, Van Nuys, California, for determination of thyroid function by the T4 (thyroxine) test. Blood for the clinical chemistry and T4 tests was obtained from the cervical trunk after decapitation.

Iodine-125 Uptake

In order to assess the effects of DEDS on thyroid function under the conditions of this inhalation experiment, I-125 uptake was measured in the extra groups of 5 male rats per exposure group by the method of Saghir, et al.[2] In this method, each rat was given, by intraperitoneal injection, 1 μCi of carrier-free $Na^{125}I$ in 0.5 ml of 0.9% saline solution. A positive control was also run on a group of 5 male rats treated with 1 mg each of propylthiouracil (PTU, a known goitrogen). The I-125 was administered 20 hours after the 10th exposure for the DEDS exposed rats and one hour after administration of PTU in the case of the positive control rats. Three hours after administration of the I-125 the rats were anesthetized by methoxyflurane, decapitated and thyroidectomized. Each thyroid was digested in 1 ml of NCS* Solubilizer for 24 hours in plastic scintillation tubes. Total radioactivity was then measured in each tube using a Nuclear Chicago automatic gamma counting system - Model #4230. Percentage uptake was calculated by comparing the radioactivity

[b]Centrifi-Chem* System 400, Methods File.

in 1 mg of thyroid tissue with that in a standard dose. The standard dose was 50 ul of a standard dosing solution: 25 ml volume containing 50 uCi of ^{125}I. Rats used in this part of the study (I-uptake) were not sent for pathologic examination, but were disposed of in accordance with regulations for radioactive waste disposal.

Pathology

Twenty-four hours after the last exposure a necropsy examination was performed on 10 rats/sex/group excluding the rats used in the iodine uptake experiment. Prior to necropsy, the rats were fasted overnight, weighed, anesthetized with methoxyflurane to facilitate the clamping of the trachea, and then killed by decapitation. All eyes were examined using a glass microscope slide technique. The eyes from 5 rats/sex/group were fixed in Zenker's solution. Eyes from the remaining rats were preserved in buffered 10% formalin. Weights of the brain, heart, liver, kidney, testes (males) and spleen (females) were determined and recorded. Due to the hematological and gross findings during the necropsy of the male rats, the spleens of females were weighed at the time of their necropsy on the following day.

The brain, liver, kidneys, lungs, spleen, thyroid, testes (males), nasal turbinates and a section of the thoracic vertebral column were collected and preserved in phosphate-buffered 10% formalin. Routine histologic procedures were used to prepare hematoxylin and eosin stained sections from liver, kidneys, lung, spleen, thyroid, testes (males) of 5

rats/sex/group. Excluding those rats exposed to 50 ppm DEDS, the vertebral columns from 5 rats/sex/group were processed for subsequent bone marrow evaluation.

Statistical Evaluation

Clinical chemistry, thyroid T4, organ weight, and body weight data were evaluated using an analysis of variance and Dunnett's test (Steel and Torrie, 1960).[8] The level of significance in all cases was $p<0.05$.

RESULTS

Chamber Analysis

Results of the analyses for diethyldisulfide in the inhalation chambers during the 10-day experiment are summarized in Table 1.

Animal Observation and Body Weights

Male and female rats in the 450 ppm exposure group had eye irritation as evidenced by blinking and moderate palpebral closure on each day during the exposure. Occasionally the rats in the 150 ppm group also showed eye irritation during exposure. On seven of the exposure days 1/4 to 1/2 of the male rats in the 450 ppm group were stained with urine in the perineal region upon removal from the exposure chambers. One to three of the females of the 450 ppm group were also urine stained after exposure on two days. All of the male rats began to have slight scrotal swelling on the fourth exposure day in the 450 and 150 ppm groups. This effect was observed only in the 450 ppm group for the remainder of the study. On the eighth study day it was observed that 3 to 4 rats of various groups had slight lung rales, but this observation was not made at any other time. There were no obvious signs of toxicity in the 50 ppm exposure group.

Individual and mean body weights for male and female rats are given in Tables 2, 3, and 11. Body weights of male rats were statistically significantly lower than control values in the 450 ppm group throughout the study and in the other two concentration groups at the last two

weighings. Body weights for female rats were statistically significantly lower in the 450 ppm group at the last three weighings and on the seventh day in the 50 ppm group. Due to the difference among day zero mean weights in the various groups, body weight change from pre-exposure body weights was calculated (Tables 4 and 5) in order to more accurately assess the effect of inhaled DEDS on body weight. The body weight changes show statistically significantly lower body weight gains for both male and female rats in each dose group for the last half of the study, and in female rats for the entire study except for day 1 of the 50 ppm group. In general, inhalation of diethyldisulfide was associated with a decreased body weight gain in both male and female rats at all concentrations of the study.

Clinical Studies

Individual and mean hematological values obtained prior to sacrifice of male and female rats are given in Tables 6 and 7. In male rats, statistically significantly elevated white blood cell counts were seen in the 450 ppm group by use of the Coulter Counter technique. This effect was accompanied by low packed cell volume and red cell counts in the same group of rats. Examination of blood smears revealed numerous nucleated and immature red blood cells. Thus, the white blood cell count was redetermined by visually comparing blood smears from this group to the controls. What was counted by the Coulter Counter included, in all due probability, nucleated red blood cells and immature red blood cells as well as white blood cells. White blood cell counts for

female rats in the 450 ppm group were determined only by visual comparison to controls. A slight increase in the total white blood cell count was observed in female rats exposed to 150 ppm DEDS. This was not a statistically significant increase and the values were within the range of white blood cell count values for historical control rats of the identical strain and age used in this study. Therefore this effect is not considered to be related to inhalation of diethyl disulfide. Packed cell volumes and red cell counts of both males and females of the 450 ppm group were statistically significantly decreased and spurious results were obtained for hemoglobin due to the turbidity of the samples. In the female high dose group the samples were centrifuged after adding lysing solution in order to obtain a better hemoglobin reading and in this group the mean hemoglobin value was statistically significantly lower than that of controls.

All of the above-mentioned blood effects are consistent with a diagnosis of hemolytic anemia brought about by the inhalation of diethyl-disulfide for 10 days at a concentration of 450 ppm. There were no effects of a hematologic nature in male or female rats exposed for 10 days to 150 or 50 ppm of DEDS.

Individual and mean clinical chemistry values for male and female rats are given in Tables 8 and 9. For males in the 450 ppm exposure group there were statistically significantly reduced mean BUN, AP and T4 values. Bilirubin was statistically significantly greater in this group; the mean SGPT activity for this group was lower than that of

controls and the other treatment groups but the difference was not statistically significant. Female rats had lower mean BUN and AP values in the 450 ppm group than in the other groups and the mean AP value was statistically significantly reduced from the control value. There was also a statistically significantly elevated bilirubin for the 450 ppm female rats. Although a statistically significantly reduced T4 level was seen in females of the 50 ppm group, this was not seen at higher concentrations and was thus not considered to be related to inhalation of diethyldisulfide. It was concluded that inhalation of 150 or 50 ppm of diethyldisulfide for 10 consecutive days had no adverse effect on BUN, SGPT, AP, bilirubin or T4 in male or female rats.

Iodine-125 Uptake

Inhalation of diethyldisulfide by male rats for 10 consecutive days at concentrations of 450, 150 and 50 ppm had no effect upon the uptake of ^{125}I by thyroid tissue of these rats as compared to positive and negative controls (Table 10). Although the mean iodine uptake of the 450 ppm group was lower than the control value, the decrease was attributable to a low uptake in only one of the five animals and is thus not indicative of a group effect. Body weights for the male rats used in this ^{125}I experiment are given in Table 11.

Pathology

Two rats from the ^{125}I group (one 50 ppm, one negative control) were found in a moribund state at the end of the seventh exposure day. Both rats showed a poor body condition at necropsy. The negative control

rat died spontaneously just prior to necropsy. Necropsy revealed both rats to be off feed and possibly water. Microscopic examination of the brains from both rats showed a suppurative meningoencephalitis caused by, in all due probability, an unidentified bacteria. Table 12 lists the results of the gross and microscopic examinations of the aforementioned rats.

Table 13 lists the gross observations made on 10 rats/sex/group after 10 consecutive days' exposure to vapors of diethyldisulfide.

Enlarged salivary glands and exophthalmus were not considered treatment-related but were, most likely, signs of a possible concurrent sialodacryoadenitis infection. Observations made at necropsy that were considered tr ment-related were darkened or congested liver, kidneys and spleen. These changes occurred in both male and female rats exposed to 450 ppm DEDS. The spleens from these rats were also enlarged, although the spleens of the male rats were not weighed. An anemic and, in some cases, a slight icteric appearance was noted in 10/10 male and 9/10 female rats exposed to 450 ppm DEDS.

Individual and mean fasted body weights, organ weights and organ to body weight ratios for male and female rats are given in Tables 14 and 15. There were no effects on the organ weight values for male rats exposed to 50 ppm DEDS. The fasted body weights of males exposed to 150 and 450 ppm DEDS were statistically significantly lower than controls and this also reflects a dose-related trend which carried over into the 50 ppm group. The low mean body weight for the 50 ppm group is not statistically significant but is consistent with body weight effects

seen during the course of the study. Statistically significantly elevated relative brain, kidney and testes weights in both the 150 and 450 ppm male groups were related to the decreased body weights. Male rats in the 450 ppm exposure group had statistically significantly decreased absolute liver and testes weights which may have been related to treatment, though these effects were not accompanied by histological findings.

Female rats exposed to 150 ppm DEDS had slightly darkened spleens. This observation may or may not be related to exposure to DEDS. Histopathologic examination of the spleens did not show a treatment related effect. At necropsy, 1 out of 10 of the females in the 450 ppm exposure group had decreased adipose reserves. The remaining necropsy observations on female rats in these two groups are not considered treatment-related.

Female rats in the 50 ppm exposure group had a statistically significantly lower relative liver weight but this is not considered to be related to the inhalation of DEDS judging by the lack of a dose-related response and the fact that the mean was low due to a low value for only one rat. There were no organ weight effects in females of the 150 ppm group. There was a statistically significantly low mean fasted body weight for female rats exposed to 450 ppm diethyldisulfide. There were also statistically significantly elevated relative heart, liver, and kidney weights. These effects in the 450 ppm female group reflect the decreased weight gain caused by the inhalation of DEDS. Absolute

and relative spleen weights for this group of female rats were also statistically significantly elevated. Spleen enlargement was due to increased congestion of the red pulp, an observation consistent with hemolytic anemia.

Histopathologic findings on 5 rats/sex/group have been listed in Table 15. Histopathologic alterations considered to be related to exposure to DEDS were seen in the liver and spleen. From the 450 ppm exposure group, 3/5 males and 2/5 females had livers with a slight degree of extramedullary hematopoiesis. Microscopic examination of the spleens from the same rats revealed all to have treatment-related changes consisting of moderate congestion of the red pulp accompanied by a moderate degree of extramedullary hematopoiesis. These findings are consistent with the animals' response to a hemolytic condition. The remaining microscopic observations listed in Table 16 were not considered to be related to exposure to diethyldisulfide.

DISCUSSION AND CONCLUSIONS

Body weight effects were the only effects attributed to inhalation of diethyldisulfide at 50 ppm in both male and female rats. Eye irritation was observed in male and female rats exposed to 150 ppm diethyldisulfide. This was accompanied by body weight and relative organ weight effects in both sexes. The female rats of this exposure group exhibited darkened spleens upon gross pathologic examination.

Inhalation of 450 ppm diethyldisulfide produced extensive body weight and organ weight effects in both male and female rats. Eye irritation and slight urine staining were observed in both sexes during and after exposure. The males also had slightly swollen scrotal sacs. Hematology revealed effects suggestive of hemolytic anemia in both males and females in the 450 ppm exposure group. This phenomenon could account for effects on bilirubin level, packed cell volume, RBC, the histological and weight changes of the spleens and histological changes of the liver. Thyroxine levels were decreased in males.

There was no effect on iodine uptake by the thyroid in male rats at any concentration tested.

The suggested detoxification mechanism for DEDS includes reduction to ethyl mercaptan, methylation to ethylmethylsulfide, and then oxidation to ethylmethylsulfone via ethylmethylsulfoxide.[9] It is interesting to note that dimethylsulfoxide (DMSO) produces a reversible hemolytic anemia and diuresis in experimental animals.[10] The anemia was produced

in dogs and rats after repeated intravenous or intraperitoneal injections.[11] Daily topical administration of 2.5 ml of 90% DMSO to rats resulted in a 10-fold increase in urinary output.[12] If, as has been reported in various industrial hygiene and analytical reports[13], diethylsulfide, dimethyldisulfide and dimethylsulfide are found in the same work areas as diethyldisulfide it would seem likely that their toxic effects may be additive because their metabolites may be DMSO itself or structurally similar compounds.

Based on the results of this study, it is not possible to predict the results of repeated inhalation of diethyldisulfide at concentrations below 50 ppm. It is certain that concentrations at or above 50 ppm are too high for humans both from an odor/comfort standpoint and for toxicity reasons. The clinical signs suggestive of a hemolytic anemia which were observed at 450 ppm have not been characterized as to time of onset nor as to reversibility.

An Industrial Hygiene Guide (IHG) may be chosen using these data if at least a 100-fold safety factor below 50 ppm is used. This could be done because the effects at 50 ppm were only on body weight and are not considered serious. It is recommended that this IHG be for total mono- and disulfides in light of the similar toxic effects attributed to DMSO and DEDS's likelihood of being the same or similar to metabolites of various mono-and disulfides.

Written by:

Reviewed By:

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13. Dow Analytical Reports

Table 1

INHALATION CHAMBER AIR ANALYSIS FOR DIETHYLDISULFIDE

Target Concentration, ppm	50	150	450	Control
Nominal Concentration, ppm	44.6	170.4	521.6	-
$\bar{X}$±S.D.	±8.80	24.19	±4.36	
Analytical Concentration, (TWA) ppm	53.45	149.64	436.91	-
$\bar{X}$±S.D.	±7.39	±13.52	±28.47	
Total Exposure Days[b]	11	11	11	11
Exposure Days Within ±10% of Mean Analytical Concentration	8	9	10	-
Exposure Days Within ±20% of Mean Analytical Concentration	10	10	11	-
Daily Temperature, °F	74.8	72.0	74.4	-[a]
$\bar{X}$±S.D.	±2.22	±1.66	±2.07	
Daily Relative Humidity, %	52.2	52.4	56.3	-[a]
$\bar{X}$±S.D.	±3.93	±8.57	±4.58	

[a]Controls were kept in an animal holding room at ambient conditions; no record was kept of temperature or humidity.

[b]Because females were placed on test one day later than males (staggered start), the total number of days during which animals were exposed is 11.

Table 2

INDIVIDUAL AND MEAN (± S.D.) BODY WEIGHTS (g) OF MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Days on Exposure		0	1	3	5	7	9
0 PPM							
Animal No.	77-3680	184	178	187	188	200	-[a]
	-3681	205	208	220	222	235	-[a]
	-3682	174	174	184	182	193	-[a]
	-3683	193	199	209	210	228	234
	-3684	190	193	204	198	212	220
	-3685	184	188	199	198	218	224
	-3686	202	204	213	213	230	233
	-3687	209	210	218	209	223	224
	-3688	200	204	214	210	230	238
	-3689	197	200	206	202	222	223
	Mean	193.8	195.8	205.4	203.2	219.1	228.0
	± S.D.	10.91	12.35	12.28	12.07	13.71	6.86
50 PPM							
	77-3740	202	216	211	215	224	224
	-3741	182	188	186	187	194	200
	-3742	203	210	212	211	219	218
	-3743	185	189	188	192	196	189
	-3744	197	206	206	209	216	214
	-3745	206	214	214	219	220	226
	-3746	194	200	198	202	208	199
	-3747	181	187	187	192	196	203
	-3748	192	202	198	201	201	201
	-3749	189	196	191	197	198	212
	Mean	193.1	200.8	199.1	202.5	207.2*	208.6*
	± S.D.	8.90	10.73	10.99	10.73	11.60	12.06
150 PPM							
	77-3720	194	203	206	204	209	210
	-3721	183	189	194	194	200	207
	-3722	203	205	209	214	218	219
	-3723	195	202	208	202	203	211
	-3724	197	207	209	209	207	213
	-3725	192	195	198	196	205	211
	-3726	206	208	209	211	216	220
	-3727	203	205	204	204	207	210
	-3728	207	212	213	209	216	226
	-3729	188	191	194	200	206	212
	Mean	196.8	201.7	204.4	204.3	208.7*	213.9*
	± S.D.	7.94	7.59	6.75	6.52	6.04	5.86
450 PPM							
	77-3700	195	186	187	190	194	191
	-3701	175	170	174	175	173	173
	-3702	196	186	189	194	192	192
	-3703	199	191	190	190	192	185
	-3704	198	188	186	186	190	191
	-3705	187	174	173	175	174	174
	-3706	179	171	167	166	168	166
	-3707	180	175	171	171	173	161
	-3708	181	172	174	176	180	173
	-3709	194	185	186	189	185	184
	Mean	188.4	179.8*	179.7*	181.2*	182.1*	179.0*
	± S.D.	9.02	8.08	8.64	9.67	9.68	11.10

*Statistically significantly lower than control mean using analysis of variance and Dunnett's test, $p<0.05$.

[a]No body weights available; rats inadvertently omitted from weighing.

Table 3

INDIVIDUAL AND MEAN (± S.D.) BODY WEIGHTS (g) OF FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Days on Exposure		0	1	3	5	7	9
0 PPM							
Animal No.	77-3690	128	142	144	144	143	132
	-3691	120	136	138	141	148	143
	-3692	114	131	135	134	138	140
	-3693	116	133	135	136	138	138
	-3694	115	136	137	140	142	145
	-3695	122	141	143	141	144	141
	-3696	132	132	136	139	143	146
	-3697	133	134	138	132	141	137
	-3698	123	118	125	132	134	131
	-3699	121	122	132	134	136	139
Mean		122.4	132.5	136.3	137.3	140.7	139.2
± S.D.		6.75	7.55	5.38	4.24	4.19	4.98
50 PPM							
	77-3750	135	138	137	138	136	137
	-3751	131	142	141	140	129	141
	-3752	124	132	130	132	126	135
	-3753	123	131	129	128	118	136
	-3754	140	147	144	145	132	146
	-3755	126	137	136	138	121	129
	-3756	131	138	134	138	125	138
	-3757	130	137	136	137	140	139
	-3758	124	130	131	134	133	133
	-3759	132	136	134	140	141	139
Mean		129.6*	136.8	135.2	137.0	130.1*	137.3
± S.D.		5.44	5.14	4.73	4.71	7.72	4.60
150 PPM							
	77-3730	143	150	146	150	153	149
	-3731	127	133	125	133	130	128
	-3732	120	126	132	125	125	122
	-3733	132	136	136	139	137	135
	-3734	134	137	139	139	142	139
	-3735	128	133	134	136	133	133
	-3736	128	133	132	134	133	135
	-3737	134	136	139	142	141	142
	-3738	127	132	131	134	135	138
	-3739	129	135	134	140	137	139
Mean		130.2*	135.1	134.8	137.2	136.6	136.2
± S.D.		6.07	6.08	5.67	6.58	7.63	7.38
450 PPM							
	77-3710	134	133	126	127	130	125
	-3711	125	126	122	121	123	118
	-3712	135	142	137	135	136	129
	-3713	124	129	122	121	119	117
	-3714	138	142	136	132	133	128
	-3715	128	132	128	125	124	118
	-3716	136	137	140	134	134	120
	-3717	133	134	130	126	125	122
	-3718	129	130	132	129	128	125
	-3719	134	135	137	133	131	129
Mean		131.6*	134.0	131.0	128.3*	128.3*	123.1*
± S.D.		4.79	5.25	6.46	5.14	5.46	4.72

*Statistically significantly different from control mean using analysis of variance and Dunnett's test, $p<0.05$.

Table 4

INDIVIDUAL AND MEAN (±S.D.) BODY WEIGHT CHANGES (g) FROM PREEXPOSURE WEIGHT FOR MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Days on Exposure		0	1	3	5	7	9
0 PPM							
Animal No.	77-3680	-	-6	3	4	16	-[a]
	-3681	-	3	15	17	30	-[a]
	-3682	-	0	10	8	19	-[a]
	-3683	-	6	16	17	35	41
	-3684	-	3	14	8	22	30
	-3685	-	4	15	14	34	40
	-3686	-	2	11	11	28	31
	-3687	-	1	9	0	14	15
	-3688	-	4	14	10	30	38
	-3689	-	3	9	5	25	26
Mean			2.0	12.6	9.4	25.3	31.6
± S.D.			3.26	4.01	5.58	7.35	9.22
50 PPM							
	77-3740	-	14	9	13	22	22
	-3741	-	6	4	5	12	18
	-3742	-	7	9	8	16	15
	-3743	-	4	3	7	11	4
	-3744	-	9	9	12	19	17
	-3745	-	8	8	13	14	20
	-3746	-	6	4	8	14	5
	-3747	-	6	6	11	15	22
	-3748	-	10	6	9	9	9
	-3749	-	7	2	8	9	23
Mean			7.7*	6.0*	9.4	14.1*	15.5*
± S.D.			2.79	2.67	2.72	4.18	7.11
150 PPM							
	77-3720	-	9	12	10	15	16
	-3721	-	5	11	11	17	24
	-3722	-	2	6	11	15	16
	-3723	-	7	13	7	8	16
	-3724	-	10	12	12	10	16
	-3725	-	3	6	4	13	19
	-3726	-	2	3	5	10	14
	-3727	-	2	1	1	4	7
	-3728	-	5	6	2	9	19
	-3729	-	3	6	12	18	24
Mean			4.8*	7.6*	7.5	11.9*	17.1*
± S.D.			2.97	4.14	4.25	4.43	4.93
450 PPM							
	77-3700	-	-9	-8	-5	-1	-4
	-3701	-	-5	-1	0	-2	-2
	-3702	-	-10	-7	-2	-4	-4
	-3703	-	-8	-9	-9	-7	-14
	-3704	-	-10	-12	-12	-8	-7
	-3705	-	-13	-14	-12	-13	-13
	-3706	-	-8	-12	-13	-11	-13
	-3707	-	-5	-9	-9	-7	-19
	-3708	-	-9	-7	-5	-1	-8
	-3709	-	-9	-8	-5	-9	-10
Mean			-8.6*	-8.7*	-7.2*	-6.3*	-9.4*
± S.D.			2.37	3.59	4.47	4.19	5.38

*Statistically significantly different from control mean using analysis of variance and Dunnett's test, $p<0.05$.

[a] No body weights available; rats inadvertently omitted from weighing.

Table 5

INDIVIDUAL AND MEAN (±S.D.) BODY WEIGHT CHANGES (g) FROM PREEXPOSURE WEIGHT FOR FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Days of Exposure		0	1	3	5	7	9
0 PPM							
Animal No.	77-3690	-	14	16	16	15	4
	-3691	-	16	18	21	28	23
	-3692	-	17	21	20	24	26
	-3693	-	17	19	20	22	22
	-3694	-	21	22	25	27	30
	-3695	-	19	21	19	22	19
	-3696	-	0	4	7	11	14
	-3697	-	1	5	-1	8	4
	-3698	-	-5	2	9	11	8
	-3699	-	1	11	13	15	18
Mean			10.1	13.9	14.9	18.3	16.8
± S.D.			9.65	7.75	7.91	7.18	9.09
50 PPM							
	77-3750	-	3	2	3	1	2
	-3751	-	11	10	9	-2	10
	-3752	-	8	6	8	2	11
	-3753	-	8	6	5	-5	13
	-3754	-	7	4	5	-8	6
	-3755	-	11	10	12	-5	5
	-3756	-	7	3	7	-6	7
	-3757	-	7	6	7	10	9
	-3758	-	6	7	10	9	9
	-3759	-	4	2	8	9	7
Mean			7.2	5.6*	7.4*	0.5*	7.7*
± S.D.			2.57	2.91	2.63	6.82	3.43
150 PPM							
	77-3730	-	7	3	7	10	6
	-3731	-	6	-2	6	3	1
	-3732	-	6	12	5	5	2
	-3733	-	4	4	7	5	3
	-3734	-	3	5	5	8	5
	-3735	-	5	6	8	5	7
	-3736	-	5	4	6	5	7
	-3737	-	2	5	8	7	8
	-3738	-	5	4	7	8	11
	-3739	-	6	5	11	8	10
Mean			4.9*	4.6*	7.0*	6.4*	6.0*
± S.D.			1.52	3.41	1.76	2.12	3.30
450 PPM							
	77-3710	-	-1	-8	-7	-4	-9
	-3711	-	1	-3	-4	-2	-7
	-3712	-	7	2	0	1	-6
	-3713	-	5	-2	-3	-5	-7
	-3714	-	4	-2	-6	-5	-10
	-3715	-	4	0	-3	-4	-10
	-3716	-	1	4	-2	-2	-16
	-3717	-	1	-3	-7	-8	-11
	-3718	-	1	3	0	-1	-4
	-3719	-	1	3	-1	-3	-5
Mean			2.4*	-0.6*	-3.3*	-3.3*	-8.5*
± S.D.			2.46	3.72	2.67	2.50	3.50

*Statistically significantly different from control mean using analysis of variance and Dunnett's test, $p<0.05$.

Table 6

INDIVIDUAL AND MEAN (± S.D.) PRETERMINAL HEMATOLOGY VALUES FOR MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

	Animal No.	PCV %	RBC x 10^6	Hgb g/100 cc	WBC x 10^3	Differential Counts: Neut. SEG	Neut. B/J	Lym.	Mon.	Eos.	Bas.
0 PPM	77-3680	51.0	9.10	16.9	13.0	14	0	83	3	0	0
	-3681	51.0	8.53	16.9	15.1	16	0	81	2	1	0
	-3682	51.5	8.75	17.1	18.8	31	0	61	7	1	0
	-3683	48.5	7.87	16.2	18.3	17	0	76	7	0	0
	-3684	52.0	8.67	17.0	15.0	24	0	67	8	1	0
	Mean	50.8	8.58	16.8	16.0	20	0	74	5	1	0
	± S.D.	1.4	0.45	0.4	2.4						
50 PPM	77-3740	51.0	8.69	16.7	11.0	21	0	76	3	0	0
	-3741	48.0	8.49	16.4	11.7	21	0	77	2	0	0
	-3742	52.0	9.02	17.8	13.5	17	0	80	3	0	0
	-3743	51.0	8.53	16.8	14.8	21	0	77	2	0	0
	-3744	50.0	8.71	16.7	14.1	27	0	67	6	0	0
	Mean	50.4	8.69	16.9	13.0	22	0	75	3	0	0
	± S.D.	1.5	0.21	0.5	1.6						
150 PPM	77-3720	49.0	8.49	16.7	14.9	17	0	82	1	0	0
	-3721	53.0	8.89	17.4	13.3	28	0	69	2	1	0
	-3722	50.0	8.75	16.9	10.8	21	0	75	3	1	0
	-3723	50.0	8.32	16.3	15.8	26	0	70	3	1	0
	-3724	50.5	8.63	16.8	13.7	23	0	72	5	0	0
	Mean	50.5	8.62	16.8	13.7	23	0	75	3	1	0
	± S.D.	1.5	0.22	0.4	1.9						
450 PPM	77-3700	39.0	5.61	15.5[a]	59.7[a]	27	0	68	3	2	0
Coulter Counter Method	-3701	39.5	6.14	16.7	66.0	20	0	77	3	0	0
	-3702	40.5	5.96	18.0	78.9	13	0	85	2	0	0
	-3703	40.0	6.04	16.6	53.6	18	0	77	2	3	0
	-3704	39.0	5.99	17.0	56.0	20	0	79	0	1	0
	Mean	39.6*	5.95*	16.8	62.8	20	0	77	2	1	0
	± S.D.	0.7	0.20	0.9	10.1						
Visual Comparison to Control	77-3700				16.0[b]						
	-3701				13.0						
	-3702				17.0						
	-3703				17.0						
	-3704				14.0						
	Mean				15.8						
	± S.D.				1.3						

*Statistically significant deviation from control mean using analysis of variance and Dunnett's test $p<0.05$.

[a]Values invalid due to technical difficulties and not used for statistical analysis.

[b]WBC were estimated in this group; values were not used for statistical analysis.

Table 7

INDIVIDUAL AND MEAN (± S.D.) PRETERMINAL HEMATOLOGY VALUES FOR FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

	Animal No.	PCV %	RBC x 10^6	Hgb g/100 cc	WBC x 10^3	Differential Counts: Neut. SEG	Neut. B/J	Lym.	Mon.	Eos.	Bas.	Retico %
0 PPM	77-3690	52.0	9.03	17.6	14.3	23	0	76	0	1	0	0.1
	-3691	53.5	8.60	17.4	16.2	16	0	81	1	2	0	0.3
	-3692	50.0	8.44	16.8	14.7	31	0	65	3	1	0	0.9
	-3693	50.0	8.15	15.4	14.2	21	0	78	1	0	0	0.4
	-3694	51.0	8.73	17.6	12.6	18	0	81	0	1	0	1.1
	Mean	51.3	8.59	17.0	14.4	22	0	76	1	1	0	0.6
	± S.D.	1.5	0.33	0.9	1.3							
50 PPM	77-3750	53.0	8.70	15.8	16.4	23	0	75	2	0	0	0.4
	-3751	54.0	9.18	18.4	13.7	19	0	75	6	0	0	0.9
	-3752	53.0	8.66	17.3	14.3	19	0	76	5	0	0	0.6
	-3753	54.0	8.45	16.9	13.7	27	0	71	2	0	0	0.5
	-3754	54.5	7.96	16.9	15.2	12	0	85	2	1	0	0.5
	Mean	53.7	8.59	17.1	14.7	20	0	77	3	0	0	0.6
	± S.D.	0.7	0.44	0.9	1.2							
150 PPM	77-3730	50.0	7.58	16.5	16.1	22	0	76	0	2	0	1.4
	77-3731	49.0	8.21	16.6	17.0	32	0	64	4	0	0	0.2
	77-3732	52.5	9.25	17.3	15.7	35	0	63	2	0	0	1.1
	77-3733	56.0	8.89	17.4	18.9	20	0	77	2	1	0	0.9
	77-3734	54.0	8.56	16.9	14.8	18	0	80	2	0	0	0.9
	Mean	52.3	8.50	16.9	16.5	25	0	72	2	1	0	0.9
	± S.D.	2.9	0.64	0.4	1.6							
450 PPM[a]	77-3710	39.0	5.91	11.3	16.0	16	0	81	1	2	0	9.6
	-3711	39.0	5.77	10.6	17.0	19	0	78	2	1	0	7.9
	-3712	40.0	5.91	10.6	15.0	17	0	79	3	1	0	5.8
	-3713	40.0	5.72	10.3	17.0	12	0	85	3	0	0	5.8
	-3714	40.0	6.58	11.2	16.0	23	0	75	1	1	0	8.7
	Mean	39.6*	5.98*	10.8*	16.2	17	0	80	2	1	0	7.6
	± S.D.	0.5	0.35	0.4	0.8							

*Statistically significant deviation fron control mean using analysis of variance and Dunnett's test, $p<0.05$

[a]WBC were estimated in this group; values were not used in statistical analysis.

Table 8

INDIVIDUAL AND MEAN (± S.D.) TERMINAL CLINICAL CHEMISTRY PARAMETERS FOR MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Dose	Animal No.	BUN mg/100 ml	SGPT mU/ml	AP mU/ml	Total Bilirubin mg/100 ml	Total Thyroxine µg/100 ml
0 PPM	77-3680	19	20	163	0.2	5.0
	-3681	22	16	172	0.2	4.7
	-3682	17	16	154	0.2	4.6
	-3683	21	21	163	0.2	3.5
	-3684	21	15	144	0.2	4.3
	-3685	17	24	175	0.3	6.7
	-3686	19	18	159	0.3	5.6
	-3687	18	19	145	0.2	4.1
	-3688	18	20	173	0.2	6.1
	-3689	19	18	144	0.3	5.5
	Mean	19	19	159	0.2	5.0
	± S.D.	2	3	12	0.0	0.1
50 PPM	77-3740	22	19	13[a]	0.2	5.7
	-3741	20	19	158	0.2	5.3
	-3742	20	27	146	0.3	4.4
	-3743	18	27	155	0.3	4.2
	-3744	20	15	143	0.2	3.5
	-3745	21	23	139	0.2	5.5
	-3746	16	16	151	0.2	4.4
	-3747	20	24	170	0.2	3.5
	-3748	24	20	145	0.3	3.8
	-3749	16	18	155	0.2	3.9
	Mean	20	21	150	0.2	4.4
	± S.D.	2	4	10	0.0	0.8
150 PPM	77-3720	18	19	152	0.1	3.2
	-3721	19	20	166	0.2	5.3
	-3722	20	16	152	0.2	4.3
	-3723	24	20	174	0.3	4.0
	-3724	20	19	139	0.2	3.1
	-3725	18	18	164	0.2	4.8
	-3726	21	14	147	0.3	5.7
	-3727	18	18	151	0.2	4.4
	-3728	19	18	142	0.3	3.7
	-3729	16	16	162	0.2	3.4
	Mean	19	18	155	0.2	4.2
	± S.D.	2	2	11	0.1	0.9
450 PPM	77-3700	15	13	110	0.4	4.0
	-3701	18	13	98	0.4	4.0
	-3702	18	14	96	0.4	3.5
	-3703	18	16	81	0.4	3.1
	-3704	17	13	104	0.4	3.8
	-3705	14	21	97	0.4	3.1
	-3706	16	16	80	0.4	2.6
	-3707	14	17	94	0.5	3.4
	-3708	18	15	107	0.5	3.1
	-3709	14	16	106	0.4	3.9
	Mean	16*	15	97*	0.4*	3.4*
	± S.D.	2	2	10	0.0	0.5

*Statistically significant deviation from control mean using analysis of variance and Dunnett's test, $p<0.05$.

Table 9

INDIVIDUAL AND MEAN (± S.D.) TERMINAL CLINICAL CHEMISTRY PARAMETERS FOR FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Dose	Animal No.	BUN mg/100 ml	SGPT mU/ml	AP mU/ml	T. Bilirubin mg/100 ml	(T4) µg/100 ml
0 PPM	77-3690	25	15	110	0.1	2.4
	-3691	24	15	115	0.2	2.4
	-3692	26	18	128	0.2	2.6
	-3693	18	16	112	0.3	2.8
	-3694	21	16	110	0.3	-[a]
	-3695	22	14	104	0.3	3.7
	-3696	23	20	125	0.3	3.2
	-3697	17	11	106	0.1	4.2
	-3698	19	17	116	0.2	3.9
	-3699	17	20	125	0.2	4.8
	Mean	21	16	115	0.2	3.3
	± S.D.	3	3	8	0.1	0.9
50 PPM	77-3750	35	17	97	0.2	2.7
	-3751	20	22	119	0.2	2.5
	-3752	24	21	120	0.2	2.1
	-3753	22	17	118	0.1	2.9
	-3754	21	17	121	0.2	2.6
	-3755	20	19	131	0.1	2.9
	-3756	22	11	112	0.1	1.7
	-3757	22	12	112	0.1	3.0
	-3758	23	17	133	0.1	2.1
	-3759	21	13	102	0.1	1.8
	Mean	23	17	116	0.1	2.4*
	± S.D.	4	4	11	0.0	0.5
150 PPM	77-3730	25	14	125	0.1	2.5
	-3731	22	13	117	0.1	1.8
	-3732	27	26	140	0.4	-[a]
	-3733	21	19	104	0.4	4.2
	-3734	18	18	113	0.3	2.2
	-3735	18	17	97	0.2	2.0
	-3736	23	13	119	0.1	3.3
	-3737	25	14	115	0.2	3.2
	-3738	25	18	131	0.3	2.7
	-3739	24	16	121	0.2	3.1
	Mean	23	17	118	0.2	2.8
	± S.D.	3	4	12	0.1	0.8
450 PPM	77-3710	17	16	67	0.6	3.2
	-3711	17	14	73	0.4	3.9
	-3712	16	16	80	0.4	3.1
	-3713	15	14	69	0.4	3.0
	-3714	17	14	62	0.3	3.6
	-3715	22	15	77	0.5	4.2
	-3716	19	10	79	0.4	3.5
	-3717	14	13	107	0.4	4.4
	-3718	15	24	86	0.4	-[a]
	-3719	16	11	60	0.6	2.6
	Mean	17	15	74*	0.4*	3.5
	± S.D.	2	4	13	0.1	0.6

*Statistically significant deviation from control mean using analysis of variance and Dunnett's test, $p<0.05$.

[a]Insufficient sample for repeat of technically deficient first trial.

Table 10

I-125 UPTAKE BY MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Animal #		Vials No.	Wt. Empty (g)	Wt. Full (g)	Wt. of Tissue (mg)	Counts per Minute[d]	Counts per Minute/mg	$\bar{X}$ Counts/ group	% Uptake
N391	Negative Controls	1	3.3476	3.3587	11.1	29528	2660		
N392		2	3.6075	3.6182	10.7	28408	2655		
N394		3	3.2783	3.2867	8.4	18[b]	(2)[c]	3159	0.81
N395 (Scratched)[a]		4	3.3468	-	-	-	-		
N396		5	3.4108	3.4190	8.2	34128	4162		
Mean ± S.D.					9.60±1.51				
N397	Positive Controls	6	3.6001	3.6099	9.8	1923	196		
N398		7	3.3043	3.3152	10.9	1789	164	183	0.05
N399		8	3.3941	3.4059	11.8	2228	189		
N400		9	3.3862	3.4034	17.2	3165	184		
Mean ± S.D.					12.43±3.29				
N386	50 ppm	10	3.4334	3.4412	7.8	33424	4285		
N387		11	3.4068	3.4168	10.0	28248	2825	3413	0.87
N388		12	3.2914	3.3016	10.2	37584	3685		
N390		13	3.2810	3.2913	10.3	29432	2857		
Mean ± S.D.					9.58±1.19				
N381	150 ppm	14	3.4093	3.4203	11.0	34576	3143		
N382		15	3.2849	3.2942	9.3	35888	3859		
N383		16	3.3829	3.3903	7.4	37051	5007	4262	1.09
N384		17	3.3603	3.3690	8.7	37344	4292		
N385		18	3.4009	3.4109	10.0	50112	5011		
Mean ± S.D.					9.28±1.36				
N376	450 ppm	19	3.3805	3.3901	9.6	29488	3072		
N377		20	3.4016	3.4151	13.5	38512	2853		
N378		21	3.3967	3.4070	10.3	32064	3113	2850	0.73
N379		22	3.3579	3.3668	8.9	32912	3698		
N380		23	3.4034	3.4182	14.8	22408	1514		
Mean ± S.D.					11.42±2.58				
	Standard[e] Dose	24				38896	-	$\bar{X}$(10)	
		25				39280	-	390400	
		26				38944	-		
	Blanks	27				-			
		28				-			
		29				-			

[a] Thyroid destroyed at sacrifice
[b] Thyroid "missed"
[c] Value not used in calculation
[d] Channel minus background mean $\frac{35+30}{2} = 32$
[e] 50 µl std - dosing solution

Table 11

INDIVIDUAL BODY WEIGHTS OF MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY (I-125 GROUP)

Days on Exposure		0	1	3	5	7	9
	Ear Tag #						
Negative Control							
	N391	146	147	160	152	173	183
	N392	159	159	171	158	178	187
	N393	152	153	158	130	127	Dead
	N394	158	158	166	143	170	181
	N395	152	150	138	130	158	155
Positive Control							
	N396	150	153	164	152	168	171[b]
	N397	144	146	157	148	166	170
	N398	158	160	177	170	191	196
	N399	149	152	166	160	164	167
	N400	162	163	176	170	188	193
50 PPM	N386	158	155	--[a]	142	146	173
	N387	152	151	—	156	164	164
	N388	157	154	—	161	159	151
	N389	162	160	—	154	119	Dead
	N390	154	148	—	153	154	160
150 PPM	N381	157	156	—	160	166	170
	N382	155	153	—	156	161	166
	N383	156	154	—	155	158	163
	N384	153	153	—	160	165	171
	N385	156	153	—	161	165	171
450 PPM	N376	145	136	—	134	141	144
	N377	148	142	—	143	148	147
	N378	160	153	—	145	151	150
	N379	154	145	—	146	150	149
	N380	156	147	—	152	155	152

[a] No body weights available; rats inadvertently omitted from weighing.

[b] Rat with Ear Tag # N396 was removed from positive control group and placed in negative control group on the last day of exposure.

TABLE 12

SUMMARY OF THE PATHOLOGIC FINDINGS IN TWO RATS PRESELECTED FOR ^{125}I UPTAKE EVALUATION THAT BECAME MORIBUND ON DAY 7 OF A 10-DAY INHALATION TOXICITY STUDY OF DIETHYLDISULFIDE

Pathology Number	Sex	Exposure Concentration	Observations	Possible or Probable Cause of Death or Moribund Condition
77-4406	Male	Negative Control	Gross Findings: Soiled hairs around external nares. Depleted adipose reserves. Gastrointestinal tract contains a decreased quantity of ingesta. Severly congested liver: Histopathologic Findings: Perivascular aggregations of inflammatory cells and probable bacteria in the brain. Inflammatory cells seen in meninges and ventricles as well.	Suppurative meningoencephalitis
77-4407	Male	50 ppm	Gross Findings: Soiled hairs around external nares. Focal area of ulceration or erosion in stomach. Histopathologic Findings: Numerous inflammatory cells and probable bacteria in ventricles and perivascular spaces of the brain.	Suppurative meningoencephalitis

Table 13

GROSS OBSERVATIONS ON MALE AND FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Sex	Male				Female			
Dose Level (ppm)	0	50	150	450	0	50	150	450
Number of Rats Per Group	10	10	10	10	10	10	10	10
No visible lesions	6/10[a]	6/10	8/10	-	9/10	10/10	2/10	-
Enlarged salivary glands	3/10	3/10	1/10	-	-	-	-	-
Exophthalmus, excessive lacrimation (probable sialodacryoadenitis)	-	1/10	1/10	-	-	-	-	-
Corneal cloudiness - unilateral	1/10	-	1/10	1/10	-	-	-	-
- bilateral	-	-	-	-	-	-	-	-
Lenticular opacity - unilateral	-	-	-	-	-	-	-	1/10
Decreased adipose reserves	-	-	-	-	-	-	-	1/10
Clear fluid filled cyst arising from thyroid (2 x 2 mm in dimension)	1/10	-	-	-	-	-	-	-
Liver nodule consistent with site of old diaphragmatic hernia	-	1/10	-	-	1/10	-	-	1/10
Anemic and/or slightly icteric appearance	-	-	-	10/10	-	-	-	9/10
Darkened liver	-	-	-	10/10	-	-	-	9/10
Darkened kidneys	-	-	-	8/10	-	-	-	8/10
Dark and enlarged spleen	-	-	-	10/10	-	-	-	10/10
Slight darkened appearance to spleen	-	-	-	-	-	-	8/10	-

[a] Data listed as number affected/number of rats examined.

- Indicates observation not present.

Table 14

TERMINAL INDIVIDUAL AND MEAN (± S.D.) BODY WEIGHT, ORGAN WEIGHT AND ORGAN TO BODY WEIGHT RATIOS FOR MALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Dose PPM	Animal Number	Fasted Body Weight g	Organ Weights (g and g/100g Body Weight)									
			Brain		Heart		Liver		Kidneys		Testes	
			g	g/100g	g	g/100g	g	g/100g	g	g/100g	g	g/100g
0	77-3680	185	1.70	0.91	0.66	0.36	5.54	2.99	1.56	0.84	2.61	1.41
0	77-3681	213	1.82	0.86	0.71	0.33	7.29	3.42	1.74	0.82	2.82	1.33
0	77-3682	178	1.72	0.97	0.62	0.35	5.56	3.13	1.54	0.87	2.58	1.45
0	77-3683	208	1.80	0.87	0.68	0.33	6.68	3.21	1.65	0.80	2.86	1.37
0	77-3684	197	1.75	0.89	0.64	0.32	6.34	3.21	1.56	0.79	2.68	1.36
0	77-3685	202	1.77	0.87	0.67	0.33	6.48	3.20	1.57	0.78	2.45	1.21
0	77-3686	212	1.74	0.82	0.68	0.32	6.49	3.07	1.64	0.78	2.56	1.21
0	77-3687	203	1.74	0.86	0.75	0.37	6.25	3.08	1.63	0.80	2.82	1.39
0	77-3688	213	1.75	0.82	0.70	0.33	6.82	3.20	1.70	0.80	2.85	1.34
0	77-3689	203	1.74	0.86	0.69	0.34	6.40	3.15	0.75	0.37	2.96	1.46
	Mean	201	1.75	0.87	0.68	0.34	6.38	3.17	1.54	0.76	2.72	1.35
	± S.D.	12	0.04	0.04	0.04	0.02	0.53	0.12	0.28	0.14	0.17	0.09
50	77-3740	201	1.73	0.86	0.69	0.34	6.31	3.15	1.63	0.81	2.72	1.36
50	77-3741	180	1.75	0.97	0.64	0.35	5.53	3.07	1.49	0.83	2.53	1.41
50	77-3742	196	1.74	0.89	0.70	0.35	6.58	3.36	1.57	0.80	2.61	1.33
50	77-3743	171	1.72	1.01	0.63	0.37	4.88	2.85	1.46	0.85	2.72	1.59
50	77-3744	192	1.72	0.90	0.62	0.32	6.04	3.15	1.58	0.83	2.74	1.43
50	77-3745	203	1.76	0.86	0.68	0.33	6.43	3.17	1.64	0.81	2.75	1.35
50	77-3746	191	1.74	0.91	0.66	0.34	5.94	3.11	1.49	0.78	2.69	1.41
50	77-3747	181	1.71	0.94	0.61	0.34	5.36	2.96	1.49	0.82	2.54	1.40
50	77-3748	183	1.69	0.92	0.69	0.38	6.08	3.32	1.59	0.87	2.56	1.40
50	77-3749	183	1.74	0.95	0.70	0.38	5.19	2.84	1.50	0.82	2.84	1.56
	Mean	188	1.73	0.92	0.66	0.35	5.83	3.10	1.54	0.82	2.67	1.42
	± S.D.	10	0.02	0.05	0.03	0.02	0.57	0.18	0.06	0.03	0.10	0.08
150	77-3720	185	1.79	0.97	0.66	0.36	5.92	3.19	1.64	0.88	2.69	1.45
150	77-3721	176	1.73	0.98	0.62	0.35	5.95	3.37	1.51	0.86	2.59	1.47
150	77-3722	194	1.70	0.87	0.71	0.37	6.38	3.34	1.74	0.89	2.60	1.34
150	77-3723	180	1.76	0.98	0.66	0.37	5.75	3.20	1.61	0.90	2.63	1.47
150	77-3724	187	1.73	0.92	0.68	0.36	6.25	3.34	1.54	0.82	2.74	1.46
150	77-3725	189	1.74	0.92	0.61	0.32	5.91	3.13	1.61	0.85	2.78	1.47
150	77-3726	196	1.72	0.88	0.71	0.36	6.50	3.32	1.69	0.86	2.83	1.44
150	77-3727	188	1.72	0.92	0.63	0.34	6.04	3.21	1.57	0.83	2.72	1.45
150	77-3728	200	1.75	0.88	0.70	0.35	6.72	3.37	1.76	0.88	2.68	1.34
150	77-3729	141	1.75	1.24	0.69	0.49	6.00	4.24	1.52	1.07	2.55	1.80
	Mean	184*	1.74	0.96*	0.67	0.37	6.19	3.39	1.62	0.89*	2.68	1.47*
	± S.D.	16	0.03	0.11	0.04	0.04	0.36	0.32	0.09	0.07	0.09	0.13
450	77-3700	175	1.74	0.99	0.68	0.39	6.55	3.75	1.72	0.99	2.64	1.51
450	77-3701	158	1.74	1.10	0.66	0.42	5.89	3.72	1.58	1.00	2.51	1.59
450	77-3702	174	1.73	1.00	0.67	0.39	6.46	3.71	1.46	0.84	2.66	1.53
450	77-3703	168	1.67	1.00	0.60	0.36	5.65	3.37	1.61	0.96	2.38	1.42
450	77-3704	170	1.67	0.98	0.69	0.40	6.19	3.63	1.66	0.98	2.45	1.44
450	77-3705	156	1.66	1.06	0.64	0.41	5.23	3.35	1.23	0.79	2.38	1.53
450	77-3706	147	1.70	1.16	0.60	0.41	5.18	3.53	1.48	1.01	2.41	1.64
450	77-3707	152	1.76	1.15	0.66	0.43	4.97	3.27	1.56	1.02	2.30	1.52
450	77-3708	156	1.76	1.13	0.35	0.22	5.30	3.39	1.50	0.96	2.25	1.44
450	77-3709	165	1.75	1.06	0.68	0.41	5.58	3.38	1.53	0.92	2.45	1.48
	Mean	162*	1.72	1.06*	0.62	0.38	5.70*	3.51*	1.53	0.95*	2.44*	1.51*
	± S.D.	10	0.04	0.07	0.10	0.06	0.55	0.18	0.13	0.08	0.13	0.07

*Statistically significant deviation from control mean using analysis of variance and Dunnett's test, $p < 0.05$.

Table 15

TERMINAL INDIVIDUAL AND MEAN (± S.D.) BODY WEIGHT, ORGAN WEIGHT, AND ORGAN TO BODY WEIGHT RATIOS FOR FEMALE RATS EXPOSED TO VAPORS OF DIETHYLDISULFIDE IN A 10-DAY INHALATION STUDY

Dose PPM	Animal Number	Fasted Body Weight g	Organ Weights (g and g/100g Body Weight)									
			Brain		Heart		Liver		Kidneys		Spleen	
			g	g/100g	g	g/100g	g	g/100g	g	g/100g	g	g/100g
0	77-3690	130	3.30[a]	2.55	0.46	0.36	3.80	2.93	1.03	0.79	0.29	0.22
0	77-3691	122	1.61	1.31	0.49	0.40	3.80	3.11	1.06	0.87	0.32	0.26
0	77-3692	118	1.63	1.38	0.44	0.37	3.67	3.10	0.99	0.84	0.28	0.23
0	77-3693	124	1.68	1.35	0.46	0.37	3.68	2.96	1.09	0.87	0.32	0.26
0	77-3694	127	1.66	1.31	0.46	0.36	3.94	3.11	1.08	0.85	0.31	0.25
0	77-3695	127	1.62	1.27	0.48	0.38	3.83	3.02	1.14	0.90	0.32	0.25
0	77-3696	124	1.62	1.31	0.48	0.39	3.75	3.03	1.09	0.88	0.35	0.28
0	77-3697	124	1.61	1.30	0.51	0.41	3.66	2.96	1.09	0.88	0.35	0.28
0	77-3698	115	1.61	1.40	0.46	0.40	3.34	2.91	1.05	0.91	0.31	0.27
0	77-3699	124	1.59	1.28	0.48	0.39	3.66	2.95	1.05	0.85	0.30	0.24
	Mean	123	1.62	1.45	0.47	0.38	3.71	3.01	1.07	0.86	0.31	0.25
	± S.D.	4	0.03	0.39	0.02	0.02	0.16	0.08	0.04	0.03	0.02	0.02
50	77-3750	123	1.64	1.34	0.46	0.38	3.70	3.02	1.09	0.89	0.30	0.24
50	77-3751	128	1.65	1.30	0.49	0.38	3.75	2.94	1.13	0.89	0.28	0.22
50	77-3752	120	1.63	1.36	0.45	0.37	3.38	2.82	1.07	0.90	0.28	0.23
50	77-3753	118	1.65	1.40	0.42	0.36	3.37	2.86	1.00	0.85	0.27	0.23
50	77-3754	130	1.68	1.29	0.46	0.35	2.87	2.20	1.14	0.87	0.30	0.23
50	77-3755	123	1.64	1.33	0.50	0.41	3.57	2.90	1.08	0.88	0.31	0.25
50	77-3756	126	1.62	1.28	0.48	0.38	3.30	2.61	1.02	0.81	0.32	0.25
50	77-3757	126	1.62	1.29	0.48	0.38	3.69	2.93	1.08	0.86	0.32	0.26
50	77-3758	119	1.60	1.34	0.44	0.37	3.49	2.94	0.95	0.80	0.26	0.22
50	77-3759	126	1.63	1.29	0.51	0.40	3.77	3.00	1.11	0.88	0.34	0.27
	Mean	124	1.64	1.32	0.47	0.38	3.49	2.82*	1.07	0.86	0.30	0.24
	± S.D.	4	0.02	0.04	0.03	0.02	0.28	0.25	0.06	0.03	0.03	0.02
150	77-3730	132	1.71	1.29	0.47	0.35	4.08	3.10	1.25	0.95	0.42	0.32
150	77-3731	115	1.58	1.37	0.45	0.39	3.61	3.13	1.06	0.92	0.30	0.26
150	77-3732	112	1.55	1.39	0.46	0.41	3.31	2.97	0.99	0.89	0.28	0.25
150	77-3733	123	1.66	1.35	0.46	0.37	3.37	2.75	1.03	0.84	0.28	0.23
150	77-3734	126	1.65	1.31	0.46	0.36	3.56	2.83	1.12	0.89	0.30	0.24
150	77-3735	123	1.60	1.31	0.46	0.38	3.69	3.01	1.02	0.83	0.34	0.28
150	77-3736	119	1.63	1.37	0.46	0.39	3.66	3.07	1.05	0.88	0.31	0.26
150	77-3737	126	1.64	1.30	0.49	0.39	3.58	2.85	1.06	0.84	0.34	0.27
150	77-3738	122	1.65	1.35	0.48	0.39	3.46	2.85	1.14	0.94	0.31	0.26
150	77-3739	125	1.59	1.27	0.50	0.40	3.52	2.83	1.13	0.91	0.31	0.25
	Mean	122	1.62	1.33	0.47	0.39	3.59	2.94	1.08	0.89	0.32	0.26
	± S.D.	6	0.05	0.04	0.02	0.02	0.21	0.13	0.08	0.04	0.04	0.02
450	77-3710	117	1.59	1.36	0.47	0.40	3.85	3.28	1.10	0.94	0.61	0.52
450	77-3711	109	1.61	1.48	0.46	0.42	3.64	3.35	1.05	0.96	0.60	0.55
450	77-3712	120	1.63	1.36	0.51	0.43	3 97	3.30	1.15	0.96	0.67	0.56
450	77-3713	107	1.58	1.48	0.49	0.46	3.57	3.35	1.11	1.04	0.62	0.58
450	77-3714	116	1.69	1.45	0.58	0.50	4.04	3.47	1.12	0.96	0.60	0.51
450	77-3715	108	1.59	1.47	0.46	0.43	3.77	3.48	1.07	0.99	0.61	0.57
450	77-3716	120	1.63	1.36	0.51	0.43	3.79	3.17	1.09	0.91	0.64	0.54
450	77-3717	112	1.61	1.45	0.50	0.45	3.70	3.32	0.82	0.74	0.68	0.61
450	77-3718	115	1.63	1.41	0.51	0.44	3.86	3.34	1.13	0.98	0.61	0.53
450	77-3719	117	1.60	1.36	0.49	0.42	3.81	3.25	1.12	0.96	0.68	0.58
	Mean	114*	1.62	1.42	0.50	0.44*	3.80	3.33*	1.07	0.94*	0.63*	0.55*
	± S.D.	5	0.03	0.05	0.03	0.03	0.14	0.09	0.09	0.08	0.03	0.03

*Statistically significant deviation from control mean using analysis of variance and Dunnett's test, $p < 0.05$.

[a]Value not used in calculation.

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