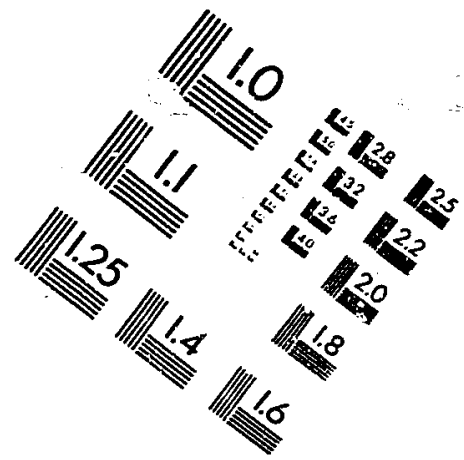
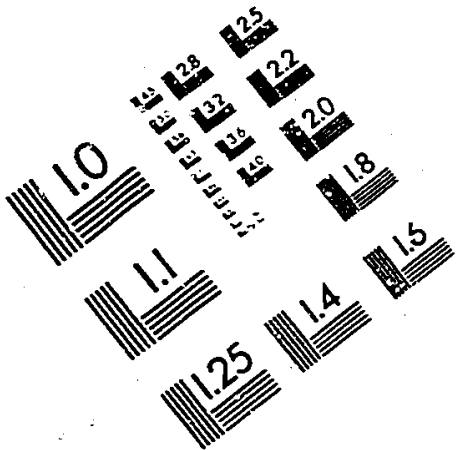




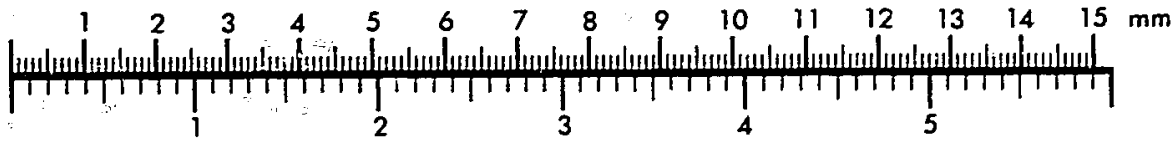
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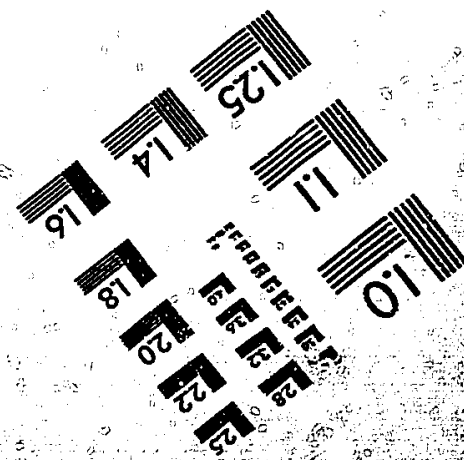
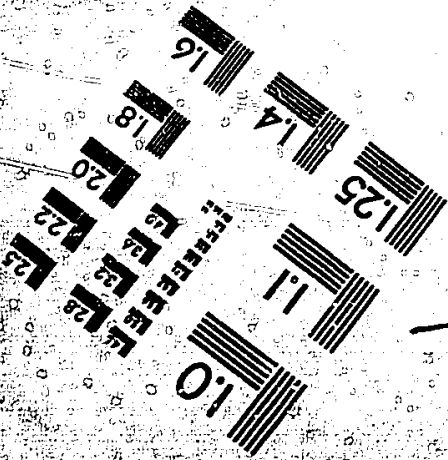
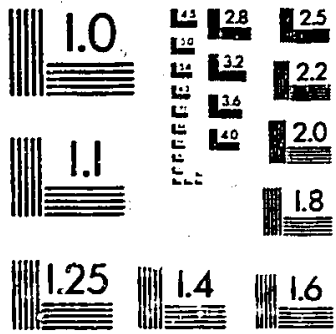
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REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN RATS WITH COVER
LETTER DATED 041493

Chemical Category

PROPIONALDEHYDE (123-38-6)

Section 8d



UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

April 14, 1993

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Attn: 8(d) Health and Safety Reporting Rule (Notification/Reporting)

Dear Sir or Madam:

As a follow-up to our May 8, 1992 letter of notification concerning a range-finding and reproductive/developmental toxicology study in rats for propionaldehyde (CASRN 123-38-6) (copy attached), Union Carbide Corporation ("Union Carbide") herewith submits the following report:

"Propionaldehyde: Combined Repeated-Exposure and Reproductive/Developmental Toxicity Study in Rats", Bushy Run Research Center, BRRC Report 91U0086, April 6, 1993.

In this report the term "CONFIDENTIAL" may appear. This term was entered for internal control at the time of issuance of the report. There is no information in this report for which Union Carbide asserts a claim of confidentiality, and the Agency may use the information as necessary in the discharge of its duties. We advise the Agency, however, that publication rights to the information are the property of Union Carbide.

Please contact the undersigned with questions, if any, at 203/794-5230.



86930000198

Very truly yours,

William C. Kuryla
William C. Kuryla, Ph.D.
Associate Director
Product Safety

WCK/cr
Attachment

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May 8, 1992

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Attn: 8(d) Health and Safety Reporting Rule (Notification/Reporting)

Dear Sir or Madam:

In accordance with 40 CFR Part 716.20 (A)(3), Union Carbide Corporation ("Union Carbide") hereby notifies the Agency of the initiation of toxicology studies for the following chemicals.

Propionaldehyde (CASRN 123-38-6):
acute toxicity and irritancy study (Bushy Run Research Center, Export, PA); Study started: March 9, 1992; Report expected: June 1992.

Propionaldehyde (CASRN 123-38-6):
rat range-finding study [SIDS] (Bushy Run Research Center, Export, PA); Study started: October 14, 1991; Report will be an appendix to the definitive study, described below (expected late 1992).

Propionaldehyde (CASRN 123-38-6):
rat definitive study [SIDS] (Bushy Run Research Center, Export, PA); Study started: December 23, 1991; Report expected: late 1992.

Please contact the undersigned with questions, if any, at 203/794-5230.

Very truly yours,

William C. Kuryla, Ph.D.
Associate Director
Product Safety

WCK/cr

FINAL PROJECT REPORT 91U0086

Propionaldehyde

*Combined Repeated-Exposure and
Reproductive/Developmental Toxicity Study
in CD[®] Rats*

April 6, 1993



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

STUDY TITLE

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD⁰ Rats

TEST SUBSTANCE

Propionaldehyde

contains NO CBI"

DATA REQUIREMENT

Not Applicable

AUTHOR

C. D. Driscoll

STUDY COMPLETION DATE

April 6, 1993

PERFORMING LABORATORY

Bushy Run Research Center (BRRC)
Union Carbide Chemicals and
Plastics Company Inc.
6702 Mellon Road
Export, PA 15632-8902

LABORATORY PROJECT ID

91U0086

SPONSOR

Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

Page 1 of 366

Union Carbide Chemicals and Plastics Company Inc.
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Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD¹ Rats

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

This study meets the requirements of the following Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA), 40 CFR Part 792; Organisation for Economic Co-operation and Development (OECD), C(81)30(Final) with exceptions. The exceptions are:

1. The Study Director had no knowledge of the procedures used for chemical analysis for interfering contaminants in the water conducted by the supplier, the NUS Corporation, Materials Engineering and Testing Co., and Lancaster Laboratories, Inc. or procedures used for diet analysis by Purina Mills, Inc.

These exceptions are not expected to compromise the integrity of the results and conclusion of the study.

Study Director:

Cynthia D. Driscoll
Cynthia D. Driscoll, Ph.D.

4-5-93

Date

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Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

SUMMARY

Young adult CD® male and female rats (15/sex/group) were exposed to propionaldehyde (CAS No. 123-38-6) vapor at concentrations of 0, 150, 750, or 1500 ppm. Exposures were conducted daily, 6 hours/day, 7 days/week, for both males and females during a 2-week pre-mating period, and a 14-day (maximum) mating phase. The males continued to be exposed until scheduled sacrifice in Week 7; a total of 52 exposures. The mated females were exposed daily through Day 20 of gestation only. The females were then allowed to deliver their litters naturally and raise their offspring until Day 4 of lactation. Clinical observations were made daily following exposures, and body weights and food consumption were measured at regular intervals throughout the study. Offspring body weight, viability, and disposition were monitored from birth until postnatal Day 4. Following the last exposure, males were fasted and blood samples were obtained for clinical pathology analyses prior to necropsy. On Day 4 of lactation, necropsies were performed on the adult females and the offspring were examined externally and sacrificed without pathologic evaluation.

The means of daily mean chamber atmosphere concentrations (\pm S.D.) were 151 ± 4.1 , 745 ± 15.2 , and 1522 ± 23.7 ppm, for target concentrations of 150, 750, and 1500 ppm, respectively. The adult males did not display any overt signs of toxicity at any time during the study. Body weights, weight gains, clinical observations, and food consumption were similar among all 3 exposure groups and controls. Successful mating performance and fertility were also unaffected. Hematology and clinical chemistry analyses revealed elevated erythrocyte counts, with a corresponding increase in hemoglobin and hematocrit values, and an increase in monocytes for the males from the 1500 ppm group. At necropsy, kidney weights, as a percentage of final body weight, were elevated in the males from the 1500 ppm group. There were no gross lesions observed that could be attributed to propionaldehyde exposure. Microscopic examination indicated an exposure-related effect on the olfactory epithelium in the anterior 2 sections of the nasal cavity. Vacuolization was primarily evident in the low and intermediate exposure groups and atrophy was seen in the intermediate and high exposure groups. Squamous metaplasia was seen in 2 males from the 1500 ppm group and 1 male in the 750 ppm group.

The adult females did not display any exposure-related clinical signs. However, body weight gains and food consumption were significantly decreased during the first week of exposures at the mid and high concentrations. During gestation, the body weights of the high concentration females were less than controls on Days 0, 7, and 14. Small, but consistent decreases in food consumption were noted in the females from the 1500 ppm group throughout gestation. During Days 14-17 of gestation, the intermediate group of females were also found to have a slight, but significant, decrease in food consumption. On Day 0 of lactation, body weights at the high and mid concentrations were significantly less than controls but were within normal limits by Day 4. At sacrifice on Day 4 of lactation, no gross lesions observed could be attributed to propionaldehyde exposure. The findings of the adult female microscopic examinations were similar to those observed in the

males. Vacuolization of the olfactory epithelium was apparent in the low and intermediate exposure groups and atrophy was seen primarily at the high concentration. None of the females at any level had findings of squamous metaplasia. The decline in the severity of the nasal lesions in females relative to males is likely to be attributable to the 6-day (approximately) period between the cessation of exposures after gd 20 and the sacrifice on lactation Day 4 for the females.

There were no significant effects of exposure on any of the reproductive parameters assessed. Litter size and viability were similar among the groups. Pup body weights on Postnatal Days 0 and 4 were not affected by exposure although the high concentration body weight gain for that period was slightly depressed.

In summary, repeated exposure to propionaldehyde vapor at concentrations of 0, 150, 750, or 1500 ppm was associated with minimal toxicity at the two highest concentrations in females, but males showed no apparent toxicity. Microscopic assessment of the nasal epithelium, however, revealed treatment-related effects at all concentrations of propionaldehyde exposure in both sexes. Reproductive parameters were not affected at any concentration. A slight decrease in body weight gain in the 1500 ppm offspring was the only finding of possible significance in the neonates.

OBJECTIVES

The objective of this study was to evaluate the potential of the test substance to 1) produce toxicity in adult male and female CD® rats, 2) affect male and female reproductive performance, and 3) produce developmental toxicity following repeated inhalation exposure.

BACKGROUND INFORMATION

This study was conducted by Union Carbide Chemicals and Plastics Company Inc. as part of voluntary participation in the OECD High Production Volume Chemical testing program. A dose range-finding study was conducted at BRRC, Project Number 91-13-25601 (see Appendix 9 of this report), to establish the maximum tolerated concentration of propionaldehyde vapor in pregnant CD® rats to aid in the dose selection process for the definitive study. In the range finding study, five groups were exposed to propionaldehyde at concentrations of 0, 500, 1000, 1500, or 2500 ppm, 6 hours/day, from gestation day (gd) 0 through 20. Concentration-related decreases in body weight, body weight gain and food consumption were observed in groups exposed to 1000 ppm or above. Fetal body weights were also decreased at the highest concentration.

TARGET CONCENTRATION SELECTION

Target propionaldehyde vapor concentrations of 0 (control), 150, 750, and 1500 ppm were selected in conjunction with the Sponsor based on the results of the range-finding study.

MATERIALS AND METHODS

The protocol, protocol amendment, and protocol deviations (BRRC Project No. 91-13-25602) detailing the design and conduct of this study are presented in Appendix 8.

Test Substance

Two 55-gallon stainless steel drums of propionaldehyde; Lot No. T-1258; CAS No. 123-38-6 were received on October 15, 1991, from Union Carbide Chemicals and Plastics Company Inc. (South Charleston, WV) and assigned BRRC Sample No. 54-351-A and 54-351-B. The test substance was a water-white odorous liquid. The test substance was stored in the original containers in a special enclosure under a nitrogen atmosphere. The purity of the test substance was determined by the GLP Analytical Skills Center at the UCC&P South Charleston, WV, Technical Center to be approximately 99% and the report is included in Appendix 1. Pertinent chemical and physical properties of propionaldehyde are listed in Appendices 1 and 8.

Animals and Husbandry

Seventy-five male and 75 female CD® rats arrived on December 23, 1991, from Charles River Laboratories, Inc. (Portage, MI). They were designated by the supplier to be approximately 56 days old (birth date was recorded as approximately October 28, 1991) and 234-275 and 177-209 g upon arrival for males and females, respectively. The females were nulliparous and nonpregnant.

Animals were housed in Room 101 from arrival to termination of the study, except during exposures. Within 2 days of receipt, the animals were examined by a Clinical Veterinarian, and representative animals were subjected to a pretest health screen including full necropsy, histologic examination of selected tissues, and serum viral antibody analyses. Based on the results of these data, the Clinical Veterinarian indicated that these animals were in good health and suitable for use.

All animals were assigned a unique number and identified by cage tags. Animals considered available for the study were also identified by a tail tattooing procedure. Animals selected for the pretest health screen were identified by a toe-clipping procedure after sacrifice.

The animals were housed 1 or 2/cage for approximately 14 days in stainless steel, wire mesh cages (22.5 x 15.5 x 18 cm). DACB® (Deotized Animal Cage Board; Shepherd Specialty Papers, Inc., Kalamazoo, MI) was placed under each cage and changed regularly. An automatic timer was set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). Temperature and relative humidity were recorded continuously (Cole-Parmer Hygrothermograph® Seven-Day Continuous Recorder, Model No. 8368-00, Cole-Parmer Instrument Co., Chicago, IL). Temperature was routinely maintained at 65-77°F; relative humidity was routinely maintained at 40-70%. Any minor exceptions to these specified ranges were noted in the raw data.

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) was available ad libitum, except during exposures, and was delivered by an automatic watering system with demand control valves mounted on each rack (water bottles were used for females while in shoe box cages). Water analyses were provided by the supplier, the NUS Corporation, Materials and Engineering Testing Co., and Lancaster Laboratories, Inc. at regular intervals. EPA standards for maximum levels of contaminants were not exceeded. Ground, certified Rodent Chow® #5002 (Purina Mills, Inc.) was available ad libitum, except during exposures. Analyses for chemical composition and possible contaminants of each feed lot were performed by Purina Mills, Inc., and the results were included in the raw data.

Animal Acclimation

The acclimation period was approximately 2 weeks. During this period, the animals were weighed at least 2 times at scheduled intervals. Detailed clinical observations were conducted in conjunction with body weight measurements. Cage-side animal observations were conducted at least once daily, and mortality checks were conducted twice daily (morning and afternoon). The animals were examined just prior to the end of the acclimation period by a Clinical Veterinarian. Animals considered unacceptable for the study, based on the clinical signs, body weights, or body weight gains, were rejected. The fate of rejected animals and the reasons for rejection were documented in the raw data.

Study Organization

Following the second pretest body weight, the animals were assigned to 3 exposure groups and a control group using a stratified randomization procedure

based on body weight. At the time of group assignment, only animals with body weights within $\pm 20\%$ of the population mean for each sex were included. The body weight range on the day of first exposure was 319.1 to 377.5 g for males and 201.3 to 243.1 g for females. The following table summarizes the organization of the study.

Group	Number of Animals		Test Vapor Concentration (ppm)
	Male	Female	
Control	15	15	0
Low	15	15	150
Mid	15	15	750
High	15	15	1500

The exposures began on January 6, 1992. Males were exposed for 6 hours/day for 52 consecutive days. Females were exposed for a minimum of 35, and a maximum of 48 consecutive days (depending upon when they mated). The 6-hour exposure period was defined as the time when the generation system was turned on and subsequently turned off. All control animals were exposed to filtered air only, using the same exposure regimen. Fifteen females/group were sacrificed during the period February 14 - 28, 1992 on Day 4 of lactation (after approximately 38 exposures and 6 days of recovery). Fifteen males/group were sacrificed on February 27, 1992 after 52 exposures.

Inhalation Chamber Description and Operation

The inhalation chambers used for this study were located in Room 138. They were constructed from stainless steel with glass windows for animal observation. The volume of each chamber was approximately 4320 liters, and the airflow was approximately 1000 liters/minute. Chamber airflow was calibrated with a Kurz Model 505 mass flowmeter. A Dwyer Magnehelic® pressure gauge (Dwyer Instruments, Inc., Michigan City, IN) was used to monitor chamber airflow. Chamber temperature and relative humidity were recorded using industrial thermometers (Control Specialties, Inc., Houston, TX) and Airguide Humidity Indicators (Airguide Instrument Company, Chicago, IL), respectively. Temperature and relative humidity measurements were recorded approximately every 30 minutes during each exposure. Prior to the start of exposures and on Exposure Days 1 and 45, the oxygen content of all the chambers was measured with an O₂ indicator (Model 245R, Mine Safety Appliances, Pittsburgh, PA).

Vapor Generation

For all exposure chambers, propionaldehyde was metered from a piston pump (Fluid Metering, Inc., Oyster Bay, NY) into a heated glass evaporator similar in design to that described by Snellings and Dodd (1990). The temperature of the evaporators was maintained at the lowest level sufficient to vaporize the liquid. The resultant vapor was carried into the chamber by a countercurrent air stream that entered the bottom of the evaporator. Prior to the start of exposures and on Exposure Days 18 and 45, temperature measurements were taken from the inside surface of the evaporators using a Fluke 51 K/J thermometer.

Observations and MeasurementsLife Evaluations

All animals were individually observed for signs of toxic effects immediately following daily exposures. Preceding and following each exposure, observations were recorded for animals exhibiting overt clinical signs. On days when exposures were not conducted, detailed observations were generally conducted in the morning.

Body weight data were collected for all males on the morning prior to initiation of the first exposure and weekly thereafter. Female body weight data were collected weekly during the pre-mating phase on Days 0, 7, and 14, during gestation of Days 0, 7, 14, and 21, and Days 0 and 4 of lactation.

Food consumption was measured weekly throughout the study for males, except during the 2-week mating period. Female food consumption was measured weekly during the pre-mating period, and at 3 to 4-day intervals during gd 0 through 20.

Mating, Gestation, and Lactation

After the 2-week prebreed exposure period was completed, the animals within each exposure group were randomly mated, one male to one female, to produce the F1 generation. The following mating procedure was used: the animals were paired for 7 days; after the first 7 days of the mating period, females of unsuccessfully mated pairs were randomly placed with another male in the same exposure group. The observation of a dropped copulation plug or the presence of vaginal sperm was considered evidence of successful mating and was designated gd 0.

Once evidence of successful mating was observed, the male and female from that mating pair were individually housed. For any mating pairs which did not show evidence of successful mating, the last scheduled mating day was considered gd 0 for that female and the animals were treated accordingly for subsequent events.

Females were observed 2 times daily beginning on gd 21 for evidence of littering. The dams were allowed to rear their young until Day 4 of lactation.

On Day 4 of lactation, F0 parental females were necropsied and the F1 pups were examined grossly and then euthanized and discarded. F0 males were necropsied after parturition of the F1 litters.

Reproductive Indices

The following indices were calculated for parental animals:

Mating index (females) =

$$\frac{\text{Number of plug-/sperm-positive females}}{\text{Total number of females paired}} \times 100$$

Mating index (males) =

$$\frac{\text{Number of males impregnating females}}{\text{Total number of males paired}} \times 100$$

Fertility index (female) =

$$\frac{\text{Number of pregnant females}}{\text{Number of plug-/sperm-positive females}} \times 100$$

Fertility index (male) =

$$\frac{\text{Number of males siring litters}}{\text{Number of males impregnating females}} \times 100$$

Gestational index =

$$\frac{\text{Number of females with live litters}}{\text{Number of females pregnant}} \times 100$$

The following indices were calculated for litters:

Live birth index =

$$\frac{\text{Number of live pups at birth}}{\text{Total number of pups born}} \times 100$$

4-Day survival index =

$$\frac{\text{Number of pups surviving 4 days}}{\text{Total number of live pups at birth}} \times 100$$

Offspring Evaluations

All pups from the F1 generation were examined as soon as possible on the day of birth (Day 0) to determine the number of viable and stillborn male and female members of each litter. Litters were evaluated twice daily for survival. Survival indices were calculated at 0 and 4 days after birth. The sex of each pup was determined and verified daily. All live pups were weighed individually on Postnatal Day 0 and 4. The body weights and sexes were recorded on an individual basis but the pups were not uniquely identified. All pups were examined for physical abnormalities at birth and on Postnatal Day 4. All pups dying during lactation were necropsied when possible to investigate the cause of death.

Clinical Pathology Evaluations

Prior to sacrifice, blood was obtained from all adult males for hematology and clinical chemistry determinations. Blood samples were collected by retroorbital bleeding in methoxyflurane anesthetized rats. All males were fasted prior to bleeding following their last exposure.

The following were measured or calculated:

Hematology

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	platelet count
mean corpuscular volume (MCV)	
mean corpuscular hemoglobin (MCH)	
mean corpuscular hemoglobin concentration (MCHC)	

Clinical Chemistry

glucose (fasting)	gamma-glutamyl transferase (GGT)
urea nitrogen	calcium
creatinine	phosphorus
total protein	sodium
total bilirubin	potassium
aspartate aminotransferase (AST)	chloride
alanine aminotransferase (ALT)	

Details of the clinical pathology procedures are included in Appendix 3.

Anatomic Pathology Evaluations

At the time of sacrifice, adult females and fasted adult males were anesthetized with methoxyflurane and euthanized by severing the brachial vessels to permit exsanguination. On the day of sacrifice, body weights were obtained to allow expression of relative organ weights. A complete necropsy, which included examination of the thoracic cavity, was performed on all animals. The liver, lungs, kidneys, thymus, uterus (females), testes and epididymides (male) were weighed and retained in 10% neutral buffered formalin (NBF) for all sacrificed animals. The following tissues were also collected and retained in 10% NBF:

gross lesions
brain
 pituitary
upper and lower respiratory tract
 (including nasal turbinates, larynx, and trachea)
heart
spleen
adrenal gland
ovaries (females)
 vagina (females)
 uterus (females)
seminal vesicles (males)

The following tissues were collected and retained in Bouin's fixative:

testes (males)
epididymides (males)

Tails were saved for identification purposes.

The underlined tissues from the control and high concentration animals were processed histologically and examined microscopically. In addition, the first 2 sections of the nasal cavity for all animals from the low and intermediate groups were examined.

Details of the anatomic pathology procedures are included in Appendix 2.

Data Analyses

The unit of comparison was the male, the pregnant dam or the litter. The data for quantitative continuous variables were intercompared for the 3 exposure groups and the control group by use of Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparisons.

Nonparametric data were statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U test when appropriate. Incidence data were compared using the Fisher's Exact Test. For all statistical tests, the probability value of < 0.05 (two-tailed) was used as the critical level of significance (Dixon, 1990; Sokal and Rohlf, 1981).

Various models of calculators, computers, and computer programs may have been used to analyze data for this study. Since various models round or truncate numbers differently, values in some tables may differ slightly from those in other tables or from independently calculated data. The integrity of the study and interpretation of the data were unaffected by these differences.

RETENTION OF RECORDS

All raw data, documentation, records, the protocol, protocol amendment, and protocol deviations, specimens, and a copy of the final report generated as a result of this study are retained in the BRRC Archives. Due to the nature of the test substance, a reserve sample was not retained in the BRRC Archives.

RESULTS AND DISCUSSION

All references of differences in group mean values in the following text refer to comparisons of statistically significant differences between the exposure/treatment group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

Chamber Atmospheres

A summary of the chamber atmosphere measurements is presented in Table 1. Detailed results and discussion of the chamber atmosphere measurements are included in Appendix 1.

During exposures, the mean of daily mean chamber temperatures for all exposure groups ranged from 20 to 21°C (Appendix 1), and the relative humidity ranged from 47 to 48% (Appendix 1). For all measurements, the chamber oxygen content was 20.8%. The evaporator temperature measurements ranged from 37 to 55°C.

The means of daily mean chamber atmosphere concentrations (\pm S.D.) were 151 (\pm 4.1), 745 (\pm 15.2), and 1522 (\pm 23.7), for target concentrations of 150, 750, and 1500 ppm, respectively. No propionaldehyde was detected (minimum detection limit 5 ppm) in the control chamber atmosphere during the study.

The distribution of propionaldehyde vapor concentration in each of the three exposure chambers was examined and the vapor concentrations were found to be uniformly distributed. A description and results of the chamber distributions are presented in Appendix 1.

Clinical Observations and Mortality

Summaries of the clinical observations are presented in Tables 2 and 6, for adult males and females, respectively. Individual animal clinical observation data are included in Appendix 4. Individual animal fate data are included in Appendix 4.

No adult males or females died prior to the scheduled sacrifice. Neither the adult males nor the adult females displayed any overt signs of toxicity at any time during the study.

Body Weights

Summaries of absolute body weights and body weight gains are presented in Tables 3 and 4 for males and Tables 7, 8, 10, and 12 for females. Individual animal body weight data are included in Appendix 4.

Adult male body weights and weight gains were similar among all three exposure groups and controls. The adult female body weight gains, but not absolute body weights, were decreased during the first week of exposures at the mid and high concentrations. During gestation, the body weights of the high concentration females were less than controls on Days 0, 7, and 14. However, weight gain during gestation was similar to controls. On Day 0 of lactation, body weights in the high and mid concentrations were less than controls but were similar to controls by Day 4.

Food Consumption

Summaries of food consumption data are presented in Table 5 for males and Tables 9 and 11 for females. Individual food consumption data are included in Appendix 4.

Although there was no significant effect upon food consumption in adult males at any interval measured, there appeared to be a slight decrease at the highest level throughout the study. During the first week of exposures, the females at the two highest concentrations displayed slight decreases in food consumption. By the second week, however, all groups had similar levels of intake. Small, but consistent, decreases in food consumption were also noted in the high dose females throughout gestation. A transient decrease in food

consumption was also noted for the intermediate group of females during Days 14-17 of gestation, but there was a tendency towards reduced consumption throughout much of gestation.

Reproductive Parameters

A summary of reproductive parameters is presented in Tables 13 and 14. Individual reproductive data are included in Appendix 5.

Successful mating performance and fertility were unaffected by exposure to propionaldehyde. Of the 15 mating pairs, only one male in each group failed to sire a litter. The mating, fertility, and gestational indices ranged from 93.3 to 100% for all groups. Gestational length, number of corpora lutea, number of uterine implants, pre and postimplantation loss, and number of pups born alive were not differentially affected as a function of exposure.

F1 Offspring

Litter Size and Sex Ratio

A summary of litter sizes and sex ratios (% males) are presented in Table 15. The corresponding individual data are included in Appendix 5.

There were no effects on litter size or sex ratio on the day of birth or Postnatal Day 4.

Viability and Survival

The summary of litter viability is included in Table 16 and a summary of pup survival indices is presented in Table 17. The corresponding individual data are included in Appendix 5.

There were no effects on F1 pup viability or survival indices.

Pup Body Weights

Pup body weights and body weight gains are summarized in Table 18. Individual pup body weight data are presented in Appendix 5.

Average pup body weights were similar among groups through the first 4 days of lactation, however, pups at the high concentration showed slightly depressed body weight gains during that period.

Clinical Pathology Evaluations

Individual adult male clinical pathology data are included in Appendix 7. Detailed results and discussion of the clinical pathology measurements are included in Appendix 3.

Hematology and clinical chemistry analyses revealed elevated erythrocyte counts, with accompanying increases in hemoglobin and hematocrit values, and an increase in monocytes in the males exposed to 1500 ppm. These findings may reflect a dehydration and irritation effect of exposure to propionaldehyde at the highest concentration.

Organ Weights, Necropsy Observations, and Microscopic Diagnoses

Summary results of organ weights and organ weights relative to body weights are presented in Tables 19 and 20 for adult males and Tables 21 and 22 for adult females. Summary results of necropsy observations are presented in Tables 23 and 24 for adult males and females, respectively. A summary of the microscopic diagnosis of the nasal cavity is presented in Tables 25 and 26 for adult males and females, respectively. Detailed results and discussion of the anatomic pathology results, including microscopic evaluations, are included in Appendix 2. Individual anatomic pathology data are included in Appendix 6.

The mean absolute thymic region weight was significantly increased in males, but not females, in the 1500 ppm group. Although no other absolute organ weights were affected, the 1500 ppm male relative kidney weight was increased. A similar change in females was not observed.

There were no gross lesions observed at necropsy that could be attributed to propionaldehyde exposure. Microscopic examination indicated an exposure-related effect on the olfactory epithelium in the anterior 2 sections of the nasal cavity in the males and females. Vacuolization was primarily evident in the low and intermediate group males and atrophy was seen in the intermediate and high group males. Squamous metaplasia was seen in 2 males from the 1500 ppm group and 1 male in the 750 ppm group. The findings of the adult female microscopic examinations were similar to those observed in the males although somewhat less severe. Vacuolization of the olfactory epithelium was apparent in the low and intermediate exposure groups and atrophy was seen primarily in the high concentration. None of the females at any level had findings of squamous metaplasia.

CONCLUSIONS

Although the lack of overt clinical signs in this study was consistent with the dose range-finding data, given the general irritating properties of the aldehyde chemical class, it was somewhat surprising. The microscopic changes observed in the nasal epithelium, however, are consistent with anticipated effects of chemical irritants. Interestingly, neither the lungs nor other portions of the respiratory tract were adversely affected. The absence of effects in other aspects of the respiratory tract is generally consistent with findings of other aldehydes (Appelman et al., 1982, 1988; Maronpot et al., 1986; Woutersen et al., 1987; Zwart et al., 1988).

Previous reports (Gage, 1970) of liver damage following six days of exposure to 1300 ppm propionaldehyde were not substantiated under the conditions of this study of 52 days of consecutive exposures.

In summary, repeated exposure to propionaldehyde vapor at concentrations of 0, 150, 750, or 1500 ppm was associated with minimal overt toxicity at the two highest concentrations in females, but males showed no apparent toxicity. Microscopic assessment of the nasal epithelium, however, revealed treatment-related effects at all concentrations of propionaldehyde exposure in both sexes. Reproductive parameters were not affected at any concentration. A slight decrease in body weight gain in the 1500 ppm offspring was the only neonatal finding of possible significance.

REVIEW AND APPROVAL

Study Director: Cynthia D. Driscoll 4/5/93
Cynthia D. Driscoll, Ph.D. Date

Director: John P. Van Miller 4/6/93
John P. Van Miller, Ph.D., DABT Date

KEY PERSONNEL

Study Director: C. D. Driscoll

Study Coordinators: M. A. Copeman
M. F. Kubena

Supervisor: L. C. Fisher

Scientists: D. A. Neptun
I. M. Pritts

Additional personnel are listed in the raw data.

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TABLE 1
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 SUMMARY OF CHAMBER ATMOSPHERE DATA

Target Concentration (ppm)	Temp (°C)	RH (%)	A (ppm)	NOM (ppm)	A/NOM
0	20.5±0.70	47.5±1.50	<MDL	-----	-----
150	20.9±0.87	46.7±1.53	151± 4.1	151± 6.4	1.00±0.046
750	20.5±1.00	48.2±1.21	745±15.2	717±18.8	1.04±0.022
1500	20.0±0.92	48.4±1.83	1522±23.7	1453± 7.8	1.05±0.019

Temp = temperature
 RH = relative humidity
 A = analytical concentration
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration
 <MDL = less than the minimum estimated detection limit

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 SUMMARY OF CLINICAL OBSERVATIONS^a

CATEGORY FINDING (LOCATION)	GRADE ^b	FO ADULT MALES PPM			
		0 (DAYS) ^c	150 (DAYS)	750 (DAYS)	1500 (DAYS)
NORMAL					
NO SIGNIFICANT CLINICAL OBSERVATIONS	P	15 (0- 52)	15 (0- 52)	15 (0- 52)	15 (0- 52)
DEAD					
SCHEDULED SACRIFICE	P	15 (52)	15 (52)	15 (52)	15 (52)
BODY					
URINE STAINS	P	0	0	0	1 (44- 52)
EYES/EARS/NOSE LACRIMATION					
(EYE-BOTH)	P	0	1 (1)	0	1
(EYE-LEFT)	P	0	0	0	0
PERINASAL ENCRUSTATION	P	1 (43)	0	0	2 (17- 49)
ORAL/DENTAL PERIORAL WETNESS					
SKIN					
ALOPECIA (PAW-FORE-BOTH)	P	0	0	0	1 (17)
EXCORIATED					
(PAW-FORE-BOTH)	P	0	0	1 (22- 31)	3 (21- 52)
(PAW-FORE-LEFT)	P	0	0	1	1
RAISED AREAS (RED AND OR BROWN) (TAIL)	P	6 (17- 52)	5 (17- 52)	7 (17- 52)	3 (17- 52)

^aNumber of animals exhibiting the finding at least once during the study.

^bGrades: P = present, 1 = mild, 2 = moderate, 3 = severe.

^cEarliest to latest day a finding of the specified grade was observed.

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF BODY WEIGHT (GRAMS)

		F0 ADULT MALES			
GROUP: PPM	0	150	750	1500	
WEEK 0					
MEAN	349.2	345.8	348.4	347.6	
S.D.	16.72	15.25	13.09	16.65	
N	15	15	15	15	
WEEK 1					
MEAN	374.2	365.8	369.7	366.2	
S.D.	19.45	22.70	15.49	19.44	
N	15	15	15	15	
WEEK 2					
MEAN	392.6	378.9	384.4	381.1	
S.D.	24.87	26.91	17.39	25.72	
N	15	15	15	15	
WEEK 3					
MEAN	416.4	401.5	410.6	405.3	
S.D.	27.02	30.20	22.19	26.79	
N	15	15	15	15	
WEEK 4					
MEAN	437.4	419.8	430.8	423.4	
S.D.	30.39	34.17	24.03	27.60	
N	15	15	15	15	
WEEK 5					
MEAN	455.5	435.7	448.2	438.2	
S.D.	35.82	36.38	26.09	31.03	
N	15	15	15	15	
WEEK 6					
MEAN	465.8	444.4	459.2	447.1	
S.D.	40.49	43.20	31.86	34.08	
N	15	15	15	15	

None significantly different from control group

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF BODY WEIGHT GAIN (GRAMS)

GROUP: PPM	F0 ADULT MALES			
	0	150	750	1500
WEEK 0 TO 1				
MEAN	25.0	20.0	21.3	18.6
S.D.	9.85	9.04	6.99	6.86
N	15	15	15	15
WEEK 1 TO 2				
MEAN	16.4	13.1	14.7	14.9
S.D.	6.87	6.44	5.33	8.19
N	15	15	15	15
WEEK 2 TO 3				
MEAN	23.8	22.6	26.2	24.3
S.D.	6.49	7.60	8.23	7.00
N	15	15	15	15
WEEK 3 TO 4				
MEAN	20.9	18.4	20.2	18.1
S.D.	5.54	6.92	5.28	4.01
N	15	15	15	15
WEEK 4 TO 5				
MEAN	18.1	15.9	17.4	14.8
S.D.	7.63	3.91	5.52	9.70
N	15	15	15	15
WEEK 5 TO 6				
MEAN	10.3	8.7	11.0	8.9
S.D.	10.93	9.62	8.49	9.44
N	15	15	15	15

None significantly different from control group

TABLE 5
 PROPIONALDEHYDE, COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

GROUP: PPM	FO ADULT MALES			
	0	150	750	1500
WEEK 0 TO 1				
MEAN	26.5	25.1	26.1	24.8
S.D.	1.68	2.78	1.88	1.98
N	15	15	15	15
WEEK 1 TO 2				
MEAN	26.4	25.4	25.4	24.5
S.D.	1.91	2.97	2.12	2.71
N	14	12	12	14
WEEK 4 TO 5				
MEAN	28.0	27.0	27.7	26.9
S.D.	2.46	2.37	1.74	2.31
N	14	13	10	15
WEEK 5 TO 6				
MEAN	27.3	26.6	27.8	25.9
S.D.	2.90	3.30	2.19	2.70
N	15	15	15	15
WEEK 6 TO 7				
MEAN	28.1	27.0	27.9	26.3
S.D.	2.31	2.89	1.43	2.79
N	15	15	15	15

None significantly different from control group
 Data not included for animals with observed food spillage.

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 SUMMARY OF CLINICAL OBSERVATIONS^a

CATEGORY FINDING (LOCATION)	FO ADULT FEMALES			
	0 (DAYS) ^c	150 (DAYS)	750 (DAYS)	1500 (DAYS)
NORMAL				
NO SIGNIFICANT CLINICAL OBSERVATIONS	P 15(0- 43)	P 15(0- 43)	P 15(0- 44)	P 15(0- 53)
DEAD				
SCHEDULED SACRIFICE	P 15(39- 43)	P 15(40- 43)	P 15(39- 44)	P 15(39- 53)
EYES/EARS/NOSE LACRIMATION(EYE-BOTH)	P 0	P 0	P 0	P 1(27- 28)
PERI OCULAR ENCRUSTATION (EYE-BOTH)	P 0	P 0	P 1 (7)	P 0
(EYE-LEFT)	P 0	P 0	P 0	P 1(29- 33)
PERINASAL ENCRUSTATION	P 0	P 1(23- 30)	P 0	P 0
SKIN				
ALOPECIA (FACE)	P 0	P 1(31- 36)	P 0	P 0
(LEG-FRONT-BOTH)	P 0	P 0	P 1(7- 43)	P 1(18- 21)
(MULTIPLE AREAS-NOS)	P 0	P 0	P 0	P 1(22- 40)
(PAW-FORE-BOTH)	P 1(31- 41)	P 0	P 0	P 0
CRUST(FACE)	P 0	P 1 (40)	P 0	P 0
RAISED AREAS (RED AND OR BROWN) (TAIL)	P 0	P 1(17- 42)	P 6(17- 43)	P 0

^aNumber of animals exhibiting the finding at least once during the study.
^bGrades: P = present, 1 = mild, 2 = moderate, 3 = severe.
^cEarliest to latest day a finding of the specified grade was observed.

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF BODY WEIGHT (GRAMS)

F0 ADULT FEMALES				
GROUP: PPM	0	150	750	1500
WEEK 0				
MEAN	220.1	219.8	219.5	218.7
S.D.	9.89	7.60	7.94	8.95
N	15	15	15	15
WEEK 1				
MEAN	230.9	227.3	223.9	221.9
S.D.	10.40	8.75	8.07	12.05
N	15	15	15	15
WEEK 2				
MEAN	236.6	234.5	232.0	233.4
S.D.	10.58	13.80	11.24	10.46
N	9	11	8	8
None significantly different from control group				

TABLE 8
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF BODY WEIGHT GAIN (GRAMS)

GROUP: PPM	F0 ADULT FEMALES			
	0	150	750	1500
WEEK 0 TO 1				
MEAN	10.9	7.4	4.4**	3.2**
S.D.	4.77	6.99	5.29	4.62
N	15	15	15	15
WEEK 1 TO 2				
MEAN	5.8	7.7	5.9	7.9
S.D.	3.69	6.17	6.29	7.56
N	9	11	8	8

** Significantly different from control group (p < .01)

TABLE 9
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

GROUP: PPM	F0 ADULT FEMALES			
	0	150	750	1500
WEEK 0 TO 1				
MEAN	18.1	17.5	16.9*	16.6**
S.D.	0.87	1.50	1.63	1.69
N	14	11	11	13
WEEK 1 TO 2				
MEAN	18.6	18.6	18.3	17.2
S.D.	0.89	1.60	1.21	1.64
N	11	14	9	14

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

Data not included for animals with observed food spillage.

TABLE 10
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF GESTATIONAL BODY WEIGHT AND WEIGHT CHANGE (GRAMS)

		FO ADULT FEMALES			
GROUP: PPM	0	150	750	1500	
<u>GESTATIONAL BODY WEIGHTS (g)</u>					
DAY 0					
MEAN	241.38	239.59	234.52	227.63**	
S.D.	12.974	11.773	12.051	8.921	
N	14	15	14 ^a	14	
DAY 7					
MEAN	275.71	273.14	266.53	260.25**	
S.D.	15.765	16.693	11.528	10.855	
N	14	15	14	14	
DAY 14					
MEAN	305.37	302.13	293.63	288.38*	
S.D.	20.166	20.499	13.367	12.537	
N	14	15	14	14	
DAY 21					
MEAN	377.39	376.35	364.31	360.45	
S.D.	29.478	49.184	23.938	18.336	
N	14	15	14	14	
<u>GESTATIONAL BODY WEIGHT CHANGES (g)</u>					
DAY 0 TO 7					
MEAN	34.33	33.56	32.02	32.62	
S.D.	5.767	7.504	5.370	3.744	
N	14	15	14	14	
DAY 7 TO 14					
MEAN	29.67	28.99	27.09	28.13	
S.D.	6.245	8.913	3.229	6.497	
N	14	15	14	14	
DAY 14 TO 21					
MEAN	72.02	74.22	70.68	72.08	
S.D.	14.320	35.019	19.982	14.573	
N	14	15	14	14	
DAY 0 TO 21 (GESTATION)					
MEAN	136.01	136.76	129.79	132.83	
S.D.	20.679	45.314	23.046	15.970	
N	14	15	14	14	

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)
^a The plug was missed for one pregnant female in the 750 ppm group, data not included.

TABLE 11
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF GESTATIONAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

GROUP: PPM	F0 ADULT FEMALES ¹¹			
	0	150	750	1500
DAY 0 TO 4				
MEAN	22.51	22.03	22.10	20.25**
S.D.	2.137	2.509	2.304	1.374
N	14	13	14	14
DAY 4 TO 7				
MEAN	24.27	23.83	22.99	21.50**
S.D.	2.300	2.453	1.667	1.755
N	14	15	14	13
DAY 7 TO 11				
MEAN	24.16	24.09	22.63	21.67**
S.D.	2.303	3.004	2.304	1.831
N	14	15	14	14
DAY 11 TO 14				
MEAN	24.65	24.63	23.39	22.48
S.D.	2.618	3.343	1.921	1.825
N	14	15	14	14
DAY 14 TO 17				
MEAN	26.42	25.17	24.01*	23.89*
S.D.	2.249	3.670	2.281	1.730
N	14	15	14	14
DAY 17 TO 21				
MEAN	24.58	24.64	23.14	22.18
S.D.	2.883	4.146	1.835	2.474
N	14	15	13	13
DAY 0 TO 7				
MEAN	23.27	22.71	22.48	20.82**
S.D.	2.164	2.419	1.811	1.469
N	14	13	14	13
DAY 7 TO 14				
MEAN	24.37	24.32	22.96	22.02*
S.D.	2.329	3.056	1.949	1.713
N	14	15	14	14
DAY 14 TO 21				
MEAN	25.37	24.87	23.37	22.88*
S.D.	2.295	3.778	1.482	2.017
N	14	15	13	13

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

Data not included for animals with observed food spillage.

TABLE 12
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF LACTATIONAL BODY WEIGHT AND WEIGHT CHANGE (GRAMS)

		P0 ADULT FEMALES			
GROUP: PPM	0	150	750	1500	
<u>LACTATIONAL BODY WEIGHTS (g)</u>					
DAY 0					
MEAN	277.18	275.59	262.64*	261.47*	
S.D.	21.870	16.896	11.954	11.294	
N	14	14	15	14	
DAY 4					
MEAN	299.72	297.12	288.44	283.73	
S.D.	20.054	19.045	15.192	12.956	
N	14	14	15	14	
<u>LACTATIONAL BODY WEIGHT CHANGES (g)</u>					
DAY 0 TO 4					
MEAN	22.54	21.53	25.80	22.26	
S.D.	10.704	10.671	9.757	9.540	
N	14	14	15	14	

* Significantly different from control group (p < .05)

TABLE 13
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

SUMMARY OF REPRODUCTIVE PARAMETERS
 F0 PARENTS

GROUP: PPM	0	150	750	1500
No. F0 pairs at study start	15	15	15	15
No. F0 pairs	15	15	15	15
No. males impregnating females ^a	15	15	14	14
No. plug/sperm-positive females	15	15	15 ^b	14
No. pregnant ^c	14	15	15	14
No. males siring litters	14	14	14	14
No. live litters on postnatal day 0	14	14	15	14
<u>INDICES^d</u>				
Mating Index (females)	100.0	100.0	100.0	93.3
Mating Index (males)	100.0	100.0	93.3	93.3
Fertility Index (females)	93.3	100.0	100.0	100.0
Fertility Index (males)	93.3	93.3	100.0	100.0
Gestational Index	100.0	93.3	100.0	100.0

^a Defined as the number of males producing plug- or sperm-positive females.

^b Copulation plug and sperm were missed in one female.

^c Determined by delivery of litters/uterine staining.

^d The indices are defined in the text.

TABLE 14
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF GESTATIONAL LENGTH AND REPRODUCTIVE PARAMETERS

		F0 ADULT FEMALES			
GROUP: PPM	0	150	750	1500	
LENGTH OF GESTATION (DAYS)					
MEAN	21.8	21.9	21.8	21.8	
S.D.	0.43	0.36	0.43	0.43	
N	14	14	14	14	
CORPORA LUTEA					
MEAN	15.4	16.0	15.0	14.7	
S.D.	1.91	2.48	1.46	1.73	
N	14	15	15	14	
UTERINE IMPLANTS					
MEAN	15.4	15.9	15.9	15.3	
S.D.	1.45	2.77	1.36	1.38	
N	14	14	15	14	
PREIMPLANTATION LOSS (%)					
MEAN	2.5	12.0	1.2	1.4	
S.D.	4.50	26.54	3.44	3.78	
N	14	15 ^a	15	14	
PUPS BORN ALIVE					
MEAN	14.2	15.0	15.0	14.5	
S.D.	1.63	2.72	1.41	1.22	
N	14	14	15	14	
POSTIMPLANTATION LOSS (%)					
MEAN	6.1	5.3	5.8	4.9	
S.D.	7.23	5.52	5.63	5.59	
N	14	14	15	14	

None significantly different from control group
^a One 150 PPM female, which did not deliver, was found to have eleven corpora lutea but no implantation sites following staining of the uterus.

TABLE 15
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF LITTER SIZE AND SEX RATIO (% MALES)

		F1 PUPS			
GROUP: PPM	0	150	750	1500	
<u>LACTATIONAL DAY 0</u>					
TOTAL BORN/LITTER					
MEAN	14.5	15.1	15.0	14.6	
S.D.	1.87	2.70	1.41	1.09	
N	14	14	15	14	
TOTAL BORN ALIVE/LITTER					
MEAN	14.2	15.0	15.0	14.5	
S.D.	1.63	2.72	1.41	1.22	
N	14	14	15	14	
SEX RATIO					
MEAN	54.9	45.1	51.8	49.3	
S.D.	9.95	16.48	10.30	9.08	
N	14	14	15	14	
<u>LACTATIONAL DAY 4</u>					
LITTER SIZE					
MEAN	14.0	14.9	14.4	14.2	
S.D.	1.62	2.79	1.40	1.31	
N	14	14	15	14	
SEX RATIO					
MEAN	55.8	45.4	51.3	49.7	
S.D.	10.05	16.71	10.41	9.31	
N	14	14	15	14	
None significantly different from control group					

TABLE 16
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 SUMMARY OF LITTER VIABILITY

GROUP: PPM	F1 PUPS			
	0	150	750	1500
<u>LACTATIONAL DAY 0</u>				
TOTAL BORN	203	211	225	204
TOTAL BORN ALIVE	199	210	225	203
NO. STILLBORN	4	1	0	1
<u>LACTATIONAL DAY 4</u>				
NO. ALIVE	196	209	216	199
NO. DEAD (DAYS 0 TO 4)	3	1	9	4
None significantly different from control group				

TABLE 17
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF PUP SURVIVAL INDICES

		F1 PUPS			
GROUP: PPM	0	150	750	1500	
LIVE BIRTH INDEX					
MEAN	98.2	99.5	100.0	99.5	
S.D.	3.66	1.78	0.00	2.06	
N	14	14	15	14	
4-DAY SURVIVAL INDEX					
MEAN	98.5	99.5	96.2	98.0	
S.D.	2.99	2.06	6.76	4.05	
N	14	14	15	14	

None significantly different from control group
 The equations used for calculating pup survival indices are recorded in the text.

TABLE 18
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF PUP BODY WEIGHT AND WEIGHT CHANGE (GRAMS) PER LITTER

		F1 PUPS			
GROUP: PPH	0	150	750	1500	
<u>PUP BODY WEIGHTS (g)</u>					
<u>LACTATIONAL DAY 0</u>					
ENTIRE LITTER					
MEAN	5.83	5.94	5.80	5.89	
S.D.	0.469	0.334	0.614	0.525	
N	14	14	15	14	
MALE PUPS					
MEAN	5.95	6.12	5.97	6.06	
S.D.	0.495	0.374	0.614	0.561	
N	14	14	15	14	
FEMALE PUPS					
MEAN	5.70	5.80	5.61	5.73	
S.D.	0.467	0.313	0.601	0.509	
N	14	14	15	14	
<u>LACTATIONAL DAY 4</u>					
ENTIRE LITTER					
MEAN	9.47	9.30	8.91	8.73	
S.D.	0.885	0.848	0.999	0.980	
N	14	14	15	14	
MALE PUPS					
MEAN	9.60	9.53	9.10	8.93	
S.D.	0.899	0.860	1.008	1.042	
N	14	14	15	14	
FEMALE PUPS					
MEAN	9.29	9.10	8.71	8.54	
S.D.	0.874	0.797	0.988	0.931	
N	14	14	15	14	
<u>PUP BODY WEIGHTS CHANGES (g)</u>					
<u>LACTATIONAL DAY 0 TO 4</u>					
ENTIRE LITTER					
MEAN	3.63	3.36	3.11	2.84**	
S.D.	0.651	0.642	0.550	1.051	
N	14	14	15	14	
MALE PUPS					
MEAN	3.65	3.42	3.13	2.86	
S.D.	0.701	0.634	0.576	1.089	
N	14	14	15	14	
FEMALE PUPS					
MEAN	3.59	3.30	3.10	2.91**	
S.D.	0.614	0.593	0.552	1.028	
N	14	14	15	14	

** Significantly different from control group (p < .01)

TABLE 19
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT WEEK 7

		F0 ADULT MALES			
GROUP: PPM	0	150	750	1500	
FINAL BODY WEIGHT					
MEAN	454.1	430.4	446.4	431.0	
S.D.	41.21	43.56	31.52	35.03	
N	15	15	15	15	
LIVER					
MEAN	11.490	10.936	11.455	11.190	
S.D.	1.4926	1.1531	1.2211	1.3477	
N	15	15	15	15	
KIDNEYS					
MEAN	3.203	3.086	3.338	3.357	
S.D.	0.3994	0.4059	0.4671	0.3229	
N	15	15	15	15	
LUNGS					
MEAN	1.552	1.532	1.572	1.522	
S.D.	0.0709	0.1315	0.1447	0.1042	
N	14	15	14	15	
THYMIC REGION					
MEAN	0.349	0.338	0.350	0.292**	
S.D.	0.0522	0.1064	0.0978	0.0577	
N	15	15	15	15	
EPIDIDYMIDES					
MEAN	1.319	1.236	1.267	1.253	
S.D.	0.1269	0.1848	0.0883	0.1000	
N	15	15	15	15	
TESTES					
MEAN	3.430	3.272	3.331	3.363	
S.D.	0.3192	0.4861	0.1552	0.2602	
N	15	15	15	15	

** Significantly different from control group (p < .01)

TABLE 20
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT WEEK 7

FO ADULT MALES				
GROUP: PPM	0	150	750	1500
LIVER				
MEAN	2.528	2.543	2.563	2.591
S.D.	0.1945	0.1392	0.1667	0.1668
N	15	15	15	15
KIDNEYS				
MEAN	0.706	0.720	0.747	0.780**
S.D.	0.0662	0.0891	0.0853	0.0513
N	15	15	15	15
LUNGS				
MEAN	0.341	0.357	0.352	0.354
S.D.	0.0292	0.0206	0.0264	0.0244
N	14	15	14	15
THYMIC REGION				
MEAN	0.077	0.079	0.078	0.068
S.D.	0.0135	0.0248	0.0208	0.0140
N	15	15	15	15
EPIDIDYMIDES				
MEAN	0.294	0.288	0.285	0.293
S.D.	0.0493	0.0422	0.0246	0.0365
N	15	15	15	15
TESTES				
MEAN	0.758	0.762	0.749	0.785
S.D.	0.0674	0.1126	0.0550	0.0810
N	15	15	15	15

** Significantly different from control group (p < .01)

TABLE 21
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT WEEK 5

FO ADULT FEMALES				
GROUP: PPM	0	150	750	1500
FINAL BODY WEIGHT				
MEAN	296.4	295.4	288.4	283.6
S.D.	23.29	19.58	15.19	12.49
N	15	15	15	15
LIVER				
MEAN	12.980	12.995	12.589	12.336
S.D.	1.4890	1.5997	1.0985	1.1210
N	15	15	15	15
KIDNEYS				
MEAN	1.991	1.973	2.040	1.968
S.D.	0.1760	0.2125	0.1821	0.1388
N	15	15	15	15
LUNGS				
MEAN	1.219	1.313	1.191	1.217
S.D.	0.0502	0.2631	0.0823	0.1113
N	15	15	15	15
THYMIC REGION				
MEAN	0.240	0.225	0.189	0.214
S.D.	0.0626	0.0437	0.0533	0.0620
N	15	15	15	15

None significantly different from control group

TABLE 22
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT WEEK 5

FO ADULT FEMALES				
GROUP: PPM	0	150	750	1500
LIVER				
MEAN	4.377	4.393	4.364	4.347
S.D.	0.3472	0.3981	0.2909	0.3140
N	15	15	15	15
KIDNEYS				
MEAN	0.674	0.669	0.708	0.695
S.D.	0.0641	0.0703	0.0627	0.0528
N	15	15	15	15
LUNGS				
MEAN	0.414	0.445	0.414	0.429
S.D.	0.0357	0.0839	0.0293	0.0351
N	15	15	15	15
THYMIC REGION				
MEAN	0.082	0.076	0.066	0.076
S.D.	0.0224	0.0164	0.0184	0.0227
N	15	15	15	15
None significantly different from control group				

TABLE 23
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
STOMACH					
CONTENTS ABNORMAL		3	0	0	0
LIVER					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	0	1	2
SIZE DECREASE		0	2	0	0
COLON					
PARASITE		1	0	0	0
SKIN					
SHAPE/CONTOUR CHANGE		5	4	7	2
ALOPECIA		0	0	0	1
SPLEEN					
ACCESSORY		1	0	0	0
LYMPH ND, S-MAN					
SIZE INCREASE		7	3	9	2
COLOR CHANGE, FOCAL/MULTIFOCAL		2	1	4	2
COLOR CHANGE, DIFFUSE		1	3	0	3
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	4	1	4
SIZE DECREASE		0	1	0	0
TESTES					
SIZE DECREASE		0	1	0	0
CONSISTENCY CHANGE		0	0	0	1
EPIDIDYMIDES					
NODULE		2	0	0	0
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		5	2	8	6
KIDNEYS					
DILATED PELVIS		0	0	0	1
GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM					

TABLE 24
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF NECROPSY OBSERVATIONS

F0 ADULT FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
STOMACH					
ULCERATED		0	0	0	1
CONTENTS ABNORMAL		0	0	0	1
LIVER					
COLOR CHANGE, DIFFUSE		0	0	1	0
COLON					
GASEOUS		0	1	1	0
ADRENAL GL					
COLOR CHANGE, FOCAL/MULTIFOCAL		1	2	4	3
COLOR CHANGE, DIFFUSE		0	0	1	1
SIZE INCREASE		1	0	0	0
SKIN					
CRUST/SCAB/SCALE		0	1	0	0
SURFACE CHANGE		0	1	4	0
ALOPECIA		1	0	1	1
SPLEEN					
SIZE INCREASE		1	0	0	0
SHAPE/CONTOUR CHANGE		1	0	0	0
LYMPH ND, S-MAN					
SIZE INCREASE		6	4	2	0
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	1	0
LYMPH ND, MED					
COLOR CHANGE, DIFFUSE		0	1	0	0
THYMIC REGION					
SIZE DECREASE		0	0	2	1
OVARIES					
CYST		0	1	0	2
LUNGS					
COLOR CHANGE, DIFFUSE		2	0	0	0
COLOR CHANGE, FOCAL/MULTIFOCAL		5	4	6	5
KIDNEYS					
DILATED PELVIS		1	1	0	0
URETER					
DILATATION/DISTENTION		1	0	0	0
GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM					

TABLE 25
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE (NASAL CAVITY)

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
NASAL CAVITY					
TOTAL NUMBER EXAMINED		15	15	15	15
EXAMINED, UNREMARKABLE		15	3	0	0
RHINITIS		0	0	7**	14**
MINIMAL		0	0	1	3
MILD		0	0	5	7
MODERATE		0	0	1	4
SQUAMOUS METAPLASIA		0	0	1	2
MILD		0	0	1	0
MODERATE		0	0	0	2
ATROPHY, OLFACTORY EPITHELIUM		0	2	10**	15**
MINIMAL		0	2	1	0
MILD		0	0	6	1
MODERATE		0	0	3	8
MARKED		0	0	0	6
VACUOLIZATION OF OLFACTORY EPITHELIUM		0	12**	14**	2
MINIMAL		0	6	2	0
MILD		0	4	3	0
MODERATE		0	2	2	0
MARKED		0	0	7	2

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

** Significantly different from control group (p < .01)

TABLE 26
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE (NASAL CAVITY)

F0 ADULT FEMALES					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
NASAL CAVITY					
TOTAL NUMBER EXAMINED		15	15	15	15
EXAMINED, UNREMARKABLE		15	0	0	0
RHINITIS					
		0	1	6*	1
MINIMAL					
		0	1	0	0
MILD					
		0	0	6	1
ATROPHY, OLFACTORY EPITHELIUM					
		0	0	2	15**
MINIMAL					
		0	0	1	0
MILD					
		0	0	0	6
MODERATE					
		0	0	0	9
MARKED					
NECROSIS OF OLFACTORY EPITHELIUM					
		0	0	0	1
MODERATE					
		0	0	0	1
VACUOLIZATION OF OLFACTORY EPITHELIUM					
		0	15**	15**	0
MINIMAL					
		0	8	0	0
MILD					
		0	7	7	0
MODERATE					
		0	0	8	0

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

Quality Assurance Unit Study Inspection Summary

Test Substance: Propionaldehyde

Study: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

Study Director: C. D. Driscoll, Ph.D.

The Quality Assurance Unit of BRRC conducted the inspections listed below and reported the results to the study director and to management on the dates indicated. It is the practice of this Quality Assurance Unit to report the results of each inspection to both the study director and management.

<u>Date</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued</u>	
		<u>To Study Director</u>	<u>To Management</u>
10-8-91	Protocol Range-Finding Study	10-11-91	10-15-91
10-8-91	Protocol Full Study	10-11-91	12-6-91
10-15-91	Event-Animal Receipt Range-Finding Study	10-25-91	12-9-91
10-23-91	Event-Exposure Range-Finding Study	10-23-91	12-9-91
11-12-91	Event-Sacrifice Range-Finding Study	11-12-91	12-9-91
12-24-91	Event-Animal Receipt Full Study	12-30-91	2-18-92
1-6-92	Event-Exposure Full Study	1-6-92	2-18-92
2-18-92	Event-Sacrifice Full Study	2-18-92	4-15-92
2-27-92	Event-Male Sacrifice Full Study	2-27-92	4-15-92

<u>Date</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued</u>	
		<u>To Study Director</u>	<u>To Management</u>
7-10-92	Protocol Amendment 1 Range-Finding and Full Studies	7-14-92	7-21-92
8-18 to 12-22-92	Raw Data and Report Range-Finding and Full Studies	1-11-93	4-2-93
9-17 to 12-14-92	Anatomic Pathology Raw Data and Report Full Study	1-11-93	4-2-93
9-22 to 12-9-92	Analytical Chemistry Raw Data and Report Full Study	1-11-93	4-2-93
9-22 to 12-10-92	Clinical Pathology Raw Data and Report Full Study	1-11-93	4-2-93
4-1-93	Archives Range-Finding and Full Studies	4-1-93	4-2-93

Linda J. Calisti 4/5/93
 Linda J. Calisti, Manager Date
 Good Laboratory Practices/Quality Assurance

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

Chamber Atmosphere Report

(27 Pages)

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SUMMARY

The concentration of propionaldehyde vapor in the exposure chamber was monitored throughout the 52 days of exposure by flame ionization gas chromatography. The concentration in each exposure chamber atmosphere was determined approximately 11 times during each 6-hour exposure. The overall mean (\pm standard deviation) chamber atmosphere concentrations were 151 (\pm 4.1), 745 (\pm 15.2), and 1522 (\pm 23.7) ppm, for target concentrations of 150, 750, and 1500, ppm, respectively. Propionaldehyde was not detected in the control chamber atmosphere.

The test substance was analyzed before and after the exposure regimen and remained over 99% pure.

The uniformity of propionaldehyde vapor concentration in each of 3 exposure chambers was examined. Each chamber was tested once prior to the start of the exposure regimen. Vapor concentrations were measured by gas chromatography using flame ionization detection. Concentrations were measured at 5 positions for each individual distribution test. In each test, these concentrations were representative of a uniform vapor distribution as indicated by low coefficient of variation (CV) values. CV values of less than 4% were found for each of the 3 distribution tests. Furthermore, the results indicate that the "normal" analytical sampling position for each chamber was properly located within the chamber such that sampling results were representative of propionaldehyde concentrations in the breathing zone of the animals.

MATERIALS AND METHODS

Test Substance

Two 55-gallon containers of propionaldehyde (CAS No. 123-38-6, Lot T-1258, BRRC Sample No. 54-351 A and B) were received from Union Carbide Chemicals and Plastics Company Inc. (UCC&P), S. Charleston, WV, on October 15, 1991. The chemical and physical properties of the test substance are described in Table 1. The compositional analyses were provided by the GLP Analytical Skills Center at the UCC&P South Charleston, WV, Technical Center. A summary of the reports is presented in Table 2; the entire report is presented as Attachment 1. The prestudy and poststudy compositional analyses indicated that the test substance was over 99% pure and had remained stable for the duration of the exposure regimen.

Test Substance Generation

The methods used to generate propionaldehyde vapor in the exposure chambers are described in the text of the main report.

Chamber Distribution Setup

The distribution tests simulated actual animal exposures, including the use of similar animal cages, cage carriers with collection trays, and airflow rates. No animals were present in the exposure chambers.

The positions of the sampling probes within the chambers are provided in Table 8. One of these positions was the "normal" analytical probe position. It is important to note the analytical sampling consisted of three "cycles," each cycle requiring approximately 30 minutes to complete. Since the chamber concentrations may vary slightly with time, the data from the three cycles (Table 9) were averaged to eliminate time dependent concentration variations. Also, the sampling occurred after the equilibration of the chamber concentration (t_{99}) had been obtained.

Analytical Instrumentation

A Perkin-Elmer Sigma 2000 gas chromatograph (GC) equipped with a flame ionization detector was used to analyze the exposure chamber atmospheres for propionaldehyde vapor. The GC operating conditions are presented in Table 3. A Spectra-Physics 4270 Integrator provided a record of the chromatograms and chromatographic analyses as well as peak integration. The data were captured using an IBM PS/2 Computer with Spectra-Physics Chromstation/2 software. In-house software was used to compute daily statistics and also to provide an alarm system which monitored chamber concentrations.

Calibration

Calibration of the gas chromatograph was achieved by injecting gas standards which were prepared by syringe injection of propionaldehyde test substance into Tedlar[™] gas bags containing UHP nitrogen or air. These standards were prepared using the mathematical relationship:

$$V = \frac{C \times V_h \times MW \times 298 \times P \times 10^{-6}}{d \times 24.45 \times T \times 760}$$

where: V = required volume of calibration liquid in milliliters at temperature T (degrees K)

C = desired calibration concentration, in ppm

V_h = volume of container, in liters

MW = molecular weight of the calibration liquid

P = barometric pressure, in millimeters of mercury

d = density of the calibration liquid in grams per milliliter at temperature T

24.45 = molecular volume at 298 degrees K and 760
millimeters of mercury, in liters

T = temperature, in degrees Kelvin

The calibration curve (Figure 1) was constructed by plotting peak areas versus the gas standard concentrations. The calibration was checked at least once each week during the exposure regimen.

RESULTS AND DISCUSSION

Chamber Atmosphere Analysis

Each chamber atmosphere was analyzed for propionaldehyde approximately twice each hour during each 6-hour exposure by flame ionization gas chromatography. The daily mean analytical concentrations are listed in Tables 4 through 7. The means of daily mean chamber atmosphere concentrations (\pm standard deviations) were 151 (\pm 4.1), 745 (\pm 15.2), and 1522 (\pm 23.7) ppm, for target concentrations of 150, 750, and 1500 ppm, respectively. No concentration of propionaldehyde above the estimated minimum detection limit of 5 ppm was detected in the control chamber atmosphere during the study.

Analytical/Nominal Concentration Ratio

The daily analytical/nominal (A/NOM) propionaldehyde concentration ratios are given in Tables 5 through 7; the nominal concentration being an estimate calculated from the quantity of test substance delivered and the chamber airflow rate. The overall mean A/NOM concentration ratios were 1.00, 1.04, and 1.05, for propionaldehyde target concentrations of 150, 750, and 1500 ppm, respectively.

Temperature and Relative Humidity

The daily mean temperature and relative humidity values for the exposure chambers are also presented in Tables 4 through 7. The means of daily mean temperature values were 20, 21, 20, and 20°C, for propionaldehyde target concentrations of 0, 150, 750, and 1500 ppm, respectively. The means of daily mean relative humidity values were 48, 47, 48, and 48%, respectively.

Chamber Distribution

The uniformity of propionaldehyde vapor concentration in 3 test substance exposure chambers was examined. Each chamber was tested prior to the exposure regimen. Concentrations were measured at 5 positions for each distribution test. The results and the statistical summaries are presented in Table 9.

In each test, these concentrations were representative of a uniform vapor distribution as indicated by low coefficient of variation (CV) values. CV values of 0.3, 0.2, and 3.2% were obtained for exposure chambers 38-1, 38-2, and 38-4, respectively. Furthermore, the results indicate that the "normal" analytical sampling position for each chamber was properly located within the chamber such that sampling results were representative of propionaldehyde concentrations in the breathing zone of the animals.

Analytical Chemist:

Irvin M. Pritts
Irvin M. Pritts, Ph.D.

4-6-93

Date

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

CHEMICAL AND PHYSICAL PROPERTIES¹

Synonyms:	Propanal; Propylaldehyde
Molecular Weight:	58.08
Molecular Formula:	C ₂ H ₅ CHO
Vapor Density (air = 1)	2.0
Appearance and Odor:	Water-white liquid; suffocating odor
Boiling Point, 760 mm Hg:	48°C
Solubility in Water:	22% @ 20°C
Evaporation Rate (but acetate=1):	19.9
Vapor Pressure at 20°C:	approx. 258 mm Hg
Specific Gravity (H ₂ O = 1):	0.7982 @ 20/20°C
Flash Point (Tag Closed Cup):	< -18°C

¹Material Safety Data Sheet, Union Carbide Chemicals and Plastics Company Inc., Revised 8/29/90.

TABLE 2
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

TEST SUBSTANCE ANALYSIS¹

Component	Prestudy Area ¹	Poststudy Area ¹
Propionaldehyde	99.77 (approx.)	99.42 (approx.)
n-Propanol	0.01	0.02
2-Methyl Butyraldehyde	0.02	0.02
Valeraldehyde	0.06	0.02
Propionic Acid	0.07	0.37
Propionaldehyde Dimers	0.03	0.04
Propionaldehyde Trimers	0.01	0.04
All Other Impurities	0.03	0.07

¹The capillary gas chromatographic compositional analyses were provided by the GLP Analytical Skills Center at the UCCSP South Charleston, WV, Technical Center. In addition, gas chromatography-mass spectrometry and nuclear magnetic resonance spectroscopy were independently used to confirm the sample's identity.

TABLE 3
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

GAS CHROMATOGRAPH OPERATING PARAMETERS

Chromatograph:	Perkin-Elmer Sigma 2000
Detector:	Flame Ionization
Column:	10% SP-1000, on 80/100 mesh Supelcoport, 10 ft. x 1/8 in. stainless steel
Column temperature:	170°C
Injector temperature:	100°C gas sample valve
Detector temperature:	250°C
Carrier flow rate:	20 mL/minute nitrogen
Sample size:	0.5 cc
Retention time:	1.4 minutes
GC attenuation:	Range = 100
Minimum detection limit:	Approximately 5 ppm
Integrator attenuation:	128

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
 AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

CHAMBER ATMOSPHERE DATA: 0 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)
1	20.0	47.6	<MDL
2	19.8	50.2	<MDL
3	20.7	48.8	<MDL
4	20.5	49.3	<MDL
5	21.0	46.8	<MDL
6	20.0	47.9	<MDL
7	20.0	47.9	<MDL
8	20.0	46.7	<MDL
9	20.0	46.1	<MDL
10	22.0	49.8	<MDL
11	22.6	49.6	<MDL
12	21.8	49.9	<MDL
13	21.7	49.9	<MDL
14	21.8	49.2	<MDL
15	20.0	47.6	<MDL
16	20.3	48.5	<MDL
17	20.0	46.9	<MDL
18	20.0	48.5	<MDL
19	20.0	46.1	<MDL
20	20.8	47.3	<MDL
21	20.0	46.8	<MDL
22	20.0	46.5	<MDL
23	21.0	46.6	<MDL
24	21.0	47.3	<MDL
25	20.8	47.2	<MDL
26	21.0	46.9	<MDL
27	20.3	45.7	<MDL
28	20.1	42.8	<MDL
29	20.7	45.8	<MDL
30	21.0	46.8	<MDL
31	21.9	46.2	<MDL
32	20.0	46.0	<MDL
33	20.0	45.5	<MDL
34	22.0	46.5	<MDL
35	20.0	44.3	<MDL
36	21.0	45.9	<MDL
37	21.0	46.6	<MDL
38	20.3	46.8	<MDL
39	20.0	49.1	<MDL
40	20.0	47.8	<MDL
41	20.3	47.4	<MDL
42	20.0	46.4	<MDL
43	20.0	49.1	<MDL
44	20.0	48.4	<MDL
45	20.0	49.1	<MDL
46	20.0	48.7	<MDL
47	20.0	48.2	<MDL
48	20.0	48.6	<MDL
49	20.0	48.0	<MDL
50	20.0	48.6	<MDL
51	20.0	48.8	<MDL
52	20.0	47.8	<MDL
Mean:	20.5	47.5	<MDL
SD:	0.70	1.50	—

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 <MDL = less than the minimum estimated detection limit

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
 AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

CHAMBER ATMOSPHERE DATA: 150 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	20.0	44.5	153	2.8	168	0.91
2	20.7	48.5	153	2.1	165	0.93
3	20.9	47.5	154	6.9	158	0.97
4	20.9	46.8	146	2.4	145	1.01
5	21.0	46.4	146	2.3	147	0.99
6	20.9	46.8	151	2.7	151	1.00
7	20.6	46.9	155	1.5	153	1.01
8	20.8	46.0	148	3.0	147	1.01
9	20.0	45.3	146	2.1	147	0.99
10	21.7	46.7	148	2.8	147	1.01
11	22.9	50.8	152	2.9	147	1.03
12	22.8	49.8	152	5.0	143	1.06
13	22.9	49.1	155	5.7	147	1.05
14	22.9	49.6	150	9.4	145	1.03
15	20.8	46.9	148	5.0	145	1.02
16	21.4	47.1	153	5.7	146	1.05
17	20.9	46.2	143	1.9	145	0.99
18	20.8	47.1	155	4.2	145	1.07
19	21.0	45.7	151	5.5	148	1.02
20	20.0	46.3	153	5.4	148	1.03
21	21.1	46.1	157	6.3	147	1.07
22	20.8	46.1	150	6.0	148	1.01
23	21.0	45.8	143	1.2	146	0.98
24	20.8	47.7	150	6.1	146	1.03
25	20.8	47.6	148	6.6	145	1.02
26	20.8	47.6	150	4.2	143	1.05
27	21.0	45.1	153	4.4	149	1.03
28	20.0	46.1	152	6.4	148	1.03
29	20.8	44.7	146	7.2	147	0.99
30	22.0	45.9	148	6.5	146	1.01
31	21.9	45.5	161	4.7	149	1.08
32	21.8	45.4	151	4.6	148	1.02
33	20.9	43.6	146	3.7	148	0.99
34	21.0	44.4	158	3.1	149	1.06
35	20.8	44.2	161	4.2	152	1.06
36	22.0	44.5	148	3.3	152	0.97
37	21.0	45.2	148	7.9	151	0.98
38	21.9	44.0	154	9.2	149	1.03
39	20.0	48.0	144	3.9	155	0.93
40	20.9	47.2	147	1.0	158	0.93
41	21.0	48.5	148	1.2	159	0.93
42	20.0	47.9	150	1.4	159	0.94
43	20.0	47.5	151	2.1	160	0.94
44	20.0	47.1	150	0.7	159	0.94
45	20.0	48.4	146	0.8	158	0.92
46	20.0	47.4	151	1.0	159	0.95
47	20.0	47.6	153	1.2	161	0.95
48	19.0	46.3	155	1.0	159	0.97
49	19.3	47.0	156	2.2	161	0.97
50	20.0	48.0	149	2.3	157	0.95
51	20.0	47.9	152	0.8	160	0.95
52	20.7	47.2	148	1.6	159	0.93
Mean:	20.9	46.7	151	—	151	1.00
SD:	0.87	1.53	4.1	—	6.4	0.046

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration

TABLE 6
 FORMALDEHYDE: COMBINED REPEATED-EXPOSURE
 AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

CHAMBER ATMOSPHERE DATA: 750 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	20.8	47.6	747	5	705	1.06
2	22.3	49.5	747	7	699	1.07
3	20.7	49.2	743	5	698	1.06
4	20.9	47.8	731	5	699	1.05
5	20.0	47.4	733	6	699	1.05
6	20.8	48.2	727	13	683	1.06
7	20.4	48.4	758	8	704	1.08
8	20.0	46.9	706	4	675	1.05
9	19.8	47.0	719	8	694	1.04
10	21.1	49.7	737	6	698	1.06
11	22.6	50.7	744	10	695	1.07
12	21.8	50.2	739	19	697	1.06
13	22.5	50.6	754	8	695	1.08
14	22.8	50.5	747	12	700	1.07
15	21.7	49.2	754	8	705	1.07
16	20.6	49.7	745	10	704	1.06
17	19.	48.1	724	9	695	1.04
18	19.5	48.6	749	12	700	1.07
19	20.0	47.2	728	7	704	1.03
20	20.9	48.8	763	25	703	1.06
21	20.0	48.6	734	7	697	1.05
22	20.7	46.8	722	11	700	1.03
23	21.0	47.7	734	15	716	1.03
24	20.8	48.3	765	4	730	1.05
25	20.8	48.8	752	14	724	1.04
26	20.8	47.8	751	4	723	1.04
27	19.0	46.5	722	7	723	1.00
28	21.0	44.8	758	9	723	1.05
29	20.1	47.2	734	15	721	1.02
30	21.8	47.4	746	12	730	1.02
31	21.8	47.8	759	9	739	1.04
32	20.8	48.0	751	17	723	1.04
33	20.0	46.5	741	11	732	1.01
34	20.9	46.7	752	5	728	1.03
35	19.0	46.0	761	6	723	1.05
36	21.9	46.4	748	14	727	1.02
37	21.9	47.1	759	23	728	1.04
38	21.3	48.5	745	3	727	1.02
39	19.9	48.3	759	9	729	1.04
40	20.0	48.0	730	5	722	1.01
41	20.0	49.7	741	8	732	1.01
42	19.9	48.4	736	4	726	1.01
43	19.8	48.3	738	4	720	1.02
44	19.9	48.5	738	16	728	1.01
45	19.2	49.0	726	8	724	1.00
46	19.0	48.9	750	14	744	1.01
47	19.0	48.8	772	8	753	1.03
48	20.0	47.8	788	7	745	1.06
49	20.0	48.7	760	7	746	1.02
50	19.0	48.8	770	3	752	1.02
51	19.0	49.4	767	4	751	1.02
52	20.0	48.2	749	5	744	1.01
Mean:	20.5	48.2	745	---	717	1.04
SD:	1.00	1.22	15.2	---	18.8	0.022

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
 AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

CHAMBER ATMOSPHERE DATA: 1500 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	19.8	47.4	1543	4	1456	1.06
2	20.3	49.8	1537	6	1449	1.06
3	20.7	49.1	1548	5	1455	1.06
4	20.0	47.4	1538	3	1450	1.06
5	19.0	47.9	1529	5	1451	1.05
6	19.8	48.1	1528	19	1433	1.07
7	21.6	48.8	1555	38	1450	1.07
8	19.8	46.9	1554	13	1455	1.07
9	19.0	47.0	1490	11	1445	1.03
10	20.8	50.5	1545	8	1444	1.07
11	21.8	51.2	1540	13	1435	1.07
12	22.8	50.9	1547	15	1437	1.08
13	21.5	51.0	1563	12	1440	1.09
14	21.8	50.7	1553	38	1440	1.08
15	20.0	49.2	1550	7	1452	1.07
16	19.9	49.8	1551	10	1456	1.07
17	20.5	47.8	1540	7	1458	1.06
18	19.8	48.5	1562	8	1456	1.07
19	20.0	47.1	1508	5	1446	1.04
20	19.9	48.6	1529	17	1450	1.05
21	19.9	48.3	1561	14	1466	1.06
22	20.0	46.8	1520	18	1455	1.04
23	20.0	47.0	1491	7	1452	1.03
24	19.8	47.8	1536	12	1456	1.05
25	19.8	48.0	1522	9	1464	1.04
26	19.8	47.6	1498	6	1445	1.04
27	20.0	45.7	1524	12	1447	1.05
28	20.5	43.3	1515	22	1456	1.04
29	19.2	47.2	1485	12	1449	1.02
30	21.4	47.8	1492	22	1452	1.03
31	20.4	47.4	1514	5	1453	1.04
32	19.8	46.6	1505	18	1450	1.04
33	19.8	45.4	1488	10	1452	1.02
34	20.7	46.5	1495	4	1451	1.03
35	20.0	46.0	1500	6	1453	1.03
36	20.8	46.6	1522	30	1461	1.04
37	20.0	46.1	1498	23	1455	1.03
38	21.9	46.7	1505	7	1456	1.03
39	19.0	48.0	1540	20	1457	1.06
40	19.4	47.8	1504	10	1468	1.02
41	19.0	48.8	1492	13	1458	1.02
42	19.0	48.6	1507	20	1468	1.03
43	19.0	51.1	1509	10	1449	1.04
44	20.0	50.4	1494	10	1446	1.03
45	18.8	51.2	1493	14	1461	1.02
46	18.9	50.7	1512	6	1464	1.03
47	19.0	50.8	1502	14	1459	1.03
48	19.0	50.0	1541	23	1446	1.07
49	19.0	50.1	1557	10	1456	1.07
50	19.0	50.6	1523	5	1463	1.04
51	20.0	51.2	1516	4	1458	1.04
52	19.0	50.0	1490	3	1455	1.02
Mean:	20.0	46.4	1522	—	1453	1.05
SD:	0.92	1.83	23.7	—	7.8	0.019

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration

TABLE 8
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

CHAMBER DISTRIBUTION STUDY
CHAMBER DESCRIPTION AND POSITION OF CHAMBER SAMPLING PROBES

CHAMBER

Construction: Stainless steel and glass.
 Manufacturer: Wahmann Manufacturing Company (Timonium, MD)
 Shape: Rectangular
 Dimensions: Height: 207 cm
 Width: 98 cm
 Depth: 213 cm

Chamber #38-1 Probe Placement (1500 ppm Target)

<u>Probe Number</u>	<u>Location (x:y:z)* Units (cm)</u>		
1	70	:	54 : 47
2	33	:	130 : 45
3 Analytical Probe	39	:	98 : 168
4	67	:	130 : 163
5	36	:	56 : 160

Chamber #38-2 Probe Placement (750 ppm Target)

<u>Probe Number</u>	<u>Location (x:y:z)* Units (cm)</u>		
1	71	:	128 : 163
2 Analytical Probe	53	:	98 : 163
3	32	:	52 : 162
4	34	:	130 : 46
5	68	:	51 : 49

Chamber #38-4 Probe Placement (150 ppm Target)

<u>Probe Number</u>	<u>Location (x:y:z)* Units (cm)</u>		
1	31	:	55 : 162
2	30	:	128 : 46
3	63	:	126 : 167
4 Analytical Probe	52	:	98 : 168
5	64	:	54 : 47

*Location described by a 3-dimensional coordinate system:
 x = width coordinate; y = depth coordinate; z = height coordinate. The origin of the coordinate system (0:0:0) is the lower left front corner of the internal chamber.

TABLE 9
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE
 AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

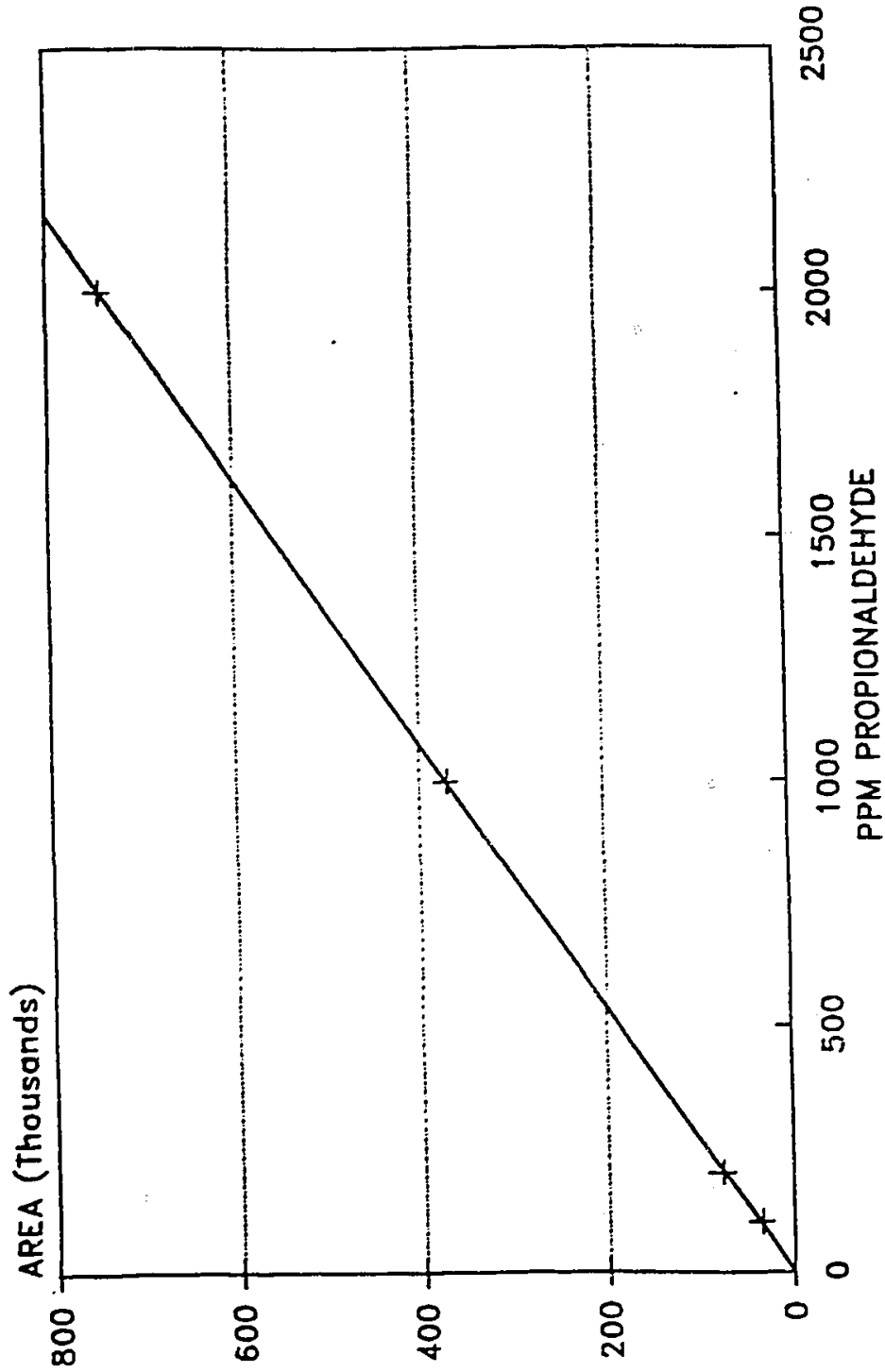
CHAMBER DISTRIBUTION DATA
 PROPIONALDEHYDE CONCENTRATION (PPM) AT CHAMBER PROBE POSITION

(Chamber 38-1)					
	1	2	3	4	5
	1522	1515	1530	1530	1532
	1537	1524	1533	1529	1535
	1529	1516	1529	1525	1523
Mean:	1529	1518	1530	1528	1530
SD:	7.2	5.0	2.1	2.5	6.5
Grand mean = 1527		SD = 5.1		% CV = 0.3	

(Chamber 38-2)					
	1	2	3	4	5
	800	796	794	806	806
	805	799	809	800	799
	797	796	800	794	800
Mean:	801	797	801	800	802
SD:	4.2	1.9	7.6	6.3	4.1
Grand mean = 800		SD = 1.9		% CV = 0.2	

(Chamber 38-4)					
	1	2	3	4	5
	146	157	157	162	155
	146	156	158	162	157
	146	155	156	152	157
Mean:	146	156	157	158	156
SD:	0.2	1.1	0.6	5.7	1.5
Grand mean = 155		SD = 4.9		% CV = 3.2	

FIGURE 1. PROPIONALDEHYDE
CALIBRATION CURVE



Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

Test Substance Characterization Report

PROPIONALDEHYDE

GLP ANALYSIS - FINAL REPORT

AUTHORS: A. E. Gabany (2)
A. M. Harrison (4)
R. A. McDowie (2) **DATE:** August 26, 1992

SUPERVISORS: P. D. Gaarenstroom
T. L. Dawson (3) **STUDY #:** 100-SLW-4

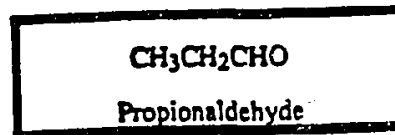
FILE NO: 39461

SUMMARY Two samples of propionaldehyde, for toxicity testing at Bushy Run Research Center, were analyzed by Good Laboratory Practice (GLP) standards to meet EPA requirements. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the sample's identity. Sample purity, measured by capillary GC, is - 99.77% for the pre-study sample and 99.42% for the post-study sample based on area percent. The slightly lower purity of the post-study sample is due to the increase of propionic acid in the sample. All raw data, documentation, records, protocols, sample and final reports are being retained.

INTRODUCTION Richard C. Wise, this study's sponsor, requested that the Bushy Run Research Center test propionaldehyde for genetic toxicity. Such studies must follow GLP standards established by the EPA that require they be conducted with authentic materials whose identity and purity are verified analytically.

A sample of propionaldehyde (100-SLW-6; lot # T-1258) was received 10/14/91 in a clear glass bottle from UCC&P, Texas City, TX for analytical characterization. This sample is a subsample of a larger quantity of propionaldehyde, (BRRC # 54-351B) tested at Bushy Run Research Center. A GLP protocol describing the analytical characterization of the sample was prepared (Appendix 1). The protocol called for structural identification by NMR and GC/MS and for the capillary GC quantitative measurement of any impurities identified by GC/MS. The post-study sample (100-SLW-6R; BRRC # 54-351B) was received on 2/28/92.

Shown at right is the structure of Propionaldehyde; its Chemical Abstracts Service Registry number (CAS #) is 123-38-6.



DISCUSSION The data from the analyses are summarized below.

NMR Analyses Proton and carbon NMR data were collected in the UCC&P NMR Skill Center using a General Electric GN-300NB spectrometer. The acquisition parameters are shown in the figures; for the ^1H NMR spectrum, the pulses used correspond to 3° flip angles; the ^{13}C flip angles were 30° ; the $^{13}\text{C}(^1\text{H})$ (proton decoupled ^{13}C) spectrum used Waltz 16 modulation for ^1H decoupling. The spectra were not acquired under quantitative conditions; the acquisition conditions were established to identify the major component and to look for any substantial impurities. The sample was dissolved in deuteriochloroform for analysis; tetramethylsilane (TMS) was added to provide an internal chemical shift reference. The TMS

KEY WORDS: RN=123-38-6.

RESEARCH AND DEVELOPMENT
UNION CARBIDE CHEMICALS AND PLASTICS COMPANY INC. (UCC&P)
SOUTH CHARLESTON, WEST VIRGINIA

and deuteriochloroform were used as received.

Figure 1 shows the ^1H NMR spectrum obtained from the sample 100-SLW-6. The observed chemical shifts, spin-spin coupling patterns, and relative intensities are appropriate for propionaldehyde. The aldehydic proton appears as a triplet at 9.78 ppm; the methyl hydrogens as a triplet at 1.09 ppm; and the methylene hydrogens as a quartet of doublets at 2.48 ppm. The minor peak at 7.57 ppm is probably due to residual protonated solvent. Several very minor peaks are observed but have not been assigned; they probably include spinning side bands, ^{13}C satellites, and minor by-products.

Figure 2 shows the $^{13}\text{C}\{^1\text{H}\}$ spectrum for the same sample. No unusual or unexpected resonances are seen; the three types of carbons present in propionaldehyde are seen: the carbonyl at 202.2 ppm, the methyl at 5.2 ppm, and the methylene at 36.5 ppm. The triplet at 77 ppm is the deuteriochloroform solvent, which was used as a secondary chemical shift reference. Several minor peaks are observed at 101.7, 27.0, 8.3, and 7.1 ppm, which could arise from expected impurities such as the trimer. The NMR spectra are totally consistent with the sample being propionaldehyde which contains no major organic impurities.

GC/MS Analysis Electron ionization (EI) and isobutane chemical ionization (CI) mass spectral data were collected in the UCC&P MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard (HP) 5890 gas chromatograph. The sample, 100-SLW-6, was analyzed by injecting 0.1 μL aliquots onto a DB-1 capillary column held at 30°C for 4 minutes, and then programmed to 250°C at 8°/minute. Figure 3 shows the EI total ion current chromatogram for the sample (scanned from m/z 10 to m/z 310 in the EI mode, and m/z 60-360 in the CI mode). The chromatogram is annotated with identifications based on the components' EI and CI spectra. The propionaldehyde trimers identified by capillary GC were confirmed by GC/CI/MS only.

Capillary GC A HP 5890 gas chromatograph equipped with a flame ionization detector was used to analyze the sample. Aliquots (1 μL) were injected via autoinjector with a 100:1 split ratio onto a DB-1 capillary column started at 60°C and held for 4 minutes, then programmed to 250° at 12°/minute (see Figure 4 for the pre-study sample and Figure 5 for the post-study sample). The averages of triplicate analyses are given below (normalized chromatogram area percent). The slightly lower purity of the post-study sample is due to the increase of propionic acid in the sample.

Component name	100-SLW-6	100-SLW-6R
Propionaldehyde	= 99.77	= 99.42
n propanol	0.01	0.02
2-methyl butyraldehyde	0.02	0.02
valeraldehyde	0.06	0.02
propionic acid	0.07	0.37
propionaldehyde dimers	0.03	0.04
propionaldehyde trimers	0.01	0.04
all other impurities	= 0.03	= 0.07

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC&P Skill Centers show that this sample is propionaldehyde. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purity, measured by capillary GC, is = 99.77% and 99.42%.

ARCHIVES All raw data, records, protocols, samples and final reports are being retained at UCC&P's South Charleston, WV, Technical Center as follows:

- raw data from GC, NMR and GC/MS studies are in 770-127 and 720-151, respectively;
- protocols, notebook and other records are to be kept in the GLP archives;
- the remainder of each sample is being kept in a locked GLP sample box in 770-333.

Final Report, GLP Study # 100-SLW-4

page 2 of 10

ACKNOWLEDGEMENTS We would like to thank Jo Ann Coffey for sample handling, collecting the GC data, and preparing the report, Greg Richards for collecting the GC/MS data, and Kathy Canterbury for collecting the NMR data.

NOTEBOOK REFERENCE: 100-SLW-4 and related pages

Confidentiality No claim of confidentiality is made for any information contained in this study as it pertains to use by any government agency to which it is submitted. This document, however, is proprietary to UCC&P and is confidential and trade secret information in all other countries and for all purposes other than those directly related to the purposes of the reviewing agency. Information contained in these studies should not be reviewed, abstracted or used by persons other than the agency without the expressed written consent of UCC&P except as required to carry out statutory requirements.

GLP Compliance This study was conducted to fully comply with the following GLP standards: FDA, 21 CFR, Part 58;
TSCA, 40 CFR, Part 792;
FIFRA, 40 CFR, Part 160.

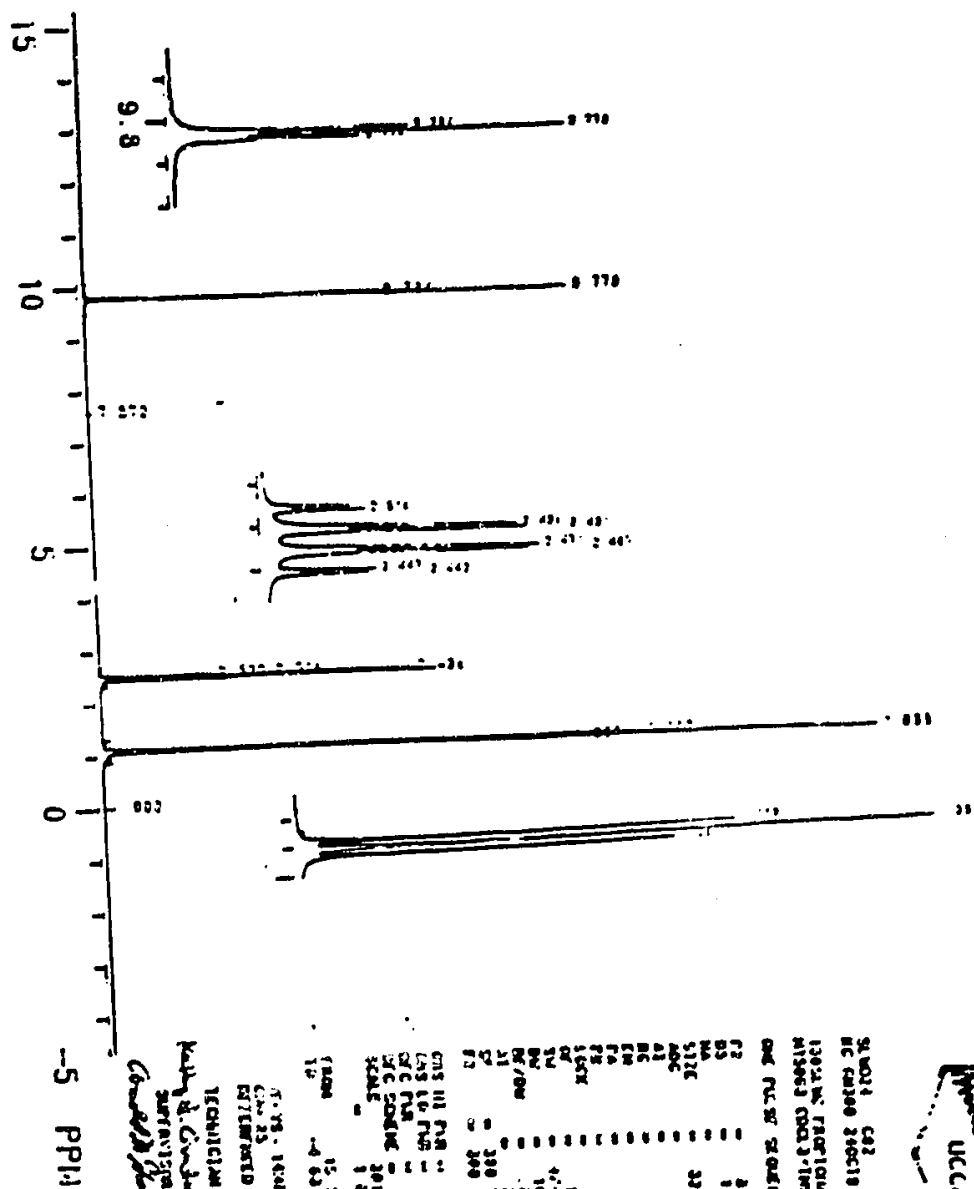
Alexander E. Gabany 8/13/92
Alexander E. Gabany, B. S., Study Director date

Arnold M. Harrison 8/13/92
Arnold M. Harrison, Ph. D., NMR Skill Center date

Richard A. McDonie 8/18/92
Richard A. McDonie, B. S. MS Skill Center date

AEG/AMH/RAM
Date Study initiated: 10/14/91
Manuscript date (Date Study completed): August 13, 1992
Attachments: 5 Figures;
Sample Protocol;
QAU statement

Figure 1 — ¹H NMR Spectrum of 100-SLW-6 (Propionaldehyde)



0.79 - 1.0425
 GMS 20
 ESTIMATED TO THE TWO
 TECHNICIAN
 Kelly & Conculumbey w/str/1
 supervisor
 Caldwell/Thomas e/str/111

 GMS 01. FM 30
 GMS 10. FM 9
 GMS 11. FM 9
 SFC CODING 2
 SFC CODING 101.20 MHz
 SCALE 1.0022 PPM/CM
 FREQ 400.1420
 PULP 12.00
 PROC 200.512000
 ACQ 2.12 SEC
 BR/OW 80
 NO 21
 NI 280.512000
 FI 200.512000
 F1 42.2012 94 Hz
 F2 166.4252
 F3 200.5120
 F4 200.5120
 F5 200.5120
 F6 200.5120
 F7 200.5120
 F8 200.5120
 F9 200.5120
 F10 200.5120
 F11 200.5120
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 F100 200.5120

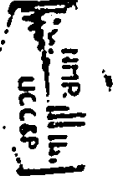
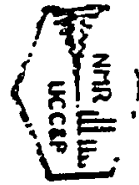
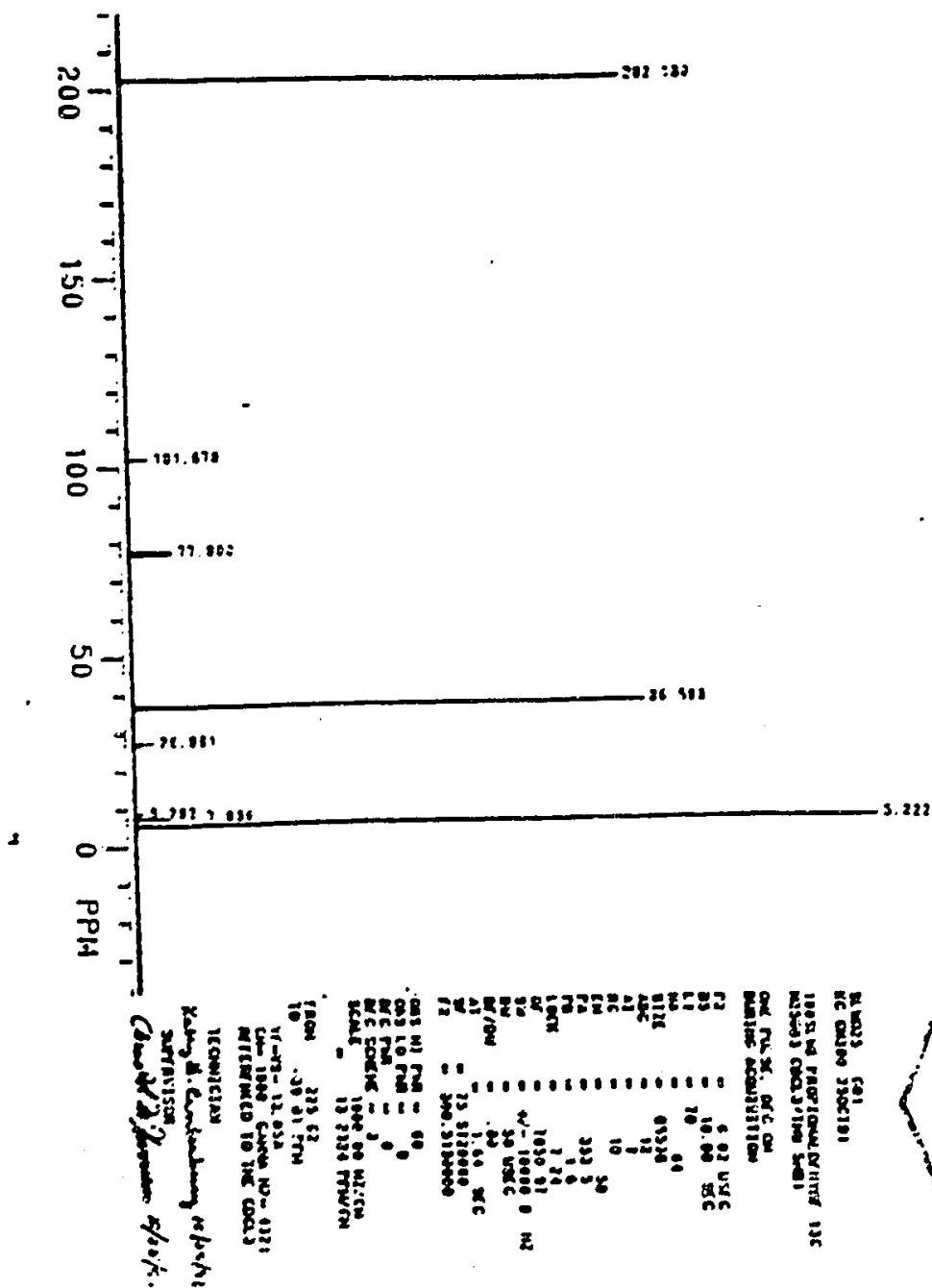
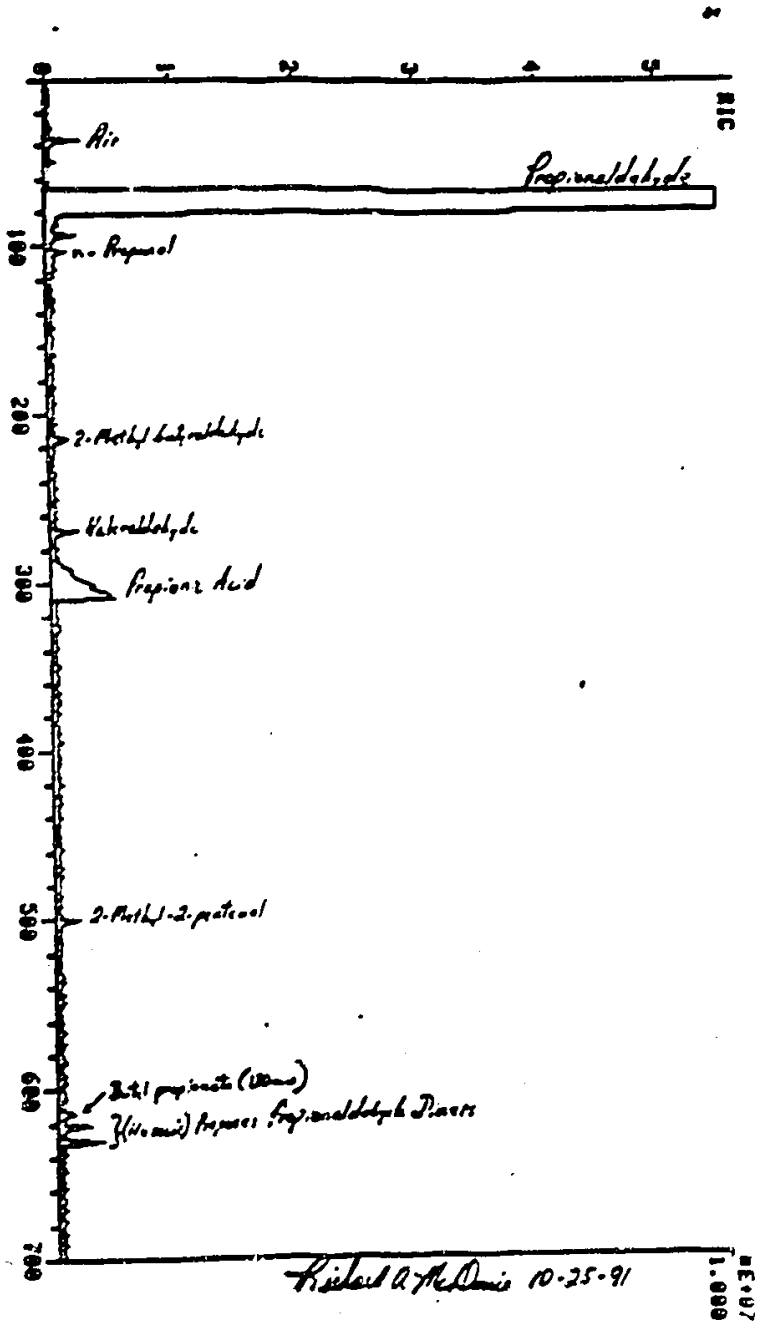


Figure 2 — ¹³C NMR Spectrum of 100-SLW-6 (Propionaldehyde)



RM003 691
 GC 0000 250C181
 100% IN PROPIONALDEHYDE 13C
 NMR3 CDCl₃ TMS SMI
 ONE PULSED, OFC ON
 PULSED ACQUISITION
 F2 6.02 USEC
 S3 10.00 USEC
 L1 70
 M4 04
 SIZE 6536
 ABC 12
 A1 10
 A5 30
 F4 232.5
 F6 1.0
 F8 1.0
 LGPR 7.24
 W 1050.81
 S2 4-10000.0 Hz
 P2 30 USEC
 M/OW .00
 A1 1.66 SEC
 W 25.510000
 F2 200.510000
 ONE HI PUL = 00
 ONE LO PUL = 0
 REC FWH = 0
 REC SCORING = 3
 1000.00 Hz/cm
 SCALE 10.2124 PPM/CM
 18001 225.52
 10 -39.81 PPM
 11-13-12.05A
 CW-1800 CASE NO- 0321
 REFERRED TO THE LOCALS
 TECHNICIAN
 Kathy A. Eisenberg wps/hk
 SUPERVISOR
 Dave W. Johnson wps/hk

Figure 3 — Capillary GC/MS RIC of 100-SLW-6 (Propionaldehyde)



CHRO1 F3921 ver 1 on UIC 802882 25-OCT-91 Elapsed: 00:17:18.5 939
 Sample PROPIONALDEHYDE Start: 1 00:12:56 1517
 Column 100-SLW-6
 Model: EI VDSMS LHM UP LR
 Oper: RMH / CLR Label under 1 > 700 Inlet 1
 Peak: 1000.00 min Baseline 1 0, 3 Masses: 10 > 310
 Area: 0, 4.00 Label 1 0, 48.00

Figure 4 — Capillary Gas Chromatogram of 100-SLW-6 (Propionaldehyde)

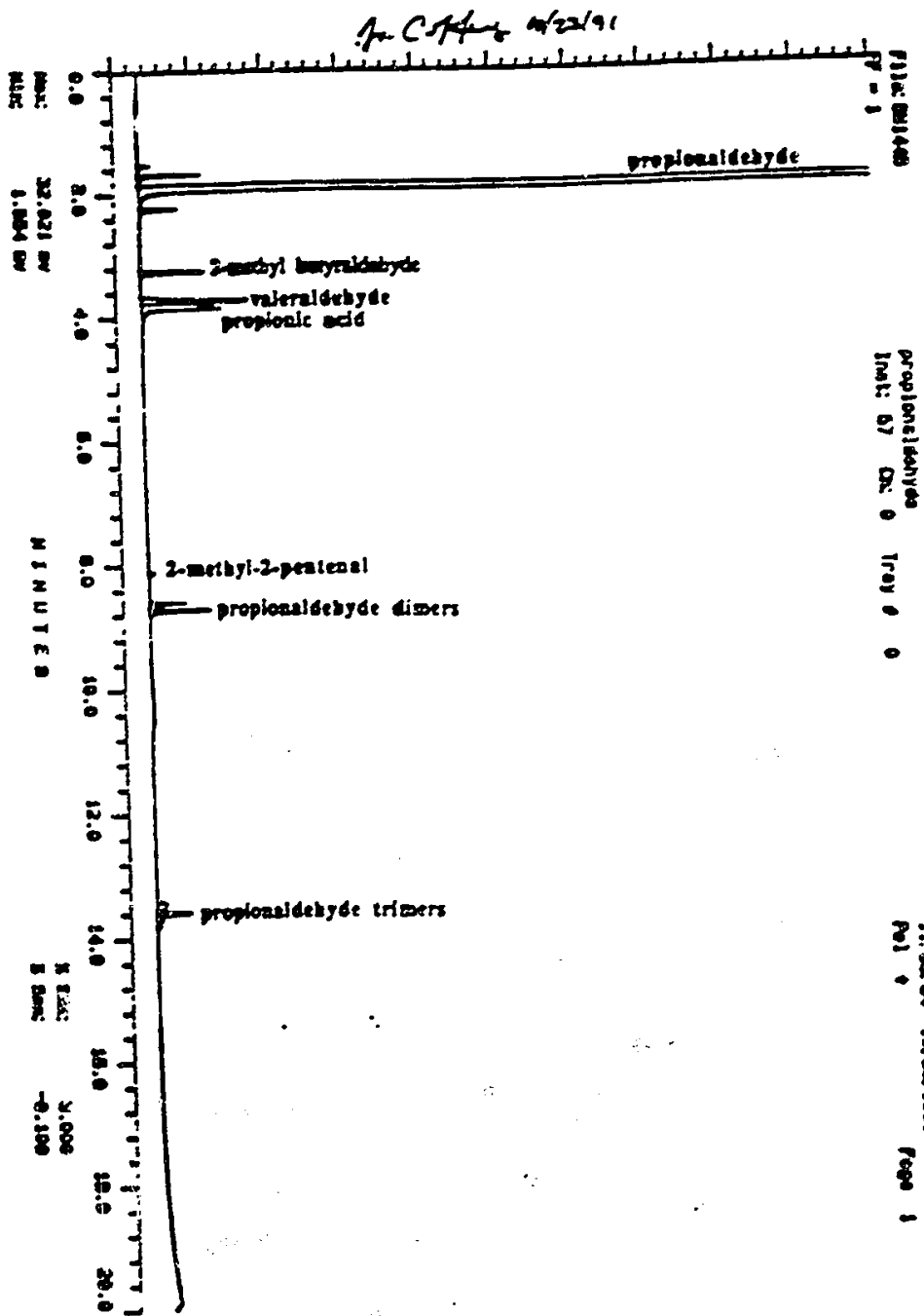
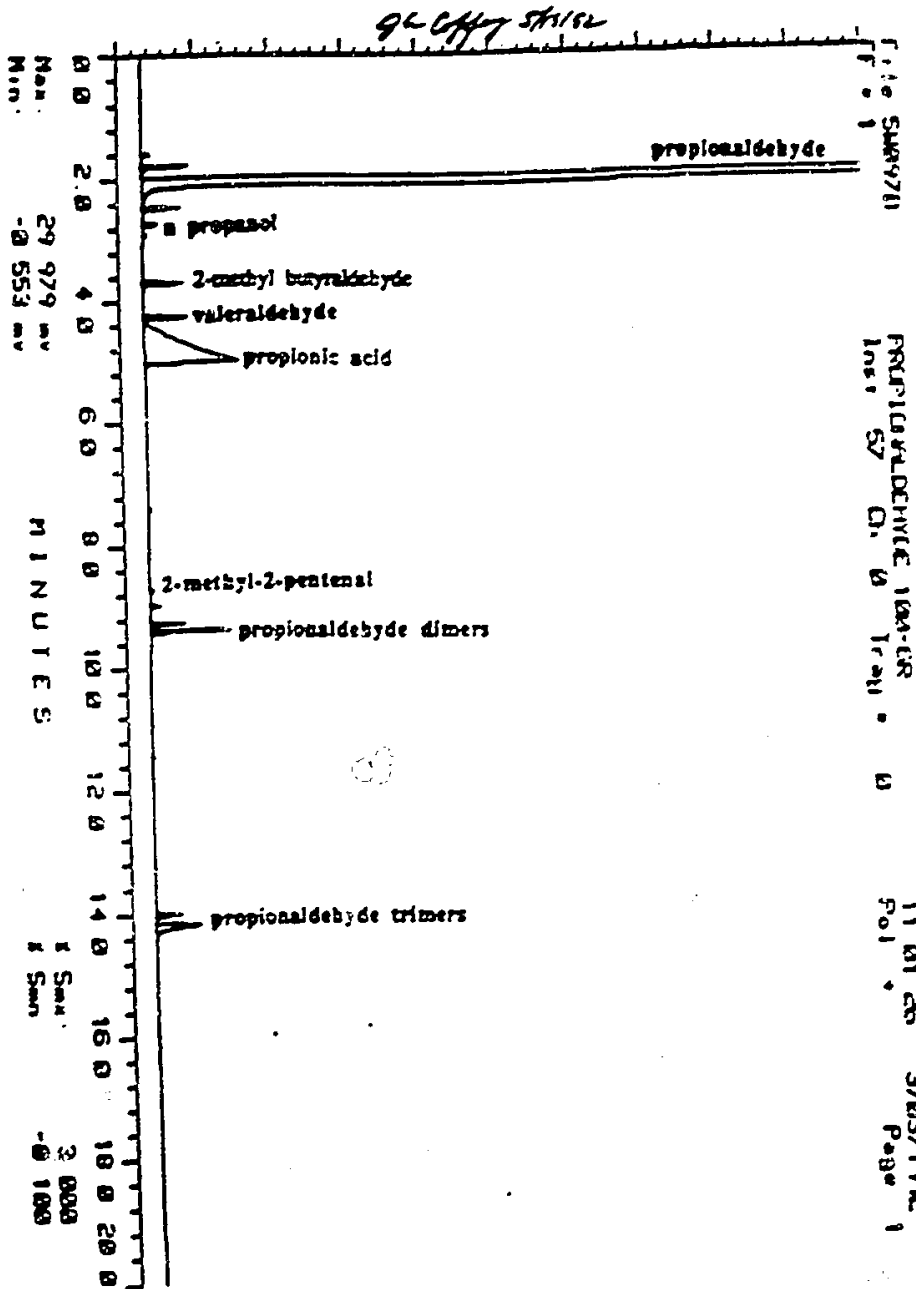


Figure 5 — Capillary Gas Chromatogram of 100-SLW-6R (Propionaldehyde)



APPENDIX 1 100-SLW-4 Protocol



PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

Title Propionaldehyde
Purpose Analytical Characterization of Sample(s) for Toxicology Studies at Busby Row Research Center (BRRC)
Study Number 100-SLW-4
Sponsor SOLVENTS AND COATING MATERIALS DIVISION (SCMD)
Union Carbide Chemicals and Plastics Company Inc. (UCC&P)
39 Old Ridgebury Road,
Danbury, Conn. 06817-0001
Testing Facility UCC&P Technical Center,
South Charleston, WV 25303 (Location 511)
Proposed Starting Date: Monday, October 14, 1991
Proposed Completion Date: December 14, 1991
Estimated Date of Final Report: January 14, 1992



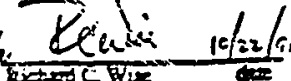
Test Substance(s) 100-SLW-4

Name	Propionaldehyde
Source	TS-2151011; UCC&P, SCMD, Texas City, Texas
CAS Registry No.	123-38-6
Description	Water-white, non-viscous liquid; suffocating odor
Purity	> 99 %
Health/Safety	Stable; highly toxic. MSDS available upon request
Storage Conditions	ambient conditions, away from heat

Study Design

- The test substance(s) will be characterized by:
- Verification of identity by proton- and carbon-NMR.
 - Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of 20.1 wt. %.
 - Quantitation of the identified impurities by capillary GC.

Reviewed and Approved by:

 Stephen L. Wellons GLP Study Director	date: 10/14/91	 Denise L. Johnson GLP Quality Assurance Unit (QAU) Representative	date: 10/14/91	 Richard C. Wise Manager of Product Safety, SCMD, Sponsor	date: 10/22/91
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This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented and signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: PROPIONALDEHYDE

Study No.: 100-SLW-4

Study Director: A.E. Gabany, B.S.

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

Date	Inspection Type	Date QAU Report Issued	
		To Study Director	To Management
Oct. 18, 1991	Protocol Compliance Review	Oct. 18, 1991	Oct. 18, 1991
Feb. 10, 1992	Laboratory Compliance Review	Feb. 10, 1992	May, 1992
Aug. 25, 1992	Final Report Compliance Review	Aug. 25, 1992	Aug 25, 1992

Denise L. Johnson 8-25-92
Denise L. Johnson | QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD¹ Rats

Anatomic Pathology Report

(21 Pages)

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SUMMARY

Young adult CD® male and female rats (15/sex/group) were exposed to propionaldehyde (CAS No. 123-38-6) vapor at concentrations of 0, 150, 750, or 1500 ppm. Exposures were conducted daily, 6 hours/day, for both males and females during a 2-week pre-mating period, and a 14-day (maximum) mating phase. The males continued to be exposed until scheduled sacrifice; a total of 52 exposures. The mated females were exposed daily through Day 20 of gestation only. The females were then allowed to deliver their litters naturally and raise their offspring until Day 4 of lactation.

All adult animals received a complete necropsy at the time of sacrifice, with selected tissues being saved and fixed for possible microscopic evaluation. On Postnatal Day 4, all pups were euthanized and discarded without pathologic evaluation. Organ weights were obtained at the time of necropsy for the adult animals. Microscopic examinations were performed on selected tissues of all parental rats from the control and high exposure groups. Subsequent to the initial evaluation, nasal tissues were evaluated from the intermediate and low exposure groups.

The kidneys in the high exposure concentration male rats were significantly heavier than controls relative to the total body weight. There were no gross lesions observed at necropsy that could be attributed to exposure to the propionaldehyde vapor. The only tissues that were affected microscopically by exposure to the vapor were in the nasal cavity. The olfactory epithelium in the anterior 2 sections of the cavity had evidence of vacuolization and atrophy, with the vacuolization primarily evident in the low and intermediate exposure groups and the atrophy seen primarily in the intermediate and high exposure groups. There was no no-observed-effect level (NOEL) seen for this tissue in this study. In addition to the effects seen in the olfactory epithelium, there was evidence of rhinitis and squamous metaplasia of the respiratory epithelium seen in some of the animals, primarily involving the intermediate and high exposure groups.

MATERIALS AND METHODS

Male and female CD® rats, purchased from Charles River Laboratories, Portage, Michigan, were exposed daily, 6 hours/day, 7 days/week to 0 (control), 150, 750, or 1500 ppm of propionaldehyde vapor. Fifteen rats/group/sex were randomly assigned to 1 of the 3 exposure groups or the control group. The exposure period included a 2-week pre-mating and a 14-day mating phase, and a period of gestation. Females were exposed only through Day 20 of gestation, while males continued to be exposed throughout the study.

Necropsy

On postnatal Day 4, the pups were euthanized and discarded without a pathologic examination. All adult rats were anesthetized with methoxyflurane and euthanized by severing their brachial vessels to permit exsanguination and received a complete necropsy.

The following tissues were saved in Bouin's fixative for microscopic examination:

testes
epididymides

The following tissues were saved in 10% neutral buffered formalin for microscopic examination:

gross lesions	brain
nasal turbinates	cerebral cortex
larynx	cerebellar cortex
trachea	medulla/pons
lungs	kidneys
heart	thymus
spleen	adrenals
liver	seminal vesicles (males)
	ovaries (females)

The following tissues were saved in 10% neutral buffered formalin, but were not processed for microscopic examination.

vagina (females)
uterus (females)
 corpus and cervix
pituitary

Lung sections included 2 coronal cuts through all lobes and mainstem bronchi.

The right kidney was sectioned transversely and the left was cut longitudinally.

The following tissues were weighed at necropsy:

liver	thymus
kidneys	testes
lungs	epididymides
	uterus

Tails were saved for animal identification purposes.

Histopathology

Microscopic examinations were performed on the tissues indicated above for male and female animals from the control and high exposure groups. Following the initial evaluation, the first 2 sections of nasal cavity were processed from the intermediate and low exposure groups for evaluation.

All tissues to be examined were paraffin embedded, sectioned at approximately 5 microns and stained with hematoxylin and eosin. Lesions were graded, when possible, into 5 categories (minimal, mild, moderate, marked and severe).

Statistics

The frequency of histologic lesions was compared between each exposure and control group using the Fisher's exact test. The probability value of < 0.05 (two-tailed) was used as the critical level of significance.

RESULTS AND DISCUSSION

Tables 1 through 4 include the organ weight data obtained at necropsy. Tables 1 and 3 include the absolute values for male and female rats, respectively, and Tables 2 and 4 include the organ weights relative to body weights for male and female rats, respectively. The only organ weights that were significantly increased were the kidney weights relative to total body weights for male rats in the high exposure concentration group. The reason for this increase could not be determined from the morphologic evaluation, but may have been due in part to the tighter values (lower standard deviation) for the kidney weights in the 1500 ppm group.

Tables 5 and 6 include the necropsy observations for the males sacrificed at Week 7 (Table 5) and the female rats (Table 6). Only those organs and tissues in which gross lesions were observed are included in the tables. There were no gross lesions that indicated an effect from the test substance administration.

Tables 7 and 8 include the microscopic diagnoses by grade for the male rats sacrificed at Week 7 and the female rats sacrificed at Week 5, respectively. The only organ in which there was an exposure-related effect was the nasal cavity, in which the anterior two sections had evidence of vacuolization and atrophy of the olfactory epithelium, with the vacuolization being evident in the lower exposure groups and the atrophy being evident in the higher exposure groups. There was rhinitis and occasional squamous metaplasia involving the respiratory epithelium in some of the rats as well, but the involvement of the olfactory epithelium was the more significant of the lesions. The effect was primarily observed in the dorsal portion of the nasal cavity from the anterior 2 sections. This selective effect, where more severe lesions were found involving the olfactory epithelium, has been reported to occur in rats exposed to acetaldehyde (Appleman, et al, 1982). The lesions observed with propionaldehyde were very similar to those reported for acetaldehyde. There were no other lesions that could be attributed to exposure to propionaldehyde vapor.

CONCLUSION

Male and female CD⁰ rats were exposed to propionaldehyde vapor at concentrations of 0 (control), 150, 750, or 1500 ppm, 6 hours/day, 7 days/week, for the duration of the study. At the termination of the study, animals were humanely euthanatized and subjected to a complete necropsy. Selected tissues were fixed and examined microscopically.

The kidneys from the high exposure concentration group male rats were significantly increased in weight relative to total body weight, but not in absolute values, the reason for which cannot be determined from the morphologic evaluation. The standard deviation for the kidney weights in the 1500 ppm group was smaller than for any other group and may have been responsible for the statistical flag. There were no gross lesions observed at necropsy that could be attributed to exposure to the propionaldehyde vapor. The only tissues that were affected microscopically by exposure to the vapor were in the nasal cavity. The olfactory epithelium in the anterior 2 sections of the cavity had evidence of vacuolization and atrophy, with the vacuolization primarily evident in the low and intermediate exposure groups and the atrophy seen primarily in the intermediate and high exposure groups. There was no NOEL seen for this tissue in this study. In addition to the effects seen in the olfactory epithelium, there was evidence of rhinitis and squamous metaplasia of the respiratory epithelium seen in some of the animals, primarily involving the intermediate and high exposure groups.

Pathologist:

E. H. Fowler
E. H. Fowler, DVM, Ph.D.
Diplomate, ACVP

4/5/93
Date

REFERENCE

Appelman, L. M., Woutersen, R. A., and Feron, V. J. (1982). Inhalation Toxicity of Acetaldehyde in Rats. I. Acute and Subacute Studies. *Toxicology*, 23, 293-307.

TABLE 1
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTION/DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT WEEK 7

		FO ADULT MALES			
GROUP: PPM		0	150	750	1500
HEART WEIGHT					
MEAN	54.1	430.4	446.4	431.0	
S.D.	11.11	43.56	31.52	35.03	
N	15	15	15	15	
LIVER					
MEAN	11.490	10.936	11.455	11.190	
S.D.	1.4926	1.1531	1.2211	1.3477	
N	15	15	15	15	
KIDNEYS					
MEAN	3.203	3.086	3.338	3.357	
S.D.	0.3994	0.3059	0.4671	0.3229	
N	15	15	15	15	
LUNGS					
MEAN	1.112	1.532	1.572	1.522	
S.D.	0.0709	0.1311	0.1417	0.1042	
N	14	15	15	15	
THYROID REGION					
MEAN	0.349	0.338	0.302	0.292**	
S.D.	0.0522	0.1064	0.0711	0.0577	
N	15	15	15	15	
EPIDIDYMIDES					
MEAN	1.319	1.236	1.236	1.253	
S.D.	0.1269	0.1849	0.1849	0.1000	
N	15	15	15	15	
TESTES					
MEAN	3.430	3.272	3.331	3.363	
S.D.	0.3192	0.4861	0.1552	0.2000	
N	15	15	15	15	

** Significantly different from control group (p < .01)

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT WEEK 7

		100 ADULT MALES			
GROUP: PPM	0	150	750	1500	
LIVER					
MEAN	2.528	2.543	2.563	2.591	
S.D.	0.1945	0.1392	0.1667	0.1668	
N	15	15	15	15	
KIDNEYS					
MEAN	0.706	0.722	0.727	0.780**	
S.D.	0.0662	0.0891	0.0853	0.0513	
N	15	15	15	15	
LUNGS					
MEAN	0.341	0.357	0.352	0.354	
S.D.	0.0292	0.0206	0.0264	0.0244	
N	14	15	14	15	
THYMIC REGION					
MEAN	0.077	0.079	0.078	0.060	
S.D.	0.0135	0.0248	0.0208	0.0140	
N	15	15	15	15	
EPIDIDYDES					
MEAN	0.294	0.288	0.285	0.293	
S.D.	0.0493	0.0422	0.0246	0.0365	
N	15	15	15	15	
TESTES					
MEAN	0.758	0.762	0.749	0.785	
S.D.	0.0674	0.1126	0.0816	0.0810	
N	15	15	15	15	
** Significantly different from control group (< .01)					

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)

		F0 ADULT FEMALES			
GROUP: PPM	0	150	750	1500	
FINAL BODY WEIGHT					
MEAN	296.4	295.4	288.4	283.6	
S.D.	23.29	19.58	15.1	12.49	
N	15	15	15	15	
LIVER					
MEAN	12.980	12.995	12.589	12.336	
S.D.	1.4890	1.5997	1.0985	1.1210	
N	15	15	15	15	
KIDNEYS					
MEAN	1.991	1.973	2.040	1.968	
S.D.	0.1760	0.2125	0.1821	0.1388	
N	15	15	15	15	
LUNGS					
MEAN	1.219	1.313	1.191	1.217	
S.D.	0.0502	0.2631	0.0823	0.1113	
N	15	15	15	15	
THYMIC REGION					
MEAN	0.240	0.225	0.189	0.214	
S.D.	0.0626	0.0437	0.0533	0.0620	
N	15	15	15	15	

None significantly different from control group

TABLE 4
 PROPRIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT

F0 ADULT FEMALES				
GROUP: PPM	0	150	750	1500
LIVER				
MEAN	4.377	4.393	4.364	4.347
S.D.	0.3472	0.3981	0.2909	0.3140
N	15	15	15	15
KIDNEYS				
MEAN	0.674	0.669	0.708	0.695
S.D.	0.0641	0.0703	0.0627	0.0519
N	15	15	15	15
LUNGS				
MEAN	0.414	0.445	0.414	0.429
S.D.	0.0357	0.0839	0.0290	0.0351
N	15	15	15	15
THYMIC REGION				
MEAN	0.092	0.076	0.066	0.076
S.D.	0.0224	0.0164	0.0184	0.0227
N	15	15	15	15

None significantly different from control group

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT WEEK 7
 FO ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
STOMACH					
CONTENTS ABNORMAL		3	0	0	0
LIVER					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	0	1	2
SIZE DECREASE		0	0	0	0
COLON					
PARASITE		1	0	0	0
SKIN					
SHAPE/CONTOUR CHANGE		5	4	7	2
ALOPECIA		0	0	0	1
SPLEEN					
ACCESSORY		1	0	0	0
LYMPH NO, L-MAN					
SIZE INCREASE		7	3	9	2
COLOR CHANGE, FOCAL/MULTIFOCAL		2	1	4	2
COLOR CHANGE, DIFFUSE		1	3	0	3
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	4	1	4
SIZE DECREASE		0	1	0	0
TESTES					
SIZE DECREASE		0	1	0	0
CONSISTENCY CHANGE		0	0	0	1
EPIDIDYMIDES					
NODULE		2	0	0	0
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		5	2	8	6
KIDNEYS					
DILATED PELVIS		0	0	0	0
GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM					

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF NECROPSY OBSERVATIONS

30 ADULT FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
STOMACH					
ULCERATED		0	0	0	1
CONTENTS ABNORMAL		0	0	0	1
LIVER					
COLOR CHANGE, DIFFUSE		0	0	1	0
COLON					
PALLOID		0	1	1	0
ADRENAL GL					
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	4	0
COLOR CHANGE, DIFFUSE		0	0	1	1
SIZE INCREASE		1	0	0	0
SKIN					
CRUST/SCAB/SCALE		0	1	0	0
SURFACE CHANGE		0	1	4	0
ALOPECIA		1	0	1	1
SPLEEN					
SIZE INCREASE		1	0	0	0
SHAPE/CONTOUR CHANGE		1	0	0	0
LYMPH ND, S-MAN					
SIZE INCREASE		6	4	2	0
COLOR CHANGE, FOCAL/MULTIFOCAL		0	0	1	0
LYMPH ND, MED					
COLOR CHANGE, DIFFUSE		0	1	0	0
THYMIC REGION					
SIZE DECREASE		0	0	2	1
OVARIES					
CYST		0	1	0	2
LUNGS					
COLOR CHANGE, DIFFUSE		2	0	0	0
COLOR CHANGE, FOCAL/MULTIFOCAL		5	4	6	5
KIDNEYS					
DILATED PELVIS		1	1	0	0
URETER					
DILATATION/DISTENTION		1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
HEART					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
STOMACH					
TOTAL NUMBER EXAMINED		3	0	0	0
EXAMINED, UNREMARKABLE		3	-	-	-
LIVER					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	15
LIPOSTOMATA					
PRESENT		1	-	-	0
ADRENAL GL					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	14
CORTICAL CELL VACUOLIZATION					
MILD		1	-	-	0
MODERATE		0	-	-	1
SKIN					
TOTAL NUMBER EXAMINED		5	0	0	3
EXAMINED, UNREMARKABLE		0	-	-	1
HYPERKERATOSIS					
MODERATE		3	-	-	1
MARKED		0	-	-	0
EPIDERMITIS					
MODERATE		1	-	-	1
MARKED		0	-	-	1
		1	-	-	0

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

None significantly different from control group

TABLE 7 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 MICE
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
SKIN (CONTINUED)					
FOLLICULITIS		4	-	-	0
MODERATE		2	-	-	0
MARKED		2	-	-	0
DERMAL FIBROSIS		1	-	-	0
MODERATE		1	-	-	0
SPLEEN					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	15
ACCESSORY SPLEEN		1	-	-	0
MILD		1	-	-	0
THYMIUS, SPLEEN					
TOTAL NUMBER EXAMINED		7	0	0	5
EXAMINED, UNREMARKABLE		6	-	-	1
HEMORRHAGE		2	-	-	3
MILD		1	-	-	1
MODERATE		1	-	-	1
MARKED		0	-	-	1
LYMPHOID HYPERPLASIA		7	-	-	3
MODERATE		3	-	-	2
MARKED		4	-	-	1
PLASMACYTOSIS		6	-	-	3
MILD		1	-	-	1
MODERATE		1	-	-	1
MARKED		3	-	-	1
SEVERE		1	-	-	0
THYMIUS REGION					
TOTAL NUMBER EXAMINED		15	0	-	15
EXAMINED, UNREMARKABLE		14	-	-	14

GROUP DESIGNATION: 1 is 0 PPM, 2 is 100 PPM, 3 is 750 PPM, 4 is 1500 PPM

None significantly different from control group

TABLE 7 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
THYMIC REGION (CONTINUED)					
HEMORRHAGE		2	-	-	1
MODERATE		2	-	-	1
BRAIN					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
TESTES					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	14
SEMINIFEROUS TUBULE ATROPHY					
MARKED		1	-	-	1
SEVERE		1	-	-	0
0		0	-	-	1
EPIDIDYMIDES					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	15
SPERM GRANULOMA					
MARKED		1	-	-	0
1		1	-	-	0
SEMINAL VESICLE					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
NASAL CAVITY					
TOTAL NUMBER EXAMINED		15	15	15	15
EXAMINED, UNREMARKABLE		15	3	0	0
RHINITIS					
MINIMAL		0	0	1	3
MILD		0	0	5	7
MODERATE		0	0	1	4

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

** Significantly different from control group (p < .01)

TABLE 7 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT WEEK 7
 F0 ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP			15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
NASAL CAVITY (CONTINUED)					
SQUAMOUS METAPLASIA		0	0	1	2
MILD		0	0	1	0
MODERATE		0	0	0	2
ATROPHY, OLFACTORY EPITHELIUM		0	2	10**	15**
MINIMAL		0	2	1	0
MILD		0	0	6	1
MODERATE		0	0	3	8
MARKED		0	0	0	6
VACUOLIZATION OF OLFACTORY EPITHELIUM		0	12**	14**	2
MINIMAL		0	0	2	0
MILD		0	4	3	0
MODERATE		0	2	2	0
MARKED		0	0	7	2
LARYNX					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
TRACHEA					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
LUNGS					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	15
ALVEOLAR MACROPHAGE CITOSIS		1	-	-	0
M		0	-	-	0
KIDNEYS					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		12	-	-	13

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

** Significantly different from control group (p < .01)

TABLE 7 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT WEEK 7
 FO ADULT MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
KIDNEYS (CONTINUED)					
NEPHRITIS, INTERSTITIAL		1	-	-	0
MILD		1	-	-	0
TUBULAR BASOPHILIA		3	-	-	2
MILD		1	-	-	0
MODERATE		1	-	-	2
MARKED		1	-	-	0

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

None significantly different from control group

TABLE 8
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

F0 ADULT FEMALES					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
HEART					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
STOMACH					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		-	-	-	1
LIVER					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
ADRENAL GL					
TOTAL NUMBER EXAMINED		15	-	-	-
EXAMINED, UNREMARKABLE		14	-	-	1
MINERALIZATION					
MARKED		1	-	-	-
CORTICAL CELL HYPERTROPHY					
MODERATE		0	-	-	1
SKIN					
TOTAL NUMBER EXAMINED		1	0	0	1
EXAMINED, UNREMARKABLE		1	-	-	1
SPLEEN					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
LYMPH ND, S-MAN					
TOTAL NUMBER EXAMINED		6	0	0	0
LYMPHOID HYPERPLASIA					
MILD		6	-	-	-
MODERATE		1	-	-	-
MARKED		3	-	-	-
		2	-	-	-

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

None significantly different from control group

TABLE 8 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

F0 ADULT FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
LYMPH ND, S-MAN (CONTINUED)					
PLASMACYTOSIS		6	-	-	-
MARKED		5	-	-	-
SEVERE		1	-	-	-
THYMIC REGION					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
BRAIN					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
OVARIES					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
NASAL CAVITY					
TOTAL NUMBER EXAMINED		15	15	15	15
EXAMINED, UNREMARKABLE		15	0	0	0
RHINITIS					
MINIMAL		0	1	6*	1
MILD		0	0	0	0
MODERATE		0	0	6	1
ATROPHY, OLFACTORY EPITHELIUM					
MINIMAL		0	0	1	0
MILD		0	0	1	0
MODERATE		0	0	0	6
MARKED		0	0	0	9
NECROSIS OF OLFACTORY EPITHELIUM					
MODERATE		0	0	0	1

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)

TABLE 8 (Continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

F0 ADULT FEMALES					
	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
NASAL CAVITY (CONTINUED)					
VACUOLIZATION OF OLFACTORY EPITHELIUM		0	15**	15**	0
MINIMAL		0	8	0	0
MILD		0	7	7	0
MODERATE		0	0	8	0
LARYNX					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
TRACHEA					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		15	-	-	15
LUNGS					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		14	-	-	14
ALVEOLAR HISTIOCYTOSIS		0	-	-	1
MILD		0	-	-	1
PERIVASCULAR INFILTRATE(S)		1	-	-	1
MINIMAL		1	-	-	0
MILD		0	-	-	1
PNEUMONITIS, INTERSTITIAL		0	-	-	1
MILD		0	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED		15	0	0	15
EXAMINED, UNREMARKABLE		11	-	-	12
HYDRONEPHROSIS		1	-	-	0
MARKED		1	-	-	0

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

** Significantly different from control group (p < .01)

TABLE 8 (Continued)
 PROPIONALDZHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

FO ADULT FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		15	15	15	15
NUMBER OF ANIMALS SACRIFICED		15	15	15	15
KIDNEYS (CONTINUED)					
MINERALIZATION		2	-	-	3
MINIMAL		0	-	-	1
MILD		1	-	-	1
MODERATE		1	-	-	1
NEPHRITIS, INTERSTITIAL		2	-	-	0
MILD		1	-	-	0
MODERATE		1	-	-	0
TUBULAR BASOPHILIA		2	-	-	0
MINIMAL		1	-	-	0
MILD		1	-	-	0
URETER					
TOTAL NUMBER EXAMINED		1	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-

GROUP LEGEND: 1 is 0 PPM, 2 is 150 PPM, 3 is 750 PPM, 4 is 1500 PPM

None significantly different from control group

**Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD⁰ Rats**

Clinical Pathology Report

(8 Pages)

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SUMMARY

Male CD® rats were exposed to propionaldehyde (0, 150, 750, or 1500 ppm) by vapor inhalation for 6 hours/day, 7 days/week during a 2-week pre-mating phase, a 14-day mating phase, and continuing for a total of 52 exposures. Blood samples were collected for clinical pathology evaluation at sacrifice (Week 7).

Male rats in the 1500 ppm group had an increase in total erythrocyte count with an increase in hemoglobin and hematocrit values indicating a possible slight dehydration effect. Monocytes were increased in male rats in the 1500 ppm group, indicating some irritation. No exposure-related differences in clinical chemistry determinations were observed in male animals from any exposure group.

MATERIALS AND METHODS

In this study, male CD® rats were exposed to propionaldehyde by vapor inhalation for 6 hours/day, 7 days/week for a total of 52 exposures. Target concentrations were 0 (control), 150, 750, and 1500 ppm.

Blood samples for all clinical pathology analyses were collected by retroorbital bleeding from methoxyflurane anesthetized rats at sacrifice. All rats were fasted prior to bleeding. All analyses were performed in a predetermined random order.

Hematology

Approximately 2.0 ml of blood was collected into blood collection tubes containing EDTA as an anticoagulant for the hematologic determinations.

The following hematologic parameters were measured or calculated: leukocyte count, erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count. These hematologic analyses were performed on an ABX MINOS™ VET (ABX, Inc., France) on the day of the sample collection. Commercially available quality control samples (Minitrol™, Roche Diagnostic Systems, Inc., Nutley, NJ) were analyzed prior to the animal samples. Blood smears for differential leukocyte counts were prepared and evaluated for all animals.

Serum Clinical Chemistry

Approximately 2.0 ml of blood was collected into blood collection tubes without anticoagulant for serum chemistry analysis.

The following clinical chemistry analyses were performed:

- | | |
|-------------------------------------|-------------------------------------|
| 1. glucose | 8. gamma glutamyl transferase (GGT) |
| 2. urea nitrogen | 9. calcium |
| 3. creatinine | 10. phosphorus |
| 4. total protein | 11. sodium |
| 5. total bilirubin | 12. potassium |
| 6. aspartate aminotransferase (AST) | 13. chloride |
| 7. alanine aminotransferase (ALT) | |

The Monarch™ 2000 Chemistry System (Instrumentation Laboratory, Lexington, MA) was used to analyze serum concentrations of glucose, urea nitrogen, creatinine, total protein, total bilirubin, AST, ALT, GGT, calcium, phosphorus, sodium, potassium, and chloride. Serum controls (SeraChem® Levels 1 and 2, Instrumentation Laboratory, Lexington, MA) were assayed with each run of samples.

Data Analyses

The results of the clinical pathology analyses for continuous variables were intercompared for the experimental groups and the control group by use of Levene's test for equality of variance, analysis of variance (ANOVA), and t-tests. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparison.

GGT and all of the parameters of the leukocyte differential count, except segmented neutrophils and lymphocytes, were considered nonparametric data but reported as means and standard deviations on the tables. These nonparametric data were statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U test when appropriate.

All statistical analyses were performed using BMDP Statistical Software (Dixon, 1990). For all statistical tests the probability value of $p < 0.05$ (two-tailed) was used as the critical level of significance.

RESULTS AND DISCUSSION

All references of differences in group mean values in the following text refer to comparisons of statistically significant differences between the treatment group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

Hematology

The summary results of hematology determinations for male rats are presented in Table 1. The individual results for these animals are found in Appendix 7.

A slight increase in total erythrocytes was observed in the 1500 ppm group. A slight increase in hemoglobin and hematocrit values, although not statistically significant, was also noted in male animals in the 1500 ppm group. These results suggest a possible dehydration effect. Monocytes were increased in male rats in the 1500 ppm group, indicating some slight irritation.

Clinical Chemistry

The summary results of serum clinical chemistry determinations for male rats are presented in Table 2. The individual results for these animals are found in Appendix 7.

No exposure-related differences in clinical chemistry determinations were observed in male animals from any exposure group.

CONCLUSION

A slight increase in total erythrocytes was observed in the 1500 ppm group indicating a possible slight dehydration effect of the exposure. Monocytes were increased in male rats in the 1500 ppm group, indicating some irritation. No exposure-related differences in clinical chemistry determinations were observed in male animals from any exposure group.

Clinical Pathologist:

Douglas A. Neptun
Douglas A. Neptun, B.S., CC(NRCC), MT(ASCP)

4/5/53
Date

REFERENCE

Dixon, W. J. BMDP Statistical Software. University of California Press, Berkeley, CA, 1990.

TABLE 1
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF HEMATOLOGY
 WEEK 7

		F0 ADULT MALES			
GROUP: PPM	0	150	750	1500	
ERYTHROCYTES (10⁶/μl)					
MEAN	8.41	8.50	8.36	8.78*	
S.D.	0.274	0.305	0.378	0.365	
N	10	10	10	10	
HEMOGLOBIN (g/dl)					
MEAN	16.7	17.1	16.7	17.4	
S.D.	0.53	0.64	0.79	0.86	
N	10	10	10	10	
HEMATOCRIT (%)					
MEAN	44.1	44.8	44.0	45.5	
S.D.	1.27	1.36	1.62	1.70	
N	10	10	10	10	
MCV (μm³)					
MEAN	52.	53.	53.	52.	
S.D.	1.5	1.4	1.3	1.7	
N	10	10	10	10	
MCH (pg)					
MEAN	19.8	20.1	20.0	19.8	
S.D.	0.55	0.53	0.65	0.84	
N	10	10	10	10	
MCHC (g/dl)					
MEAN	37.8	38.2	38.0	38.2	
S.D.	0.80	0.93	0.67	0.76	
N	10	10	10	10	
PLATELETS (10³/μl)					
MEAN	745.	760.	733.	730.	
S.D.	73.8	106.8	62.8	79.9	
N	10	9	10	10	
LEUKOCYTES (10³/μl)					
MEAN	10.4	9.6	9.6	11.4	
S.D.	1.73	2.21	2.68	3.31	
N	10	10	10	10	
SEGMENTED NEUTROPHILS (cells/μl)					
MEAN	2658.	1636.	2682.	2294.	
S.D.	1516.1	603.5	1340.7	1355.8	
N	10	10	10	10	
LYMPHOCYTES (cells/μl)					
MEAN	7074.	7381.	6343.	8180.	
S.D.	1266.0	2161.0	1596.7	2220.2	
N	10	10	10	10	
MONOCYTES (cells/μl)					
MEAN	437.	389.	440.	723.*	
S.D.	241.2	190.8	332.9	315.8	
N	10	10	10	10	

* Significantly different from control group (p < .05)

TABLE 1 (continued)
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD^C RATS
 SUMMARY OF HEMATOLOGY
 WEEK 7

		F0 ADULT MALES			
GROUP: PPM	0	150	750	1500	
BASOPHILS (cells/μl)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	
EOSINOPHILS (cells/μl)					
MEAN	211.	174.	106.	164.	
S.D.	142.2	130.7	89.	89.8	
N	10	10	10	10	
BANDED NEUTROPHILS (cells/μl)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	
LARGE MONOCYTES (cells/μl)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	
IMMATURE GRANULOCYTES (cells/μl)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	
IMMATURE ERYTHROCYTES (cells/μl)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	
NUCLEATED RBCs (cells/100 WECs)					
MEAN	0.	0.	0.	0.	
S.D.	0.0	0.0	0.0	0.0	
N	10	10	10	10	

None significantly different from control group

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 SUMMARY OF CLINICAL CHEMISTRY
 WEEK 7

GROUP: PPM	F0 ADULT MALES			
	0	150	750	1500
GLUCOSE (g/l)				
MEAN	1.21	1.17	1.20	1.17
S.D.	0.109	0.147	0.110	0.086
N	10	10	10	10
UREA NITROGEN (mg/l)				
MEAN	150.	163.	168.	154.
S.D.	17.6	20.3	21.9	17.3
N	10	10	10	10
CREATININE (mg/l)				
MEAN	7.	7.	8.	7.
S.D.	0.7	0.7	1.1	0.9
N	10	10	10	10
TOTAL PROTEIN (g/l)				
MEAN	67.	66.	67.	67.
S.D.	4.6	3.1	3.8	3.6
N	10	10	10	10
TOTAL BILIRUBIN (mg/l)				
MEAN	2.	2.	2.	2.
S.D.	0.0	0.0	0.0	0.3
N	10	10	10	10
CALCIUM (mg/l)				
MEAN	95.	95.	95.	97.
S.D.	2.2	3.5	1.3	2.1
N	10	10	10	10
INORGANIC PHOSPHORUS (mg/l)				
MEAN	66.	63.	62.	64.
S.D.	4.9	5.0	4.6	8.4
N	10	10	10	10
SODIUM (mmol/l)				
MEAN	142.	142.	141.	141.
S.D.	1.9	1.7	1.9	1.2
N	10	10	10	10
POTASSIUM (mmol/l)				
MEAN	5.4	5.2	5.3	5.4
S.D.	0.41	0.50	0.28	0.35
N	10	10	10	10
CHLORIDE (mmol/l)				
MEAN	110.	109.	108.	109.
S.D.	1.7	1.5	0.8	1.6
N	10	10	10	10
ASPARTATE AMINOTRANSFERASE (IU/l)				
MEAN	68.	64.	76.	70.
S.D.	8.7	8.3	11.2	10.5
N	10	10	10	10
ALANINE AMINOTRANSFERASE (IU/l)				
MEAN	31.	33.	33.	32.
S.D.	4.1	3.9	6.0	6.9
N	10	10	10	10
γ-Glutamyl Transferase (IU/l)				
MEAN	4.	4.	4.	4.
S.D.	0.7	0.0	0.4	0.5
N	10	10	10	10

None significantly different from control group

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD² Rats

Individual Animal Data: In-Life

(28 Pages)

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TABLE 1
PROPIONALDERIVIDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

ABBREVIATIONS

INDIVIDUAL ANIMAL DATA: IN-LIFE

Abbreviations for the locations of clinical signs appear in parentheses next to the clinical signs in the following tables. The number included with the abbreviation is the number of times that clinical sign for that location was entered into the computer for that animal during the course of the study. The following is a list of three letter abbreviations for locations of clinical signs that may appear in this appendix.

ABD ABDOMEN	LHL LEG-HIND-LEFT
ANS ANUS	LHR LEG-HIND-RIGHT
AXB AXILLA-BOTH	LNS LOCATION NOT SPECIFIED
AXL AXILLA-LEFT	MTH MOUTH
AXR AXILLA-RIGHT	MUL MULTIPLE AREAS, NOS*
ECK BACK	NCK NECK
EDY ENTIRE BODY	NSE NOSE
CHS CHEST	PAL PAWS-ALL
EAB EAR-BOTH	FFB PAW-FORE-BOTH
EAL EAR-LEFT	PFL PAW-FORE-LEFT
EAR EAR-RIGHT	FFR PAW-FORE-RIGHT
ELB EYELID-BOTH	PHB PAW-HIND-BOTH
ELL EYELID-LEFT	PHL PAW-HIND-LEFT
ELR EYELID-RIGHT	PHR PAW-HIND-RIGHT
EYB EYE-BOTH	PNS PENIS
EVL EYE-LEFT	SCR SCROTUM
EYR EYE-RIGHT	SDB SIDE-BOTH
FAC FACE	SDL SIDE-LEFT
GEN GENITAL	SDR SIDE-RIGHT
HED HEAD	SHB SHOULDER-BOTH
HFB HIP-BOTH	SHL SHOULDER-LEFT
HPL HIP-LEFT	SHR SHOULDER-RIGHT
HPR HIP-RIGHT	TAL TAIL
INB INGUINAL-BOTH	TEE TEETH
INL INGUINAL-LEFT	TRA TREATMENT AREA
INR INGUINAL-RIGHT	TSB TESTIS-BOTH
LAL LEGS-ALL	TSL TESTIS-LEFT
LFB LEG-FORE-BOTH	TSR TESTIS-RIGHT
LFL LEG-FORE-LEFT	VAG VAGINA
LFR LEG-FORE-RIGHT	* NOS NOT OTHERWISE SPECIFIED
LHB LEG-HIND-BOTH	

TABLE 1 (Continued)
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

ABBREVIATIONS

INDIVIDUAL ANIMAL DATA: IN-LIFE

The following is a list of abbreviations or words that may appear in this appendix in reference to individual body weight or food consumption value.

- r/s = indicates that the animal was removed from the consumption period due to spillage.
- r/e = indicates that the animal was removed from the consumption period due to excreta in the feeder
- r/o = indicates that the animal was removed from the consumption period for reasons specified in the raw data.
- r/dead = indicates that the animal was removed from the consumption period because it died or was sacrificed during the period in which this abbreviation appears.
- dead = indicates that the animal died prior to the period in which this word appears.
- sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.
- a = combined interval value removed due to removal of at least one individual interval value (see individual interval footnotes).
- no bwt = no body weights were collected because the animal was in gestation.
- r = data not collected during mating period.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD® RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 PPM	28200	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28171	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28156	NORMAL	53	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	43	PERINASAL ENCRUSTATION
	28173	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28191	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28162	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28153	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28155	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28198	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
28178	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
	SKIN	2	27- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)	
28201	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
28180	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
28159	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
	SKIN	2	17- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)	
28167	NORMAL	53	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
	SKIN	1	52	RAISED AREAS (RED AND OR BROWN) (TAL 1)	
28174	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
150 PPM	28184	NORMAL	53	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	1	17	RAISED AREAS (RED AND OR BROWN) (TAL 1)
	28187	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
	FATE	1	52	SCHEDULED SACRIFICE	

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
150 PPM	28195	NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	17-52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28181	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28185	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28199	NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	17-52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28150	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28210	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28212	NORMAL	51	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	1	LACRIMATION (EYE 1)
	750 PPM	28194	NORMAL	2	18-52
		SKIN	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28168		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28160		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28169		NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	17-52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
28188		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28193		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28146		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28203		NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
28149	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
28190	NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
	SKIN	2	18-52	RAISED AREAS (RED AND OR BROWN) (TAL 2)	
28192	NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
750 PPM	28192	SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28211	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28176	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28209	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28182	SKIN	2	17- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
		NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28186	SKIN	2	17- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
		NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
	29147	FATE	1	52	SCHEDULED SACRIFICE
	28158	NORMAL	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	10	22- 31	EXCORIATED (PFB 10)
	28208	NORMAL	51	0- 51	ALOPECIA (PFB 10)
		FATE	1	52	SCHEDULED SACRIFICE
1500 PPM	28148	SKIN	3	18- 52	RAISED AREAS (RED AND OR BROWN) (TAL 3)
		NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28197	SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
		NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	44- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28196	NORMAL	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28153	SKIN	2	17- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
		NORMAL	22	0- 20	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	32	21- 52	ALOPECIA (PFB 32)
	28157	NORMAL	6	21- 26	EXCORIATED (PFL 6)
		FATE	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
	28166	NORMAL	1	52	SCHEDULED SACRIFICE
	28189	FATE	54	0- 52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		NORMAL	1	52	SCHEDULED SACRIFICE
	FATE	52	0- 51	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	SKIN	1	52	SCHEDULED SACRIFICE	
	SKIN	2	50- 52	RAISED AREAS (RED AND OR BROWN) (TAL 2)	

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1500 PPM	28207	NORMAL	46	0-44	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	8	45-52	ALOPECIA (PFB 8)
	28179	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		BODY	9	44-52	URINE STAINS
	28214	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
	28213	NORMAL	31	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	49	PERINASAL ENCRUSTATION
		SKIN	22	27-48	ALOPECIA (PFB 22)
	28205	NORMAL	53	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	17	PERINASAL ENCRUSTATION
		ORAL/DENTAL	1	17	PERIORAL WETNESS
	28206	NORMAL	52	0-51	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	52	SCHEDULED SACRIFICE
		SKIN	2	17-52	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28172	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS
	FATE	1	52	SCHEDULED SACRIFICE	
28183	NORMAL	53	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
	EYES/EARS/NOSE	1	2	LACRIMATION (EVL 1)	
28202	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	
28204	NORMAL	54	0-52	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	52	SCHEDULED SACRIFICE	

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

WEEK	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)							
		F0 ADULT MALES GROUP: 0 PPM							
		0	1	2	3	4	5	6	7
	28200	320.1	342.8	350.9	376.7	391.1	405.3	389.8	379.5
	28171	328.4	362.9	375.9	397.7	423.2	448.3	465.8	453.7
	28156	333.8	371.3	390.7	423.9	440.6	461.4	480.6	468.6
	28173	337.1	356.2	367.6	390.5	405.8	415.5	423.0	410.5
	28191	331.9	349.9	358.4	378.1	396.3	409.8	412.8	400.3
	28162	346.8	377.1	401.3	431.8	455.4	479.0	488.1	480.0
	28153	348.5	375.1	390.8	417.2	436.4	450.7	458.5	449.2
	28155	354.2	383.2	403.9	440.5	473.1	488.7	505.1	492.5
	28198	344.7	354.1	370.1	383.2	403.0	403.2	418.2	402.2
	28178	356.1	372.6	393.4	410.9	426.8	451.9	467.1	453.8
	28201	365.6	385.6	406.6	424.2	445.1	460.0	480.6	464.6
	28180	358.4	387.3	416.6	437.1	463.5	485.4	503.9	502.3
	28159	371.3	418.8	445.8	472.9	497.8	528.4	544.1	530.2
	28167	363.7	380.9	409.0	426.7	440.1	457.4	473.4	460.6
	28174	377.5	395.1	408.7	435.4	462.2	487.4	475.7	463.1
MEAN		349.2	374.2	392.6	416.4	437.4	455.5	465.8	454.1
S.D.		16.72	19.45	24.87	27.02	30.39	35.82	40.49	41.21
N		15	15	15	15	15	15	15	15

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

WEEK	INDIVIDUAL BODY WEIGHT (GRAMS)							
	FO ADULT MALES GROUP: 150 PPH							
	0	1	2	3	4	5	6	7
ANIMAL								
28184	323.5	341.2	354.4	383.7	388.0	400.2	403.4	378.3
28187	323.6	326.6	332.7	351.5	361.4	369.1	373.6	360.5
28195	329.2	346.0	358.5	375.5	400.4	418.2	431.9	419.2
28181	332.7	342.8	356.9	384.3	400.2	421.0	423.5	405.5
28165	337.2	351.5	349.3	369.4	379.4	394.9	379.7	372.3
28199	339.8	360.7	370.9	390.5	412.7	429.2	437.9	433.2
28150	345.7	373.9	394.8	419.1	440.3	457.8	467.6	453.9
28210	342.6	362.6	378.2	393.4	413.9	427.4	435.8	423.9
28212	349.1	372.6	378.8	399.0	425.0	440.1	458.5	445.6
28194	348.0	366.3	383.0	403.7	429.4	448.1	457.3	440.0
28168	361.5	380.4	390.1	429.3	444.8	455.1	456.0	434.5
28160	362.8	395.0	412.3	433.3	456.5	478.2	504.2	490.2
28169	360.8	383.3	401.4	416.9	429.8	446.4	460.2	446.3
28188	374.3	414.9	438.3	475.0	502.2	522.4	542.2	530.5
28193	356.3	369.5	383.9	397.4	413.6	427.7	433.9	422.4
MEAN	345.8	365.8	378.9	401.5	419.8	435.7	444.4	430.4
S.D.	15.25	22.70	26.91	30.20	34.17	36.38	43.20	43.56
N	15	15	15	15	15	15	15	15

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS

WEEK	INDIVIDUAL BODY WEIGHT (GRAMS)								
	0	1	2	3	4	5	6	7	
ANIMAL									
28146	327.5	358.1	377.7	390.1	411.5	435.9	441.8	428.8	
28203	334.2	359.7	375.3	408.3	428.7	453.6	456.4	443.4	
28149	350.8	378.5	395.0	417.8	433.7	450.0	465.6	452.1	
28190	328.3	337.5	341.2	356.2	369.3	379.1	376.6	368.5	
28192	343.9	356.4	378.1	407.2	431.8	445.6	462.5	443.5	
28211	341.0	366.9	379.6	400.0	418.5	431.6	447.8	439.7	
28176	343.1	358.9	379.7	399.5	417.1	432.6	443.3	427.9	
28209	343.2	356.8	365.9	395.2	417.9	425.8	432.0	413.8	
28182	350.4	370.8	385.8	419.8	451.3	468.8	483.1	466.8	
28186	350.0	370.4	380.9	407.6	422.5	442.7	456.8	440.9	
28147	352.2	378.4	387.8	415.4	434.5	452.2	446.4	430.4	
28158	361.3	391.8	405.0	449.4	461.6	484.9	503.2	498.0	
28208	366.3	379.5	402.7	423.1	443.0	464.7	485.9	467.8	
28148	362.5	389.0	405.5	430.2	453.1	467.8	484.5	477.7	
28197	371.0	392.1	406.0	439.2	467.0	479.5	502.4	485.7	
MEAN	348.4	369.7	384.4	410.6	430.8	448.2	459.2	446.4	
S.D.	13.09	15.49	17.39	22.19	24.03	26.09	31.86	31.52	
N	15	15	15	15	15	15	15	15	

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

WEEK	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)							
		0	1	2	3	4	5	6	7
		FO ADULT MALES GROUP: 1500 PPM							
		318.1	335.0	347.1	368.6	386.1	398.6	401.0	386.0
	28196	325.1	338.6	339.2	368.0	393.2	417.7	439.4	425.7
	28163	333.5	351.2	372.2	389.1	404.8	415.7	421.7	412.2
	28157	331.8	350.2	364.3	397.0	415.3	424.9	430.6	410.5
	28166	339.3	359.1	366.6	389.9	411.0	414.4	411.4	389.6
	28189	342.1	362.4	376.8	405.1	426.4	444.5	456.7	445.3
	28207	356.1	386.1	415.2	455.6	481.1	517.7	530.5	507.9
	28179	349.1	363.0	368.8	388.6	405.2	417.4	430.3	413.2
	28214	343.1	359.2	375.4	399.9	411.9	439.6	465.8	448.1
	28213	360.0	390.6	412.4	441.6	462.4	480.3	498.0	485.3
	28206	347.1	366.2	374.7	391.4	404.6	427.4	420.1	405.6
	28172	359.3	363.6	373.7	402.2	417.3	426.9	439.3	421.3
	28183	360.7	376.1	397.5	405.6	422.1	429.9	432.9	402.0
	28202	375.3	403.6	428.3	447.7	462.8	472.2	467.8	464.3
	28204	372.7	387.7	413.8	429.5	446.4	449.5	460.8	447.6
	MEAN	347.6	366.2	381.1	405.3	423.4	438.2	447.1	431.0
	S.D.	16.65	19.44	25.72	26.79	27.60	31.03	34.08	35.03
	N	15	15	15	15	15	15	15	15

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 FO ADULT MALES GROUP: 0 PPM

WEEK	1	2	4	5	6	7
ANIMAL						
28200	24.5	23.9	F	25.9	21.0	25.1
28171	26.3	27.0	F	28.5	29.5	29.3
28156	28.4	27.8	F	r/s	29.7	30.1
28173	24.5	23.9	F	24.9	24.6	25.0
28191	23.3	23.6	F	25.7	25.0	24.8
28162	26.7	27.0	F	29.4	26.7	27.9
28153	25.9	25.7	F	27.8	26.3	28.6
28155	27.0	26.4	F	29.5	28.8	29.5
28198	27.0	r/s	F	23.6	25.1	25.8
28178	26.0	26.3	F	27.8	27.6	28.4
28201	27.5	26.8	F	28.8	30.3	31.0
28180	27.6	27.1	F	29.7	29.7	30.7
28159	30.1	31.2	F	32.2	32.4	31.5
28167	25.3	26.2	F	26.7	27.7	27.1
28174	26.7	26.3	F	31.5	25.1	26.0
MEAN	26.5	26.4		28.0	27.3	28.1
S.D.	1.68	1.91		2.46	2.90	2.31
N	15	14		14	15	15

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT MALES GROUP: 150 PPM

WEEK	1	2	4	5	6	7
ANIMAL						
28184	23.7	23.9	F	25.9	23.9	24.8
28187	19.5	19.3	F	21.6	20.9	21.5
28195	22.6	F/S	F	26.8	26.3	26.5
28181	21.9	22.2	F	25.7	24.9	24.1
28165	23.1	23.8	F	25.5	20.6	23.2
28199	23.8	23.5	F	27.0	26.0	26.5
28150	27.5	27.9	F	30.8	30.1	31.1
28210	26.2	F/S	F	28.9	26.4	27.0
28212	25.4	26.0	F	26.2	26.9	26.5
28194	25.9	26.3	F	27.3	26.4	25.7
28168	25.2	F/S	F	F/S	27.2	28.2
28160	29.6	28.6	F	F/S	32.4	31.7
28169	27.1	27.2	F	28.6	28.2	28.8
28188	29.6	29.9	F	30.4	31.6	30.5
28193	25.1	25.8	F	26.4	27.1	28.1
MEAN	25.1	25.4		27.0	26.6	27.0
S.D.	2.78	2.97		2.37	3.30	2.89
N	15	12		13	15	15

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT MALES GROUP: 750 PPM

WEEK	1	2	4	5	6	7
ANIMAL						
28146	29.5	28.1	F	r/s	23.7	29.8
28203	26.0	25.3	F	27.7	26.8	26.0
28149	27.7	27.6	F	28.3	28.0	28.5
28190	21.2	19.5	F	23.1	21.5	24.0
28192	25.3	25.6	F	27.7	27.4	27.8
28211	25.7	25.7	F	26.9	27.6	28.3
28176	26.1	26.8	F	r/s	27.8	27.6
28209	24.7	24.7	F	r/s	26.6	27.4
28182	27.1	r/s	F	r/s	31.1	28.7
28186	27.3	r/s	F	28.7	28.4	28.9
28147	27.2	r/s	F	28.7	26.8	28.4
28158	26.7	25.9	F	29.2	27.8	29.1
28208	24.7	25.9	F	28.2	29.9	28.0
28148	25.3	25.5	F	28.2	27.9	27.6
28197	27.4	24.9	F	29.0	29.9	30.1
MEAN	26.1	25.4		27.7	27.8	27.9
S.D.	1.88	2.12		1.74	2.19	1.43
N	15	12		10	15	15

TABLE 4
 PROPRIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

WEEK	ANIMAL	INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)						
		1	2	4	5	6	7	
	28196	22.0	21.5	F	24.7	23.5	23.7	
	28163	23.2	21.7	F	26.7	27.3	26.5	
	28157	24.2	24.0	F	25.1	24.7	25.3	
	28166	23.1	23.9	F	26.9	25.2	25.5	
	28189	23.6	22.9	F	24.5	21.9	23.1	
	28207	25.3	F/S	F	28.2	26.9	26.7	
	28179	27.6	29.2	F	34.1	33.2	35.2	
	28214	24.7	24.2	F	26.8	25.3	25.7	
	28213	22.3	23.0	F	27.3	28.6	26.7	
	28205	26.0	26.8	F	28.3	27.8	26.7	
	28206	24.0	24.1	F	26.5	23.0	24.5	
	28172	24.0	20.3	F	25.5	24.9	25.7	
	28183	25.7	26.0	F	25.3	25.3	24.4	
	28202	27.6	28.9	F	27.5	24.6	26.3	
	28204	28.5	27.1	F	27.1	26.8	28.2	
MEAN		24.8	24.5		26.9	25.9	26.3	
S.D.		1.98	2.71		2.31	2.70	2.79	
N		15	14		15	15	15	

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 PPH	28229	NORMAL	41	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	39	SCHEDULED SACRIFICE
	28228	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
	28244	NORMAL	41	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	39	SCHEDULED SACRIFICE
	28287	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28239	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28240	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28242	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	42	SCHEDULED SACRIFICE
	28276	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	42	SCHEDULED SACRIFICE
	28245	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28226	NORMAL	32	0-30	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	30	SCHEDULED SACRIFICE
150 PPH	28255	NORMAL	11	31-41	ALOPECIA (PPH 11)
		FATE	1	41	SCHEDULED SACRIFICE
	28249	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28275	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
	28278	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	42	SCHEDULED SACRIFICE
	28256	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
28277	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	42	SCHEDULED SACRIFICE	
28272	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	40	SCHEDULED SACRIFICE	
28270	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	42	SCHEDULED SACRIFICE	
28288	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	43	SCHEDULED SACRIFICE	
28253	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	41	SCHEDULED SACRIFICE	
28264	NORMAL	42	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS	

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
150 PPM	28264	FATE	1	42	SCHEDULED SACRIFICE
		SKIN	2	17-42	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28233	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	42	SCHEDULED SACRIFICE
	28225	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
	28238	NORMAL	27	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	8	23-30	PERINASAL ENCRUSTATION
		SKIN	1	40	CRUST (FAC 1)
			6	31-36	ALOPECIA (FAC 6)
	28257	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	42	SCHEDULED SACRIFICE
	28267	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS
	FATE	1	42	SCHEDULED SACRIFICE	
28280	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	43	SCHEDULED SACRIFICE	
28258	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	40	SCHEDULED SACRIFICE	
28262	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	41	SCHEDULED SACRIFICE	
28220	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	41	SCHEDULED SACRIFICE	
750 PPM	28266	NORMAL	41	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	39	SCHEDULED SACRIFICE
	28281	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28236	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
	28250	NORMAL	41	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	39	SCHEDULED SACRIFICE
	28271	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28263	NORMAL	45	0-43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
	28223	NORMAL	40	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
28283	NORMAL	2	17-40	RAISED AREAS (RED AND OR BROWN) (TAL 2)	
	SKIN	39	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	40	SCHEDULED SACRIFICE	
	EYES/EARS/NOSE	1	7	PERIOULAR ENCRUSTATION (EYE 1)	
	SKIN	2	17-40	RAISED AREAS (RED AND OR BROWN) (TAL 2)	

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
750 PPM	28260	NORMAL	45	0-44	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	44	SCHEDULED SACRIFICE
		SKIN	1	17	RAISED AREAS (RED AND OR BROWN) (TAL 1)
	28259	NORMAL	14	0-16	NC SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	43	SCHEDULED SACRIFICE
		SKIN	2	17-43	RAISED AREAS (RED AND OR BROWN) (TAL 2)
			30	7-43	ALOPECIA (LFB 30)
	28252	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28222	NORMAL	40	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
		SKIN	2	17-40	RAISED AREAS (RED AND OR BROWN) (TAL 2)
	28224	NORMAL	42	0-40	NC SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
28221	NORMAL	40	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	40	SCHEDULED SACRIFICE	
	SKIN	2	17-40	RAISED AREAS (RED AND OR BROWN) (TAL 2)	
28230	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	42	SCHEDULED SACRIFICE	
1500 PPM	28265	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28269	NORMAL	40	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	39	SCHEDULED SACRIFICE
	28279	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28268	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28254	NORMAL	42	0-40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	40	SCHEDULED SACRIFICE
	28243	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
	28247	NORMAL	43	0-41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	41	SCHEDULED SACRIFICE
28285	NORMAL	44	0-42	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	42	SCHEDULED SACRIFICE	
28231	NORMAL	19	0-17	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	17	SCHEDULED SACRIFICE	
	SKIN	23	18-40	ALOPECIA (LFB 4, MUL 19)	
28246	NORMAL	34	0-39	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	39	SCHEDULED SACRIFICE	
	EYES/EARS/NOSE	5	29-33	PERIOPICULAR ENCRUSTATION (EYL 5)	
		2	27-28	LACRIMATION (EVB 2)	

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL CLINICAL OBSERVATIONS
 F0 ADULT FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY		FINDING
				DAYS	DAYS	
1500 PPM	28234	NORMAL	44	0-	42	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1		42	SCHEDULED SACRIFICE
	28241	NORMAL	45	0-	43	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1		43	SCHEDULED SACRIFICE
	28251	NORMAL	42	0-	40	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1		40	SCHEDULED SACRIFICE
	28284	NORMAL	43	0-	41	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1		41	SCHEDULED SACRIFICE
	28237	NORMAL	55	0-	53	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1		53	SCHEDULED SACRIFICE

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

INDIVIDUAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 0 PPM

WEEK	0	1	2	3
ANIMAL				
28229	212.0	219.2	no bwt.	no bwt.
28228	219.0	238.0	245.3	no bwt.
28244	210.5	221.6	no bwt.	no bwt.
28287	208.9	222.0	228.2	no bwt.
28239	208.0	220.7	222.2	no bwt.
28240	216.1	227.7	no bwt.	no bwt.
28242	228.1	236.8	246.3	no bwt.
28276	208.2	227.8	229.7	no bwt.
28245	225.7	234.8	no bwt.	no bwt.
28226	215.5	219.4	229.6	no bwt.
28255	223.6	233.3	no bwt.	no bwt.
28249	224.1	237.3	231.4	no bwt.
28275	238.3	251.9	253.4	no bwt.
28278	226.5	233.1	243.2	no bwt.
28256	236.3	250.6	no bwt.	no bwt.
MEAN	220.1	230.9	236.6	
S.D.	9.89	10.40	10.58	
N	15	15	9	

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

INDIVIDUAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 150 PPM

WEEK	0	1	2	3
ANIMAL				
28277	201.3	214.1	218.6	no bwt.
28272	223.9	220.0	no bwt.	no bwt.
28270	214.7	229.4	no bwt.	no bwt.
28288	212.2	216.2	222.0	no bwt.
28253	213.2	212.5	218.7	no bwt.
28264	221.5	223.3	224.7	no bwt.
28233	217.7	224.2	232.6	no bwt.
28225	228.0	232.1	235.6	no bwt.
28238	224.4	231.2	no bwt.	no bwt.
28257	221.7	233.6	243.2	no bwt.
28267	213.3	235.9	242.2	no bwt.
28280	226.4	234.9	237.5	no bwt.
28258	226.4	233.3	no bwt.	no bwt.
28262	227.5	242.3	265.8	no bwt.
28220	225.6	226.4	239.1	no bwt.
MEAN	219.8	227.3	234.5	
S.D.	7.60	8.75	13.80	
N	15	15	11	

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS

INDIVIDUAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 750 PPM

WEEK	0	1	2	3
ANIMAL				
28266	208.0	217.4	no bwt.	no bwt.
28281	206.3	207.3	217.6	no bwt.
28236	208.2	218.1	217.1	no bwt.
28250	209.1	210.8	no bwt.	no bwt.
28271	223.0	224.4	no bwt.	no bwt.
28263	223.7	237.2	241.4	no bwt.
28223	219.4	219.3	no bwt.	no bwt.
28283	222.9	227.4	240.3	no bwt.
28260	220.5	229.6	241.7	no bwt.
28259	229.6	228.6	226.5	no bwt.
28252	219.8	227.0	227.2	261.4
28222	234.6	223.5	no bwt.	no bwt.
28224	230.6	227.3	no bwt.	no bwt.
28221	225.9	227.8	no bwt.	no bwt.
28230	221.7	233.3	244.2	no bwt.
MEAN	219.5	223.9	232.0	261.4
S.D.	7.94	8.07	11.24	0.00
N	15	15	8	1

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 1500 PPM

WEEK	0	1	2	3
ANIMAL				
28265	214.6	216.7	no bwt.	no bwt.
28269	211.6	205.7	no bwt.	no bwt.
28279	211.4	215.0	no bwt.	no bwt.
28268	212.2	215.8	no bwt.	no bwt.
28254	213.5	221.4	no bwt.	no bwt.
28283	212.1	213.4	227.9	no bwt.
28247	209.5	207.0	229.5	no bwt.
28285	217.8	222.4	230.8	no bwt.
28231	215.7	221.5	225.0	no bwt.
28246	221.5	219.7	no bwt.	no bwt.
28234	219.1	222.2	223.4	no bwt.
28241	223.2	231.6	235.2	no bwt.
28251	224.4	229.8	no bwt.	no bwt.
28284	230.4	230.8	240.1	no bwt.
28237	243.1	255.4	255.6	294.5
MEAN	218.7	221.9	233.4	294.5
S.D.	8.95	12.05	10.46	0.00
N	15	15	8	1

TABLE 7
 PROPIONALDEHYDS: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 0 PPM

WEEK	1	2
ANIMAL		
28229	16.8	16.9
28228	16.4	18.3
28244	16.8	r/s
28287	18.5	18.3
28239	18.4	18.8
28240	18.6	19.3
28242	18.1	18.3
28276	19.5	r/s
28245	17.9	19.3
28226	16.6	17.5
28255	18.2	r/s
28249	18.5	19.3
28275	19.2	20.1
28278	18.1	18.3
28256	r/s	r/s
MEAN	18.1	18.6
S.D.	0.87	0.89
N	14	11

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 150 PPM

WEEK	1	2
ANIMAL		
28277	r/s	18.4
28272	r/s	r/s
28270	18.8	18.2
28288	15.9	17.2
28253	15.6	16.5
28264	15.2	16.0
28233	r/s	19.9
28225	19.0	18.3
28238	18.5	19.0
28257	17.8	19.0
28267	19.8	18.4
28280	17.3	18.6
28258	17.2	18.8
28262	r/s	22.7
28220	17.6	19.1
MEAN	17.5	18.6
S.D.	1.50	1.60
N	11	14

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD ♀ RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 750 PPM

WEEK	1	2
ANIMAL		
28266	16.5	19.1
28281	16.4	r/s
28236	r/s	19.4
28250	14.0	15.9
28271	r/s	19.5
28263	r/s	19.5
28223	16.2	17.3
28283	19.9	r/s
28260	17.3	18.3
28259	r/s	r/s
28252	16.6	17.8
28222	16.0	17.8
28224	16.7	r/s
28221	17.0	r/s
28230	19.6	r/s
MEAN	16.9	18.3
S.D.	1.63	1.21
N	11	9

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS
 INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 1500 PPM

WEEK	1	2
ANIMAL		r/s
28265	16.6	14.6
28269	13.4	16.2
28279	15.1	17.2
28268	16.0	17.6
28254	17.5	18.4
28243	r/s	19.6
28247	19.4	16.5
28285	15.1	18.5
28231	18.2	14.2
28246	r/s	15.8
28234	14.6	17.0
28241	17.0	18.4
28251	17.6	19.0
28284	17.2	18.5
28237	18.3	
MEAN	16.6	17.2
S.D.	1.69	1.64
N	13	14

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD² Rats

Reproductive Parameters

(35 Pages)

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TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

REPRODUCTIVE PARAMETERS

The following is a list of abbreviations or words that may appear in this appendix in reference to individual food consumption values.

- r/s = indicates that the animal was removed from the consumption period due to spillage.
- r/e = indicates that the animal was removed from the consumption period due to excreta in the feeder
- r/o = indicates that the animal was removed from the consumption period for reasons specified in the raw data.
- r/dead = indicates that the animal was removed from the consumption period because it died or was sacrificed during the period in which this abbreviation appears.
- r/l = indicates that the data is not included because there were no live pups left in litter.
- r/c = indicates that the animal was removed from the consumption period due to excessive bedding in the feeder.
- dead = indicates that the animal died prior to the period in which this word appears.
- sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.
- a = Combined interval value removed due to removal of at least one individual interval value (see individual interval footnotes).

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL MATING AND PREGNANCY DATA
 F0 ADULTS GROUP: 0 PPM

FEMALE NUMBER	MALE NUMBER	MALE NUMBER AFTER SWITCH ^a	IMPREGNATION DATE	DELIVERY DATE	GESTATION LENGTH IN DAYS	UTERINE STAINING RESULTS
28229	28155		20-JAN-92	10-FEB-92	21	
28228	28178		23-JAN-92	14-FEB-92	22	
28244	28162		20-JAN-92	10-FEB-92	21	
28287	28198		21-JAN-92	DID NOT DELIVER	--	
28239	28153		21-JAN-92	12-FEB-92	22	NO IMPLANTATION SITES
28240	28200		20-JAN-92	11-FEB-92	22	
28242	28167		23-JAN-92	13-FEB-92	21	
28276	28156		22-JAN-92	13-FEB-92	22	
28245	28171		20-JAN-92	11-FEB-92	22	
28226	28159		21-JAN-92	12-FEB-92	22	
28255	28191		20-JAN-92	11-FEB-92	22	
28249	28201		21-JAN-92	12-FEB-92	22	
28275	28173		23-JAN-92	14-FEB-92	22	
28278	28180		22-JAN-92	13-FEB-92	22	
28256	28174		20-JAN-92	11-FEB-92	22	

^a Date of switch, January 26, 1992. No switches occurred as all pairs had mated by this date.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL MATING AND PREGNANCY DATA
 F0 ADULTS GROUP: 150 PPM

FEMALE NUMBER	MALE NUMBER	MALE NUMBER AFTER SWITCH ^a	IMPREGNATION DATE	DELIVERY DATE	GESTATION LENGTH IN DAYS	UTERINE STAINING RESULTS
28277	28181		23-JAN-92	13-FEB-92	21	
28272	28187		20-JAN-92	11-FEB-92	22	
28270	28165		22-JAN-92	13-FEB-92	22	
28288	28195		23-JAN-92	14-FEB-92	22	
28253	28212		21-JAN-92	12-FEB-92	22	
28264	28160		23-JAN-92	13-FEB-92	21	
28233	28139		22-JAN-92	13-FEB-92	22	
28225	28150		23-JAN-92	14-FEB-92	22	
28238	28184		20-JAN-92	DID NOT DELIVER	--	PREGNANT - 1 RESORPTION
28257	28210		22-JAN-92	13-FEB-92	22	
28267	28194		22-JAN-92	13-FEB-92	22	
28280	28193		23-JAN-92	14-FEB-92	22	
28258	28168		20-JAN-92	11-FEB-92	22	
28262	28188		21-JAN-92	12-FEB-92	22	
28220	28169		21-JAN-92	12-FEB-92	22	

^a Date of switch, January 26, 1992. No switches occurred as all pairs had mated by this date.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS

INDIVIDUAL MATING AND PREGNANCY DATA
 F0 ADULTS GROUP: 750 PPH

FEMALE NUMBER	MALE NUMBER	MALE NUMBER AFTER SWITCH ^a	IMPREGNATION DATE	DELIVERY DATE	GESTATION LENGTH IN DAYS	UTERINE STAINING RESULTS
28266	28147		20-JAN-92	10-FEB-92	21	
28281	28176		21-JAN-92	12-FEB-92	22	
28236	28146		23-JAN-92	14-FEB-92	22	
28250	28158		20-JAN-92	10-FEB-92	21	
28271	28186		20-JAN-92	11-FEB-92	22	
28263	28190		23-JAN-92	14-FEB-92	22	
28223	28148		20-JAN-92	11-FEB-92	22	
28283	28192		21-JAN-92	11-FEB-92	21	
28260	28149		24-JAN-92	15-FEB-92	22	
28259	28197		23-JAN-92	14-FEB-92	22	
28252	28203		2-FEB-92 ^b	12-FEB-92	10 ^c	
28222	28182	28146	20-JAN-92	11-FEB-92	22	
28224	28208		20-JAN-92	11-FEB-92	22	
28221	28209		20-JAN-92	11-FEB-92	22	
28230	28211		22-JAN-92	13-FEB-92	22	

^a Date of switch, January 26, 1992.

^b No evidence of successful mating. Assigned a gestation day 0 on last scheduled mating day.

^c Missed copulation plug, apparent successful mating with the first male.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS
 INDIVIDUAL MATING AND PREGNANCY DATA
 FO ADULTS GROUP: 1500 PPM

FEMALE NUMBER	MALE NUMBER AFTER SWITCH ^a	IMPREGNATION DATE	DELIVERY DATE	GESTATION LENGTH IN DAYS	UTERINE STAINING RESULTS
28265	28166	20-JAN-92	11-FEB-92	22	
28269	28205	20-JAN-92	10-FEB-92	21	
28279	28207	20-JAN-92	11-FEB-92	22	
28268	28179	20-JAN-92	11-FEB-92	22	
28254	28189	20-JAN-92	11-FEB-92	22	
28243	28206	21-JAN-92	12-FEB-92	22	
28247	28204	21-JAN-92	12-FEB-92	22	
28285	28214	22-JAN-92	13-FEB-92	22	
28231	28172	21-JAN-92	11-FEB-92	21	
28246	28163	20-JAN-92	10-FEB-92	21	
28234	28157	22-JAN-92	13-FEB-92	22	
28241	28202	23-JAN-92	14-FEB-92	22	
28251	28183	20-JAN-92	11-FEB-92	22	
28284	28196	21-JAN-92	11-FEB-92	22	
28237	28213	2-FEB-92 ^b	12-FEB-92	22	
	28214		DID NOT DELIVER	--	NO IMPLANTATION SITES

^a Date of switch, January 26, 1992.

^b No evidence of successful mating. Assigned a gestation day 0 on last scheduled mating day.

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 0 PPH

PREGNANCY STATUS	DAY 0	7	14	21	26	36	43
28229 P	222.19	252.34	272.16	338.48			
28228 P	253.45	285.33	319.51	386.18			
28244 P	238.08	274.97	300.22	382.06			
28287 NP	227.75	242.13	245.20	242.43	249.39		
28239 P	225.63	256.98	286.50	367.25			
28240 P	240.71	271.66	305.41	362.94			
28242 P	253.31	296.94	334.19	417.12			
28276 P	232.50	261.71	282.86	358.03			
28245 P	235.10	278.70	312.05	385.28			
28226 P	231.91	259.13	290.13	332.08			
28255 P	239.97	269.04	295.27	376.87			
28249 P	232.73	269.52	295.62	353.67			
28275 P	259.92	289.33	312.20	377.51			
28278 P	247.86	289.74	330.08	405.92			
28256 P	265.92	304.50	339.03	440.05			
MEAN	241.38	275.71	305.37	377.39	0.00		
S.D.	12.974	15.765	20.166	29.478	0.000		
N	14	14	14	14	0		

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, mp=MISSED PLUG
 NP, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD® RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 150 PPM

PREGNANCY STATUS	DAY 0	7	14	21	26	36	43
28277 P	231.01	271.90	310.19	403.85			
28272 P	229.09	264.32	291.05	349.20			
28270 P	237.15	272.13	300.87	382.59			
28288 P	223.09	252.71	289.93	366.85			
28253 P	226.64	243.34	277.75	379.06			
28254 P	231.34	263.40	295.74	377.17			
28233 P	236.61	273.03	296.81	369.54			
28225 P	244.48	286.28	312.27	418.41			
28238 P	242.45	269.34	277.15	242.56	270.65		
28257 P	242.87	274.11	300.85	383.06			
28267 P	251.97	288.83	311.81	403.09			
28280 P	249.54	274.73	299.12	366.24			
28258 P	240.33	271.60	299.27	371.22			
28262 P	270.03	317.65	365.69	481.23			
28220 P	235.19	273.79	303.52	351.19			
MEAN	239.59	273.14	302.13	376.35	270.65		
S.D.	11.773	16.693	20.499	49.184	0.000		
N	15	15	15	15	1		

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, mp=MISSED PLUG
 mp, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 FROPIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 750 PPM

PREGNANCY STATUS	DAY 0	7	14	21	26	36	43
28266 P	224.04	249.26	274.36	342.20			
28281 P	217.27	253.82	283.94	376.17			
28236 P	230.29	266.52	295.13	362.98			
28250 P	213.37	251.57	271.09	336.17			
28271 P	235.92	263.48	288.17	362.03			
28263 P	252.18	287.62	318.45	415.81			
28223 P	226.95	254.02	278.93	352.78			
28283 P	248.18	279.57	307.04	383.78			
28260 P	249.65	272.66	301.62	367.52			
28259 P	234.95	269.97	297.69	386.37			
28252 mp	279.41	322.47					
28222 P	235.18	266.86	291.43	362.80			
28224 P	233.27	263.33	294.72	370.36			
28221 P	232.56	274.23	304.02	365.21			
28230 P	249.44	278.55	304.18	316.14			
MEAN	234.52	266.53	293.63	364.31			
S.D.	12.051	11.528	13.367	23.938			
N	14	14	14	14			

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, mp=HISSED PLUG
 mp, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 1500 PPM

PREGNANCY STATUS	DAY 0	7	14	21	26	36	43
28265 P	227.93	257.42	280.75	342.98			
28269 P	210.69	238.62	271.36	356.77			
28279 P	216.09	241.84	268.55	328.56			
28268 P	224.22	256.70	292.52	328.37			
28254 P	232.85	264.39	285.82	372.70			
28243 P	229.43	261.92	288.34	372.26			
28247 P	228.07	264.17	285.23	360.72			
28285 P	230.13	269.34	294.34	374.17			
28231 P	223.22	252.90	275.58	339.20			
28246 P	217.47	254.78	280.67	375.03			
28234 P	227.98	263.79	304.25	377.39			
28241 P	238.98	270.73	310.55	381.71			
28251 P	237.06	269.39	297.20	366.91			
28284 P	242.64	277.47	302.11	369.58			
28237 NP	301.17	292.70	288.85	274.47	282.42		
MEAN	227.63	260.25	288.38	360.45	0.00		
S.D.	8.921	10.855	12.537	18.336	0.000		
N	14	14	14	14	0		

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, MD=MISSSED PLUG
 mp, NP AND RFS HEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 FO ADULT FEMALES GROUP: 0 PPH

ANIMAL	PS	GDD	DAY	0-4	4-7	7-11	11-14	14-17	17-21	0-7	7-14	14-21
28229	P	21		20.44	22.81	21.38	21.41	24.25	22.23	21.46	21.39	23.09
28228	P	22		20.07	21.35	22.82	24.02	23.40	23.38	21.05	23.34	23.39
28244	P	21		23.71	24.36	23.34	22.32	25.73	24.76	23.99	22.90	25.18
28287	NP			18.80	18.92	17.49	18.12	18.98	22.40	18.85	17.76	20.94
28239	P	22		22.80	23.94	25.00	24.70	26.07	25.53	23.29	24.87	25.76
28240	P	22		22.72	23.44	23.63	24.67	28.04	18.68	23.03	24.07	22.69
28242	P	21		24.58	27.37	26.14	27.81	30.13	26.69	25.83	26.86	28.16
28276	P	22		21.39	22.84	23.83	22.54	23.70	23.91	22.01	23.28	23.82
28245	P	22		22.64	24.54	23.38	24.35	27.57	26.51	23.45	23.80	26.96
28226	P	22		20.79	21.10	19.99	24.15	25.34	21.41	20.92	21.78	23.09
28255	P	22		20.52	22.08	23.55	22.41	25.14	24.26	21.19	23.06	24.63
28249	P	22		22.88	25.17	25.17	24.46	27.19	26.09	23.86	24.86	26.56
28275	P	22		20.56	23.19	23.44	22.95	24.53	22.74	21.69	23.23	23.51
28278	P	22		24.24	27.61	28.57	29.97	30.30	27.89	25.68	29.17	28.92
28256	P	22		27.78	29.01	27.96	29.31	28.47	30.05	28.31	28.54	29.37
MEAN				22.51	24.27	24.16	24.65	26.42	24.58	23.27	24.37	25.37
S.D.				2.137	2.300	2.303	2.518	2.249	2.883	2.164	2.329	2.295
N				14	14	14	14	14	14	14	14	14

PS=PREGNANCY STATUS, GDD=GESTATION DAY OF DELIVERY
 P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, mp=HISSED PLUG
 mp, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 150 PPM

ANIMAL	PS	GDD	DAY	0-4	4-7	7-11	11-14	14-17	17-21	0-7	7-14	14-21
28277	P	21		24.55	26.47	27.61	29.45	27.90	26.58	25.37	28.40	27.14
28272	P	22		23.45	24.82	24.19	24.36	25.16	21.69	24.04	24.26	23.18
28270	P	22		23.23	25.39	23.51	22.91	23.64	24.23	24.15	23.25	23.98
28288	P	22		20.69	21.99	21.50	24.46	26.36	23.58	21.25	22.82	24.77
28253	P	22		18.11	18.03	19.73	21.28	23.38	25.81	18.08	20.39	24.77
28264	P	21		18.41	22.65	21.30	24.19	24.60	23.70	20.23	22.54	24.08
28233	P	22	r/s		24.33	23.36	22.72	22.00	23.45	a	23.08	22.83
28225	P	22	r/s		26.18	25.65	25.11	25.43	27.75	a	25.42	26.75
28238	P	22		21.83	22.77	21.68	19.63	16.87	15.79	22.23	20.80	16.25
28257	P	22		21.07	22.44	23.20	23.82	24.68	25.22	21.66	23.47	24.99
28267	P	22		22.81	26.74	24.17	24.88	27.34	29.05	24.49	24.47	28.32
28280	P	22		22.35	24.99	24.42	23.41	23.10	23.06	23.48	23.99	23.08
28258	P	22		20.45	20.87	24.41	22.99	26.52	20.35	20.33	23.80	22.99
28262	P	22		27.61	26.61	32.50	33.65	34.26	34.36	27.18	32.99	34.32
28220	P	22		21.76	23.23	24.10	26.56	26.24	25.03	22.39	25.15	25.54
MEAN				22.03	23.83	24.09	24.63	25.17	24.64	22.71	24.32	24.87
S.D.				2.509	2.453	3.004	3.343	3.670	4.146	2.419	3.056	3.778
N				13	15	15	15	15	15	13	15	15

PS=PREGNANCY STATUS, GDD=GESTATION DAY OF DELIVERY
 P=NOT PREGNANT, RFS=REMOVED FROM STUDY, MP=MISSED PLUG
 RP, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 750 PPM

ANIMAL	PS	GDD	DAY	0-4	4-7	7-11	11-14	14-17	17-21	0-7	7-14	14-21
26266 P	21		20.53	23.82	21.87	21.60	22.47	21.20	21.94	21.75	21.74	
28281 P	22		20.52	24.33	23.15	22.06	22.20	23.16	22.15	22.69	22.75	
28236 P	22		19.51	21.75	22.51	26.80	23.67	23.66	20.47	24.35	23.67	
28250 P	21		21.16	21.62	20.57	21.43	21.36	20.11	21.36	20.94	20.65	
28271 P	22		22.13	22.86	21.27	22.43	23.83	21.69	22.45	21.77	22.61	
28263 P	22		26.88	24.31	27.18	24.84	27.08	25.67	25.78	26.17	26.27	
28223 P	22		20.73	22.28	20.29	20.22	21.46	21.72	21.39	20.26	21.61	
28283 P	21		23.58	25.15	25.40	24.32	24.34	23.59	24.25	24.94	23.91	
28260 P	22		21.68	19.46	19.87	21.91	22.32	24.59	20.73	20.74	23.61	
28259 P	22		20.85	22.23	21.38	22.72	24.92	23.44	21.44	21.95	24.08	
28252 mp	10		20.12	21.51					20.71			
28222 P	22		20.61	22.71	21.26	23.50	23.21	24.76	21.51	22.22	24.09	
28224 P	22		20.41	21.68	21.36	24.84	27.71	21.22	20.95	22.85	24.00	
28221 P	22		26.18	24.01	24.67	24.83	23.13	25.97	25.25	24.74	24.76	
28230 P	22		24.57	25.71	26.00	25.99	28.48	r/o	25.06	26.00	a	
MEAN			22.10	22.99	22.63	23.39	24.01	23.14	22.48	22.96	23.37	
S.D.			2.304	1.667	2.304	1.921	2.281	1.835	1.811	1.949	1.482	
N			14	14	14	14	14	13	14	14	13	

PS=PREGNANCY STATUS, GDD=GESTATION DAY OF DELIVERY
 P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, mp=MISSED PLUG
 mp, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 F0 ADULT FEMALES GROUP: 1500 PPM

ANIMAL	PS	GDD	DAY	0-4	4-7	7-11	11-14	14-17	17-21	0-7	7-14	14-21
28265	P	22		19.34	20.84	20.33	19.87	21.77	18.09	19.98	20.13	19.67
28269	P	21		17.55	18.37	18.55	19.92	21.29	21.76	17.90	19.14	21.56
28279	P	22		18.00	18.90	19.46	20.30	20.77	17.84	18.39	19.82	19.09
28268	P	22		19.50	r/a	22.13	22.51	24.93	19.68	a	22.29	21.93
28254	P	22		21.25	22.43	19.96	21.50	23.84	23.35	21.75	20.62	23.56
28243	P	22		22.18	23.37	23.03	22.46	24.41	22.25	22.69	22.79	23.18
28247	P	22		20.58	23.54	23.58	22.14	23.99	23.49	21.85	22.97	23.71
28285	P	22		20.48	23.68	23.23	24.59	24.65	r/s	21.85	23.81	a
28231	P	21		21.66	21.95	23.35	24.30	24.82	25.27	21.78	23.76	25.08
28246	P	21		19.02	19.82	18.95	20.88	24.26	22.03	19.36	19.77	22.99
28234	P	22		21.23	20.04	22.37	23.74	24.91	22.53	20.72	22.96	23.55
28241	P	22		21.14	21.85	21.95	25.68	27.44	26.16	21.44	23.55	26.71
28251	P	22		21.02	22.30	22.93	23.68	22.89	23.86	21.57	23.25	23.44
28284	P	22		20.58	22.39	23.60	23.16	24.44	21.97	21.36	23.41	23.03
28237	NP			19.91	21.22	r/s	30.50	r/s	r/s	20.47	a	a
MEAN				20.25	21.50	21.57	22.48	23.89	22.18	20.82	22.02	22.88
S.D.				1.374	1.755	1.831	1.825	1.730	2.474	1.469	1.713	2.017
N				14	13	14	14	14	13	13	14	13

PS=PREGNANCY STATUS, GDD=GESTATION DAY OF DELIVERY
 P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, MP=MISSED PLUG
 MP, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL LACTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 0 PPM

ANIMAL	LACTATION DAY 0	4
28279	257.73	268.58
28228	279.24	296.81
28244	287.52	292.78
28239	260.18	288.05
28240	270.35	309.17
28242	304.32	311.40
28276	266.44	287.40
28245	290.25	314.30
28226	255.41	278.01
28255	260.73	291.93
28249	246.05	279.53
28275	280.12	308.65
28278	297.83	332.86
28256	324.31	336.57
MEAN	277.18	299.72
S.D.	21.870	20.054
N	14	14



TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL LACTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 150 PPM

ANIMAL	LACTATION DAY 0	4
28277	292.97	298.89
28272	261.35	291.44
28270	272.76	297.98
28288	253.94	262.55
28253	259.43	280.50
28264	271.54	287.40
28233	267.53	287.30
28225	286.52	330.07
28257	272.61	293.46
28267	282.10	311.62
28280	276.94	303.85
28258	269.87	302.66
28262	321.82	333.13
28220	268.92	278.82
MEAN	275.59	297.12
S.D.	16.896	19.045
N	14	14

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD® RATS
 INDIVIDUAL LACTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 750 PPM

ANIMAL	LACTATION DAY 0	4
28256	258.28	267.59
28281	266.48	293.80
28236	260.19	283.11
28250	243.78	266.97
26	254.74	291.03
28263	283.50	325.30
28223	253.87	276.73
28283	282.76	295.10
28260	273.27	291.57
28259	256.00	291.39
28252	254.63	269.69
28222	268.41	289.54
28224	267.72	300.60
28221	270.29	301.73
28230	245.70	282.47
MEAN	262.64	288.44
S.D.	11.954	15.192
N	15	15

TABLE 5
 PROPIONALDEHYDS: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL LACTATIONAL BODY WEIGHT (GRAMS)
 F0 ADULT FEMALES GROUP: 1500 PPM

ANIMAL	LACTATION DAY 0	4
28265	244.49	272.39
28269	255.91	271.94
28279	237.87	260.94
28268	260.61	283.26
28254	268.04	289.96
28243	254.34	283.68
28247	269.30	275.15
28285	263.10	294.64
28231	251.98	276.16
28246	273.80	283.20
28234	269.06	289.27
28241	275.42	314.14
28251	264.10	295.81
28284	272.52	281.64
MEAN	261.47	283.73
S.D.	11.294	12.956
N	14	14

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD® RATS

INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 0 FPM

DAM #	LACTATION DAYS	B A																	
		0	1	2	3	4	17	0	1	2	3	4	17	0	1	2	3	4	17
28229	MALES	6	6	6	6	6	6												
	FEMALES	6	5	5	5	5	5												
	DEAD		1																
28228	MALES	5	5	5	5	5	5												
	FEMALES	8	8	8	8	8	8												
28244	MALES	8	8	8	8	8	8												
	FEMALES	7	7	7	7	7	7												
28239	MALES	8	9	8	8	8	8												
	FEMALES	8	7	7	7	7	7												
	MISSING		1																
28240	MALES	9	9	9	9	9	9												
	FEMALES	8	8	8	8	8	8												
28242	MALES	10	10	10	10	10	10												
	STILLBORN	1																	
28276	FEMALES	6	6	6	6	6	6												
	MALES	8	8	8	8	8	8												
28245	FEMALES	5	5	5	5	5	5												
	MALES	8	8	8	8	8	8												
28226	MALES	8	8	8	8	8	8												
	FEMALES	4	4	4	4	4	4												
	STILLBORN	1																	
28255	MALES	7	7	7	7	7	7												
	FEMALES	7	7	7	7	7	7												
28249	MALES	9	9	9	9	9	9												
	FEMALES	5	5	5	5	5	5												

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD® RATS

INDIVIDUAL LITTER VIABILITY
 F2 PUPS GROUP: 0 PPM

DAM #	LACTATION DAYS	B								A							
		0	1	2	3	4	17	0	1	2	3	4	17				
28275	MALES	8	8	8	8	8	8	8	8	8	8	8	8				
	FEMALES	5	5	5	5	5	5	5	5	5	5	5	5				
28278	MALES	5	5	5	5	5	5	5	5	5	5	5	5				
	FEMALES	10	10	10	10	10	10	10	10	10	10	10	10				
28256	MALES	10	10	10	10	10	10	10	10	10	10	10	10				
	STILLBORN	2															
	FEMALES	6	6	5	5	5	5	5	5	5	5	5	5				
	DEAD			1													

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 150 PPM

DAM #	LACTATION DAYS	B A																
		0	1	2	3	4	17	6	6	6	6	6	6	6	6	6	6	6
28277	MALES FEMALES	6	6	6	6	6	6	10	10	10	10	10	10	10	10	10	10	10
28272	MALES FEMALES	5	5	5	5	5	5	7	7	7	7	7	7	7	7	7	7	7
28270	MALES FEMALES	4	4	4	4	4	4	12	12	12	12	12	12	12	12	12	12	12
28288	MALES FEMALES STILLBORN	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
28253	MALES FEMALES	4	4	4	4	4	4	12	12	12	12	12	12	12	12	12	12	12
28264	MALES FEMALES	8	8	8	8	8	8	7	7	7	7	7	7	7	7	7	7	7
28233	MALES FEMALES	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7
28225	MALES FEMALES	5	5	5	5	5	5	13	13	13	13	13	13	13	13	13	13	13
28257	MALES FEMALES	5	5	5	5	5	5	10	10	10	10	10	10	10	10	10	10	10
28267	MALES FEMALES	8	8	8	8	8	8	9	9	9	9	9	9	9	9	9	9	9
28280	MALES FEMALES MISSING	7	7	7	7	7	7	6	5	5	5	5	5	5	5	5	5	5
28258	MALES FEMALES	9	9	9	9	9	9	7	7	7	7	7	7	7	7	7	7	7

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 150 PPM

DAM #	LACTATION DAYS	0	1	2	3	4	17	B		A
								MALES	FEMALES	
28262	MALES		9	9	9	9	9			
	FEMALES		11	11	11	11	11			
28220	MALES		8	8	8	8	8			
	FEMALES		1	1	1	1	1			

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL LITTER VIABILITY
 F1 F 3 GROUP: 750 PPM

DAM #	LACTATION DAYS	B A																	
		0	1	2	3	4	17	0	1	2	3	4	17	0	1	2	3	4	17
28266	MALES FEMALES	9	9	9	9	9	9	5	5	5	5	5	5	9	9	9	9	9	9
28281	MALES FEMALES	12	12	12	12	12	12	4	4	4	4	4	4	12	12	12	12	12	12
28236	MALES FEMALES	5	5	5	5	5	5	9	9	9	9	9	9	5	5	5	5	5	5
28250	MALES FEMALES	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
28271	MALES FEMALES	7	7	7	7	7	7	8	8	8	8	8	8	7	7	7	7	7	7
28253	MALES FEMALES MISSING	8	8	8	8	8	8	9	9	8	8	8	8	1					
28223	MALES FEMALES	9	9	9	9	9	9	6	6	6	6	6	6	9	9	9	9	9	9
28283	MALES DEAD FEMALES DEAD	6	5	5	5	5	5	1	1					10	10	8	8	8	8
28260	MALES MISSING FEMALES MISSING	7	7	7	6	6	6	9	9	9	8	8	8	1					
28259	MALES FEMALES	7	7	7	7	7	7	8	8	8	8	8	8	7	7	7	7	7	7
28252	MALES FEMALES	7	7	7	7	7	7	5	5	5	5	5	5	7	7	7	7	7	7

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDS: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD • RATS

INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 750 PPM

DAM #	LACTATION DAYS	B		A			
		0	1	2	3	4	17
28222	MALES	8	8	7	7	7	
	MISSING FEMALES	5	5	5	5	5	
28224	MALES	8	8	8	8	8	
	FEMALES	7	7	7	7	7	
28221	MALES	6	6	6	6	6	
	DEAD FEMALES	1	7	7	7	7	
28230	MALES	7	7	7	7	7	
	FEMALES	9	9	9	9	9	

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 1500 PPM

DAM #	LACTATION DAYS	0	1	2	3	4	B		A
							5	17	
28265	MALES	6	5	5	5	5			
	DEAD		1						
	FEMALES	10	9	9	9	9			
	MISSING		1						
28269	MALES	7	7	7	7	7			
	FEMALES	8	8	8	8	8			
	MALES	5	5	5	5	5			
28279	FEMALES	9	9	9	9	9			
	MALES	7	7	7	7	7			
	FEMALES	7	7	6	6	6			
	DEAD		1						
28254	MALES	8	8	8	8	8			
	FEMALES	7	7	7	7	7			
	MALES	10	10	10	10	10			
28243	FEMALES	5	5	5	5	5			
	MALES	7	7	7	7	7			
	STILLBORN	1							
28247	FEMALES	5	5	5	5	5			
	MALES	6	6	6	6	6			
	FEMALES	7	6	6	6	6			
	MISSING		1						
28285	MALES	5	5	5	5	5			
	FEMALES	8	8	8	8	8			
	MALES	9	9	9	9	9			
28246	FEMALES	6	6	6	6	6			
	MALES	8	8	8	8	8			
	FEMALES	8	8	8	8	8			

B= BEFORE CULLING, A= AFTER CULLING

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL LITTER VIABILITY
 F1 PUPS GROUP: 1500 PPH

DAM #	LACTATION DAYS	B		A			
		0	1	2	3	4	17
28241	MALES	7	7	7	7	7	7
	FEMALES	9	9	9	9	9	9
28251	MALES	8	8	8	8	8	8
	FEMALES	6	6	6	6	6	6
28284	MALES	7	7	7	7	7	7
	FEMALES	8	8	8	8	8	8

B= BEFORE CULLING, A= AFTER CULLING

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

LACTATION DAY:	0		INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER F1 PUPS GROUP:																		
	LITTER	MEAN	H	F	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX	PS UE PX						
28229	5.37	5.15			1 M	5.61	2 M	5.47	3 M	5.65	4 M	4.72	5 M	5.18	6 M	5.60	7 F	5.21	8 F	5.27	
					9 F	5.48	10 F	4.98	11 F	5.07	12 F	4.90			6.92	6 F	6.41	7 F	6.18	8 F	7.28
28228	6.89	6.50			1 M	7.01	2 M	6.77	3 M	7.29	4 M	6.47	5 M	6.92	6 F	6.54					
					9 F	6.12	10 F	6.42	11 F	6.65	12 F	6.39	13 F	6.54							
28244	5.60	5.24			1 M	5.88	2 M	5.40	3 M	5.78	4 M	5.58	5 M	5.70	6 M	5.45	7 M	5.48	8 M	5.53	
					9 F	5.74	10 F	5.42	11 F	5.47	12 F	4.76	13 F	5.42	14 F	4.82	15 F	5.03			
28239	6.02	5.75			1 M	6.02	2 M	6.19	3 M	5.47	4 M	6.28	5 M	6.48	6 M	5.41	7 M	5.92	8 M	6.42	
					9 F	5.45	10 F	5.97	11 F	5.73	12 F	5.72	13 F	5.56	14 F	5.89	15 F	5.97	16 F	5.73	
28240#	5.31	5.08			1 M	5.92	2 M	5.20	3 M	5.26	4 M	5.03	5 M	4.85	6 M	5.27	7 M	5.49	8 M	5.44	
					9 F	5.35	10 F	4.85	11 F	4.75	12 F	5.03	13 F	5.17	14 F	5.15	15 F	4.98	16 F	5.32	
					17 F	5.13				4.95	4 M	6.10	5 M	5.28	6 M	5.56	7 M	5.11	8 M	5.75	
28242#	5.41	5.16			9 M	5.14	10 F	5.04	11 F	5.43	12 F	5.44	13 F	5.34	14 F	5.31	15 F	5.01	16 F	4.52	
					17 M	5.0															
28276	5.92	5.83			1 M	6.08	2 M	5.88	3 M	5.62	4 M	5.56	5 M	5.55	6 M	5.97	7 M	5.11	8 M	6.61	
					9 F	5.77	10 F	6.08	11 F	5.81	12 F	5.71	13 F	5.80							
28245	6.32	6.32			1 M	5.91	2 M	5.86	3 M	6.53	4 M	6.36	5 M	6.46	6 M	5.72	7 M	6.16	8 M	6.53	
					9 F	6.25	10 F	6.52	11 F	6.18	12 F	6.54	13 F	6.09							
28226	6.33	5.90			1 M	6.63	2 M	6.84	3 M	6.37	4 M	5.58	5 M	6.04	6 M	6.45	7 M	6.53	8 M	6.19	
					9 F	5.87	10 F	5.90	11 F	5.64	12 F	6.19	13 F	5.0							
28255	6.66	6.08			1 M	6.86	2 M	7.20	3 M	6.39	4 M	6.73	5 M	6.45	6 M	6.22	7 M	6.76	8 F	5.97	
					9 F	6.11	10 F	5.72	11 F	6.12	12 F	6.30	13 F	6.45	14 F	5.87					
28249	5.79	5.39			1 M	5.38	2 M	6.04	3 M	5.89	4 M	5.64	5 M	5.91	6 M	5.60	7 M	6.15	8 M	5.46	
					9 M	6.01	10 F	5.16	11 F	5.48	12 F	5.79	13 F	5.19	14 F	5.31					
28275	6.35	6.24			1 M	5.96	2 M	5.72	3 M	6.86	4 M	6.96	5 M	6.07	6 M	6.51	7 M	6.32	8 M	6.41	
					9 F	5.44	10 F	6.46	11 F	6.42	12 F	6.58	13 F	6.30							
28278	5.82	5.64			1 M	6.02	2 M	5.86	3 M	5.96	4 M	5.07	5 M	6.17	6 F	5.87	7 F	5.85	8 F	5.37	
					9 F	5.89	10 F	5.52	11 F	5.75	12 F	5.77	13 F	5.28	14 F	5.74	15 F	5.41			
28255#	5.57	5.54			1 M	5.77	2 M	6.36	3 M	5.09	4 M	5.09	5 M	5.32	6 M	6.15	7 M	5.39	8 M	5.00	
					9 M	5.92	10 F	5.58	11 F	5.38	12 F	5.63	13 F	5.29	14 F	5.24	15 F	6.10	16 F	5.56	
					17 M	5.0	18 M	5.0													
MEAN	5.95	5.70																			
S.D.	0.50	0.47																			
N	14	14																			

S = STILLBORN
 # = AT LEAST ONE PUP IN LITTER MISSEXED

TABLE 7
PROPIONALDEHYDS: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS.
INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER
F1 PUPS GROUP: 150 PPM

LACTATION DAY:	LITTER	MEAN		P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	
		N	F																	
0	28277	5.56	5.36	1 M	5.73	2 M	5.69	3 M	5.28	4 M	5.29	5 M	5.78	6 M	5.58	7 F	5.40	8 F	5.28	
	28272	5.95	6.09	9 F	5.19	10 F	5.65	11 F	5.39	12 F	5.14	13 F	5.46	14 F	5.21	15 F	5.62	16 F	5.29	
	28270	5.72	5.41	9 F	6.10	10 F	6.60	11 F	6.27	12 F	5.54	5.84	5 F	4.70	6 F	5.50	7 F	5.69	8 F	5.55
	28288	6.07	5.50	9 F	5.66	2 M	5.70	3 M	5.70	4 M	5.84	5 F	4.70	6 F	5.50	7 F	5.69	8 F	5.55	
	28253	6.58	5.88	9 F	5.66	10 F	5.66	11 F	4.63	12 F	4.63	13 F	5.40	14 F	5.40	15 F	5.37	16 F	5.73	
	28264	5.48	5.32	9 F	5.42	10 F	6.38	11 F	5.46	12 F	4.83	13 F	5.62	14 F	5.64	15 F	5.0	5.0	5.16	
	28233	6.49	6.10	9 F	5.97	10 F	5.98	11 F	5.90	12 F	6.21	13 F	6.33	14 F	4.93	15 F	6.01	16 F	4.73	
	28275	5.79	5.77	9 F	5.49	2 M	5.64	3 M	5.40	4 M	5.36	5 M	5.29	6 M	5.61	7 M	5.78	8 M	5.30	
	28257	5.99	5.83	9 F	5.10	10 F	5.43	11 F	5.45	12 F	5.71	13 F	5.19	14 F	5.29	15 F	5.07	16 F	6.00	
	28267	6.27	5.64	9 F	6.28	2 M	6.65	3 M	6.37	4 M	6.81	5 M	6.57	6 M	6.28	7 F	6.31	8 F	6.10	
	28280	6.39	5.98	9 F	6.59	10 F	6.15	11 F	5.98	12 F	5.90	13 F	5.88	14 F	5.15	15 F	5.29	16 F	6.37	
	28258	6.27	5.90	9 F	6.10	10 F	6.13	11 F	5.22	12 F	5.99	13 F	5.99	14 F	5.95	15 F	5.67	16 F	5.43	
	28262	6.53	6.06	9 F	6.21	18 F	5.56	17 F	6.42	3 M	5.78	4 M	6.23	5 M	5.89	7 F	5.69	8 F	5.65	
	28220	6.51	6.34	9 F	5.68	10 F	6.12	11 F	5.94	2 M	6.42	3 M	5.96	4 M	6.22	15 F	5.85	5.85	5.93	
	MEAN	6.12	5.80	9 F	6.22	2 M	6.01	3 M	6.04	4 M	5.98	5 M	6.58	6 M	6.75	7 M	6.63	8 M	5.93	
	S.D.	0.37	0.31	9 F	5.62	10 F	5.83	11 F	5.69	12 F	5.04	13 F	6.05	14 F	5.52	15 F	4.99	16 F	6.15	
	N	14	14	17 F	5.85	17 F	5.85	17 F	5.99	4 M	5.80	5 M	7.10	6 M	6.27	7 M	6.05	8 F	6.12	
		14	14	9 F	6.51	2 M	6.98	3 M	5.99	4 M	5.99	5 M	7.10	6 M	6.27	7 M	6.05	8 F	6.12	
		14	14	9 F	5.63	10 F	6.12	11 F	6.33	12 F	6.20	13 F	5.47	14 F	6.60	15 F	6.41	16 F	5.97	
		14	14	9 M	6.20	2 M	6.26	3 M	6.25	4 M	6.27	5 M	6.31	6 M	5.77	15 F	5.83	16 F	5.96	
		14	14	9 M	6.16	10 F	5.68	11 F	6.06	12 F	6.16	13 F	5.82	14 F	5.77	15 F	5.83	16 F	5.96	
		14	14	9 M	6.20	2 M	6.56	3 M	6.72	4 M	6.62	5 M	6.77	6 M	6.37	7 M	6.05	8 M	6.64	
		14	14	9 M	6.76	10 F	5.91	11 F	5.70	12 F	6.03	13 F	6.35	14 F	5.68	15 F	6.59	16 F	5.71	
		14	14	17 F	5.82	18 F	5.99	19 F	5.91	20 F	5.99	21 F	6.43	22 F	6.79	23 F	6.67	24 F	6.51	
		14	14	1 M	6.23	2 M	6.43	3 M	6.47	4 M	6.43	5 M	6.59	6 M	6.79	7 M	6.67	8 M	6.51	
		14	14	S F	6.34															

S = STILLBORN

TABLE 7
 PROPIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPEMEXAL TOXICITY STUDY IN CD- RATS

INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER
 F1 PUPS GROUP: 1500 PPM

LITTER	LACTATION DAY: J	MEAN	N	P S		P S		P S		P S		P S		P S		P S		P S	
				U E	P X	U E	P X	U E	P X	U E	P X	U E	P X	U E	P X	U E	P X	U E	P X
28265	5.50	5.13	9 F	5.61	2 M	5.71	3 M	5.27	4 M	5.89	13 F	5.43	6 M	5.11	7 F	5.01	8 F	5.11	8 F
28269	5.76	5.55	9 F	5.22	10 F	5.15	11 F	4.97	12 F	5.02	13 F	5.10	14 F	5.22	15 F	5.57	16 F	4.98	4.98
28279	7.73	7.22	9 F	7.69	2 M	8.30	3 M	7.83	4 M	7.41	5 M	7.44	6 F	5.39	15 F	5.42			
28268	5.61	5.63	9 F	7.43	10 F	7.23	11 F	7.38	12 F	7.40	13 F	6.53	14 F	7.30					
28254#	6.12	5.77	9 F	5.65	2 M	5.12	3 M	5.39	4 M	6.19	5 M	5.37	6 M	5.71	7 M	5.84	8 F	5.51	5.51
28243	6.13	5.65	9 M	6.12	2 M	6.50	3 M	5.82	4 M	6.01	5 M	6.04	6 M	6.17	7 M	6.11	8 M	5.95	5.95
28247#	6.34	5.80	9 M	6.01	2 M	6.41	3 M	5.79	12 F	5.88	13 F	5.82	14 F	5.72	15 F	5.64			
28285	6.21	5.75	9 F	6.54	10 M	6.12	11 F	5.51	12 F	5.98	13 F	5.35	14 F	6.14	15 F	5.28			
28231	5.74	5.36	9 F	5.72	10 F	5.77	11 F	5.60	12 F	5.52	13 M	8.0		6.30	7 F	6.20	8 F	6.00	6.00
28246	5.44	5.33	9 F	5.02	10 F	5.86	11 F	5.99	12 F	5.67	13 F	5.68		5.22	7 F	5.23	8 F	5.07	5.07
28234	6.13	5.77	9 M	5.63	2 M	5.86	3 M	5.86	4 M	5.75	5 M	5.60		5.60					
28241	5.97	5.55	9 M	5.84	10 F	5.35	11 F	5.15	12 F	5.46	13 F	5.21	14 F	5.22	15 F	5.31	16 F	6.28	6.28
28251	6.29	5.99	9 F	5.13	2 M	6.17	3 M	6.93	4 M	6.12	5 M	5.99	6 M	6.47	7 M	5.97	8 M	6.23	6.23
28284	5.90	5.57	9 F	5.97	10 F	5.85	11 F	5.80	12 F	5.65	13 F	5.70	14 F	5.88	15 F	5.39	16 F	5.70	5.70
			9 F	6.11	2 M	5.94	3 M	6.01	4 M	6.21	5 M	6.04	6 M	5.91	7 M	5.56	8 F	5.91	5.91
			9 F	5.28	10 F	5.08	11 F	5.77	12 F	5.24	13 F	5.24	14 F	5.97	15 F	5.77	16 F	5.70	5.70
			9 F	6.64	2 M	6.33	3 M	6.68	4 M	5.66	5 M	6.38	6 M	6.43	7 M	6.17	8 M	6.03	6.03
			9 F	5.86	10 F	5.71	11 F	6.29	12 F	5.90	13 F	5.85	14 F	6.32	7 M	6.34	8 F	4.32	4.32
			9 F	4.69	2 M	5.72	3 M	5.79	4 M	6.16	5 M	6.34	6 M	6.23	7 M	5.97	15 F	5.94	5.94
			9 F	5.59	10 F	5.48	11 F	5.85	12 F	5.81	13 F	5.59	14 F	5.97	15 F	5.97	15 F	5.94	5.94

S = STILLBORN
 # = AT LEAST ONE PUP IN LITTER MISSEED

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

LACTATION DAY:	4	MEAN		INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER F1 PUPS GROUP:																		
		M	F	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE	PS UE			
28229	8.17	8.35		1 M	8.15	2 M	8.84	3 M	9.13	4 M	7.95	5 M	6.35	6 M	7.92	7 F	8.64	7 F	D 1	8 F	8.32	
				9 F	8.41	10 F	9.03	11 F	9.05	12 M	7.95											
28228	9.30	9.11		1 M	8.51	2 M	9.64	3 M	9.56	4 M	9.26	5 M	9.51	6 F	9.00	7 F	9.14	8 F	9.14	8 F	9.14	
				9 F	9.37	10 F	8.71	11 F	9.85	12 F	8.85											
28244	8.94	8.46		1 M	8.95	2 M	8.55	3 M	9.03	4 M	8.57	5 M	9.11	6 M	8.69	7 M	9.41	8 M	9.20	8 M	9.20	
				9 F	9.14	10 F	8.34	11 F	7.96	12 F	8.35	13 F	8.74	14 F	9.16	15 F	7.56					
28239	9.57	9.33		1 M	9.77	2 M	10.17	3 M	9.82	4 M	9.20	5 M	8.20	6 M	8.97	7 M	10.52	8 M	9.92	8 M	9.92	
				9 F	M 1	10 F	9.90	11 F	9.27	12 F	9.44	13 F	9.18	14 F	8.92	15 F	9.70	16 F	8.88	16 F	8.88	
28240	9.08	8.71		1 M	8.93	2 M	9.89	3 M	9.56	4 M	9.40	5 M	8.42	6 M	9.05	7 M	8.33	8 M	9.14	8 M	9.14	
				9 M	9.00	10 F	9.57	11 F	8.90	12 F	7.97	13 F	7.99	14 F	8.44	15 F	8.14	16 F	8.93	16 F	8.93	
				17 F	9.72																	
28242	8.11	7.85		1 M	7.68	2 M	8.69	3 M	8.11	4 M	7.07	5 M	10.08	6 M	8.72	7 M	6.48	8 M	9.02	8 M	9.02	
				9 M	8.14	10 M	7.13	11 F	8.21	12 F	8.86	13 F	7.56	14 F	9.15	15 F	5.87	16 F	7.45	16 F	7.45	
				17 M	S 0																	
28276	10.27	10.04		1 M	11.16	2 M	10.73	3 M	10.72	4 M	9.25	5 M	10.26	6 M	9.78	7 M	10.41	8 M	9.86	8 M	9.86	
				9 F	9.92	10 F	9.86	11 F	10.20	12 F	10.21	13 F	10.03									
28245	10.80	10.66		1 M	11.18	2 M	10.42	3 M	10.19	4 M	11.61	5 M	11.64	6 M	10.63	7 M	10.40	8 M	10.34	8 M	10.34	
				9 F	10.46	10 F	11.34	11 F	10.96	12 F	10.51	13 F	10.04									
28226	11.11	10.58		1 M	11.45	2 M	10.22	3 M	10.95	4 M	10.74	5 M	11.25	6 M	11.21	7 M	11.81	8 M	11.81	8 M	11.81	
				9 F	10.25	10 F	10.93	11 F	10.76	12 F	10.36	13 F	S 0									
28255	9.92	9.31		1 M	9.85	2 M	9.65	3 M	9.64	4 M	10.26	5 M	9.89	6 M	10.73	7 M	9.39	8 F	9.85	8 F	9.85	
				9 F	9.32	10 F	9.80	11 F	8.77	12 F	9.18	13 F	9.21	14 F	9.03	15 F	9.03	16 F	9.01	16 F	9.01	
28249	9.63	8.80		1 M	9.37	2 M	9.86	3 M	9.95	4 M	9.02	5 M	10.02	6 M	9.33	7 M	9.85	8 M	9.01	8 M	9.01	
				9 M	10.28	10 F	9.74	11 F	8.01	12 F	8.05	13 F	9.35	14 F	8.84							
28275	10.55	10.41		1 M	10.42	2 M	9.99	3 M	10.49	4 M	10.60	5 M	10.71	6 M	10.85	7 M	11.63	8 M	9.71	8 M	9.71	
				9 F	10.96	10 F	10.71	11 F	10.78	12 F	8.94	13 F	10.64									
28278	9.84	9.63		1 M	10.36	2 M	9.75	3 M	8.95	4 M	9.54	5 M	10.61	6 F	10.46	7 F	9.21	8 F	9.18	8 F	9.18	
				9 F	9.94	10 F	10.02	11 F	9.58	12 F	9.95	13 F	8.73	14 F	9.25	15 F	9.93	16 F	8.78	16 F	8.78	
28255	9.13	8.83		1 M	8.83	2 M	9.35	3 M	9.62	4 M	9.00	5 M	8.01	6 M	9.79	7 M	9.69	8 M	8.78	8 M	8.78	
				9 M	9.50	10 F	D 2	11 M	8.58	12 F	8.41	13 F	8.49	14 F	8.57	15 F	9.69	16 F	9.97	16 F	9.97	
				17 M	S 0	18 M	S 0															

MEAN 9.60 9.29
 S.D. 0.90 0.87
 N 14 14

D= DEAD, M= HISSING, S= STILLBORN

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER
 F1 PUPS GROUP: 150 PPM

LITTER	LACTATION DAY: 4		MEAN		P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT	P S U E	P X WEIGHT																				
	M	F	M	F																																								
28277	8.45	8.16	1 M	8.61	2 M	8.53	3 M	8.15	4 M	8.15	5 M	8.31	6 M	8.98	7 F	8.37	8 F	8.24	9 F	8.58	10 F	7.38	11 F	7.04	13 F	8.27	15 F	8.65	16 F	8.16	17 F	8.54	2 M	9.76	3 M	9.01	5 M	10.00	6 F	10.29	7 F	8.99	8 F	10.37
28272	9.38	9.83	1 M	9.07	2 M	9.64	3 M	9.39	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28270	9.46	8.81	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28288	9.31	8.36	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28253	9.51	8.61	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28264	8.55	8.23	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28233	9.72	9.41	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28225	9.35	8.98	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28257	9.05	8.74	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28267	9.88	8.98	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28200	11.00	10.67	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28258	9.24	9.09	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28262	9.21	8.79	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44
28220	11.37	10.66	1 M	9.28	2 M	9.28	3 M	8.28	4 M	9.74	5 F	9.55	6 F	9.54	7 F	7.53	8 F	8.71	9 F	9.51	10 F	9.23	11 F	8.63	12 F	8.14	14 F	7.47	15 F	9.18	16 F	8.82	17 F	9.20	2 M	9.53	3 M	8.78	5 M	9.77	7 M	9.22	8 F	9.44

MEAN 9.53 9.10
 S.D. 0.80 0.80
 N 14 14
 M= MISSING, S= STILLBORN

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS

LACTATION DAY:	LITTER	MEAN		INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER															
		M	F	P S		U E		P S		U E		P S		U E					
4				P X	W E I G H T	P X	W E I G H T	P X	W E I G H T	P X	W E I G H T	P X	W E I G H T	P X	W E I G H T	P X	W E I G H T		
	28266	7.91	7.33	1 M	7.78	2 M	7.92	3 M	7.71	4 M	7.51	5 M	7.94	6 M	8.03	7 M	8.09	8 M	8.25
				9 M	7.94	10 F	7.37	11 F	8.32	12 F	7.39	13 F	6.61	14 F	6.97				
	28281	9.30	8.83	1 M	8.89	2 M	9.12	3 M	9.96	4 M	8.61	5 M	9.05	6 M	9.46	7 M	8.82	8 M	9.17
				9 M	9.57	10 M	9.68	11 M	10.38	12 M	8.88	13 F	9.81	14 F	9.76	15 F	7.94	16 F	7.82
	28236	9.42	9.06	1 M	9.30	2 M	9.17	3 M	9.77	4 M	9.22	5 M	9.65	6 F	9.12	7 F	9.37	8 F	9.57
				9 F	8.93	10 F	9.14	11 F	9.43	12 F	8.54	13 F	8.69	14 F	8.75				
	28250	7.29	7.20	1 M	7.75	2 M	6.94	3 M	7.14	4 M	6.97	5 M	6.78	6 M	7.41	7 M	8.12	8 M	7.20
				9 F	7.62	10 F	6.77	11 F	7.21	12 F	6.86	13 F	7.46	14 F	7.81	15 F	7.42	16 F	6.47
	28271	9.43	9.07	1 M	9.66	2 M	9.15	3 M	9.94	4 M	9.57	5 M	8.50	6 M	10.62	7 M	8.60	8 F	8.89
				9 F	8.96	10 F	9.33	11 F	9.45	12 F	8.52	13 F	9.23	14 F	9.31	15 F	8.90		
	28263	9.34	8.91	1 M	9.38	2 M	8.85	3 M	9.63	4 M	9.97	5 M	9.02	6 M	9.84	7 M	9.21	8 M	8.80
				9 F	M 2	10 F	8.91	11 F	9.70	12 F	9.61	13 F	8.86	14 F	9.90	15 F	9.28	16 F	7.25
				17 F	8.77														
	28223	8.55	8.24	1 M	9.04	2 M	8.47	3 M	8.20	4 M	8.75	5 M	8.67	6 M	8.67	7 M	8.00	8 M	8.52
				9 M	8.60	10 F	8.01	11 F	8.40	12 F	8.62	13 F	7.33	14 F	8.76	15 F	8.32		
	28283	8.00	7.18	1 M	D 1	2 M	7.68	3 M	8.69	4 M	7.98	5 M	7.74	6 M	7.93	7 F	D 2	8 F	D 2
				9 F	6.87	10 F	7.45	11 F	6.85	12 F	7.51	13 F	6.84	14 F	7.03	15 F	7.71	16 F	7.19
				17 M	D 0														
	28260	9.10	8.76	1 M	M 3	2 M	9.15	3 M	9.71	4 M	8.45	5 M	9.61	6 M	8.91	7 M	8.79	8 F	M 3
				9 F	9.05	10 F	8.41	11 F	9.03	12 F	8.67	13 F	9.51	14 F	8.48	15 F	8.73	16 F	8.16
	28259	9.72	9.24	1 M	9.67	2 M	10.24	3 M	8.93	4 M	9.42	5 M	11.28	6 M	8.86	7 M	9.64	8 F	9.37
				9 F	8.60	10 F	9.42	11 F	9.40	12 F	9.32	13 F	8.93	14 F	9.23	15 F	9.66		
	28252	10.75	10.29	1 M	10.65	2 M	10.63	3 M	11.03	4 M	10.33	5 M	10.42	6 M	10.66	7 M	11.51	8 F	10.53
				9 F	10.15	10 F	9.37	11 F	10.64	12 F	10.77								
	28222	9.97	9.58	1 M	M 2	2 M	9.81	3 M	10.05	4 M	10.14	5 M	9.96	6 M	10.11	7 M	10.27	8 M	9.42
				9 F	9.66	10 F	9.33	11 F	9.90	12 F	9.85	13 F	9.18						
	28224	9.39	8.92	1 M	9.71	2 M	8.98	3 M	9.94	4 M	9.35	5 M	8.85	6 M	9.07	7 M	9.55	8 M	9.55
				9 F	9.09	10 F	9.65	11 F	8.36	12 F	8.64	13 F	8.71	14 F	9.03	15 F	8.99		
	20221	10.56	10.21	1 M	10.89	2 M	10.26	3 M	10.28	4 M	10.79	5 M	10.37	6 M	10.79	7 F	10.63	8 F	10.13
				9 F	9.81	10 F	11.18	11 F	10.61	12 F	9.61	13 F	9.53	14 M	D 0				
	28230	7.82	7.83	1 M	8.77	2 M	7.92	3 M	8.37	4 M	7.56	5 M	7.57	6 M	7.17	7 M	7.37	8 F	8.58
				9 F	8.62	10 F	8.13	11 F	7.62	12 F	7.20	13 F	7.99	14 F	8.38	15 F	6.90	16 F	7.06

MEAN 9.10 8.71
 S.D. 1.01 0.99
 N 15 15

D= DEAD, M= MISSING

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL PUP BODY WEIGHT (GRAMS) PER LITTER
 F1 PUPS GROUP: 1500 PPM

LACTATION DAY: 4	LITTER	MEAN	N	F	PS		UE		PS		UE		PS		UE		PS		UE		PS		UE	
					P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT	P X	WEIGHT
	28265	8.05	8.02	1 M	D 1	2 M	8.75	3 M	7.42	4 M	8.01	5 M	8.31	6 M	7.78	7 F	M 1	8 F	8.02					
	28269	8.62	8.36	9 F	7.63	10 F	8.94	11 F	7.86	12 F	7.93	13 F	7.91	14 F	8.10	15 F	8.24	16 F	7.57					
	28279	8.59	8.04	1 M	8.34	2 M	9.22	3 M	8.58	4 M	8.98	5 M	7.86	6 M	8.99	7 M	8.35	8 F	8.22					
	28268	9.63	9.71	9 F	8.73	10 F	8.21	11 F	8.48	12 F	7.98	13 F	9.06	14 F	8.10	15 F	8.06							
	28254	9.40	8.96	1 M	8.63	2 M	8.06	3 M	9.19	4 M	8.50	5 M	8.57	6 F	8.56	7 F	7.72	8 F	7.99					
	28243	9.09	8.16	9 F	7.23	10 F	8.42	11 F	8.01	12 F	8.18	13 F	7.92	14 F	8.32									
	28247	9.39	8.90	1 M	9.18	2 M	9.45	3 M	9.77	4 M	9.51	5 M	9.99	6 M	9.40	7 M	10.13	8 F	D 2					
	28285	10.49	9.66	9 F	10.05	10 F	9.93	11 F	9.49	12 F	10.04	13 F	9.75	14 F	9.02									
	28231	8.41	7.93	1 M	8.90	10 F	8.78	11 F	9.01	12 F	9.52	5 M	9.23	6 M	9.02	7 M	9.30	8 M	9.14					
	28246	8.13	8.41	1 M	9.16	2 M	8.67	3 M	9.13	4 M	9.40	5 M	9.07	6 M	3.84	7 M	5.15	8 M	9.16					
	28234	9.43	9.24	9 M	8.62	10 M	9.71	11 F	8.33	12 F	6.89	13 F	8.65	14 F	8.27	15 F	8.67							
	28241	9.60	8.58	1 M	9.25	10 F	9.07	11 F	8.61	12 F	8.24	13 M	5.0											
	28251	9.89	9.46	1 M	10.69	2 M	10.15	3 M	10.26	4 M	10.78	5 M	10.36	6 M	10.71	7 F	M 1	8 F	9.73					
	28284	6.24	6.11	9 F	10.06	10 F	10.25	11 F	9.69	12 F	9.87	13 F	8.35											
				1 M	8.72	2 M	8.28	3 M	8.04	4 M	8.66	5 M	8.37	6 F	7.73	7 F	8.05	8 F	7.53					
				9 F	7.88	10 F	8.08	11 F	8.60	12 F	7.76	13 F	7.81											
				1 M	7.71	2 M	8.92	3 M	5.40	4 M	8.68	5 M	9.00	6 M	8.56	7 M	8.15	8 M	8.02					
				9 M	8.72	10 F	8.28	11 F	8.52	12 F	8.59	13 F	8.06	14 F	8.57	15 F	8.45							
				1 M	9.51	2 M	9.49	3 M	9.97	4 M	9.12	5 M	8.93	6 M	8.90	7 M	9.46	8 M	10.03					
				9 F	8.61	10 F	8.56	11 F	8.16	12 F	8.79	13 F	9.57	14 F	9.36	15 F	11.21	16 F	9.68					
				1 M	9.84	2 M	9.80	3 M	9.23	4 M	9.16	5 M	9.79	6 M	9.25	7 M	10.11	8 F	9.67					
				9 F	9.11	10 F	9.38	11 F	6.03	12 F	8.04	13 F	10.57	14 F	7.54	15 F	9.39	16 F	9.86					
				1 M	9.05	2 M	9.24	3 M	10.11	4 M	9.88	5 M	10.57	6 M	10.09	7 M	9.99	8 M	10.21					
				9 F	9.57	10 F	9.69	11 F	9.56	12 F	9.01	13 F	9.02	14 F	9.88									
				1 M	6.97	2 M	6.51	3 M	4.91	4 M	5.60	5 M	6.42	6 M	6.15	7 M	7.13	8 F	6.49					
				9 F	6.16	10 F	5.78	11 F	6.89	12 F	5.05	13 F	6.59	14 F	5.50	15 F	6.40							

MEAN 8.93 8.54
 S.D. 1.04 0.93
 N 14 14

D= DEAD, M= MISSING, S= STILLBORN

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

Individual Anatomic Pathology Data

(41 Pages)

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TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

NECROPSY PROTOCOL

F0 ADULT MALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	ORAL/PHARYNGEAL	TONGUE	ESOPHAGUS
STOMACH	LIVER	PANCREAS	DUODENUM	JEJUNUM
ILEUM	CECUM	COLON	RECTUM	ANUS
PITUITARY	THYROID GL	PARATHYROID GL	ADRENAL GL	SKIN
SUBCUTIS	HEAD	EARS	NARES/NOSE	MAMMARY GL
PAWS/FEET	TAIL	SPLEEN	LYMPH ND, S-MAN	LYMPH ND, MED
LYMPH ND, MES	THYMIC REGION	BONE/JOINT	BONE, STERNUM	BONE, FEMUR
BONE, VERTEBRA	SKELETAL MUSCLE	DIAPHRAGM	BRAIN	SPINAL CORD
NERVE, SCIATIC	EYE	HARDEPIAN GL	LACRIMAL GL	TESTES
EPIDIDYMIDES	VASA DEFERENTIA	SEMINAL VESICLE	COAGULATING GL	PROSTATE
PENIS	LARYNX	TRACHEA	LUNGS	KIDNEYS
URETER	URINARY BLADDER	URETHRA		

The following organs were weighed at necropsy:

LIVER	THYMIC REGION	TESTES	EPIDIDYMIDES	LUNGS
KIDNEYS				

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	F0 ADULT
ANIMAL	28200	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	SKIN
LIVER	10.602	2.794	GROSS: SHAPE/CONTOUR CHANGE
KIDNEYS	2.905	0.765	PUNCTATE RED AREAS ON TAIL
LUNGS	1.557	0.410	MICRO: (4) FOLLICULITIS
THYMIC REGION	0.266	0.070	MICRO: 3 HYPERKERATOSIS
EPIDIDYMIDES	1.382	0.364	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TESTES	3.385	0.892	HEART LIVER ADRENAL GL
TERMINAL BODY WT.	379.5		SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			NASAL CAVITY LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28171	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	LYMPH ND, S-MAN
LIVER	12.664	2.791	GROSS: SIZE INCREASE
KIDNEYS	3.247	0.716	SLIGHT
LUNGS	1.575	0.347	MICRO: 3 LYMPHOID HYPERPLASIA
THYMIC REGION	0.399	0.088	MICRO: 3 PLASMACYTOSIS
EPIDIDYMIDES	1.186	0.261	KIDNEYS
TESTES	3.487	0.769	MICRO: (4) TUBULAR BASOPHILIA
TERMINAL BODY WT.	453.7		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			NASAL CAVITY LARYNX TRACHEA
			LUNGS
ANIMAL	28156	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	LUNGS
LIVER	11.486	2.451	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS	3.030	0.647	ALL LOBES 1MM RED FOCAL AREAS
LUNGS	1.437	0.307	SCATTERED THROUGHOUT
THYMIC REGION	0.321	0.069	MICRO: EXAMINED - NO SIGNIFICANT LESIONS
EPIDIDYMIDES	1.244	0.265	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TESTES	3.381	0.722	HEART LIVER ADRENAL GL
TERMINAL BODY WT.	468.6		SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			NASAL CAVITY LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28173	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	SKIN
LIVER	9.817	2.391	GROSS: SHAPE/CONTOUR CHANGE
KIDNEYS	3.142	0.765	TWO 1X1 MM RAISED AREAS
LUNGS	1.395	0.340	MICRO: 4 FOLLICULITIS
THYMIC REGION	0.346	0.084	SUPPURATIVE INFLAMMATION WITH BROKEN
EPIDIDYMIDES	1.197	0.292	HAIR SHAFTS
TESTES	3.100	0.755	LYMPH ND, S-MAN

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	FO ADULT	
<hr/>				
ANIMAL	28173 (CONTINUED)			
TERMINAL BODY WT.	410.5			
		GROSS:	SIZE INCREASE ONE NODE, 12X12X7 MM	
		MICRO+ 4	PLASMOCYTOSIS	
		MICRO: 3	LYMPHOID HYPERPLASIA	
		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
		HEART	LIVER ADRENAL GL	
		SPLEEN	THYMIC REGION BRAIN	
		TESTES	EPIDIDYMIDES SEMINAL VESICLE	
		NASAL CAVITY	LARYNX TRACHEA	
		LUNGS	KIDNEYS	
<hr/>				
ANIMAL	28191	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	9.549	2.385	STOMACH	
KIDNEYS	2.965	0.741	GROSS:	
LUNGS	1.541	0.385	CONTENTS ABNORMAL	
THYMIC REGION	0.348	0.087	CONTAINS BRIGHT YELLOW FLUID	
EPIDIDYMIDES	1.688	0.422	EPIDIDYMIDES	
TESTES	3.240	0.809	GROSS:	NODULE
TERMINAL BODY WT.	400.3		YELLOW, 6X6X4MM, TIP OF HEAD	
			MICRO: EXAMINED	- NO SIGNIFICANT LESIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
			HEART	STOMACH LIVER
			ADRENAL GL	SPLEEN THYMIC REGION
			BRAIN	TESTES EPIDIDYMIDES
			SEMINAL VESICLE	NASAL CAVITY LARYNX
			TRACHEA	LUNGS KIDNEYS
<hr/>				
ANIMAL	28162	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	11.130	2.319	STOMACH	
KIDNEYS	3.281	0.683	GROSS:	
LUNGS	1.506	0.314	CONTENTS ABNORMAL	
THYMIC REGION	0.412	0.086	CONTAINS REDDISH-ORANGE FLUID	
EPIDIDYMIDES	1.270	0.265	LIVER	
TESTES	3.171	0.661	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
TERMINAL BODY WT.	480.0		TAN PUNCTATE FOCI, MULTIPLE, VISCERAL	
			SURFACE, ALL LOBES	
			MICRO: EXAMINED	- NO SIGNIFICANT LESIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
			HEART	STOMACH LIVER
			ADRENAL GL	SPLEEN THYMIC REGION
			BRAIN	TESTES EPIDIDYMIDES
			SEMINAL VESICLE	NASAL CAVITY LARYNX
			TRACHEA	LUNGS KIDNEYS
<hr/>				
ANIMAL	28153	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	10.682	2.378	LIVER	
KIDNEYS	3.144	0.700	GROSS:	
LUNGS	1.529	0.340	COLOR CHANGE, FOCAL/MULTIFOCAL	
THYMIC REGION	0.372	0.083	TAN FOCUS BETWEEN MEDIAN LOBES	
EPIDIDYMIDES	1.355	0.302	MICRO+ P	LIPOSTOMATA
TESTES	3.793	0.844	ATTACHMENT OF FALCIFORM LIGAMENT	
			LYMPH ND, S-MAN	
			GROSS:	SIZE INCREASE

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	FO ADULT

ANIMAL	28153 (CONTINUED)		
TERMINAL BODY WT.	449.2		
			2-3X NORMAL, LEFT
		MICRO+ 4	LYMPHOID HYPERPLASIA
		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
		HEART	ADRENAL GL SPLEEN
		THYMIC REGION	BRAIN TESTES
		EPIDIDYMIDES	SEMINAL VESICLE NASAL CAVITY
		LARYNX	TRACHEA LUNGS
		KIDNEYS	
ANIMAL	28155	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	12.011	2.439	LYMPH ND, S-MAN
KIDNEYS	3.609	0.733	GROSS: SIZE INCREASE
LUNGS	1.549	0.315	3X NORMAL, LEFT
THYMIC REGION	0.296	0.060	MICRO+ 3 LYMPHOID HYPERPLASIA
EPIDIDYMIDES	1.329	0.270	LYMPH ND, S-MAN
TESTES	3.772	0.766	GROSS: COLOR CHANGE, DIFFUSE
TERMINAL BODY WT.	492.5		DARK RED, BILATERAL
		MICRO+ 3	HEMORRHAGE
		MICRO: 2	PLASMACYTOSIS
		THYMIC REGION	
		GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
			MULTIPLE DARK RED FOCI
		MICRO+ 3	HEMORRHAGE
		LUNGS	
		GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
			MULTIPLE DARK RED FOCI, ALL LOBES
		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL.	
		HEART	LIVER ADRENAL GL
		SPLEEN	BRAIN TESTES
		EPIDIDYMIDES	SEMINAL VESICLE NASAL CAVITY
		LARYNX	TRACHEA LUNGS
		KIDNEYS	
ANIMAL	28198	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	9.084	2.259	COLON
KIDNEYS	2.472	0.615	GROSS: PARASITE
THYMIC REGION	0.423	0.105	PINWORM
EPIDIDYMIDES	1.368	0.340	EPIDIDYMIDES
TESTES	2.848	0.708	GROSS: NODULE
TERMINAL BODY WT.	402.		4X4X3MM, TIP OF HEAD, YELLOW
			RIGHT
		MICRO+ (4)	SPERM GRANULOMA
			UNILATERAL
		LUNGS	
		GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
			DARK RED FOCI, LEFT LOBE
		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
		HEART	LIVER ADRENAL GL
		SPLEEN	THYMIC REGION BRAIN
		TESTES	SEMINAL VESICLE NASAL CAVITY
		LARYNX	TRACHEA LUNGS
		KIDNEYS	

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TABLE 2
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	PO ADULT
ANIMAL	28178	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	11.339	2.498	SKIN
KIDNEYS	3.651	0.804	GROSS: SHAPE/CONTOUR CHANGE
LUNGS	1.601	0.353	RAISED AREAS, BROWN, 1X1X1MM, TAIL
THYMIC REGION	0.364	0.080	MICRO+((3)) HYPERKERATOSIS
EPIDIDYMIDES	1.408	0.310	MICRO: (4) EPIDERMITIS
TESTES	3.713	0.818	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	453.8		HEART LIVER ADRENAL GL
			SPLZEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			NASAL CAVITY LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28201	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	11.749	2.529	STOMACH
KIDNEYS	3.068	0.660	GROSS: CONTENTS ABNORMAL
LUNGS	1.618	0.348	CONTAINS BRIGHT YELLOW MATERIAL
THYMIC REGION	0.420	0.090	LUNGS
EPIDIDYMIDES	1.379	0.297	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
TESTES	5.124	0.672	PUNCTATE RED FOCI, LEFT, RIGHT
TERMINAL BODY WT.	464.6		APICAL, RIGHT CARDIAC
			AND RIGHT DIAPHRAGMATIC LOBES
			MICRO: EXAMINED - NO SIGNIFICANT LESIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART STOMACH LIVER
			ADRENAL GL SPLZEN THYMIC REGION
			BRAIN TESTES EPIDIDYMIDES
			SEMINAL VESICLE NASAL CAVITY LARYNX
			TRACHEA LUNGS KIDNEYS
ANIMAL	28180	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	14.874	2.961	ADRENAL GL
KIDNEYS	3.024	0.602	MICRO: 2 CORTICAL CELL VACUOLIZATION
LUNGS	1.587	0.316	LYMPH ND, S-MAN
THYMIC REGION	0.350	0.070	GROSS: SIZE INCREASE
EPIDIDYMIDES	1.311	0.261	TWO NODES, 10X10X2 MM, 16X12X4 MM
TESTES	3.459	0.689	MICRO+ 5 PLASMACYTOSIS
TERMINAL BODY WT.	502.3		LYMPH ND, S-MAN
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			TAN WITH RED FOCI, BOTH NODES
			MICRO: 4 LYMPHOID HYPERPLASIA
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER SPLZEN
			THYMIC REGION BRAIN TESTES
			EPIDIDYMIDES SEMINAL VESICLE NASAL CAVITY
			LARYNX TRACHEA LUNGS
			KIDNEYS

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	FO ADULT
ANIMAL	28159	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	13.379	2.524	SKIN
KIDNEYS	4.132	0.779	GROSS:
LUNGS	1.659	0.313	SHAPE/CONTOUR CHANGE
THYMIC REGION	0.331	0.062	ONE BROWN PUNCTATE RAISED AREA NEAR
EPIDIDYMIDES	1.212	0.229	BASE OF TAIL
TESTES	3.991	0.753	MICRO+ (3) FOLLICULITIS
TERMINAL BODY WT.	530.2		SPLEEN
			GROSS:
			ACCESSORY
			4X5X2MM ATTACHED TO ONE POLE
			MICRO+ (2) ACCESSORY SPLEEN
			LYMPH ND, S-MAN
			GROSS:
			SIZE INCREASE
			RIGHT SIDE ONE 20X10X4MM
			MICRO+ 4 LYMPHOID HYPERPLASIA
			MICRO: 4 PLASMACYTOSIS
			THYMIC REGION
			GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			MULTIPLE PUNCTATE RED FOCAL AREAS
			SCATTERED THROUGHOUT
			MICRO+((3)) HEMORRHAGE
			TESTES
			MICRO: (4) SEMINIFEROUS TUBULE ATROPHY
			UNILATERAL, PERIPHERY OF TESTICLE
			KIDNEYS
			MICRO: ((3)) TUBULAR BASOPHILIA
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			BRAIN EPIDIDYMIDES SEMINAL VESICLE
			NASAL CAVITY LARYNX TRACHEA
			LUNGS
ANIMAL	28167	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	11.980	2.601	SKIN
KIDNEYS	3.523	0.765	GROSS:
LUNGS	1.548	0.336	SHAPE/CONTOUR CHANGE
THYMIC REGION	0.335	0.073	MULTIPLE, DARK BROWN RAISED AREAS,
EPIDIDYMIDES	1.253	0.272	NEAR TATTOOING NUMBERS
TESTES	3.738	0.812	MICRO+ 3 DERMAL FIBROSIS
TERMINAL BODY WT.	460.6		MICRO: (3) FOLLICULITIS
			((3)) HYPERKERATOSIS
			LYMPH ND, S-MAN
			GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			MULTIPLE DARK RED FOCI, BILATERAL
			MICRO+((2)) HEMORRHAGE
			LYMPH ND, S-MAN
			GROSS:
			SIZE INCREASE
			15X10X5MM, LEFT
			MICRO+ 4 PLASMACYTOSIS
			MICRO: 4 LYMPHOID HYPERPLASIA
			LUNGS
			GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			DARK RED FOCI, ALL RIGHT LOBES
			KIDNEYS

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM MALE FO ADULT

 ANIMAL 28167 (CONTINUED)

MICRO: (2) TUBULAR BASOPHILIA
 (2) NEPHRITIS, INTERSTITIAL
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 TESTES EPIDIDYMIDES SEMINAL VESICLE
 NASAL CAVITY LARYNX TRACHEA
 LUNGS

ANIMAL 28174 27-FEB-92 STUDY DAY 52

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	12.006	2.592
KIDNEYS	2.847	0.615
LUNGS	1.620	0.350
THYMIC REGION	0.252	0.054
EPIDIDYMIDES	1.202	0.260
TESTES	3.243	0.700
TERMINAL BODY WT.	463.1	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 LUNGS

MICRO: (3) ALVEOLAR HISTIOCYTOSIS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 TESTES EPIDIDYMIDES SEMINAL VESICLE
 NASAL CAVITY LARYNX TRACHEA
 KIDNEYS

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 150 PPM MALE			FO ADULT	
<u>ANIMAL</u>	<u>28184</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>		
LIVER	9.508	2.513	THYMIC REGION	
KIDNEYS	2.601	0.688	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
LUNGS	1.366	0.361		MULTIPLE DARK RED FOCI
THYMIC REGION	0.238	0.073	TESTES	
EPIDIDYMIDES	0.673	0.178	GROSS:	SIZE DECREASE
TESTES	1.846	0.488		0.50 OF NORMAL, LEFT
TERMINAL BODY WT.	378.3		NASAL CAVITY	
			MICRO: 1	VACUOLIZATION OF OLFACTORY EPITHELIUM
<u>ANIMAL</u>	<u>26187</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>		
LIVER	8.840	2.452	NASAL CAVITY	
KIDNEYS	2.539	0.704	MICRO: ((1))	VACUOLIZATION OF OLFACTORY EPITHELIUM
LUNGS	1.338	0.371	LUNGS	
THYMIC REGION	0.273	0.076	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
EPIDIDYMIDES	1.147	0.318		LEFT LOBE 1MM RED FOCAL AREAS
TESTES	3.192	0.885		SCATTERED THROUGHOUT
TERMINAL BODY WT.	360.5			
<u>ANIMAL</u>	<u>28195</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>		
LIVER	10.300	2.600	SKIN	
KIDNEYS	3.162	0.754	GROSS:	SHAPE/CONTOUR CHANGE
LUNGS	1.492	0.356		RAISED AREAS, BROWN, ADJACENT TO
THYMIC REGION	0.477	0.114	MICRO: EXAMINED -	NO SIGNIFICANT LESIONS
EPIDIDYMIDES	1.251	0.298		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TESTES	3.074	0.733	NASAL CAVITY	
TERMINAL BODY WT.	419.2			
<u>ANIMAL</u>	<u>28181</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>		
LIVER	9.830	2.424	LIVER	
KIDNEYS	3.264	0.805	GROSS:	SIZE DECREASE
LUNGS	1.509	0.372		SLIGHT, ALL LOBES
THYMIC REGION	0.415	0.102	LYMPH ND, S-MAN	
EPIDIDYMIDES	1.306	0.322	GROSS:	SIZE INCREASE
TESTES	3.766	0.929		SLIGHT, BILATERAL
TERMINAL BODY WT.	405.5		LYMPH ND, S-MAN	
			GROSS:	COLOR CHANGE, DIFFUSE
				RED AND TAN, RIGHT
			THYMIC REGION	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				MULTIPLE DARK RED FOCI
			NASAL CAVITY	
			MICRO: 2	VACUOLIZATION OF OLFACTORY EPITHELIUM
			1	ATROPHY, OLFACTORY EPITHELIUM
			LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL

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 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 150 PPM		MALE		FO ADULT	

ANIMAL	28181	(CONTINUED)			
ANIMAL	28165	27-FEB-92	STUDY DAY	52	MULTIPLE DARK RED FOCI, ALL LOBES
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN		
LIVER	9.616	2.591	GROSS:	COLOR CHANGE, DIFFUSE	
KIDNEYS	2.954	0.891		DARK RED, RIGHT	
LUNGS	1.380	0.371	NASAL CAVITY		
THYMIC REGION	0.270	0.073	MICRO: 1	VACUOLIZATION OF OLFACTORY EPITHELIUM	
EPIDIDYMIDES	1.381	0.371			
TESTES	3.587	0.963			
TERMINAL BODY WT.	372.3				

ANIMAL	28199	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	11.224	2.591	GROSS:	SHAPE/CONTOUR CHANGE	
KIDNEYS	3.081	0.711		ONE RAISED RED AREA, TAIL	
LUNGS	1.405	0.324	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
THYMIC REGION	0.577	0.122	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
EPIDIDYMIDES	1.417	0.327	NASAL CAVITY		
TESTES	3.227	0.745			
TERMINAL BODY WT.	433.2				

ANIMAL	28150	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN		
LIVER	11.392	2.510	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL	
KIDNEYS	2.863	0.631		MULTIPLE DARK RED FOCI, BILATERAL	
LUNGS	1.481	0.326	THYMIC REGION		
THYMIC REGION	0.359	0.079	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL	
EPIDIDYMIDES	1.159	0.255		MULTIPLE DARK RED FOCI	
TESTES	3.263	0.719	NASAL CAVITY		
TERMINAL BODY WT.	453.9		MICRO: 1	VACUOLIZATION OF OLFACTORY EPITHELIUM	

ANIMAL	28210	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN		
LIVER	11.238	2.651	GROSS:	SIZE INCREASE	
KIDNEYS	3.797	0.896		4X NORMAL, BILATERAL	
LUNGS	1.616	0.381	NASAL CAVITY		
THYMIC REGION	0.269	0.063	MICRO: 3	VACUOLIZATION OF OLFACTORY EPITHELIUM	
EPIDIDYMIDES	1.222	0.288			
TESTES	3.192	0.753			
TERMINAL BODY WT.	423.9				

ANIMAL	28212	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	12.398	2.782	GROSS:	SHAPE/CONTOUR CHANGE	
KIDNEYS	2.813	0.631		PUNCTATE RED AREAS, TAIL	
LUNGS	1.621	0.364	LYMPH ND, S-MAN		
THYMIC REGION	0.545	0.123	GROSS:	COLOR CHANGE, DIFFUSE	

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 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:		150 PPM	MALE	FO ADULT	
<hr/>					
ANIMAL	28212 (CONTINUED)				
EPIDIDYMIDES	1.281	0.287			DARK RED
TESTES	3.247	0.729	NASAL CAVITY		
TERMINAL BODY WT.	445.6		MICRO: 1		VACUOLIZATION OF OLFACTORY EPITHELIUM
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ANIMAL	28194	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.			
LIVER	10.344	2.351	LIVER		
KIDNEYS	2.562	0.582	GROSS:		SIZE DECREASE
LUNGS	1.573	0.357			SLIGHT, ALL LOBES
THYMIC REGION	0.217	0.049	NASAL CAVITY		
EPIDIDYMIDES	1.166	0.255	MICRO: 2		VACUOLIZATION OF OLFACTORY EPITHELIUM
TESTES	2.870	0.652			
TERMINAL BODY WT.	440.0				
<hr/>					
ANIMAL	28168	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.			
LIVER	10.614	2.443	LYMPH ND, S-MAN		
KIDNEYS	3.105	0.715	GROSS:		SIZE INCREASE
LUNGS	1.481	0.341			NORMAL, LEFT SIDE
THYMIC REGION	0.211	0.049	THYMIC REGION		
EPIDIDYMIDES	1.240	0.285	GROSS:		SIZE DECREASE
TESTES	3.291	0.757			0.50 OF NORMAL
TERMINAL BODY WT.	434.5		NASAL CAVITY		
			MICRO: 2		VACUOLIZATION OF OLFACTORY EPITHELIUM
<hr/>					
ANIMAL	28160	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.			
LIVER	12.592	2.569	GROSS: EXAMINED - NO SIGNIFICANT LESIONS		
KIDNEYS	3.446	0.703	NASAL CAVITY		
LUNGS	1.629	0.332	MICRO: 1		VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.268	0.055			
EPIDIDYMIDES	1.296	0.264			
TESTES	3.664	0.747			
TERMINAL BODY WT.	490.2				
<hr/>					
ANIMAL	28169	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.			
LIVER	12.393	2.777	SKIN		
KIDNEYS	3.841	0.861	GROSS:		SHAPE/CONTOUR CHANGE
LUNGS	1.599	0.358			1X1 MM RED RAISED AREAS, TAIL
THYMIC REGION	0.332	0.074	NASAL CAVITY		
EPIDIDYMIDES	1.311	0.294	MICRO: 2		VACUOLIZATION OF OLFACTORY EPITHELIUM
TESTES	3.457	0.775			
TERMINAL BODY WT.	446.3				
<hr/>					
ANIMAL	28188	27-FEB-92	STUDY DAY	52	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.			
LIVER	12.142	2.289	GROSS: EXAMINED - NO SIGNIFICANT LESIONS		
KIDNEYS	3.361	0.634	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
LUNGS	1.813	0.342			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			NASAL CAVITY		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 150 PPM			MALE		F0 ADULT	
<hr/>						
<u>ANIMAL</u>	<u>28188 (CONTINUED)</u>					
THYMIC REGION	0.328	0.062				
EPIDIDYMIDES	1.501	0.283				
TESTES	3.984	0.751				
TERMINAL BODY WT.	530.5					
<hr/>						
<u>ANIMAL</u>	<u>28193</u>	<u>27-FEB-92</u>	<u>STUDY DAY</u>	<u>52</u>		
<u>TYPE OF DEATH: SCHEDULED SACRIFICE</u>						
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	<u>THYMIC REGION</u>			
LIVER	10.978	2.599	GROSS:		COLOR CHANGE, FOCAL/MULTIFOCAL	
KIDNEYS	2.876	0.681			MULTIPLE DARK RED FOCI	
LUNGS	1.676	0.397	NASAL CAVITY			
THYMIC REGION	0.286	0.068	MICRO:	3	VACUOLIZATION OF OLFACTORY EPITHELIUM	
EPIDIDYMIDES	1.192	0.282		1	ATROPHY, OLFACTORY EPITHELIUM	
TESTES	3.415	0.809				
TERMINAL BODY WT.	422.4					

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TABLE 2
PROPIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD¹ FATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:		750 PPM		MALE		FO ADULT	
ANIMAL	28146	27-FEB-92	STUDY DAY 52				
TYPE OF DEATH: SCHEDULED SACRIFICE							
ORGAN WEIGHT	ABS. (G)	REL.					
LIVER	10.821	2.524	LYMPH ND, S-MAN				
KIDNEYS	2.762	0.644	CROSS:	SIZE INCREASE			
LUNGS	1.712	0.399		ONE NODE, 12X10X4 MM			
THYMIC REGION	0.210	0.051	NASAL CAVITY				
EPIDIDYMIDES	1.297	0.302	MICRO:	2	RHINITIS		
TESTES	3.221	0.751		3	ATROPHY, OLFACTORY EPITHELIUM		
TERMINAL BODY WT.	28.8			4	VACUOLIZATION OF OLFACTORY EPITHELIUM		
ANIMAL	28203	27-FEB-92	STUDY DAY 52				
TYPE OF DEATH: SCHEDULED SACRIFICE							
ORGAN WEIGHT	ABS. (G)	REL.					
LIVER	11.368	2.564	LYMPH ND, S-MAN				
KIDNEYS	3.261	0.736	CROSS:	SIZE INCREASE			
LUNGS	1.651	0.372		ONE NODE 17X12X4 MM			
THYMIC REGION	0.308	0.069	NASAL CAVITY				
EPIDIDYMIDES	1.331	0.300	MICRO:	4	VACUOLIZATION OF OLFACTORY EPITHELIUM		
TESTES	3.522	0.794		3	ATROPHY, OLFACTORY EPITHELIUM		
TERMINAL BODY WT.	443.4						
ANIMAL	28149	27-FEB-92	STUDY DAY 52				
TYPE OF DEATH: SCHEDULED SACRIFICE							
ORGAN WEIGHT	ABS. (G)	REL.					
LIVER	11.650	2.577	GROSS: EXAMINED	- NO SIGNIFICANT LESIONS			
KIDNEYS	3.418	0.756	NASAL CAVITY				
LUNGS	1.461	0.323	MICRO:	2	RHINITIS		
THYMIC REGION	0.236	0.052		2	VACUOLIZATION OF OLFACTORY EPITHELIUM		
EPIDIDYMIDES	1.236	0.274					
TESTES	3.295	0.729					
TERMINAL BODY WT.	452.1						
ANIMAL	28190	27-FEB-92	STUDY DAY 52				
TYPE OF DEATH: SCHEDULED SACRIFICE							
ORGAN WEIGHT	ABS. (G)	REL.					
LIVER	8.952	2.429	SKIN				
KIDNEYS	2.765	0.750	GROSS:	SHAPE/CONTOUR CHANGE			
LUNGS	1.296	0.352		MULTIPLE PUP: PATE BROWN RAISED AREAS			
THYMIC REGION	0.256	0.069		ALONG TAIL			
EPIDIDYMIDES	1.249	0.339	NASAL CAVITY				
TESTES	3.115	0.845	MICRO:	3	VACUOLIZATION OF OLFACTORY EPITHELIUM		
TERMINAL BODY WT.	368.5			2	ATROPHY, OLFACTORY EPITHELIUM		
ANIMAL	28192	27-FEB-92	STUDY DAY 52				
TYPE OF DEATH: SCHEDULED SACRIFICE							
ORGAN WEIGHT	ABS. (G)	REL.					
LIVER	10.212	2.272	SKIN				
KIDNEYS	3.136	0.698	GROSS:	SHAPE/CONTOUR CHANGE			
LUNGS	1.444	0.321		TAN AND BROWN RAISED AREAS, TAIL,			
THYMIC REGION	0.446	0.099		1X1X1MM			
EPIDIDYMIDES	1.175	0.261	LYMPH ND, S-MAN				
			GROSS:	SIZE INCREASE			

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	750 PPM	MALE	FO ADULT
<hr/>			
ANIMAL	28192	(CONTINUED)	
TESTES	3.239	0.720	20X11X4MM, LEFT
TERMINAL BODY WT.	449.5		
			LYMPH ND, S-MAN GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED DARK RED AND RED, LEFT
			NASAL CAVITY MICRO: 2 VACUOLIZATION OF OLFACTORY EPITHELIUM 2 ATROPHY, OLFACTORY EPITHELIUM
			LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED PUNCTATE FOCI, ALL LOBES
<hr/>			
ANIMAL	28211	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	11.621	2.643	NASAL CAVITY MICRO: 4 VACUOLIZATION OF OLFACTORY EPITHELIUM 2 ATROPHY, OLFACTORY EPITHELIUM
KIDNEYS	3.985	0.906	
THYMIC REGION	0.264	0.060	LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL PUNCTATE RED FOCI, SCATTERED ON ALL LOBES
EPIDIDYMIDES	1.390	0.316	
TESTES	3.685	0.938	
TERMINAL BODY WT.	439.7		
<hr/>			
ANIMAL	28176	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	10.285	2.404	LYMPH ND, S-MAN GROSS: SIZE INCREASE 2X NORMAL, LEFT
KIDNEYS	3.087	0.722	
LUNGS	1.656	0.387	NASAL CAVITY MICRO: ((1)) VACUOLIZATION OF OLFACTORY EPITHELIUM ((2)) RHINITIS
THYMIC REGION	0.438	0.102	
EPIDIDYMIDES	1.251	0.292	LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MULTIPLE PUNCTATE RED FOCI, ALL LOBES
TESTES	3.507	0.620	
TERMINAL BODY WT.	427.9		
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ANIMAL	28209	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	10.549	2.519	SKIN GROSS: SHAPE/CONTOUR CHANGE BROWN MULTIPLE PUNCTATE RAISED AREAS ON TAIL
KIDNEYS	3.054	0.729	
LUNGS	1.391	0.332	LYMPH ND, S-MAN GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MULTIPLE PUNCTATE RED FOCAL AREAS ON ONE NODE LEFT SIDE
THYMIC REGION	0.325	0.078	
EPIDIDYMIDES	1.051	0.251	NASAL CAVITY MICRO: 2 RHINITIS 4 VACUOLIZATION OF OLFACTORY EPITHELIUM 2 ATROPHY, OLFACTORY EPITHELIUM
TESTES	3.175	0.759	
TERMINAL BODY WT.	418.8		LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL LEFT LOBE SEVERAL BROWN IMM FOCAL AREAS SCATTERED THROUGHOUT

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TABLE 2
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 750 PPM MALE			FO ADULT	
ANIMAL	28182	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	11.388	2.440	SKIN	
KIDNEYS	3.067	0.657	GROSS:	SHAPE/CONTOUR CHANGE
LUNGS	1.602	0.343		MULTIPLE RED RAISED AREAS, TAIL
THYMIC REGION	0.495	0.106	LYMPH ND, S-MAN	
EPIDIDYIMIDES	1.309	0.280	GROSS:	SIZE INCREASE
TESTES	3.230	0.692		ONE NODE 12X10X3 MM
TERMINAL BODY WT.	466.8		LYMPH ND, S-MAN	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				PUNCTATE RED FOCI
			NASAL CAVITY	
			MICRO: 3	VACUOLIZATION OF OLFACTORY EPITHELIUM
			LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				SCATTERED PUNCTATE RED FOCI, ALL LOBES
ANIMAL	28186	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	13.176	2.989	LYMPH ND, S-MAN	
KIDNEYS	3.730	0.846	GROSS:	SIZE INCREASE
LUNGS	1.704	0.386		2X NORMAL TO 12X9X3 MM
THYMIC REGION	0.508	0.115	LYMPH ND, S-MAN	
EPIDIDYIMIDES	1.337	0.303	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
TESTES	3.230	0.733		TAN WITH RED FOCI
TERMINAL BODY WT.	440.9		THYMIC REGION	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				RED FOCAL AREAS
			NASAL CAVITY	
			MICRO: 2	RHINITIS
			((1))	VACUOLIZATION OF OLFACTORY EPITHELIUM
			LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				SCATTERED PUNCTATE RED FOCI, ALL LOBES
ANIMAL	28147	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	11.037	2.564	LIVER	
KIDNEYS	3.005	0.717	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
LUNGS	1.468	0.341		2X2MM TAN FOCUS BETWEEN MEDIAN LOBES
THYMIC REGION	0.324	0.075	NASAL CAVITY	
EPIDIDYIMIDES	1.150	0.267	MICRO: 4	VACUOLIZATION OF OLFACTORY EPITHELIUM
TESTES	3.347	0.778	2	ATROPHY, OLFACTORY EPITHELIUM
TERMINAL BODY WT.	430.4		LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				DARK RED FOCAL AREA, AZYGOS LOBE
ANIMAL	28158	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	12.733	2.557	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	3.334	0.670	NASAL CAVITY	
LUNGS	1.659	0.333	MICRO: 4	VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.312	0.063	3	ATROPHY, OLFACTORY EPITHELIUM

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TABLE 2
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 750 PPM MALE			FO ADULT	

ANIMAL	28158	(CONTINUED)		
EPIDIDYMIDES	1.243	0.250		
TESTES	3.334	0.670		
TERMINAL BODY WT.	498.0			
ANIMAL	28208	27-FEB-92	STUDY DAY	52
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	SKIN	
LIVER	12.241	2.617	GROSS:	SHAPE/CONTOUR CHANGE
KIDNEYS	3.406	0.728		RAISED AREA NEAR THE 2 ON THE
LUNGS	1.509	0.323		TATTOOING NUMBERS
THYMIC REGION	0.268	0.057	LYMPH ND, S-MAN	
EPIDIDYMIDES	1.341	0.287	GROSS:	SIZE INCREASE
TESTES	3.223	0.689		2X NORMAL, RIGHT; 15X5X3MM, LEFT
TERMINAL BODY WT.	467.8		NASAL CAVITY	
			MICRO: 4	VACUOLIZATION OF OLFACTORY EPITHELIUM
			2	ATROPHY, OLFACTORY EPITHELIUM
			((1))	RHINITIS
			LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				DARK RED FOCI, ALL RIGHT LOBES
ANIMAL	28148	27-FEB-92	STUDY DAY	52
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	SKIN	
LIVER	12.239	2.562	GROSS:	SHAPE/CONTOUR CHANGE
KIDNEYS	3.424	0.717		BROWN RAISED AREAS, TAIL, SEVERAL,
LUNGS	1.657	0.347		1X1X1MM
THYMIC REGION	0.445	0.093	LYMPH ND, S-MAN	
EPIDIDYMIDES	1.308	0.274	GROSS:	SIZE INCREASE
TESTES	3.468	0.726		21X11X6MM, LEFT
TERMINAL BODY WT.	477.7		NASAL CAVITY	
			MICRO: 1	ATROPHY, OLFACTORY EPITHELIUM
ANIMAL	28197	27-FEB-92	STUDY DAY	52
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.	SKIN	
LIVER	13.551	2.790	GROSS:	SHAPE/CONTOUR CHANGE
KIDNEYS	4.553	0.937		SEVERAL RAISED RED AREAS, TAIL
LUNGS	1.804	0.371	LYMPH ND, S-MAN	
THYMIC REGION	0.413	0.085	GROSS:	SIZE INCREASE
EPIDIDYMIDES	1.334	0.275		20X10X5 MM, ONE NODE
TESTES	3.373	0.695	NASAL CAVITY	
TERMINAL BODY WT.	485.7		MICRO: 3	RHINITIS
			((2))	SQUAMOUS METAPLASIA
			(2)	VACUOLIZATION OF OLFACTORY EPITHELIUM

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1500 PPM MALE			FO ADULT	
ANIMAL	28196	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	9.219	2.388	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
KIDNEYS	3.350	0.860	NASAL CAVITY	
LUNGS	1.441	0.373	MICRO: (2) RHINITIS	
THYMIC REGION	0.326	0.084	3 ATROPHY, OLFACTORY EPITHELIUM	
EPIDIDYMIDES	1.226	0.310	ANTERIOR TWO SECTIONS, DORSAL PORTION	
TESTES	3.160	0.819	KIDNEYS	
TERMINAL BODY WT.	386.0		MICRO: ((3)) TUBULAR BASOPHILIA	
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:				
	HEART	LIVER	ADRENAL GL	
	SPLEEN	THYMIC REGION	BRAIN	
	TESTES	EPIDIDYMIDES	SEMINAL VESICLE	
	LARYNX	TRACHEA	LUNGS	
ANIMAL	28163	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	12.012	2.022	LIVER	
KIDNEYS	3.147	0.739	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
LUNGS	1.536	0.361	TAN PUNCTATE FOCAL AREA, CENTER OF	
THYMIC REGION	0.259	0.061	LEFT LATERAL LOBE	
EPIDIDYMIDES	1.353	0.310	SKIN	
TESTES	3.307	0.777	GROSS: ALOPECIA	
TERMINAL BODY WT.	425.7		FOREPAW, BILATERAL	
NASAL CAVITY				
			MICRO: 2 RHINITIS	
			3 ATROPHY, OLFACTORY EPITHELIUM	
			ANTERIOR TWO SECTIONS, DORSAL PORTION	
LUNGS				
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
			PUNCTATE RED FOCI, ALL LOBES	
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:				
	HEART	LIVER	ADRENAL GL	
	SKIN	SPLEEN	THYMIC REGION	
	BRAIN	TESTES	EPIDIDYMIDES	
	SEMINAL VESICLE	LARYNX	TRACHEA	
	LUNGS	KIDNEYS		
ANIMAL	28157	27-FEB-92	STUDY DAY 52	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.		
LIVER	11.230	2.725	LYMPH ND, S-MAN	
KIDNEYS	3.125	0.750	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
LUNGS	1.404	0.350	DARK RED FOCI, LEFT	
THYMIC REGION	0.272	0.066	MICRO: 2 HEMORRHAGE	
EPIDIDYMIDES	1.330	0.323	MICRO: 3 LYMPHOID HYPERPLASIA	
TESTES	3.619	0.878	2 PLASMACYTOSIS	
TERMINAL BODY WT.	412.2		THYMIC REGION	
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
			MULTIPLE DARK RED FOCI	
NASAL CAVITY				
			MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM	
			1 RHINITIS	
			4 VACUOLIZATION OF OLFACTORY EPITHELIUM	
LUNGS				

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	MALE	FO ADULT
<u>ANIMAL</u>	<u>28157 (CONTINUED)</u>		
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED FOCI, ALL RIGHT LOBES
			KIDNEYS GROSS: DILATED PELVIS MILD, RIGHT
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			LARYNX TRACHEA LUNGS
			KIDNEYS
<u>ANIMAL</u>	<u>28166</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	GROSS: EXAMINED -- NO SIGNIFICANT LESIONS
LIVER	10.510	2.560	NASAL CAVITY
KIDNEYS	2.897	0.706	MICRO: 2 RHINITIS
LUNGS	1.388	0.338	3 ATROPHY, OLFACTORY EPITHELIUM
THYMIC REGION	0.359	0.087	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
EPIDIDYMIDES	1.302	0.317	HEART LIVER ADRENAL GL
TESTES	3.373	0.822	SPLEEN THYMIC REGION BRAIN
TERMINAL BODY WT.	410.5		TESTES EPIDIDYMIDES SEMINAL VESICLE
			LARYNX TRACHEA LUNGS
			KIDNEYS
<u>ANIMAL</u>	<u>28189</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	SKIN
LIVER	8.800	2.259	GROSS: SHAPE/CONTOUR CHANGE
KIDNEYS	3.102	0.796	SEVERAL PUNCTATE BROWN FOCAL AREAS
LUNGS	1.314	0.337	NEAR BASE OF TAIL
THYMIC REGION	0.240	0.062	MICRO+ (4) HYPERKERATOSIS
EPIDIDYMIDES	1.210	0.311	LYMPH ND, S-MAN
TESTES	3.082	0.791	GROSS: COLOR CHANGE, DIFFUSE
TERMINAL BODY WT.	389.6		DARK RED
			MICRO+ ((3)) HEMORRHAGE
			NASAL CAVITY
			MICRO: 2 RHINITIS
			3 ATROPHY, OLFACTORY EPITHELIUM
			ANTERIOR TWO SECTIONS, DORSAL PORTION
			KIDNEYS
			MICRO: ((3)) TUBULAR BASOPHILIA
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			LARYNX TRACHEA LUNGS
<u>ANIMAL</u>	<u>28207</u>	<u>27-FEB-92</u>	<u>STUDY DAY 52</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	THYMIC REGION
LIVER	11.666	2.620	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS	3.487	0.783	MULTIPLE DARK RED FOCI
LUNGS	1.549	0.348	NASAL CAVITY

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	MALE	FO ADULT
ANIMAL 28207 (CONTINUED)			
THYMIC REGION	0.279	0.063	MICRO: ((3)) SQUAMOUS METAPLASIA
EPIDIDYMIDES	1.219	0.274	3 RHINITIS
TESTES	3.429	0.770	4 ATROPHY, OLFACTORY EPITHELIUM
TERMINAL BODY WT.	445.3		ANTERIOR TWO SECTIONS, DORSAL PORTION
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
HEART			LIVER
SPLEEN			THYMIC REGION
TESTES			EPIDIDYMIDES
LARYNX			TRACHEA
KIDNEYS			LUNGS
ANIMAL 28179 27-FEB-92 STUDY DAY 52			
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	12.885	2.537	LYMPH ND, S-MAN
KIDNEYS	3.703	0.729	GROSS: SIZE INCREASE
LUNGS	1.495	0.294	3X NORMAL, LEFT
THYMIC REGION	0.275	0.054	MICRO+ 4 LYMPHOID HYPERPLASIA
EPIDIDYMIDES	1.308	0.258	LYMPH ND, S-MAN
TESTES	3.751	0.739	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
TERMINAL BODY WT.	507.9		MULTIPLE DARK RED FOCI, LEFT
MICRO+ (4) HEMORRHAGE			
LYMPH ND, S-MAN			
GROSS: COLOR CHANGE, DIFFUSE			
DARK RED, RIGHT			
MICRO: (3) PLASMACYTOSIS			
NASAL CAVITY			
MICRO: 3 RHINITIS			
3 ATROPHY, OLFACTORY EPITHELIUM			
ANTERIOR TWO SECTIONS, DORSAL PORTION			
LUNGS			
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL			
DARK RED FOCI, ALL LOBES			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
HEART			LIVER
SPLEEN			THYMIC REGION
TESTES			EPIDIDYMIDES
LARYNX			TRACHEA
KIDNEYS			LUNGS
ANIMAL 28214 27-FEB-92 STUDY DAY 52			
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	10.523	2.547	NASAL CAVITY
KIDNEYS	3.021	0.731	MICRO: 2 RHINITIS
LUNGS	1.551	0.375	3 ATROPHY, OLFACTORY EPITHELIUM
THYMIC REGION	0.342	0.083	LUNGS
EPIDIDYMIDES	1.355	0.328	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
TESTES	3.633	0.879	DARK RED FOCAL AREA, LEFT LOBE
TERMINAL BODY WT.	413.2		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART			
LIVER			
SPLEEN			
THYMIC REGION			
TESTES			
EPIDIDYMIDES			
LARYNX			
TRACHEA			
KIDNEYS			
LUNGS			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	M,LE	FO ADULT
ANIMAL	28213	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	TESTES
LIVER	12.636	2.820	GROSS: CONSISTENCY CHANGE
KIDNEYS	3.342	0.746	RIGHT, SOFT
LUNGS	1.491	0.333	MICRO+ (5) SEMINIFEROUS TUBULE ATROPHY
THYMIC REGION	0.407	0.091	UNILATERAL, PERIPHERAL
EPIDIDYMIDES	1.014	0.226	NASAL CAVITY
TESTES	3.205	0.715	MICRO: 1 RHINITIS
TERMINAL BODY WT.	448.1		4 ATROPHY, OLFACTORY EPITHELIUM
			ANTERIOR TWO SECTIONS, DORSAL PORTION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			EPIDIDYMIDES SEMINAL VESICLE LARYNX
			TRACHEA LUNGS KIDNEYS
ANIMAL	28205	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	12.806	2.639	NASAL CAVITY
KIDNEYS	4.077	0.829	MICRO: 2 RHINITIS
LUNGS	1.777	0.356	3 ATROPHY, OLFACTORY EPITHELIUM
THYMIC REGION	0.293	0.042	4 VACUOLIZATION OF OLFACTORY EPITHELIUM
EPIDIDYMIDES	1.123	0.231	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TESTES	2.916	0.601	HEART LIVER ADRENAL GL
TERMINAL BODY WT.	485.3		SPLEEN THYMIC REGION BRAIN
			TESTES EPIDIDYMIDES SEMINAL VESICLE
			LARNG TRACHEA LUNGS
			KIDNEYS
ANIMAL	28206	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	SPIN
LIVER	9.610	2.171	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS	3.257	0.801	SEVERAL RAISED AREAS, TAIL
LUNGS	1.677	0.199	MICRO: (3) EPIDERMITIS
THYMIC REGION	0.254	0.063	THYMIC REGION
EPIDIDYMIDES	1.412	0.348	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
TESTES	3.743	0.923	RED FOCAL AREAS
TERMINAL BODY WT.	405.6		MICRO+ (3) HEMORRHAGE
			NASAL CAVITY
			MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM
			LUNGS
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			PUNCTATE TO 1X1 MM RED FOCI, ALL LOBES
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN BRAIN TESTES
			EPIDIDYMIDES SEMINAL VESICLE LARYNX
			TRACHEA LUNGS KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	MALE	FO ADULT
ANIMAL	28172	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	11.567	2.746	LIVER GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL 2X2MM TAN FOCUS, RIGHT LATERAL LOBE
KIDNEYS	3.513	0.834	
LUNGS	1.499	0.356	NASAL CAVITY MICRO: 1 RHINITIS 4 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.251	0.060	
EPIDIDYMIDES	1.206	0.305	
TESTES	3.458	0.821	
TERMINAL BODY WT.	421.3		LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED FOCI, RIGHT DIAPHRAGMATIC LOBE AND LEFT LOBE
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
HEART	LIVER	ADRENAL GL	
SPLEEN	THYMIC REGION	BRAIN	
TESTES	EPIDIDYMIDES	SEMINAL VESICLE	
LARYNX	TRACHEA	LUNGS	
KIDNEYS			
ANIMAL	28183	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	9.916	2.467	LYMPH ND, S-MAN GROSS: SIZE INCREASE 2X NORMAL
KIDNEYS	3.074	0.765	
LUNGS	1.517	0.377	MICRO: 4 PLASMACYTOSIS MICRO: 3 LYMPHOID HYPERPLASIA
THYMIC REGION	0.228	0.057	
EPIDIDYMIDES	1.211	0.301	NASAL CAVITY MICRO: 2 RHINITIS 4 ATROPHY, OLFACTORY EPITHELIUM INVOLVES SOME OF THE OLFACTORY EPITHELIUM ALL SECTIONS
TESTES	3.165	0.787	
TERMINAL BODY WT.	402.0		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART	LIVER	ADRENAL GL	
SPLEEN	THYMIC REGION	BRAIN	
TESTES	EPIDIDYMIDES	SEMINAL VESICLE	
LARYNX	TRACHEA	LUNGS	
KIDNEYS			
ANIMAL	20202	27-FEB-92	STUDY DAY 52
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	12.356	2.661	LYMPH ND, S-MAN GROSS: COLOR CHANGE, DIFFUSE ONE NODE LEFT SIDE, DARK RED
KIDNEYS	3.442	0.741	
LUNGS	1.683	0.364	NASAL CAVITY MICRO: ((3)) RHINITIS ((3)) SQUAMOUS METAPLASIA PRESENT ON NASAL SEPTUM AND TURBINATES
THYMIC REGION	0.328	0.071	
EPIDIDYMIDES	1.223	0.263	4 ATROPHY, OLFACTORY EPITHELIUM INVOLVES DORSAL EPITHELIUM BACK TO THE THIRD SECTION
TESTES	3.532	0.761	
TERMINAL BODY WT.	464.3		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART	LIVER	ADRENAL GL	
SPLEEN	LYMPH ND, S-MAN	THYMIC REGION	

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TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1500 PPM MALE

FO ADULT

ANIMAL 28202 (CONTINUED)

BRAIN SEMINAL VESICLE LUNGS TESTES LARYNX KIDNEYS EPIDIDYMIDES TRACHEA

ANIMAL 28204 27-FEB-92 STUDY DAY 52

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.
LIVER	12.111	2.706
KIDNEYS	3.877	0.866
LUNGS	1.529	0.341
THYMIC REGION	0.357	0.080
EPIDIDYMIDES	1.216	0.272
TESTES	3.071	0.686
TERMINAL BODY WT.	447.6	

ADRENAL GL
 MICRO: 3 CORTICAL CELL VACUOLIZATION
 THYMIC REGION
 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
 RED FOCAL AREAS

NASAL CAVITY
 MICRO: 2 ATROPHY, OLFACTORY EPITHELIUM
 3 RHINITIS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

HEART LIVER SPLEEN
 THYMIC REGION BRAIN TESTES
 EPIDIDYMIDES SEMINAL VESICLE LARYNX
 TRACHEA LUNGS KIDNEYS

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TABLE 3
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

NECROPSY PROTOCOL

F0 ADULT FEMALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	ORAL/PHARYNGEAL	TONGUE	ESOPHAGUS
STOMACH	LIVER	PANCREAS	DUODENUM	JF/JUNUM
ILEUM	CECUM	COLON	RECTUM	ANUS
PITUITARY	THYROID GL	PARATHYROID GL	ADRENAL GL	SKIN
SUBCUTIS	HEAD	EARS	NARES/NOSE	MAMMARY GL
PAWS/FEET	TAIL	SPLEEN	LYMPH ND, S-MAN	LYMPH ND, MED
LYMPH ND, MES	THYMIC REGION	BONE/JOINT	BONE, STERNUM	BONE, FEMUR
BONE, VERTEBRA	SKELETAL MUSCLE	DIAPHRAGM	BRAIN	SPINAL CORD
NERVE, SCIATIC	EYE	HARDERIAN GL	LACRIMAL GL	OVARIES
OVIDUCT	UTERUS	CERVIX	VAGINA	VULVA
LARYNX	TRACHEA	LUNGS	KIDNEYS	URETER
URINARY BLADDER	URETHRA			

The following organs were weighed at necropsy:

LIVER THYMIC REGION LUNGS KIDNEYS

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	FO ADULT
ANIMAL	28229	14-FEB-92	STUDY DAY 39
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	10.898	4.058	LUNGS
KIDNEYS	2.033	0.757	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
LUNGS	1.179	0.439	DARK RED FOCAL AREA, 1X1MM, LEFT LOBE
THYMIC REGION	0.273	0.102	KIDNEYS
TERMINAL BODY WT.	268.6		MICRO: ((2)) MINERALIZATION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS
ANIMAL	28228	18-FEB-92	STUDY DAY 43
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	11.959	4.029	ADRENAL GL
KIDNEYS	1.858	0.626	GROSS: SIZE INCREASE
LUNGS	1.286	0.433	SLIGHT, LEFT
THYMIC REGION	0.167	0.054	MICRO+((4)) MINERALIZATION
TERMINAL BODY WT.	296.8		SPLEEN
			GROSS: SHAPE/CONTOUR CHANGE
			INDENTED AT ONE POLE
			LYMPH ND, S-MAN
			GROSS: SIZE INCREASE
			3-4X NORMAL, LEFT
			MICRO+ 4 PLASMOCYTOSIS
			MICRO: 4 LYMPHOID HYPERPLASIA
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER SPLEEN
			THYMIC REGION BRAIN OVARIES
			NASAL CAVITY LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28244	14-FEB-92	STUDY DAY 39
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	13.023	4.448	ADRENAL GL
KIDNEYS	2.009	0.686	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
LUNGS	1.277	0.436	BILATERAL, ONE BROWN FOCAL AREA
THYMIC REGION	0.376	0.128	PUNCTATE
TERMINAL BODY WT.	292.8		LYMPH ND, S-MAN
			GROSS: SIZE INCREASE
			LEFT SIDE, 2X NORMAL, ONE NODE
			MICRO+ 4 PLASMOCYTOSIS
			MICRO: 3 LYMPHOID HYPERPLASIA
			LUNGS
			GROSS: COLOR CHANGE, DIFFUSE
			ALL LOBES, PALE PINK
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS KIDNEYS

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TABLE 4
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	F0 ADULT
ANIMAL	28287	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	10.056	4.033	LYMPH ND, S-MAN
KIDNEYS	1.825	0.732	GROSS: SIZE INCREASE
LUNGS	1.249	0.501	2-3X NORMAL ALL NODES
THYMIC REGION	0.245	0.098	MICRO: 4 LYMPHOID HYPERPLASIA
TERMINAL BODY WT.	249.4		MICRO: 4 PLASMACYTOSIS
			LUNGS
			MICRO: ((1)) PERIVASCULAR INFILTRATE(S)
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA KIDNEYS
ANIMAL	28239	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	14.247	4.946	SPLEEN
KIDNEYS	2.187	0.759	GROSS: SIZE INCREASE
LUNGS	1.287	0.447	SLIGHT
THYMIC REGION	0.258	0.090	LYMPH ND, S-MAN
TERMINAL BODY WT.	288.0		GROSS: SIZE INCREASE
			TWO NODES: 10X6X3 MM, 12X8X3 MM
			MICRO: 5 PLASMACYTOSIS
			MICRO: 2 LYMPHOID HYPERPLASIA
			LUNGS
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			ONE 2X2 MM WHITE FOCUS, LEFT LOBE
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS KIDNEYS
ANIMAL	28240	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	15.389	4.978	LUNGS
KIDNEYS	2.453	0.793	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
LUNGS	1.178	0.381	PUNCTATE RED FOCI, RIGHT
THYMIC REGION	0.169	0.055	DIAPHRAGMATIC LOBE
TERMINAL BODY WT.	309.2		KIDNEYS
			GROSS: DILATED PELVIS
			SEVERE, BILATERAL
			MICRO: 4 HYDRONEPHROSIS
			BILATERAL
			MICRO: ((3)) NEPHRITIS, INTERSTITIAL
			UNILATERAL, LEFT KIDNEY
			((2)) TUBULAR BASOPHILIA
			ASSOCIATED WITH INFLAMMATION IN LEFT
			KIDNEY
			URETER
			GROSS: DILATATION/DISTENTION
			2X NORMAL, BILATERAL
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

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TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	FG ADULT
<u>ANIMAL</u>	<u>28240 (CONTINUED)</u>		
			HEART SPLEEN OVARIES TRACHEA
			LIVER THYMIC REGION NASAL CAVITY LUNGS
			ADRENAL GL BRAIN LARYNX URETER
<u>ANIMAL</u>	<u>28242</u>	<u>17-FEB-92</u>	<u>STUDY DAY 42</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	<u>LYMPH ND, 5-MAN</u>
LIVER	11.789	3.786	GROSS: SIZE INCREASE
KIDNEYS	1.974	0.634	2X NORMAL, SEVERAL NODES
LUNGS	1.288	0.414	MICRO: 4 PLASMOCYTOSIS
THYMIC REGION	0.213	0.068	MICRO: 3 LYMPHOID HYPERPLASIA
TERMINAL BODY WT.	311.4		KIDNEYS
			MICRO: (2) NEPHRITIS, INTERSTITIAL (1) TUBULAR BASOPHILIA
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS
<u>ANIMAL</u>	<u>28276</u>	<u>17-FEB-92</u>	<u>STUDY DAY 42</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	<u>LUNGS</u>
LIVER	11.999	4.175	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS	1.822	0.634	MOTTLED PINK AND TAN, ALL LOBES
LUNGS	1.138	0.396	MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THYMIC REGION	0.290	0.101	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	287.4		HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS KIDNEYS
<u>ANIMAL</u>	<u>28245</u>	<u>15-FEB-92</u>	<u>STUDY DAY 40</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	<u>GROSS: EXAMINED - NO SIGNIFICANT LESIONS</u>
LIVER	14.018	4.460	KIDNEYS
KIDNEYS	2.140	0.681	MICRO: ((3)) MINERALIZATION
LUNGS	1.219	0.388	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
THYMIC REGION	0.155	0.049	HEART LIVER ADRENAL GL
TERMINAL BODY WT.	314.3		SPLEEN THYMIC REGION BRAIN
			OVARIES NASAL CAVITY LARYNX
			TRACHEA LUNGS
<u>ANIMAL</u>	<u>28226</u>	<u>16-FEB-92</u>	<u>STUDY DAY 41</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	<u>SKIN</u>
LIVER	13.464	4.843	GROSS: ALOPECIA
KIDNEYS	1.762	0.634	BILATERAL, FRONT PAWS, PARTIAL, 3X5MM
LUNGS	1.167	0.420	AREA
THYMIC REGION	0.246	0.088	LUNGS
TERMINAL BODY WT.	278.0		GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM FEMALE

FG ADULT

ANIMAL 28226 (CONTINUED)

ALL LOBES MOTTLED LIGHT BROWN TO LIGHT PINK
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SKIN SPLEEN THYMIC REGION
 BRAIN OVARIES NASAL CAVITY
 LARYNX TRACHEA LUNGS
 KIDNEYS

ANIMAL 28255 15-FEB-92 STUDY DAY 40

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	13.155	4.506
KIDNEYS	1.968	0.674
LUNGS	1.218	0.417
THYMIC REGION	0.256	0.088
TERMINAL BODY WT.	291.9	

LUNGS
 GROSS: COLOR CHANGE, DIFFUSE DARK PINK, ALL LOBES
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 OVARIES NASAL CAVITY LARYNX
 TRACHEA LUNGS KIDNEYS

ANIMAL 28249 16-FEB-92 STUDY DAY 41

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	12.317	4.406
KIDNEYS	1.900	0.680
LUNGS	1.166	0.417
THYMIC REGION	0.205	0.073
TERMINAL BODY WT.	279.5	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 OVARIES NASAL CAVITY LARYNX
 TRACHEA LUNGS KIDNEYS

ANIMAL 28275 18-FEB-92 STUDY DAY 43

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	13.170	4.267
KIDNEYS	2.033	0.659
LUNGS	1.184	0.384
THYMIC REGION	0.205	0.066
TERMINAL BODY WT.	308.6	

LYMPH ND, S-MAN
 GROSS: SIZE INCREASE
 3X NORMAL, LEFT
 MICRO: 4 PLASMOCYTOSIS
 MICRO: 3 LYMPHOID HYPERPLASIA
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 OVARIES NASAL CAVITY LARYNX
 TRACHEA LUNGS KIDNEYS

ANIMAL 28278 17-FEB-92 STUDY DAY 42

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	14.254	4.282
KIDNEYS	1.856	0.558
LUNGS	1.207	0.363
THYMIC REGION	0.217	0.065
TERMINAL BODY WT.	332.9	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 OVARIES NASAL CAVITY LARYNX
 TRACHEA LUNGS KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPRIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD-1 RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	FO ADULT
ANIMAL	28256	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	14.953	4.443	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	2.040	0.606	MICRO: EXAMINED - NO SIGNIFICANT LESIONS
LUNGS	1.240	0.368	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
THYMIC REGION	0.339	0.101	HEART
TERMINAL BODY WT.	336.6		LIVER
			ADRENAL GL
			THYMIC REGION
			BRAIN
			OVARIES
			NASAL CAVITY
			LARYNX
			TRACHEA
			LUNGS
			KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	150 PPM	FEMALE	FO ADULT

ANIMAL	28277	17-FEB-92	STUDY DAY 42
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	13.889	4.640	ADRENAL GL GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL BILATERAL, PUNCTATE BROWN FOCUS
KIDNEYS	2.00	0.700	
LUNGS	1.294	0.420	LYMPH ND, S-MAN
THYMIC REGION	0.291	0.097	GROSS: SIZE INCREASE ONE NODE ON RIGHT SIDE 3X NORMAL
TERMINAL BODY WT.	298.9		NASAL CAVITY MICRO: 1 VACUOLIZATION OF OLFACTORY EPITHELIUM

ANIMAL	28272	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	13.910	4.773	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	1.942	0.666	NASAL CAVITY
LUNGS	1.195	0.410	MICRO: 1 VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.173	0.059	
TERMINAL BODY WT.	291.4		

ANIMAL	28270	17-FEB-92	STUDY DAY 42
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	12.512	4.199	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	2.430	0.815	NASAL CAVITY
LUNGS	1.139	0.382	MICRO: 1 VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.244	0.082	
TERMINAL BODY WT.	298.0		

ANIMAL	28288	18-FEB-92	STUDY DAY 43
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	12.112	4.613	NASAL CAVITY
KIDNEYS	1.736	0.661	MICRO: 1 VACUOLIZATION OF OLFACTORY EPITHELIUM
LUNGS	1.248	0.475	LUNGS
THYMIC REGION	0.191	0.073	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED TAN AND RED, ALL LOBES
TERMINAL BODY WT.	262.5		

ANIMAL	28253	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	13.230	4.717	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	1.939	0.694	NASAL CAVITY
LUNGS	1.270	0.453	MICRO: 1 VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.239	0.085	
TERMINAL BODY WT.	280.5		

ANIMAL	28264	17-FEB-92	STUDY DAY 43
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	13.193	4.590	SKIN
KIDNEYS	1.937	0.674	GROSS: SURFACE CHANGE MULTIPLE BROWN 1MM RAISED AREAS ALONG LENGTH OF TAIL
LUNGS	1.346	0.468	

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TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	150 PPM	FEMALE	FO ADULT		
<hr/>					
ANIMAL	28264	(CONTINUED)			
THYMIC REGION	0.184	0.064	NASAL CAVITY		
TERMINAL BODY WT.	287.4		MICRO: 2	VACUOLIZATION OF OLFACTORY EPITHELIUM	
<hr/>					
ANIMAL	28233	17-FEB-92	STUDY DAY 42		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	LYMPH ND, S-MAN		
LIVER	12.478	4.343	GROSS:	SIZE INCREASE	
KIDNEYS	1.025	0.670		2X NORMAL	
LUNGS	1.337	0.465	NASAL CAVITY		
THYMIC REGION	0.262	0.091	MICRO: 1	VACUOLIZATION OF OLFACTORY EPITHELIUM	
TERMINAL BODY WT.	287.3				
<hr/>					
ANIMAL	28225	18-FEB-92	STUDY DAY 43		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	COLON		
LIVER	14.775	4.476	GROSS:	GASEOUS	
KIDNEYS	2.058	0.624	LYMPH ND, MED		
LUNGS	1.195	0.362	GROSS:	COLOR CHANGE, DIFFUSE	
THYMIC REGION	0.218	0.066		DARK RED	
TERMINAL BODY WT.	330.1		NASAL CAVITY		
			MICRO: 2	VACUOLIZATION OF OLFACTORY EPITHELIUM	
			LUNGS		
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL	
				MULTIPLE DARK RED FOCI, ALL LOBES	
<hr/>					
ANIMAL	28238	15-FEB-92	STUDY DAY 40		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	SKIN		
LIVER	9.031	3.337	GROSS:	CRUST/SCAB/SCALE	
KIDNEYS	2.006	0.741		LEFT PERINASAL REGION 2X2MM RED CRUST	
LUNGS	1.355	0.501	NASAL CAVITY		
THYMIC REGION	0.322	0.119	MICRO: 2	VACUOLIZATION OF OLFACTORY EPITHELIUM	
TERMINAL BODY WT.	270.6				
<hr/>					
ANIMAL	28257	17-FEB-92	STUDY DAY 42		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	LYMPH ND, S-MAN		
LIVER	12.400	4.225	GROSS:	SIZE INCREASE	
KIDNEYS	1.894	0.645		TWO NODES, 10X6X4 MM, 15X8X4 MM	
LUNGS	1.127	0.384	NASAL CAVITY		
THYMIC REGION	0.217	0.074	MICRO: 2	VACUOLIZATION OF OLFACTORY EPITHELIUM	
TERMINAL BODY WT.	293.5		LUNGS		
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL	
				1X1 MM RED FOCI, LEFT LOBE	
<hr/>					
ANIMAL	28267	17-FEB-92	STUDY DAY 42		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS		
LIVER	14.510	4.656	NASAL CAVITY		
KIDNEYS	1.482	0.476	MICRO: ((1))	RHINITIS	
LUNGS	2.223	0.713	1	VACUOLIZATION OF OLFACTORY EPITHELIUM	
THYMIC REGION	0.193	0.062			
TERMINAL BODY WT.	311.6				

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TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REFRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	150 PPM	FEMALE	FO ADULT

ANIMAL	28280	18-FEB-92	STUDY DAY 43
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	12.878	4.238	NASAL CAVITY
KIDNEYS	2.112	0.695	MICRO: 1
LUNGS	1.225	0.403	KIDNEYS
THYMIC REGION	0.223	0.073	GROSS:
TERMINAL BODY WT.	303.9		
			VACUOLIZATION OF OLFACTORY EPITHELIUM
			DILATED PELVIS
			MODERATE, RIGHT

ANIMAL	28258	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	14.665	4.845	NASAL CAVITY
KIDNEYS	2.001	0.661	MICRO: 2
LUNGS	1.216	0.402	LUNGS
THYMIC REGION	0.178	0.059	GROSS:
TERMINAL BODY WT.	302.7		
			VACUOLIZATION OF OLFACTORY EPITHELIUM
			COLOR CHANGE, FOCAL/MULTIFOCAL
			BROWN FOCAL AREAS, RIGHT LOBES

ANIMAL	28262	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	14.721	4.419	ADRENAL GL
KIDNEYS	2.203	0.661	GROSS:
LUNGS	1.373	0.412	
THYMIC REGION	0.250	0.075	
TERMINAL BODY WT.	333.1		
			COLOR CHANGE, FOCAL/MULTIFOCAL
			BILATERAL ONE BROWN PUNCTATE FOCAL
			AREA
			LYMPH ND, S-MAN
			GROSS:
			SIZE INCREASE
			ALL NODES, 3-4X NORMAL
			NASAL CAVITY
			MICRO: 2
			VACUOLIZATION OF OLFACTORY EPITHELIUM

ANIMAL	28220	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	
LIVER	10.642	3.817	OVARIES
KIDNEYS	1.838	0.659	GROSS:
LUNGS	1.191	0.427	
THYMIC REGION	0.186	0.067	
TERMINAL BODY WT.	278.8		
			CYST
			LEFT 10MM IN DIAMETER, FILLED WITH
			CLEAR RED FLUID
			NASAL CAVITY
			MICRO: 2
			VACUOLIZATION OF OLFACTORY EPITHELIUM

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE; COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	750 PPM	FEMALE	FO ADULT
ANIMAL	28266	14-FEB-92	STUDY DAY 39
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	11.162	4.171	NASAL CAVITY
KIDNEYS	2.213	0.827	MICRO: 2 RHINITIS
LUNGS	1.219	0.456	2 VACUOLIZATION OF OLFACTORY EPITHELIUM
THYMIC REGION	0.242	0.090	
TERMINAL BODY WT.	267.6		
ANIMAL	28281	16-FEB-92	STUDY DAY 41
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN
LIVER	14.382	4.895	GROSS: SIZE INCREASE
KIDNEYS	2.168	0.738	SLIGHT TO 2X NORMAL
LUNGS	1.166	0.397	NASAL CAVITY
THYMIC REGION	0.229	0.078	MICRO: 2 VACUOLIZATION OF OLFACTORY EPITHELIUM
TERMINAL BODY WT.	293.8		
ANIMAL	28236	18-FEB-92	STUDY DAY 43
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	COLON
LIVER	11.857	4.188	GROSS: GASEOUS
KIDNEYS	1.841	0.650	NASAL CAVITY
LUNGS	1.081	0.382	MICRO: 2 RHINITIS
THYMIC REGION	0.186	0.066	2 VACUOLIZATION OF OLFACTORY EPITHELIUM
TERMINAL BODY WT.	283.1		
ANIMAL	28250	14-FEB-92	STUDY DAY 39
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	ADRENAL GL
LIVER	12.259	4.592	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS	2.053	0.769	BILATERAL, PUNCTATE BROWN FOCAL
LUNGS	1.138	0.426	AREAS, SEVERAL
THYMIC REGION	0.099	0.037	LYMPH ND, S-MAN
TERMINAL BODY WT.	267.0		GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			RIGHT SIDE MOTTLED RED AND CREAM
			THYMIC REGION
			GROSS: SIZE DECREASE
			0.50 OF NORMAL
			NASAL CAVITY
			MICRO: 2 RHINITIS
			2 VACUOLIZATION OF OLFACTORY EPITHELIUM
			LUNGS
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			ALL LOBES MOTTLED LIGHT BROWN AND
			PALE PINK
ANIMAL	28271	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	12.319	4.233	NASAL CAVITY
KIDNEYS	1.737	0.597	MICRO: 3 VACUOLIZATION OF OLFACTORY EPITHELIUM
LUNGS	1.124	0.386	
THYMIC REGION	0.200	0.069	

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TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	750 PPM	FEMALE	FO ADULT

<u>ANIMAL</u>	<u>28271</u>	<u>(CONTINUED)</u>	
TERMINAL BODY WT.	291.0		
<u>ANIMAL</u>	<u>28263</u>	<u>18-FEB-92</u>	<u>STUDY DAY 43</u>
<u>TYPE OF DEATH: SCHEDULED SACRIFICE</u>			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	14.076	4.327	ADRENAL GL
KIDNEYS	2.206	0.678	GROSS:
LUNGS	1.329	0.409	
THYMIC REGION	0.176	0.054	LYMPH ND, S-MAN
TERMINAL BODY WT.	325.3		GROSS:
			SIZE INCREASE
			2X NORMAL, RIGHT
			NASAL CAVITY
			MICRO: 2
			RHINITIS
			3
			VACUOLIZATION OF OLFACTORY EPITHELIUM
			LUNGS
			GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			MOTTLED DARK RED AND TAN, ALL LOBES
			DARK RED FOCAL AREA, 1X2X2MM, RIGHT
			DIAPHRAGMATIC LOBE
<u>ANIMAL</u>	<u>28223</u>	<u>15-FEB-92</u>	<u>STUDY DAY 40</u>
<u>TYPE OF DEATH: SCHEDULED SACRIFICE</u>			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	13.283	4.800	LIVER
KIDNEYS	1.953	0.706	GROSS:
LUNGS	1.250	0.452	
THYMIC REGION	0.197	0.071	ADRENAL GL
TERMINAL BODY WT.	276.7		GROSS:
			COLOR CHANGE, DIFFUSE
			DARK RED, ALL LOBES
			NASAL CAVITY
			MICRO: 3
			VACUOLIZATION OF OLFACTORY EPITHELIUM
			LUNGS
			GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			DARK RED FOCAL AREAS, ALL LOBES
<u>ANIMAL</u>	<u>28283</u>	<u>15-FEB-92</u>	<u>STUDY DAY 40</u>
<u>TYPE OF DEATH: SCHEDULED SACRIFICE</u>			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	12.305	4.170	SKIN
KIDNEYS	2.178	0.738	GROSS:
LUNGS	1.265	0.429	
THYMIC REGION	0.207	0.070	NASAL CAVITY
TERMINAL BODY WT.	295.1		MICRO: ((2))
			RHINITIS
			3
			VACUOLIZATION OF OLFACTORY EPITHELIUM
			2
			ATROPHY, OLFACTORY EPITHELIUM
<u>ANIMAL</u>	<u>28260</u>	<u>19-FEB-92</u>	<u>STUDY DAY 44</u>
<u>TYPE OF DEATH: SCHEDULED SACRIFICE</u>			
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	11.953	4.100	NASAL CAVITY
KIDNEYS	1.808	0.620	MICRO: 2
LUNGS	1.070	0.367	LUNGS
THYMIC REGION	0.290	0.099	GROSS:
			COLOR CHANGE, FOCAL/MULTIFOCAL
			MOTTLED RED AND TAN, ALL LOBES

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TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	750 PPM	FEMALE	FO ADULT		
<hr/>					
<u>ANIMAL</u>	<u>28221</u>	<u>(CONTINUED)</u>			
THYMIC REGION	0.194	0.064	GROSS:	SURFACE CHANGE TAIL, SEVERAL RAISED BROWN AREAS 1X1X1MM	
TERMINAL BODY WT.	301.7		NASAL CAVITY MICRO: 3	VACUOLIZATION OF OLFACTORY EPITHELIUM	
<u>ANIMAL</u>	<u>28230</u>	<u>17-FEB-22</u>	<u>STUDY DAY</u>	<u>42</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE					
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	THYMIC REGION		
LIVER	12.881	4.560	GROSS:	SIZE DECREASE 0.50 OF NORMAL	
KIDNEYS	1.837	0.650	NASAL CAVITY		
LUNGS	1.282	0.454	MICRO: 3	VACUOLIZATION OF OLFACTORY EPITHELIUM ATROPHY, OLFACTORY EPITHELIUM	
THYMIC REGION	0.075	0.027	LUNGS		
TERMINAL BODY WT.	282.5		GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL MOTTLED LIGHT BROWN AND LIGHT PINK	

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TABLE 4
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	FEMALE	F0 ADULT
ANIMAL	28265	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	13.461	4.942	ADRENAL GL
KIDNEYS	1.778	0.653	GROSS:
LUNGS	1.067	0.392	COLOR CHANGE, FOCAL/MULTIFOCAL
THYMIC REGION	0.133	0.049	BILATERAL, SEVERAL BROWN PUNCTATE FOCI
TERMINAL BODY WT.	272.4		NASAL CAVITY
			MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM
			ANTERIOR TWO SECTIONS, DORSAL PORTION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28269	14-FEB-92	STUDY DAY 39
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	12.250	4.505	ADRENAL GL
KIDNEYS	1.951	0.717	GROSS:
LUNGS	1.227	0.451	COLOR CHANGE, FOCAL/MULTIFOCAL
THYMIC REGION	0.278	0.102	BILATERAL, PUNCTATE BROWN FOCI, 2 ON EACH
TERMINAL BODY WT.	271.9		NASAL CAVITY
			MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM
			ANTERIOR TWO SECTIONS, DORSAL PORTION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28279	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	10.542	4.040	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	1.881	0.721	NASAL CAVITY
LUNGS	1.067	0.409	MICRO: ((2)) RHINITIS
THYMIC REGION	0.227	0.087	PRESENT ONLY IN ANTERIOR SECTION
TERMINAL BODY WT.	260.9		PRESENT ON LATERAL TURBINATE AND LATERAL WALL
			3 ATROPHY, OLFACTORY EPITHELIUM
			PRESENT IN SECOND AND THIRD SECTIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL	28268	15-FEB-92	STUDY DAY 40
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	11.942	4.216	STOMACH
KIDNEYS	1.888	0.667	GROSS:
LUNGS	1.187	0.419	ULCERATED
THYMIC REGION	0.169	0.060	GLANDULAR PORTION, MARKED
TERMINAL BODY WT.	283.3		STOMACH
			GROSS:
			CONTENTS ABNORMAL
			BRIGHT YELLOW SEMI-SOLID MATERIAL
			OVARIES

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	FEMALE	F0 ADULT
<u>ANIMAL</u>	<u>28268</u>	<u>(CONTINUED)</u>	
			GROSS: CYST 2X2X2 MM, RIGHT (BRUKEN AT NECROPSY)
			NASAL CAVITY MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART STOMACH LIVER ADRENAL GL SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEYS
<u>ANIMAL</u>	<u>28254</u>	<u>15-FEB-92</u>	<u>STUDY DAY 40</u>
	TYPE OF DEATH: SCHEDULED SACRIFICE		
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	11.915	4.109	ADRENAL GL
KIDNEYS	1.926	0.664	GROSS: COLOR CHANGE, DIFFUSE LIGHT RED, BILATERAL
LUNGS	1.134	0.391	NASAL CAVITY
THYMIC REGION	0.241	0.083	MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
TERMINAL BODY WT.	290.0		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEY
<u>ANIMAL</u>	<u>28243</u>	<u>16-FEB-92</u>	<u>STUDY DAY 41</u>
	TYPE OF DEATH: SCHEDULED SACRIFICE		
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	12.668	4.466	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
KIDNEYS	1.959	0.691	NASAL CAVITY
LUNGS	1.253	0.442	MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.204	0.072	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	283.7		HEART LIVER ADRENAL GL SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEYS
<u>ANIMAL</u>	<u>28247</u>	<u>16-FEB-92</u>	<u>STUDY DAY 41</u>
	TYPE OF DEATH: SCHEDULED SACRIFICE		
<u>ORGAN WEIGHT</u>	<u>ABS. (G)</u>	<u>REL.</u>	
LIVER	11.224	4.079	NASAL CAVITY
KIDNEYS	2.025	0.736	MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
LUNGS	1.094	0.398	LUNGS
THYMIC REGION	0.201	0.073	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL PUNCTATE RED FOCI, ALL LOBES
TERMINAL BODY WT.	275.1		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEYS
<u>ANIMAL</u>	<u>28285</u>	<u>17-FEB-92</u>	<u>STUDY DAY 42</u>
	TYPE OF DEATH: SCHEDULED SACRIFICE		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

FO ADULT

GROUP: 1500 PPM FEMALE

ANIMAL	28285 (CONTINUED)		
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	13.212	4.484	ADRENAL GL MICRO: ((3)) CORTICAL CELL HYPERTROPHY
KIDNEYS	1.844	0.626	NASAL CAVITY MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
LUNGS	1.351	0.459	((3)) NECROSIS OF OLFACTORY EPITHELIUM THIRD SECTION
THYMIC REGION	0.256	0.087	
TERMINAL BODY WT.	294.6		

LUNGS
 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
 ONE PUNCTATE BLACK FOCUS, RIGHT
 DIAPHRAGMATIC LOBE

KIDNEYS
 MICRO: ((2)) MINERALIZATION
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER SPLEEN
 THYMIC REGION BRAIN OVARIES
 LARYNX TRACHEA LUNGS

ANIMAL	28231	15-FEB-92	STUDY DAY 40
TYPE OF DEATH:	SCHEDULED SACRIFICE		
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	11.554	4.184	SKIN GROSS: ALOPECIA MULTIPLE AREAS PARTIAL, ABDOMINAL REGION AND LEFT SIDE
KIDNEYS	2.128	0.771	
LUNGS	1.199	0.434	NASAL CAVITY MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.182	0.066	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: HEART LIVER ADRENAL GL SKIN SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEYS
TERMINAL BODY WT.	276.2		

ANIMAL	28246	14-FEB-92	STUDY DAY 39
TYPE OF DEATH:	SCHEDULED SACRIFICE		
ORGAN WEIGHT	ABS.(G)	REL.	
LIVER	12.610	4.453	ADRENAL GL GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL BROWN PUNCTATE FOCI, BILATERAL
KIDNEYS	1.883	0.665	
LUNGS	1.386	0.489	NASAL CAVITY MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.340	0.120	
TERMINAL BODY WT.	283.2		LUNGS GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL DARK RED FOCI, LEFT LOBE THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: HEART LIVER ADRENAL GL SPLEEN THYMIC REGION BRAIN OVARIES LARYNX TRACHEA LUNGS KIDNEYS

ANIMAL	28234	17-FEB-92	STUDY DAY 42
TYPE OF DEATH:	SCHEDULED SACRIFICE		
ORGAN WEIGHT	ABS.(G)	REL.	OVARIES

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1500 PPM	FEMALE	FO ADULT
ANIMAL 28234 (CONTINUED)			
LIVER	13.934	4.817	GROSS: CYST
KIDNEYS	1.759	0.608	10X5X2 MM, LEFT
LUNGS	1.106	0.382	NASAL CAVITY
THYMIC REGION	0.198	0.068	MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM
TERMINAL BODY WT.	289.3		ANTERIOR TWO SECTIONS, DORSAL PORTION
			LUNGS
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			PUNCTATE RED FOCI, LEFT LOBES
			KIDNEYS
			MICRO: ((1)) MINERALIZATION
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS
ANIMAL 28241 18-FEB-92 STUDY DAY 43			
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	THYMIC REGION
LIVER	14.019	4.463	GROSS: SIZE DECREASE
KIDNEYS	2.055	0.654	0.50 OF NORMAL
LUNGS	1.315	0.419	NASAL CAVITY
THYMIC REGION	0.130	0.041	MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM
TERMINAL BODY WT.	314.1		ANTERIOR TWO SECTIONS, DORSAL PORTION
			LUNGS
			GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
			MULTIPLE DARK RED FOCI, ALL LOBES
			MICRO+((2)) PERIVASCULAR INFILTRATE(S)
			MICRO: (2) ALVEOLAR HISTIOCYTOSIS
			(2) PNEUMONITIS, INTERSTITIAL
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			KIDNEYS
ANIMAL 28251 15-FEB-92 STUDY DAY 40			
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	13.231	4.473	NASAL CAVITY
KIDNEYS	2.142	0.724	MICRO: 3 ATROPHY, OLFACTORY EPITHELIUM
LUNGS	1.193	0.403	ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.141	0.048	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	295.8		HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS KIDNEYS
ANIMAL 28284 16-FEB-92 STUDY DAY 41			
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	12.074	4.287	NASAL CAVITY
KIDNEYS	2.049	0.728	MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM
LUNGS	1.297	0.461	ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.208	0.074	KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
 INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

FO ADULT
 GROUP: 1500 PPM FEMALE

ANIMAL 28284 (CONTINUED)
 TERMINAL BODY WT. 281.6

MICRO: ((3)) MINERALIZATION
 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
 HEART LIVER ADRENAL GL
 SPLEEN THYMIC REGION BRAIN
 OVARIES LARYNX TRACHEA
 LUNGS

ANIMAL 28237 28-FEB-92 STUDY DAY 53
 TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS. (G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS
LIVER	10.409	3.686	NASAL CAVITY
KIDNEYS	2.247	0.796	MICRO: 4 ATROPHY, OLFACTORY EPITHELIUM
LUNGS	1.385	0.490	ANTERIOR TWO SECTIONS, DORSAL PORTION
THYMIC REGION	0.307	0.109	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	282.4		HEART LIVER ADRENAL GL
			SPLEEN THYMIC REGION BRAIN
			OVARIES LARYNX TRACHEA
			LUNGS KIDNEYS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

**Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD¹ Rats**

Individual Clinical Pathology Data

(12 Pages)

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TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
ABBREVIATIONS

The following abbreviations appear in hematology reports when the parameter is reported.

WBC = LEUKOCYTES ($10^3/\mu\text{l}$)
RBC = ERYTHROCYTES ($10^6/\mu\text{l}$)
HGB = HEMOGLOBIN (g/dl)
HCT = HEMATOCRIT (%)
MCV = MEAN CORPUSCULAR VOLUME (μm^3)
MCH = MEAN CORPUSCULAR HEMOGLOBIN (pg)
MCHC = MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)
PLAT = PLATELETS ($10^3/\mu\text{l}$)
SEGS = SEGMENTED NEUTROPHILS (cells/ μl)
LMPH = LYMPHOCYTES (cells/ μl)
MONO = MONOCYTES (cells/ μl)
BASO = BASOPHILS (cells/ μl)
EOS = EOSINOPHILS (cells/ μl)
BAND = BANDED NEUTROPHILS (cells/ μl)
LMON = LARGE MONOCYTES (cells/ μl)
IGRN = IMMATURE GRANULOCYTES (cells/ μl)
IERY = IMMATURE ERYTHROCYTES (cells/ μl)
NRBC = NUCLEATED RBCs (cells/100 WBCs)
RET = RETICULOCYTES (% of RBCs)
PT = PROTHROMBIN TIME (sec)
APTT = ACTIVATED PARTIAL THROMBOPLASTIN TIME (sec)
HBOD = HEINZ BODY (%)
MHGB = METHEMOGLOBIN (g/dl)
CLOT = CLOTTED
QNS = QUANTITY NOT SUFFICIENT
LA = LAB ACCIDENT
NOS = NO SAMPLE
DE = DATA ELIMINATED

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS
ABBREVIATIONS

The following abbreviations appear in serum clinical chemistry reports when the parameter is reported.

GLU = GLUCOSE (g/l)
UN = UREA NITROGEN (mg/l)
CREA = CREATININE (mg/l)
AST = ASPARTATE AMINOTRANSFERASE (IU/l)
ALT = ALANINE AMINOTRANSFERASE (IU/l)
TP = TOTAL PROTEIN (g/l)
ALB = ALBUMIN (g/l)
GLOB = GLOBULIN (g/l)
A/G = ALBUMIN/GLOBULIN RATIO
TBIL = TOTAL BILIRUBIN (mg/l)
DBIL = DIRECT BILIRUBIN (mg/l)
IBIL = INDIRECT BILIRUBIN (mg/l)
CPK = CREATINE KINASE (IU/l)
LDH = LACTATE DEHYDROGENASE (IU/l)
GGT = GAMMA-GLUT. TRANSFERASE (IU/l)
SDH = SORBITOL DE. DROGENASE (IU/l)
CHOL = CHOLESTEROL (g/l)
TRIG = TRIGLYCERIDES (g/l)
ALP = ALKALINE PHOSPHATASE (IU/l)
CA = CALCIUM (mg/l)
PHOS = INORGANIC PHOSPHORUS (mg/l)
NA = SODIUM (mmol/l)
K = POTASSIUM (mmol/l)
CL = CHLORIDE (mmol/l)
GLDH = GLUTAMATE DEHYDROGENASE (IU/l)
HB = SERUM HEMOGLOBIN (mg/l)
QNS = QUANTITY NOT SUFFICIENT
NOS = NO SAMPLE
LA = LAB ACCIDENT
DE = DATA ELIMINATED

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 0 PPM
 WEEK 7

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLAT	WBC	SEGS	LMPH
28200	8.64	16.7	44.4	51.	19.3	37.6	850.	8.1	1053.	6480.
28156	8.26	16.4	43.2	52.	19.8	37.9	776.	8.6	2752.	5332.
28173	8.48	16.6	43.2	51.	19.5	38.4	780.	10.8	1728.	8640.
28162	8.35	16.1	42.9	51.	19.2	37.5	744.	9.2	920.	7360.
28155	8.67	17.4	45.3	52.	20.0	38.4	600.	8.7	1653.	6438.
28198	8.23	16.5	45.6	55.	20.0	36.1	667.	11.1	2442.	7881.
28201	8.13	16.0	42.0	52.	19.6	38.0	683.	10.7	3852.	6206.
28180	7.91	16.7	43.5	55.	21.1	38.3	799.	13.6	4760.	8704.
28159	8.64	16.9	45.3	52.	19.5	37.3	764.	12.1	5324.	5445.
28167	8.74	17.7	45.3	52.	20.2	39.0	785.	11.0	2200.	8250.
MEAN	8.41	16.7	44.1	52.	19.8	37.8	745.	10.4	2668.	7074.
S.D.	0.274	0.53	1.27	1.5	0.55	0.80	73.8	1.73	1516.1	1266.0
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
28200	405.	0.	162.	0.	0.	0.	0.	0.
28156	344.	0.	172.	0.	0.	0.	0.	0.
28173	324.	0.	108.	0.	0.	0.	0.	0.
28162	368.	0.	552.	0.	0.	0.	0.	0.
28155	435.	0.	174.	0.	0.	0.	0.	0.
28198	555.	0.	222.	0.	0.	0.	0.	0.
28201	535.	0.	107.	0.	0.	0.	0.	0.
28180	0.	0.	136.	0.	0.	0.	0.	0.
28159	968.	0.	363.	0.	0.	0.	0.	0.
28167	440.	0.	110.	0.	0.	0.	0.	0.
MEAN	437.	0.	211.	0.	0.	0.	0.	0.
S.D.	241.2	0.0	142.2	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	10	10	10	10

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 150 PPM
 WEEK 7

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLAT	WBC	SEGS	LMPH
28184	8.42	17.4	45.3	54.	20.6	38.4	CLOT	7.3	1387.	5621.
28187	8.26	16.1	43.8	53.	19.4	36.7	646.	9.4	846.	7708.
28181	8.45	17.4	46.2	55.	20.5	37.6	628.	10.7	2354.	8239.
28165	8.70	17.1	45.6	52.	19.6	37.5	660.	8.8	880.	7304.
28199	8.01	16.4	42.9	54.	20.4	38.2	854.	8.8	1320.	6688.
28150	8.64	17.0	44.4	51.	19.6	38.2	781.	10.4	1352.	8216.
28212	8.83	18.4	45.6	52.	20.6	40.3	858.	15.1	2114.	12533.
28194	8.96	17.5	45.6	51.	19.5	38.3	828.	8.3	2324.	5395.
28168	8.61	17.2	44.4	52.	19.9	38.7	906.	7.7	2387.	4851.
28160	8.13	16.7	43.8	54.	20.5	38.1	683.	9.3	1395.	7254.
MEAN	8.50	17.1	44.8	53.	20.1	38.2	760.	9.6	1636.	7381.
S.D.	0.305	0.64	1.06	1.4	0.53	0.93	106.8	2.21	603.5	2161.0
N	10	10	10	10	10	10	9	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
28184	146.	0.	146.	0.	0.	0.	0.	0.
28187	470.	0.	376.	0.	0.	0.	0.	0.
28181	107.	0.	0.	0.	0.	0.	0.	0.
28165	616.	0.	0.	0.	0.	0.	0.	0.
28199	616.	0.	176.	0.	0.	0.	0.	0.
28150	520.	0.	312.	0.	0.	0.	0.	0.
28212	302.	0.	151.	0.	0.	0.	0.	0.
28194	249.	0.	332.	0.	0.	0.	0.	0.
28168	308.	0.	154.	0.	0.	0.	0.	0.
28160	558.	0.	93.	0.	0.	0.	0.	0.
MEAN	389.	0.	174.	0.	0.	0.	0.	0.
S.D.	190.8	0.0	130.7	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	10	10	10	10

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 750 PPM
 WEEK 7

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLAT	WBC	SEGS	LMPH
28149	8.26	17.0	44.1	53.	20.5	38.5	713.	7.6	1140.	6156.
28192	8.93	18.1	47.4	53.	20.2	38.1	732.	16.0	4640.	10080.
28211	8.29	16.1	42.9	52.	19.4	37.5	734.	6.4	1408.	4608.
28176	8.07	15.9	42.9	53.	19.7	37.0	637.	9.9	4356.	4950.
28209	8.39	17.5	45.0	54.	20.8	38.8	706.	10.3	3090.	6901.
28182	7.66	15.4	41.1	54.	20.1	37.4	640.	9.9	2772.	6336.
28186	8.23	17.0	43.8	53.	20.6	38.8	763.	10.3	2060.	7519.
28158	8.77	16.5	44.4	51.	18.8	37.1	828.	6.8	1156.	5304.
28208	8.23	16.7	43.8	53.	20.2	38.1	791.	8.8	2024.	6336.
28148	8.77	16.9	44.1	50.	19.2	38.3	790.	9.7	4171.	5238.
MEAN	8.36	16.7	44.0	53.	20.0	38.0	733.	9.6	2682.	6343.
S.D.	0.378	0.79	1.62	1.3	0.65	0.67	62.8	2.68	1340.7	1556.7
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	IERY	NRBC
28149	228.	0.	76.	0.	0.	0.	0.	0.
28192	1280.	0.	0.	0.	0.	0.	0.	0.
28211	320.	0.	64.	0.	0.	0.	0.	0.
28176	495.	0.	99.	0.	0.	0.	0.	0.
28209	309.	0.	0.	0.	0.	0.	0.	0.
28182	693.	0.	99.	0.	0.	0.	0.	0.
28186	412.	0.	309.	0.	0.	0.	0.	0.
28158	204.	0.	136.	0.	0.	0.	0.	0.
28208	264.	0.	176.	0.	0.	0.	0.	0.
28148	194.	0.	97.	0.	0.	0.	0.	0.
MEAN	440.	0.	106.	0.	0.	0.	0.	0.
S.D.	332.9	0.0	89.6	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	10	10	10	10

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL HEMATOLOGY
 MALES GROUP: 1500 PPM
 WEEK 7

ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLAT	WBC	SEGS	LMPH
28196	8.13	16.4	43.8	54.	20.1	37.4	762.	10.9	1308.	8629.
28163	9.15	17.4	46.5	51.	19.0	37.4	695.	6.0	1536.	4544.
28157	8.35	17.4	45.3	54.	20.8	38.4	765.	10.6	1166.	8692.
28189	9.02	19.3	49.2	55.	21.3	39.2	590.	10.8	1296.	8748.
28179	8.48	17.1	44.1	52.	20.1	38.7	822.	14.5	4640.	8410.
28214	8.58	16.3	43.5	51.	18.9	37.4	740.	8.9	1068.	7209.
28205	8.96	17.1	44.4	50.	19.0	38.5	663.	10.2	2040.	7446.
28206	9.06	17.2	45.9	51.	18.9	37.4	664.	11.7	3510.	6903.
28183	9.12	18.0	46.5	51.	19.7	38.7	860.	18.8	4324.	13348.
28202	8.99	17.9	45.6	51.	19.9	39.2	739.	10.8	2052.	7668.
MEAN	8.78	17.4	45.5	52.	19.8	38.2	730.	11.4	2294.	8180.
S.D.	0.365	0.86	1.70	1.7	0.84	0.76	79.9	3.31	1355.8	2220.2
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	IGRN	TERY	NRBC
28196	654.	0.	109.	0.	0.	0.	0.	0.
28163	192.	0.	128.	0.	0.	0.	0.	0.
28157	742.	0.	0.	0.	0.	0.	0.	0.
28189	540.	0.	216.	0.	0.	0.	0.	0.
28179	1305.	0.	145.	0.	0.	0.	0.	0.
28214	534.	0.	89.	0.	0.	0.	0.	0.
28205	510.	0.	204.	0.	0.	0.	0.	0.
28206	1053.	0.	234.	0.	0.	0.	0.	0.
28183	940.	0.	188.	0.	0.	0.	0.	0.
28202	756.	0.	324.	0.	0.	0.	0.	0.
MEAN	723.	0.	164.	0.	0.	0.	0.	0.
S.D.	315.8	0.0	89.8	0.0	0.0	0.0	0.0	0.0
N	10	10	10	10	10	10	10	10

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD¹ RATS

INDIVIDUAL CLINICAL CHEMISTRY
 MALES GROUP: 0 PPM
 WEEK 7

ANIMAL	GLU	UN	CSREA	TP	TBIL	CA	PHOS	NA	K	CL
28200	1.23	191.	6.	61.	2.	91.	68.	143.	4.8	111.
28156	1.07	161.	6.	61.	2.	93.	69.	143.	5.1	110.
28173	1.25	170.	7.	70.	2.	95.	62.	137.	4.7	106.
28162	1.38	153.	8.	66.	2.	95.	68.	143.	5.7	109.
28155	1.11	124.	7.	71.	2.	96.	57.	143.	5.6	112.
28198	1.07	163.	7.	69.	2.	97.	67.	141.	5.3	110.
28201	1.11	161.	7.	62.	2.	97.	59.	142.	5.3	111.
28180	1.32	157.	8.	71.	2.	99.	70.	142.	5.9	109.
28159	1.27	173.	7.	70.	2.	95.	68.	141.	5.6	108.
28167	1.25	146.	7.	73.	2.	96.	72.	140.	5.8	109.
MEAN	1.21	160.	7.	67.	2.	95.	66.	142.	5.4	110.
S.D.	0.109	17.6	0.7	4.6	0.0	2.2	4.9	1.9	0.41	1.7
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	AST	ALT	GGT
28200	66.	37.	4.
28156	61.	32.	5.
28173	60.	25.	4.
28162	70.	33.	5.
28155	83.	36.	5.
28198	62.	15.	5.
28201	55.	28.	4.
28180	73.	32.	4.
28159	75.	32.	4.
28167	76.	31.	3.
MEAN	68.	31.	4.
S.D.	8.7	4.1	0.7
N	10	10	10

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL CLINICAL CHEMISTRY
 MALES GROUP: 150 PPM
 WEEK 7

ANIMAL	GLU	UN	CREA	TP	TBIL	CA	PHOS	NA	K	CL
28184	1.00	179.	7.	64.	2.	93.	66.	143.	4.7	108.
28187	1.03	162.	7.	64.	2.	96.	62.	143.	4.6	110.
28181	1.14	163.	6.	60.	2.	93.	62.	141.	4.8	109.
28165	1.22	156.	7.	64.	2.	92.	70.	143.	5.3	112.
28199	1.25	170.	7.	66.	2.	93.	64.	143.	5.3	109.
28150	1.37	141.	7.	66.	2.	96.	58.	141.	5.3	111.
28212	1.42	208.	8.	69.	2.	100.	70.	143.	6.2	110.
28194	0.99	158.	7.	70.	2.	98.	60.	141.	5.7	108.
28168	1.15	157.	8.	69.	2.	89.	55.	138.	5.0	107.
28160	1.13	135.	6.	64.	2.	99.	67.	140.	4.8	108.
MEAN	1.17	163.	7.	66.	2.	95.	63.	142.	5.2	109.
S.D.	0.147	20.3	0.7	3.1	0.0	3.5	5.0	1.7	0.50	1.5
N	10	10	10	10	10	10	10	10	10	10
ANIMAL	AST	ALT	GGT							
28184	74.	32.	4.							
28187	48.	30.	4.							
28181	62.	37.	4.							
28165	60.	33.	4.							
28199	62.	41.	4.							
28150	67.	31.	4.							
28212	59.	32.	4.							
28194	75.	35.	4.							
28168	71.	33.	4.							
28160	58.	27.	4.							
MEAN	64.	33.	4.							
S.D.	8.3	3.9	0.0							
N	10	10	10							

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL CLINICAL CHEMISTRY
 MALES GROUP: 750 PPM
 WEEK 7

ANIMAL	GLU	UN	CREA	TP	TBIL	CA	PHOS	NA	K	CL
28149	1.32	145.	8.	64.	2.	97.	72.	141.	5.8	108.
28192	1.09	133.	7.	71.	2.	95.	62.	141.	5.4	108.
28211	1.17	168.	6.	64.	2.	93.	61.	141.	5.2	110.
28176	1.13	192.	7.	65.	2.	94.	64.	138.	5.2	108.
28209	1.05	181.	7.	65.	2.	96.	58.	142.	5.2	108.
28182	1.43	156.	7.	66.	2.	96.	60.	138.	5.1	108.
28186	1.19	196.	8.	69.	2.	95.	62.	143.	5.6	109.
28158	1.20	171.	10.	66.	2.	95.	62.	144.	4.8	108.
28208	1.19	146.	7.	68.	2.	97.	54.	141.	5.1	109.
28148	1.18	188.	8.	76.	2.	96.	60.	140.	5.3	107.
MEAN	1.20	168.	8.	67.	2.	95.	62.	141.	5.3	108.
S.D.	0.110	21.9	1.1	3.8	0.0	1.3	4.6	1.9	0.28	0.8
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	AST	ALT	GGT
28149	77.	27.	4.
28192	90.	33.	4.
28211	76.	31.	4.
28176	63.	28.	4.
28209	68.	34.	4.
28182	73.	36.	4.
28186	71.	29.	3.
28158	98.	47.	4.
28208	63.	28.	3.
28148	78.	36.	4.
MEAN	76.	33.	4.
S.D.	11.2	6.0	0.4
N	10	10	10

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY STUDY IN CD⁰ RATS

INDIVIDUAL CLINICAL CHEMISTRY
 MALES GROUP: 1500 PPM
 WEEK 7

ANIMAL	GLU	UN	CREA	TP	TBIL	CA	PHOS	NA	K	CL
28196	1.08	168.	6.	64.	2.	95.	75.	142.	4.8	109.
28163	1.16	153.	7.	68.	1.	99.	60.	141.	5.8	109.
28157	1.07	166.	7.	70.	2.	99.	60.	141.	5.4	108.
28189	1.23	175.	9.	61.	2.	96.	79.	143.	5.4	109.
28179	1.23	143.	7.	69.	2.	93.	57.	140.	5.0	107.
28214	1.30	164.	6.	62.	2.	96.	62.	141.	5.2	110.
28205	1.12	152.	7.	69.	2.	95.	64.	139.	5.6	106.
28206	1.30	151.	8.	68.	2.	98.	54.	141.	5.3	111.
28183	1.10	113.	7.	71.	2.	96.	58.	139.	5.9	110.
28202	1.15	153.	7.	70.	2.	99.	72.	141.	5.7	107.
MEAN	1.17	154.	7.	67.	2.	97.	64.	141.	5.4	109.
S.D.	0.086	17.3	0.9	3.6	0.3	2.1	8.4	1.2	0.35	1.6
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	AST	ALT	GGT
28196	62.	29.	5.
28163	71.	32.	4.
28157	76.	36.	4.
28189	87.	32.	4.
28179	58.	20.	4.
28214	58.	27.	3.
28205	63.	30.	4.
28206	82.	44.	4.
28183	79.	40.	4.
28202	64.	27.	4.
MEAN	70.	32.	4.
S.D.	10.5	6.9	0.5
N	10	10	10

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD⁰ Rats

Protocol, Protocol Amendment and Protocol Deviations

(29 Pages)



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD¹ (Sprague-Dawley) Rats

BIRC PROJECT NUMBER: 91-13-25602

SPONSOR: Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

TESTING FACILITY: Bushy Run Research Center (BIRC)
Union Carbide Chemicals and
Plastics Company Inc.
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center: Cynthia D. Driscoll 12/6/91
Cynthia D. Driscoll, Ph.D. Date
Study Director

Linda J. Calisti 12/6/91
Linda J. Calisti, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

John P. Van Miller 12/6/91
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Chemicals and
Plastics Company Inc.:

Tipton Tyler 12/17/91
Tipton E. Tyler, Ph.D., DABT Date
Associate Director of Applied Toxicology

Division: Product 12-17-91
Richard C. Wise Date
Manager, Product Safety

Union Carbide Chemicals and Plastics Company Inc.
Excellence Through Quality

EQ

OBJECTIVES

The objective of this study is to evaluate the potential of the test substance to 1) produce toxicity in adult male and female CD® (Sprague-Dawley) rats, 2) affect male and female reproductive performance, and 3) produce developmental toxicity following repeated inhalation exposure.

GENERAL INFORMATION

Sponsor Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company (UCC&P) Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

Project Monitor Tipton R. Tyler, Ph.D., DABT

Testing Facility Bushy Run Research Center, Export, PA 15632-8902

Personnel

Developmental Toxicology and Animal Care

Supervisor

Inhalation Toxicology

Attending Veterinarian

R. R. Altman
P. J. Benson, B.S.
T. R. Brownfield, B.S.
B. L. Butler, A.H.T., AALAS Cert. II
M. A. Copeman, A.A., B.A.
D. L. Fait, B.S., AALAS Cert. II
L. C. Fisher, B.S., AALAS Cert. III
H. F. Kubena, B.S., AALAS Cert. III
T. L. Neepser-Bradley, Ph.D.
D. J. Tarasi, A.H.T., A.S., AALAS Cert. II

I. M. Pritts, Ph. D.
L. E. Lipko, AALAS Cert. II

M. K. Walter, DVM, Diplomate ACVP

All personnel who participate in the conduct of the study will be documented in the raw data.

Starting Date of Acclimation December 23, 1991.

Starting Date of Test Substance Exposure January 6, 1992.

Proposed Date for Completion of In-Life Phase February 28, 1992.

Proposed Date for Submission of the Draft Final Report To be added by amendment.

Basis for the Study

This study will consist of three exposure groups and an air-only control group. At the time of the study start, each group will consist of 15

rats/sex. Exposures will begin when the rats are at least 70 days of age and continue daily, 6 hr/day, 7 days/week, throughout the entire study. The exposure period will include a 2-week pre-mating phase, a 14-day (maximum) mating phase, the period of gestation and lactation (females exposed only through day 20 of gestation, males continue to be exposed through approximately the last lactation day 4). Female exposures will cease after gd 20 due to the technical considerations of an inhalation reproduction study, and thus allow for natural delivery and evaluation of the offspring.

The portions of this study conducted at the Bushy Run Research Center will be performed in compliance with the U.S. EPA Good Laboratory Practice Regulations, 40 CFR Part 792 and Annex 2 of the OECD Guidelines for Testing Chemicals (c(81)30 (Final)).

Alteration of Design

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. BREC reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered in jeopardy. In this event, the Sponsor shall be notified of the alteration as soon as possible, and written verification of the change will be the responsibility of the Study Director. All protocol modifications will be signed by the Study Director and a representative of the Sponsor.

METHODS

Test Substance

Chemical Name	Propionaldehyde
Source	UCC&P Texas City, Texas
CAS Registry Number	123-38-6
Sponsor Identification Number	T-1258
BREC Number	54-351A and 54-351B
Description	Water-white liquid; suffocating odor
Percent Active Material	Approximately 98.5% by weight (approximately 1.5% water added to shipping containers as required by DOT regulations).
Solubility	22% at 20°C by weight in water

Boiling Point	760 mm Hg 48°C
Stability of Test Substance	The test substance is considered to be stable under proper storage conditions. Compositional analysis of the test substance will be used as a measure of stability.
Storage Conditions	The test substance will be stored in stainless steel drums, the original containers, in a special enclosure under a nitrogen atmosphere.
Estimated Quantity Needed	Approximately two, 55 gallon drums of the compound will be used throughout all phases of this study. After the assigned studies have been completed, all unused test substance will be returned to the Sponsor.
Reserve Sample	Due to the nature of the test substance, a reserve sample will not be retained and stored by BRRC.
Test Substance Characterization	Prior to initiation of the range-finding study and following the definitive study, a compositional analysis of the test substance will be performed by the Sponsor.
Safety	A Material Safety Data Sheet (MSDS; Attachment 1) supplied by the Sponsor will be reviewed by all personnel prior to the initiation of the study. This review will be documented. This chemical is extremely flammable; keep away from heat, sparks and flame; reactive with oxygen. Normal precautions for untested chemicals will be used. These procedures include the use of disposable paper or plastic coats or jumpsuits, hats, booties or shoe covers, and butyl or PVC coated gloves while in the animal rooms. Eye protection will include the use of safety glasses.
<u>Test Animals</u>	
Species	Crl:CD®RR rats, commonly referred to as CD® rats
Supplier	Charles River Breeding Laboratories, Portage, Michigan
Rationale	The rat is the preferred species for this type of toxicity testing. The CD® albino rat was selected due to its high fecundity and routine use in rodent reproduction and developmental toxicity studies.
Number and Sex	A total of 75 males and 75 nulliparous, nonpregnant females will be ordered from which 60 of each sex will be selected for the study.

Age and Weight

The rats will be approximately 63 days of age on scheduled animal receipt date. The males will weigh approximately 230-275 g and the females approximately 175-210 g upon arrival.

**Acclimation
and Pretest
Evaluations**

Shortly after their arrival at the laboratory, the animals will be transported to the room selected for the study. Once in the room, the animals will be removed from the shipping cartons and examined. All animals with evidence of disease or physical abnormalities will be discarded and their rejection from the shipment will be recorded. If an unusually large number of rats show evidence of disease or physical abnormalities, the shipment of rats will be rejected for use in the study. A total of 10 rats (5 male and 5 female) will be randomly selected for a health screen as discussed below.

All remaining rats will be housed two per cage for an acclimation period of approximately two weeks.

During the acclimation period, animals will be fed the same diet which will be used during the study. Animals will be observed twice daily for any overt clinical signs of disease or abnormality. Individual detailed physical examinations will be conducted twice prior to the mating period. Animals showing abnormalities deemed by the Study Director or other appropriate supervisory personnel to render the animal unacceptable for placement on the study will be sacrificed and discarded on the day observed. If an unusually large number of rats show signs of disease, the shipment of rats will be rejected for use in the study.

Rats will be weighed twice during the acclimation period, once during each week of acclimation. Any rat whose weight gain during this period is not considered normal for this age and strain of rat, or whose absolute body weight at the second weighing is outside 20% of the population mean for their sex, will not be considered for use in the study.

Quality Control

Quality control will be performed within two days after the receipt of the animals. The pretest health screen will consist of a viral screen, examinations for fecal parasites, necropsy examinations, and histopathological evaluations of selected tissues. The screen will be performed on 5 animals/sex selected directly from the shipping cartons with as many cartons as possible being represented. The gross examinations and the viral screen will be conducted on all 10 rats selected for the health screen.

The following viruses will be included in the viral screen:

Pneumonia virus of mice (PVM)
Reovirus type 3 (Rec3)
Kilham rat virus
Toolan H-1
Sendai
Lymphocytic choriomeningitis (LCM)
Rat coronavirus
SDA
Minute virus of mice (MVN)
Mycoplasma pulmonis
Polyoma virus
Encephalomyelitis (GDVII)
Mouse adenovirus FL/K87 (MAD)

Fecal examination for parasites will be conducted using a cellophane tape test on the 10 animals selected for the prestudy screen, and by zinc sulfate flotation from cecal contents obtained at their necropsy.

Histopathology will be performed on three sacrificed animals/sex. At least the following tissues will be examined: liver, kidneys, trachea, lungs, heart, spleen, salivary glands, submandibular lymph nodes, and nasal cavities.

The purpose of this screen is to determine the suitability of the population of animals proposed for this study. Therefore, the results of this screen will be available before the study begins.

Identification

Animals shall be uniquely identified prior to initiation of the study by cage identification and ear tags or tail tattoos. The individual animal numbers will be documented in the study records.

Culled Animals

Animals received with the initial shipment but not used in the study will be euthanized or used for training or methods development. Records will be kept documenting the fate of all animals received for the study.

Husbandry

The experiment will be carried out under standard laboratory conditions in the Chemical Hygiene Fellowship Building of BRRRC. The animals will be housed one to two per cage during the acclimation period. Thereafter, they will be housed individually except during mating and lactation. Stainless steel cages with wire mesh floors will be used throughout the study with the exceptions noted below.

Study animals will be housed two per cage (one male:one female from the same exposure level) during the mating period. Females will be caged individually once they have successfully mated (or at the end of the mating period). Successfully mated females will be transferred to shoebox cages and furnished with appropriate nesting materials on Day 20 of gestation following exposure.

Stainless steel cages will be changed at the end of the acclimation period and just prior to the mating period. Male caging will be changed at least once every two weeks thereafter. Mated females will remain in the same stainless steel cages from gd 0 through gd 20 at which time they will be transferred to shoebox cages. Paperboard kept under each cage will be changed regularly and daily during mating.

For exposures, animals will be transferred, one per cage (except during mating) to stainless steel wire-mesh cages. Stainless steel shelf pans will be placed under each row of cages to prevent urinary and fecal contamination of animals at lower levels.

Animal room temperature and humidity will be recorded continuously using an automatic recorder. Temperature will be maintained at 66-77°F and relative humidity will be maintained at 40-70%. The temperature and humidity will be checked by a technician at each room check and a record will be kept indicating that it was done. Appropriate corrective action will be taken whenever readings outside the specified limits are observed. If the temperature or humidity remains outside the prescribed range for more than 24 hours, the Sponsor's representative will be notified.

The accuracy of the temperature and humidity recording devices will be checked periodically and calibrated when necessary. The verification and calibration data will be recorded. Any time the continuous recording equipment is found to be malfunctioning, the temperature and humidity of the animal room will be manually measured and recorded at each room check.

Fluorescent lighting will provide illumination 12 hours per day using an automatic timer. There will be at least ten air changes per hour.

Diet

Certified Ground Rodent Chow® (#5002, Ralston Purina Company) will be available ad libitum except during exposures. The analyses of chemical composition and possible contaminants of each batch of diet will be

performed by Balston Purina Company (St. Louis, MO) and the results of their analysis will be checked by the Study Director.

Water

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum, except during exposures, by an automatic watering system with demand control valves mounted on each rack. Water pressure and function of the individual cage rack systems will be checked at each room check and a record will be kept indicating it was done. Drinking water contaminant levels will be measured at regular intervals per EPA specifications, to include the 129 "priority" pollutants, identified in the Federal Register 45 (98), Appendix D, Part 122, and shall comply with human requirements.

Study Design

Number of Groups

The study will consist of a control and three exposure groups.

Number of Animals per Group

The study will begin with 15 rats/sex/group in order to yield at least 8 pregnant females per group.

Organization

Group	Number of Animals (per Sex)	Test Vapor Concentration (ppm)
Control	15	0
Low	15	150
Mid	15	750
High	15	1500

Group Assignment

Following approximately two weeks of acclimation, animals will be assigned to one of four groups, using a computer-generated, weight-stratified, randomization procedure. The stratified randomization procedure will assign animals to groups such that the body weights of all groups are homogenous, within a sex, by statistical analysis at study initiation.

Animals not assigned to the study will be euthanized and discarded, used for training of BRRC staff or used for methods development. The fate of all animals not selected for use in this study will be documented in the raw data.

Duration of Exposures

Exposures will begin when the rats are at least 70 days of age and continue daily, 6 hr/day, 7 days/week, throughout the entire study. The exposure period will include a 2-week pre-mating phase, a 14-day (maximum) mating phase, the period of gestation and lactation (females will be exposed only through day 20 of gestation, males continue to be exposed through approximately the last lactation day 4). The females will be exposed only through gd 20 due to the technical considerations of an inhalation reproduction study, allowing for natural delivery and evaluation of the offspring.

Administration of Test Substance and Inhalation Chamber Operation**Route and Justification**

The route of exposure will be by inhalation. Inhalation is a potential route of human exposure and is considered to be a meaningful way to evaluate the toxicity of the test substance.

Exposure Chambers

Four stainless steel chambers (approximately 4.3 cubic meters) with glass doors and windows for animal observations will be used. The chamber size adequate to ensure that the total "volume" of test animals shall not exceed 5% of the volume of the test chamber. The exposure chambers in room 138 will be utilized.

Chambers will be provided with air at a flowrate of approximately 14 air changes per hour to ensure an adequate oxygen content of 19%. Oxygen content will be measured at the start of the study. The rate of airflow will be monitored and recorded approximately every 30 minutes. All chambers will be maintained at a slightly negative pressure to prevent any vapor from entering the room containing the chambers.

The temperature and relative humidity of the exposure chambers will be monitored continuously and recorded approximately 12 times during each exposure. Temperature will be maintained at 68-75°F (22 ± 2°C) and relative humidity will be maintained between 40 and 60%.

To compensate for any (undetected) differences in environment or test substance concentration within the chamber, all exposure cage positions will be rotated weekly. A description of the rotation will be provided in the raw data.

Target Exposure Concentration Selection

Three graduated concentration levels of the test substance as a vapor will be selected by the Sponsor, for evaluation in three groups of rats. An additional group, a concurrent control, will be placed in an inhalation chamber and exposed to air only.

**Test Vapor
Generation**

The test liquid will be metered from a piston pump into a heated glass evaporator similar in design to that described by Snellings and Dodd (1990). Temperatures in the evaporator will be maintained at the lowest level sufficient to vaporize the liquid, and will be recorded.

Test Vapor Analysis

Chamber concentration of the test substance will be determined approximately once each hour by a gas chromatographic (GC) technique. The details of the GC method will be described in the study report. The analytical monitoring system will be set to alarm at concentrations $<$ or $>$ 10% of the target chamber concentrations. The chamber sampling probes will be placed in the breathing zone of the animals. The daily nominal (estimated) chamber concentrations will also be determined.

**Chamber
Concentration
Distribution**

The uniformity of the vapor in each of the three exposure chambers and the reproducibility of target vapor concentrations will be examined prior to initiation of the study. For each individual distribution test, vapor concentrations will be measured at five positions situated in the breathing zone of the study animals.

Experimental Evaluations**Mortality
Checks and
Clinical Signs**

All animals assigned to study will be observed for mortality twice daily, seven days per week. During the 5-day work week, the first daily mortality check will be conducted prior to exposures or before 9:00 a.m., and the second one will generally be conducted following exposures or after 2:00 p.m. On weekends, the first daily mortality check will be conducted prior to exposures or before 9:00 a.m. and the second mortality check will be conducted following exposure or, if exposures are not conducted, after noon.

Study animals will be given detailed examinations for clinical signs of toxicity once daily following exposure. Overt signs of toxicity will be monitored visually in the morning while transferring animals to the exposure cages.

From gestation Day 21 through Lactation Day 4, when dams are not exposed to the test substance, detailed clinical observations of the dams will be conducted once daily before noon. Their litters will be examined as soon as possible after birth, Day 0 of lactation, and again on Day 4 of lactation to determine the number, sex, and condition of viable and

dead pups. Overt signs of toxicity will be monitored visually in conjunction with the afternoon mortality checks.

Observed mortality and/or clinical signs will be recorded on the day observed. Lack of clinical signs during daily detailed physical examinations will also be recorded.

Body Weight

The body weights of the male rats will be determined and recorded on the study days 0 (first exposure day), 7, 14, 21, 28, and on the day of termination.

Females will be weighed on study days 0, 7, and 14 of the pre-mating period, Days 0, 7, 14, and 21 of gestation, and Days 0 and 4 of lactation. Body weight gains will be computed. Females which do not produce live litters will be weighed weekly until scheduled sacrifice.

Litter weights, by sex, will be determined on Days 0 and 4 of lactation.

Food Consumption

Individual food consumption measurements will be collected weekly for all males except during the mating period when food consumption will not be measured. Food consumption measurements will be conducted weekly for all females during the pre-mating periods of this study. During gestation, food consumption will be measured at three-to four-day intervals for determination of food consumption during the following gestational intervals: gestation day (gd) 0-7, 7-14 and 14-21. During lactation, food consumption will not be measured. Food consumption for females which do not deliver live litters will be measured weekly until sacrifice.

During the course of the study, the area under the cage will be examined for food spillage during each daily room check and significant food spilled will be noted in the raw data. Significant food spillage will be defined as any amount that can be easily measured. No effort will be made to make this measurement. Food consumption data for animals with recorded spills will not be used in summarization of results within a particular interval.

**Mating
Procedures**

The animals will be mated at approximately 13 weeks of age, one male:one female, on the basis of random selection of mates within an exposure group. The mating period will be of 14 days duration.

The observation of a dropped or vaginal copulation plug or of vaginal sperm will be considered evidence

of successful mating. Females will be examined twice daily (a.m. and p.m.) during the cohabitation period for the presence of dropped or vaginal copulation plugs, and once daily (p.m. following exposures) for the presence of vaginal sperm. The day a copulation plug or vaginal sperm is observed will be designated gestational day (gd) 0. Once successful mating has been observed, the male and female from that mating pair will be individually housed.

Each male and female mating pair will be co-housed for a maximum period of 7 days. If at the end of the 7 days there is no evidence of mating, the female will be co-housed with another male from the same exposure level that has mated successfully previously. For any mating pairs which do not show evidence of successful mating, the last scheduled mating day will be considered gd 0 for that female and the animals will be treated accordingly for subsequent events.

Gestation

On gd 20, after exposure, each female will be transferred to a shoebox cage. Females will be observed twice daily (a.m. and p.m.) after transfer for evidence of littering.

Lactation

After delivery, the dams will be allowed to rear their young to Day 4 postpartum, at which time the dam and the litter will be euthanized.

Clinical Pathology

At the end of the exposure period, ten males selected at random from each of the exposure concentrations will be fasted for approximately 16 hours before being lightly anesthetized using methoxyflurane for blood collection by orbital sinus puncture. Fixed blood smears will be prepared and stored. The following hematological parameters will be measured:

- erythrocyte counts
- hemoglobin
- hematocrit
- erythrocyte indices, including:
 - mean corpuscular hemoglobin
 - mean corpuscular volume
 - mean corpuscular hemoglobin concentration
- platelet count
- total leukocyte count
- differential leukocyte count

Clinical chemistry tests will include:

- glucose
- urea nitrogen
- creatinine

total protein
total bilirubin
calcium
phosphorus
sodium
potassium
chloride
AST
ALT
gamma glutamyl transferase

Necropsy and Pathology

ADULTS

All parental animals in all groups will be subjected to a complete necropsy.

Parental males will be euthanized after the last litter reaches lactation day 4 (approximately). Parental females will be euthanized on day 4 of lactation. Females that fail to litter will be euthanized approximately 5 days after their expected delivery date.

On the day of scheduled sacrifice, animals will be anesthetized with methoxyflurane and humanely sacrificed by exsanguination.

The necropsy will include: examination of external surfaces; all orifices; cranial cavity; carcass; external and cut surfaces of the brain and spinal cord; the thoracic, abdominal, and pelvic cavities and their viscera; and cervical tissues and organs.

The number of implantation sites and corpora lutea for each female will also be determined at necropsy.

The following tissues will be weighed and preserved in buffered neutral 10% formalin:

liver
kidney(2)
lungs
thymus

The following tissues will be weighed and preserved in Bouin's fixative:

testes
epididymides

The following tissues will be preserved in buffered neutral 10% formalin for all adult animals:

upper and lower respiratory tract
 (including nasal turbinates)
 brain (3 sections including medulla oblongata,
 pons, cerebellar cortex and cerebral cortex)
 heart
 spleen
 adrenals
 ovaries (females only)
 seminal vesicles (males only)
 target organs if previously identified
 all gross lesions

The following tissues will be preserved in buffered neutral 10% formalin but not processed further unless deemed necessary by the Study Director or Pathologist:

vagina (females only)
 uterus (females only)
 pituitary

**Microscopic
 Evaluation
 of Adult
 Fixed Tissues**

Histopathologic evaluation will be performed on all retained tissues, except as noted above, from the control and high exposure concentration males and females. Organs demonstrating pathology in these animals will be reported to the Sponsor and, at the Sponsor's request and at additional cost to the Sponsor, such organs will be examined in the other dose groups.

OFFSPRING

On postnatal day 4, pups will be weighed, examined externally, sexed, euthanized and discarded without pathological evaluation.

**Dead or Moribund
 Animals**

Necropsies will be performed seven days per week on animals not surviving to scheduled sacrifice (including pups) in an attempt to determine the cause of death. The pregnancy status of moribund females or females that are found dead following the mating period, will be determined at necropsy.

Any animal showing signs of severe debilitation or toxicity, particularly if death appears imminent, will be humanely sacrificed by carbon dioxide asphyxiation to prevent loss of tissues through autolysis. For mated females, the uterus will be examined and the status of implantation sites will be recorded.

Organ weights of animals that are found dead or sacrificed moribund will not be determined at necropsy.

**Abortion or
Premature
Delivery**

If signs of abortion or premature delivery are observed, the animal will be euthanized by carbon dioxide asphyxiation and a complete necropsy will be performed. The uterus will be opened and examined, and site descriptions will be identified and recorded. Ovarian corpora lutea of pregnancy will be counted. Maternal tissues will be retained in fixative only as deemed necessary by the gross findings.

Organ weights of animals that abort or deliver early will not be determined at necropsy.

**Nonpregnant
Females**

The fixed uteri from any females which fail to produce a litter will be stained with potassium ferricyanide for confirmation of pregnancy status. This staining procedure does not interfere with possible subsequent histologic evaluation.

**Statistical
Evaluation**

The unit of comparison will be the male, the female (prebreeding exposure parameters), the pregnant female or the litter. Data collected for nonpregnant females and females which abort or deliver early, will not be included in the statistical analyses.

The data for continuous, parametric variables will be intercompared for the exposure and control groups by use of Levene's test for homogeneity of variance, by analysis of variance and by t-tests. The t-tests will be used, if the analysis of variance is significant, to delineate which groups differ from the control group. If Levene's test indicates homogeneous variances, the groups will be compared by an analysis of variance for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicates heterogeneous variances, the groups will be compared by an analysis of variance for unequal variances followed, when appropriate, by separate variance t-tests. For discontinuous data, the Kruskal-Wallis test followed, when appropriate, by Mann-Whitney U tests. Frequency data will be compared using Fisher's exact test. All statistical tests, except the frequency comparisons, will be performed using BMDP Statistical Software (Dixon, 1990). The frequency data tests are described in Biometry (Sokal, R. R. and Rohlf, F. J., W. H. Freeman and Company: San Francisco, 1969). The probability value of $p < 0.05$ (two-tailed) will be used as the critical level of significance for all tests.

RECORDS

All raw data and reports from this study will be retained by BRRC for at least 10 years after completion of the study. Tissues preserved in fixative will be retained for at least five years. Paraffin blocks and tissue slides will be retained indefinitely.

Prior to discarding any of the above data or materials, the Sponsor will be contacted and given the option of obtaining it or arranging for continued storage. All data and materials mentioned above will remain the sole property of the Sponsor and can be removed from BRRC at the Sponsor's discretion.

REPORT

Draft Final Report

A draft of the final report will be submitted to the Sponsor within six months after the completion of the terminal sacrifice. This report will be a comprehensive report which will include all information necessary to provide a complete and accurate description and evaluation of the test procedures and results. It will include: a summary; appropriate text discussions of the experimental design, materials and methods and results; and summary mean or incidence tables of in-life and necropsy data.

Final Report

The draft final report will be reviewed by the Sponsor, and comments on the report will be provided to BRRC within six weeks from the date of submission of the draft version. BRRC will consider these comments in preparing the final report. Assuming the Sponsor's comments are received at the specified time and no major revisions are required, BRRC will submit a final report within twelve weeks of issuance of the draft report.

The final report will be audited by the QA department and contain a signed quality assurance statement. In addition, it will contain appendices with individual animal data and other pertinent information.

ANIMAL USE POLICY

It is the goal of BRRC, through the establishment and activities of the Institutional Animal Care and Use Committee (IACUC), to comply with the U.S. Animal Welfare Act and the subsequent rules promulgated by the U.S. Department of Agriculture and in effect on the date of this protocol. It has been determined that the work described herein minimizes the number of animals used, is necessary, and uses the most appropriate species and strain in order to provide meaningful results and the most useful information for comparative purposes relative to previous studies. Furthermore, this study will be conducted humanely, and to the best of our knowledge, neither unnecessarily duplicates any previous work, nor can it be accomplished using currently available, validated non-animal models.

GOOD LABORATORY PRACTICE COMPLIANCE

The Bushy Run Research Center, through the administration of a quality assurance program by the Good Laboratory Practices Committee and Quality Assurance Unit, assures compliance of all phases of toxicological studies conducted at the Bushy Run Research Center with existing regulations and generally accepted good laboratory practices.

The study will be subjected to periodic inspections and the final report will be reviewed by the BRRC Quality Assurance Unit. All quality assurance inspection records and the Master Schedule will be made available to the Sponsor during Sponsor visits.

REFERENCES

Organization for Economic Cooperation and Development (OECD) (1981). OECD Principles of Good Laboratory Practice, c(81)30(Final).

Proposed OECD Guidelines for Testing of Chemicals (1990). Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test.

Snellings, W. M. and D. E. Dodd (1990). Inhalation studies. In: Handbook of In Vivo Toxicity Testing (D. L. Arnold, H. C. Grice and D. R. Krewski, eds.) pp 189-246, Academic Press, New York.

Sokal, R. R. and F. J. Rohlf (1969). Biometry, W. H. Freeman and Co., San Francisco, pp 369-371, 299-340, 370-372, 589-595.

ATTACHMENT 1

PAGE 1

FOR INTERNAL USE ONLY

UNION CARBIDE CORPORATION
Solvents and Coatings Materials Division

MATERIAL SAFETY DATA SHEET

EFFECTIVE DATE: 08/29/90

Union Carbide urges each customer or recipient of this MSDS to study it carefully to become aware of and understand the hazards associated with the product. The reader should consider consulting reference works or individuals who are experts in ventilation, toxicology, and fire prevention, as necessary or appropriate to use and understand the data contained in this MSDS.

To promote safe handling, each customer or recipient should: (1) notify its employees, agents, contractors and others whom it knows or believes will use this material of the information in this MSDS and any other information regarding hazards or safety; (2) furnish this same information to each of its customers for the product; and (3) request its customers to notify their employees, customers, and other users of the product of this information.

I. IDENTIFICATION

PRODUCT NAME: PROPIONALDEHYDE
 CHEMICAL NAME: Propionaldehyde
 CHEMICAL FAMILY: Aldehydes
 FORMULA: C₃H₆O
 MOLECULAR WEIGHT: 58.08
 SYNONYMS: Propanal; Propylaldehyde
 CAS # AND 123-28-6
 CAS NAME: Propanal

II. PHYSICAL DATA

BOILING POINT, 760 mm Hg: 48 C (118.4 F)
 SPECIFIC GRAVITY(H₂O = 1): 0.7982
 FREEZING POINT: -80 C (-112 F)
 VAPOR PRESSURE AT 20°C: 238 mm Hg
 VAPOR DENSITY (air = 1): 2.0
 EVAPORATION RATE (Butyl Acetate = 1): 19.9
 SOLUBILITY IN WATER by wt: 22% @ 20 C
 APPEARANCE AND ODOR: Water-white liquid; suffocating odor
 PERCENT VOLATILES (by volume): 100

Copyright 1990 Union Carbide Chemicals & Plastics Tech. Corp.
 UNION CARBIDE is a trademark of Union Carbide Corporation
 EMERGENCY PHONE NUMBER: 1-800-UCC-HELP (Number available at all times)

UNION CARBIDE CORPORATION
 Solvents and Coatings Materials Division
 29 Old Ridgebury Road, Danbury, Ct. 06817-0001

ATTACHMENT 1 (Continued)

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PRODUCT NAME: PROPIONALDEHYDE

III. INGREDIENTS

MATERIAL	%	TLV (mg/m ³)	Hazard
Propionaldehyde (CAS 8123-28-6)	100	None established	Harmful if inhaled; eye irritant, flamm

IV. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT

<0 F (<-18 C) Tag Closed Cup; <0 F (<-18 C) Tag Open Cup

FLAMMABLE LIMITS IN AIR, by volume:

LOWER: 2.6
UPPER: 17.0

EXTINGUISHING MEDIA:

Apply alcohol-type or all-purpose-type foams by manufacturer's recommended techniques for large fires. Use CO₂ or dry chemical media for small fires.

SPECIAL FIRE FIGHTING PROCEDURES:

Use water spray to cool fire-exposed containers and structures. Use water spray to disperse vapors; reignition is possible. Use self-contained breathing apparatus and protective clothing. Use remote spray monitors or fight fire from behind shields.

UNUSUAL FIRE AND EXPLOSION HAZARDS:

Vapors form from this product and may travel or be moved by air currents and ignited by pilot lights, other flames, sparks, heaters, electrical equipment, static discharges or other ignition sources at locations distant from product handling point.

Vapors may settle in low or confined areas, or travel a long distance to an ignition source and flash back explosively.

This material may produce a floating fire hazard.

ATTACHMENT 1 (Continued)

PAGE 2

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

V. HEALTH HAZARD DATA**EXPOSURE LIMIT(S):**

None established by ACGIH or OSHA.

EFFECTS OF SINGLE OVEREXPOSURE**SWALLOWING:**

Moderately toxic. Severely irritating to the gastrointestinal tract causing a burning sensation in the mouth and throat, nausea, headache, dizziness, abdominal discomfort, vomiting and diarrhea.

SKIN ABSORPTION:

No evidence of adverse effects from available information.

INHALATION:

Vapors may be irritating to the respiratory tract. High concentrations may cause headache, nausea, vomiting, coughing, and difficulty breathing, narcosis, and may result in the inhalation of potentially lethal amounts of material.

SKIN CONTACT:

May cause slight irritation, seen as mild local redness.

EYE CONTACT:

Causes severe irritation, seen as marked excess redness and swelling of the conjunctiva.

EFFECTS OF REPEATED OVEREXPOSURE:

Repeated or prolonged exposure may result in the development of dermatitis.

MEDICAL CONDITIONS AGGRAVATED BY OVEREXPOSURE:

Breathing of vapor and/or mist may aggravate asthma and inflammatory or fibrotic pulmonary disease.

SIGNIFICANT LABORATORY DATA WITH POSSIBLE RELEVANCE TO HUMAN HEALTH HAZARD EVALUATION:

Rats exposed to 1200 ppm for six days experienced liver damage.

OTHER EFFECTS OF OVEREXPOSURE:

None currently known.

EMERGENCY AND FIRST AID PROCEDURES:**SWALLOWING:**

If patient is conscious and has a gag reflex, give two glasses of water and induce vomiting. Call a physician immediately.

SKIN:

Immediately flush skin with plenty of water while removing contaminated clothing and shoes. Obtain medical attention. Wash clothing before wearing again. Discard shoes.

INHALATION:

Remove to fresh air. Give artificial respiration if not breathing. Oxygen may be given by qualified personnel if breathing is difficult.

ATTACHMENT 1 (Continued)

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FOR INTERNAL USE ONLY

ECOLOGICAL NAME: PROPIONAL DEHYDE

Obtain medical attention.

EYES:

Immediately flush eyes thoroughly with water and continue washing for at least 15 minutes. Obtain medical attention, preferably from an ophthalmologist, urgently.

NOTES TO PHYSICIAN:

There is no specific antidote. Treatment of overexposure should be directed at the control of symptoms and the clinical condition of the patient.

VI. REACTIVITY DATA**STABILITY:** Stable**CONDITIONS TO AVOID:**

Avoid contamination with basic materials. Contamination with basic materials (examples: sodium hydroxide, caustic soda, amines, ammonia, etc.) can result in a rapid exothermic reaction.

Avoid contamination with strong mineral acids:

Contamination with strong mineral acids can result in a rapid exothermic reaction.

Avoid air (oxygen):

Contact with air results in carboxylic acid formation. Oxidation can also cause formation of hazardous peroxides or peracids.

INCOMPATIBILITY (MATERIALS TO AVOID):

Alcohols, alkalies, amines, ammonia, caustics, halogen-containing compounds, oxygen, strong mineral acids.

HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS:

Burning will produce carbon monoxide and/or carbon dioxide.

Carbon monoxide is highly toxic if inhaled; carbon dioxide in sufficient concentrations can act as an asphyxiant.

HAZARDOUS POLYMERIZATION: MAY OCCUR**CONDITIONS TO AVOID:**

May react with evolution of heat in the presence of alkalies, amines, and acids.

VII. SPILL OR LEAK PROCEDURES**STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED**

Eliminate sources of ignition. Wear suitable, protective equipment; avoid contact with liquid and vapors. Collect for disposal. Highly toxic to aquatic life. Avoid discharge to sewers or waterways.

WASTE DISPOSAL METHOD:

Incinerate in a furnace where permitted under appropriate Federal, State and local regulations. This product can be toxic to the microorganisms in a

ATTACHMENT 1 (Continued)

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FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

wastewater treatment plant; however, a solution of about 10 ppm concentration was found to be biodegradable in laboratory studies.

VIII. SPECIAL PROTECTION INFORMATIONRESPIRATORY PROTECTION (SPECIFY TYPE):

Self-contained breathing apparatus in high vapor concentrations.

VENTILATION:

This product should be stored and handled in vapor-tight equipment, under an atmosphere of oxygen-free nitrogen. When this is done, general (mechanical) room ventilation should be satisfactory. Special, local ventilation is needed at points where vapors can be expected to escape to the workplace air.

PROTECTIVE GLOVES:

Butyl or PVC coated

EYE PROTECTION:

Monogoggles

OTHER PROTECTIVE EQUIPMENT:

Eye bath, safety shower

IX. SPECIAL PRECAUTIONSPRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE:

DANGER! Extremely Flammable.
Harmful if inhaled.
Causes eye irritation.

Keep away from heat, sparks, and flame.
Avoid breathing vapor.
Avoid contact with eyes.
Keep container closed.
Use with adequate ventilation.
Wash thoroughly after handling.

FOR INDUSTRY USE ONLY

OTHER PRECAUTIONS:

STORAGE: Reacts with oxygen; store under oxygen-free nitrogen.
(See Incompatibility).

ATTACHMENT 1 (Continued)

PAGE 4

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

PROCESS HAZARD: Sudden release of hot organic chemical vapors or mists from process equipment operating at elevated temperature and pressure, or sudden ingress of air into vacuum equipment, may result in ignitions without the presence of obvious ignition sources. Published "autoignition" or "ignition" temperature values cannot be treated as safe operating temperatures in chemical processes without analysis of the actual process conditions.

Any use of this product in elevated-temperature processes should be thoroughly evaluated to establish and maintain safe operating conditions. Further information is available in a technical bulletin entitled "Ignition Hazards of Organic Chemical Vapors."

TRANSFER HAZARD: Vapors of this product may be ignited by static sparks. Use proper bonding and grounding during liquid transfer as described in National Fire Protection Association document NFPA 77.

X. REGULATORY INFORMATIONSTATUS ON SUBSTANCE LISTS:

THE CONCENTRATIONS SHOWN ARE MAXIMUM OR CEILING LEVELS (WEIGHT %) TO BE USED FOR CALCULATIONS FOR REGULATIONS. TRADE SECRETS ARE INDICATED BY "TS".

FEDERAL EPA

COMPREHENSIVE ENVIRONMENTAL RESPONSE, COMPENSATION, AND LIABILITY ACT OF 1980 (CERCLA) REQUIRES NOTIFICATION OF THE NATIONAL RESPONSE CENTER OF RELEASE OF QUANTITIES OF HAZARDOUS SUBSTANCES EQUAL TO OR GREATER THAN THE REPORTABLE QUANTITIES (RQs) IN 40 CFR 302.4.

COMPONENTS PRESENT IN THIS PRODUCT AT A LEVEL WHICH COULD REQUIRE REPORTING UNDER THE STATUTE ARE:
None

Superfund Amendments and Reauthorization Act of 1986 (SARA) Title III requires Emergency Planning Based on Threshold Planning Quantities (TPQs) and release Reporting Based on Reportable Quantities (RQs) in 40 CFR 355 (Used for SARA 302, 311 AND 312).

Components Present in this Product at a level which could require Reporting under the statute are:
None

SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT OF 1986 (SARA) TITLE III REQUIRES SUBMISSION OF ANNUAL REPORTS OF RELEASE OF TOXIC CHEMICALS THAT APPEAR IN 40 CFR 372 (FOR SARA 313). THIS INFORMATION MUST BE INCLUDED IN ALL MSDS THAT ARE COPIED AND DISTRIBUTED FOR THIS MATERIAL.

COMPONENTS PRESENT IN THIS PRODUCT AT A LEVEL WHICH COULD REQUIRE REPORTING UNDER THE STATUTE ARE:

CHEMICAL
Propionaldehyde

CAS NUMBER
123-38-6

UPPER LIMIT
CONCENTRATION %
100

ATTACHMENT 1 (Continued)

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FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDESTATE RIGHT-TO-KNOW**CALIFORNIA PROPOSITION 65**

This product does not contain materials which the State of California has found to cause cancer, birth defects, or other reproductive harm.

Massachusetts 105 CMR 470.000 Right-to-know, Substance List (MSL) Hazardous Substances and Extraordinarily Hazardous Substances on the MSL must be identified when present in products.

Components present in this product at a level which could require reporting under the statute are:

HAZARDOUS SUBSTANCES (=) 1X

CHEMICAL	CAS NUMBER	UPPER BOUND CONCENTRATION X
Propionaldehyde	123-28-6	100

Pennsylvania Right-to-know, Hazardous Substance List Hazardous Substances and Special Hazardous Substances on the List must be identified when present in products.

Components present in this product at a level which could require reporting under the statute are:

HAZARDOUS SUBSTANCES (=) 1X

CHEMICAL	CAS NUMBER	UPPER BOUND CONCENTRATION X
Propionaldehyde	123-28-6	100

TSCA INVENTORY STATUS

The ingredients of this product are on the TSCA inventory.

CALIFORNIA RULE 443.1 VOC'S:
VOC 797 g/l; Vapor pressure 258 mm Hg @ 20 C

OTHER REGULATORY INFORMATION:

None

NOTE

The opinions expressed are those of qualified experts within Union Carbide. We believe that the information contained is current as of the date of this Material Safety Data Sheet. Since the use of this information and of these opinions and the conditions of the use of the product are not within the control of Union Carbide, it is the user's obligation to determine the conditions of safe use of the product.

ATTACHMENT 1 (Continued)

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FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONAL DENYDE

DATE: 08/29/90

REVISION DATE: 08/29/90

REVISED SECTIONS

Section III: INGREDIENTS CORRECTION

PRODUCT: 70771

F NUMBER: C0322D

Printed in USA



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL AMENDMENT 1

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD¹ Rats

BRRC PROJECT NUMBER: 91-13-25602

SPONSOR: Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Chemicals and
Plastics Company Inc.
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center:

Cynthia D. Driscoll 7/15/92
Cynthia D. Driscoll, Ph.D. Date
Study Director

Linda J. Calisti 7/21/92
Linda J. Calisti, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

John P. Van Miller 7/22/92
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Chemicals
and Plastics Company Inc.:

Tipton R. Tyler 7/13/92
Tipton R. Tyler, Ph.D., DABT Date
Associate Director of Applied Toxicology

Division:

Richard C. Wise 8-3-92
Richard C. Wise Date
Manager, Product Safety

Union Carbide Chemicals and Plastics Company Inc.
Excellence Through Quality



The protocol is amended as follows:

Item 1

Location of Protocol Deletion	Page 1, Title
Description of Protocol Deletion	(Sprague-Dawley)
Rationale	The parenthetical designation of (Sprague-Dawley) in reference to Charles River CD® rats has been removed in order to accurately reflect the strain designation as provided by the supplier.

Item 2

Location of Protocol Deletion	Page 2, Objectives
Description of Protocol Deletion	(Sprague-Dawley)
Rationale	See rationale for Item 1.

Item 3

Location of Protocol Deletion	Page 4, Supplier
Description of Protocol Deletion	Breeding
Rationale	The correct name of the supplier is Charles River Laboratories.

Item 4

Location of Protocol Change	Page 15, Nonpregnant Females
Description of Protocol Change	The uteri from females which fail to produce a litter will be stained with ammonium sulfide for confirmation of pregnancy status.
Rationale	Fresh tissue was stained with ammonium sulfide rather than having fixed tissue stained with potassium ferricyanide. Either chemical can be used to stain the uterus to detect very early resorptions.

repretex\protocol\apropion
July 15, 1992

PROTOCOL DEVIATIONS

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD® Rats

BRRC PROJECT NUMBER: 91-13-25602

The following deviations from the written protocol for this study or from BRRC Standard Operating Procedures occurred during this study:

1. In the protocol, it was stated that the date for submission of the Draft Final Report would be added to the protocol by amendment. The Draft Final Report was issued on June 17, 1992, but an amendment was not written.
2. Male rats were weighed on Day 35, 42, and 49 of the study. These weights were in addition to those specified in the protocol.

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Study in CD⁰ Rats

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD⁰ Rats

(119 Pages)

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Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD® Rats

SUMMARY

Young adult CD® female rats (7/group) were exposed to propionaldehyde (CAS No. 123-38-6) vapor at concentrations of 0, 500, 1000, 1500, or 2500 ppm. Inhalation exposures were conducted daily, 6 hours each day, from gestation day (gd) 0-20, following successful mating with naive males of the same strain. Clinical observations were made daily following exposures, and maternal body weights were measured on gd 0, 7, 14, and 21. Food consumption was measured at least weekly throughout the study. At scheduled sacrifice on gd 21, the dams were evaluated for liver and gravid uterine weights, number of corpora lutea, and number and status of implantation sites (including early and late resorptions, and dead and live fetuses). Fetuses were dissected from the uterus, weighed, and examined externally for malformations, variations, and gender determinations.

The means of daily mean chamber atmosphere concentrations (\pm S.D.) were 490 ± 7.7 , 1009 ± 13.2 , 1509 ± 9.9 , and 2592 ± 39.0 , for target concentrations of 500, 1000, 1500, and 2500 ppm, respectively.

The pregnancy rate was equivalent among groups and ranged from 85.7 to 100%. No females died, delivered early, or were removed from the study prior to scheduled sacrifice. One female in the 1000 ppm group was found to have only non-viable implants. Six to 7 live litters were available for evaluation from each group.

None of the groups displayed any exposure-related clinical signs. Maternal toxicity was evident, however, as exposure-related decreases in body weight, body weight gains, and food consumption. At 2500 ppm, body weights were reduced on gd 14 and 21, body weight gains were depressed during the first week of exposures (gd 0 to 7) and for the entire period of gestation (gd 0 to 21), and food consumption was reduced throughout the study. During the same intervals, the 1500 ppm group showed similar, but less severe, decreases in body weight, body weight gain, and food consumption. At 1000 ppm, body weight gain was depressed during the first week of exposures, but absolute body weights were not significantly affected. Food consumption, however, was also decreased throughout gestation. No effects on any of these measures were observed at 500 ppm.

At sacrifice, corrected body weight was decreased in the 1000 and 2500 ppm groups, and a similar tendency was present at 1500 ppm. Exposure-related effects in corrected weight change were observed at 1000 ppm and above. There were no exposure-related differences in gestational parameters including total number of implants, and the number of viable and nonviable implants.

The 2500 ppm exposure group fetal body weights were reduced, however, there was no evidence of any treatment-related external malformations or variations.

In summary, repeated exposure to propionaldehyde vapor at concentrations of 1000 ppm to 2500 ppm was associated with overt maternal toxicity. In this study, the "no-observed-adverse-effect level" (NOAEL) for maternal toxicity was 500 ppm, and the NOAEL for developmental toxicity was 1500 ppm. Based upon these data, exposure concentrations of 0, 150, 750, and 1500 ppm were selected for use in a follow-up study.

OBJECTIVES

The objective of this study was to establish the concentration-response range of propionaldehyde administered by inhalation for maternal and/or developmental toxicity in CD¹ rats. This information was used to select appropriate exposure concentrations for use in the definitive repeated exposure study designed to assess the reproductive and developmental toxicity potential of propionaldehyde.

BACKGROUND INFORMATION

This study was conducted by UCC&P as part of voluntary participation in the OECD High Production Volume Chemical testing program. Based upon previous studies of propionaldehyde (Gage, 1970; Steinhagen and Barrow, 1984), concentrations of 0, 500, 1000, 1500, and 2500 ppm were selected for use in this study to establish the maximum tolerated concentration of propionaldehyde vapor in pregnant CD¹ rats.

TARGET CONCENTRATION SELECTION

Target propionaldehyde vapor concentrations of 0 (control), 500, 1000, 1500, and 2500 ppm were selected in conjunction with the Sponsor based upon the available literature.

MATERIALS AND METHODS

The protocol, protocol amendment, and protocol deviation (BRRC Project No. 91-13-25601) detailing the design and conduct of this study are presented in Attachment 5.

Test Substance

Two 55-gallon stainless steel drums of propionaldehyde; Lot No. T-1258; CAS No. 123-38-6 were received on October 15, 1991, from Union Carbide Corporation (South Charleston, WV) and assigned BRRC Sample No. 54-351-A and B. The test substance was a water-white odorous liquid. The test substance was stored in the original containers in a special enclosure under a nitrogen atmosphere. The purity of the test substance was determined by the GLP Analytical Skills Center at the UCC&P South Charleston, WV, Technical Center to be approximately 99% and the report is included in Appendix 1. Pertinent chemical and physical properties of propionaldehyde are listed in Attachments 1 and 5.

Animals and Husbandry

Sixty male and 60 female CD[®] rats arrived on October 14, 1991, from Charles River Laboratories, Inc. (Portage, MI). The males were designated by the supplier to be approximately 70 days old (birth date was recorded as approximately August 5, 1991) and 286-350 g upon arrival. Females were approximately 63 days old (birth date approximately August 15, 1991), 186-221 g, nulliparous, and nonpregnant upon arrival.

Animals were housed in Room 101 from arrival to termination of the study, except during exposures. Within 2 days of receipt, the animals were examined by a Clinical Veterinarian, and representative animals were subjected to a pretest health screen including full necropsy, histologic examination of selected tissues, and serum viral antibody analyses. Based on the results of these data, the Clinical Veterinarian indicated that these animals were in good health and suitable for use.

All animals were assigned a unique number and identified by cage tags. Animals considered available for the study were also identified by an ear tag. Animals selected for the pretest health screen were identified by a toe-clipping procedure after sacrifice.

The animals were housed 1-2/cage for approximately 7 days in stainless steel, wire mesh cages (30.5 x 15.5 x 18.0 cm). DACB[®] (Deotized Animal Cage Board; Shepherd Specialty Papers, Inc., Kalamazoo, MI) was placed under each cage and changed regularly. An automatic timer was set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). Temperature and relative humidity were recorded continuously (Cole-Parmer Hygrothermograph[®] Seven-Day Continuous Recorder, Model No. 8368-00, Cole-Parmer Instrument Co., Chicago, IL). Temperature was routinely maintained at 65-77°F; relative humidity was routinely maintained at 40-70%. Any minor exceptions to these specified ranges were noted in the raw data.

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) was available ad libitum, except during exposures, and was delivered by an automatic watering system with demand control valves mounted on each rack (water bottles were used for females while in shoe box cages). Water analyses were provided by the supplier, the NUS Corporation, Materials and Engineering Testing Co., and Lancaster Laboratories, Inc. at regular intervals. EPA standards for maximum levels of contaminants were not exceeded. Ground, certified Rodent Chow[®] #5002 (Purina Mills, Inc.) was available ad libitum, except during exposures. Analyses for chemical composition and possible contaminants of each feed lot were performed by Purina Mills, Inc., and the results were included in the raw data.

Animal Acclimation

The acclimation period was approximately 1 week. During this period, the animals were weighed at least 2 times at scheduled intervals. Detailed clinical observations were conducted in conjunction with body weight measurements. Cage-side animal observations were conducted at least once daily, and mortality checks were conducted twice daily (morning and

afternoon). The animals were examined just prior to the end of the acclimation period by a Clinical Veterinarian. Animals considered unacceptable for the study, based on the clinical signs, body weights, or body weight gains, were rejected. The fate of rejected animals and the reasons for rejection were documented in the raw data.

Study Organization

On each gd 0, prior to initializing exposures, the animals were assigned to one of 4 exposure groups and a control group using a stratified randomization procedure based on body weight. At the time of group assignment, only animals with body weights within $\pm 20\%$ of the population mean were included. The female body weight range on the first day of exposure was 206.14 to 241.76 g. The following table summarizes the organization of the study.

Group	Number of Female Animals	Test Vapor Concentration (ppm)
Control	7	0
Low	7	150
Mid	7	750
High	7	1500

The exposures began on October 22, 1991 and continued through November 13, 1991. Females were exposed 6 hour/day, 7 days/week, on gd 0-20. The 6-hour exposure period was defined as the time when the generation system was turned on and subsequently turned off. All control animals were exposed to filtered air only using the same exposure regimen. Seven females/group were sacrificed on gd 21 during the period of November 12 - 14, 1991.

Inhalation Chamber Description and Operation

The inhalation chambers used for this study were located in Room 138. They were constructed from stainless steel with glass windows for animal observation. The volume of each chamber volume was approximately 4320 liters, and the airflow was approximately 1000 liters/minute. Chamber airflow was calibrated with a Kurz Model 505 mass flowmeter. A Dwyer Magnehelic® pressure gauge (Dwyer Instruments, Inc., Michigan City, IN) was used to monitor chamber airflow. Chamber temperature and relative humidity were recorded using industrial thermometers (Control Specialties, Inc., Houston, TX) and Airguide Humidity Indicators (Airguide Instrument Company, Chicago, IL), respectively. Temperature and relative humidity measurements were recorded approximately every 30 minutes during each exposure. Prior to the start of exposures, and on Exposure Day 2, the oxygen content of all the chambers was measured with an O₂ indicator (Model 245R, Mine Safety Appliances, Pittsburgh, PA).

Vapor Generation

For all exposure chambers, propionaldehyde was metered from a piston pump (Fluid Metering, Inc., Oyster Bay, NY) into a heated glass evaporator similar in design to that described by Snellings and Dodd (1990). The temperature of the evaporators was maintained at the lowest level sufficient to vaporize the liquid. The resultant vapor was carried into the chamber by a countercurrent air stream that entered the bottom of the evaporator. Prior to the start of exposures and on day 21 of the exposure regimen, temperature measurements were taken from the inside surface of the evaporators using a Fluke 51 K/J thermometer.

Observations and Measurements

Maternal In-Life Evaluations

All animals were individually observed for signs of toxicity immediately following daily exposures. Preceding and following each exposure, observations were recorded for animals exhibiting overt clinical signs. On days when exposures were not conducted, detailed observations were generally conducted in the morning. Female body weight data were collected on gd 0, 7, 14, and 21. Food consumption was measured at least weekly throughout the gestation period.

Maternal Necropsy and Laparotomy

At scheduled sacrifice on gd 21, all surviving dams were sacrificed by carbon dioxide asphyxiation and necropsied. The maternal body cavities were opened by midline thoracolaparotomy. The gravid uterus, ovaries (including corpora lutea), cervix, vagina, and peritoneal and thoracic cavities were examined grossly. Ovarian corpora lutea of pregnancy were counted. Maternal liver weights were determined. Each uterus was externally examined for signs of hemorrhage, removed from the peritoneal cavity, weighed and dissected longitudinally to expose the contents. All live and dead fetuses and resorption sites (early and late) were noted and recorded. Uteri from females that appeared nongravid were placed in a 10% ammonium sulfide solution for detection of early resorptions (Salewski, 1964).

Fetal Examinations

All live fetuses were weighed, examined externally for gender determinations and for variations and malformations including cleft palate.

Data Analyses

The unit of comparison was the pregnant female or the litter. The data for quantitative continuous variables were intercompared for the 4 exposure groups and the control group by use of Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests were used when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances,

all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparisons.

Nonparametric data were statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U test when appropriate. Incidence data were compared using the Fisher's Exact Test. For all statistical tests, the probability value of < 0.05 (two-tailed) was used as the critical level of significance. (Dixon, 1990; Sokal and Rohlf, 1981).

Various models of calculators, computers, and computer programs may have been used to analyze data for this study. Since various models round or truncate numbers differently, values in some tables may differ slightly from those in other tables or from independently calculated data. The integrity of the study and interpretation of the data were unaffected by these differences.

RETENTION OF RECORDS

All raw data, documentation, records, the protocol, protocol amendment, and protocol deviation, specimens, and a copy of the final report generated as a result of this study are retained in the BRRC Archives. Due to the nature of the test substance, a reserve sample was not retained in the BRRC Archives.

RESULTS AND DISCUSSION

All references of differences in group mean values in the following text refer to comparisons of statistically significant differences between the exposure group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

Chamber Atmosphere

A summary of the chamber atmosphere measurements is presented in Table 1. Detailed results and discussion of the chamber atmosphere measurements are included in Attachment 1.

During exposures, the mean of daily mean chamber temperatures for all exposure groups ranged from 20 to 21°C (Attachment 1), and the relative humidity ranged from 46 to 49%. For all measurements, the chamber oxygen content was 20.8%. The evaporator temperature measurements ranged from 43 to 83°C.

The means of daily mean chamber atmosphere concentrations (\pm S.D.) were 490 (\pm 7.7), 1009 (\pm 13.2), 1509 (\pm 9.9), and 2592 (\pm 39.0), for target concentrations of 500, 1000, 1500, and 2500 ppm, respectively. No propionaldehyde was detected (minimum detection limit 5 ppm) in the control chamber atmosphere during the study.

Animal Fate

The distribution and fate for all female rats placed on study are presented in Table 2. Individual animal data are included in Attachment 2.

No females delivered early or died prior to scheduled sacrifice. The overall pregnancy rate was equivalent for all groups and ranged from 85.7 to 100%. One pregnant female from the 1000 ppm group bore a litter which had no viable fetuses. Six to 7 litters were available for evaluation.

All subsequent summary tables and discussion involve data from gravid dams only.

Clinical Observations

Summaries of the clinical observations are presented in Table 3. Individual clinical observation data are included in Attachment 2.

No treatment-related clinical signs of toxicity were observed during the study.

Body Weights

Summaries of absolute body weights and body weight gains are presented in Table 4. Individual animal body weight data are included in Attachment 2.

There was a nonsignificant exposure-related decrease in body weights in groups exposed to 1000 ppm and above by gd 7. By gd 14, significant decreases in body weight occurred at 2500 and 1500 ppm and body weights remained depressed through gd 21. Body weight gains for gd 0-7 were decreased at 1000 ppm and above. Although weight gains continued to be somewhat lower than controls in the groups exposed to 1000 ppm or greater, a significant overall decrease for gd 0-21 was seen only in the two highest concentrations.

Food Consumption

Summaries of food consumption data are presented in Table 5. Individual food consumption data are included in Attachment 2.

Significant decreases in food consumption were evident throughout gestation for all groups exposed to 1000 ppm or greater.

Maternal Necropsy and Laparotomy

A summary of necropsy observations in dams at scheduled sacrifice is presented in Table 6. Maternal organ weights and terminal body weight are presented in Table 7. Gestational parameters are presented in Table 8. Individual maternal necropsy and laparotomy data are presented in Attachment 3.

At necropsy, there was no evidence of any lesions that could be attributed to propionaldehyde exposure. Terminal body weight was lower in the 1500 and 2500 ppm groups, and there was a similar tendency for the 1000 ppm group. Corrected weight gain was less than controls in the 1000, 1500, and 2500 ppm

groups, and the outcome for corrected body weight was similar. Relative and absolute liver weights were significantly depressed only in the 1000 ppm group.

There were no effects of exposure on the number of ovarian corpora lutea, on the number of total implants, number of viable or nonviable (early and late resorptions, and dead fetuses) implants, or on sex ratio.

Fetal Examinations

Fetal body weights per litter (males, females and total fetuses) are presented in Table 8. The summary incidence and frequency of fetal malformations and variations observed in the study are presented in Tables 9 and 10, respectively. Malformations and variations for individual fetuses grouped by litters are presented in Attachment 4. Individual fetal body weights (by uterine location, sex and litter) are also presented in Attachment 4.

Fetal body weights were reduced in the 2500 ppm exposure group. A statistically significant decrease in fetal body weight also occurred in the 500 ppm group, but was not considered to be related to exposure due to the lack of a dose-response relationship. No external malformations were observed in any group, and there was no evidence of any treatment-related variations.

The decrease in fetal body weight at 2500 ppm was observed in conjunction with a significant degree of maternal toxicity. Although not directly addressed in this study, a previous report (Steinhagen and Barrow, 1984) of brief exposures (less than 1 hour) to propionaldehyde in B6C3F1 mice and Fischer 344 rats at 2078 and 6789 ppm for mice and rats respectively, resulted in a 50% decrease in respiratory rate. The effect on fetal body weight, therefore, may be due in part to effects of propionaldehyde exposure on the dam's respiratory rate. Although the effective concentration range appears to vary across species, and perhaps strains, repeated exposure to 2500 ppm, and perhaps lower, may have had a significant impact on respiratory rate in the present study.

The observation of reduced fetal weights in the 500 ppm exposure group is not considered to be related to exposure due to the lack of a clear relationship to concentration, the significance of this finding is questionable and not considered biologically significant.

CONCLUSIONS

In summary, repeated exposure to propionaldehyde vapor at concentrations of 1000, 1500, or 2500 ppm was associated with overt maternal toxicity. In this study, the NOAEL for maternal toxicity was 500 ppm, and the NOAEL for developmental toxicity was 1500 ppm. Based upon these data, exposure concentrations of 0, 150, 750, and 1500 ppm were selected for use in a follow-up study.

KEY PERSONNEL

Study Director: C. D. Driscoll
Study Coordinators: M. A. Copeman
M. F. Kubena
Supervisors: L. C. Fisher
Scientists: D. A. Neptun
I. M. Pritts

Additional personnel are listed in the raw data.

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TABLE 1
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 SUMMARY OF CHAMBER ATMOSPHERE DATA

Target Concentration (ppm)	Temp (°C)	RH (%)	A (ppm)	NOM (ppm)	A/NOM
0	20.0±0.49	49.2±1.40	<MDL	----	-----
500	21.3±0.51	46.0±0.94	490± 7.7	507± 8.1	0.97±0.011
1000	20.7±0.53	46.6±0.76	1009±13.2	986± 6.0	1.02±0.013
1500	20.6±0.85	47.4±0.61	1509± 9.9	1450± 6.7	1.04±0.008
2500	20.2±0.59	48.0±0.55	2592±39.0	2503±43.1	1.04±0.008

Temp = temperature

RH = relative humidity

A = analytical concentration

NOM = nominal concentration

A/NOM = analytical concentration/nominal concentration

<MDL = less than the minimum estimated detection limit

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

SUMMARY OF DISTRIBUTION AND FATE^a

GROUP: PPM	0	500	1000	1500	2500
FEMALES ON STUDY	7	7	7	7	7
FEMALES THAT DIED	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
PREGNANT	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES THAT ABORTED	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES THAT DELIVERED	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES REMOVED FROM STUDY	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES EXAMINED AT LAPAROTOMY	7 100.0	7 100.0	7 100.0	7 100.0	7 100.0
NONPREGNANT	1 14.3	0 0.0	0 0.0	0 0.0	0 0.0
PREGNANT	6 85.7	7 100.0	7 100.0	7 100.0	7 100.0
FEMALES WITH NON-VIABLE IMPLANTS ONLY	0 0.0	0 0.0	1 14.3	0 0.0	0 0.0
FEMALES WITH VIABLE FETUSES	6 100.0	7 100.0	6 85.7	7 100.0	7 100.0
FEMALES THAT WERE PREGNANT	6 85.7	7 100.0	7 100.0	7 100.0	7 100.0

^a For all parameters, the data are presented as the number of dams on top and the percentage beneath.

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
 FEMALES

CATEGORY	FINDING (LOCATION)	GESTATIONAL DAYS	PPM				
			0	500	1000	1500	2500
NORMAL	NO SIGNIFICANT CLINICAL OBSERVATIONS	0- 21	6 ^a	7	7	7	7
DEAD	SCHEDULED SACRIFICE	0- 21	6	7	7	7	7
BODY	UROGENITAL DISCHARGE, RED	0- 21	0	0	1	0	0
EYES/EARS/NOSE	LACRIMATION (EYE-RIGHT)	0- 21	0	0	1	0	0
OTHER	PERIOCULAR ENCRUSTATION (EYE-BOTH, EYE-LEFT)	0- 21	0	0	0	2	1
	MISSING EAR TAG	0- 21	0	0	0	0	1

^a Number of animals exhibiting finding at least once within the specified range of days.
 None significantly different from control group

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 SUMMARY OF GESTATIONAL BODY WEIGHT AND WEIGHT CHANGE (GRAMS)

FEMALES						
GROUP: PPM	0	500	1000	1500	2500	
<u>GESTATIONAL BODY WEIGHTS (g)</u>						
DAY 0						
MEAN	226.01	226.67	224.68	225.18	226.52	
S.D.	8.918	9.892	10.909	10.867	12.556	
N	6	7	7	7	7	
DAY 7						
MEAN	260.89	257.37	246.62	248.37	241.88	
S.D.	4.288	13.262	19.156	10.892	11.780	
N	6	7	7	7	7	
DAY 14						
MEAN	297.24	291.40	275.71	280.45**	270.21**	
S.D.	7.150	16.341	27.711	9.035	16.316	
N	6	7	7	7	7	
DAY 21						
MEAN	389.90	380.65	352.54	360.21**	347.14**	
S.D.	6.863	23.533	57.266	16.721	20.151	
N	6	7	7	7	7	
<u>GESTATIONAL BODY WEIGHT CHANGES (g)</u>						
DAY 0 TO 7						
MEAN	34.88	30.70	21.93**	23.18**	15.37**	
S.D.	6.477	6.940	9.558	5.994	5.766	
N	6	7	7	7	7	
DAY 7 TO 14						
MEAN	36.35	34.03	29.09	32.08	28.33	
S.D.	5.732	6.647	10.079	5.901	4.926	
N	6	7	7	7	7	
DAY 14 TO 21						
MEAN	92.66	89.25	76.83	79.76	76.93	
S.D.	4.399	9.229	31.412	10.439	8.120	
N	6	7	7	7	7	
DAY 0 TO 21 (GESTATION)						
MEAN	163.89	153.98	127.86	135.03**	120.63**	
S.D.	6.853	17.573	47.919	15.415	14.168	
N	6	7	7	7	7	

** Significantly different from control group (p < .01)

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 SUMMARY OF GESTATIONAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

		FEMALES				
GROUP: PPM	0	500	1000	1500	2500	
DAY 0 TO 7						
MEAN	21.98	20.84	18.70**	19.00**	18.40**	
S.D.	1.609	1.311	2.023	0.988	1.362	
N	6	7	7	7	7	
DAY 7 TO 11						
MEAN	24.38	22.71	20.13**	21.21**	20.43**	
S.D.	1.099	1.828	2.000	1.516	1.817	
N	6	7	7	7	7	
DAY 11 TO 14						
MEAN	25.23	23.46	21.80**	22.54**	21.45**	
S.D.	0.860	1.623	2.490	1.323	1.636	
N	6	7	7	7	7	
DAY 14 TO 17						
MEAN	26.42	25.30	22.93**	24.12*	22.27**	
S.D.	1.275	1.855	3.097	1.878	1.420	
N	6	7	7	7	7	
DAY 17 TO 21						
MEAN	26.96	25.82	23.16**	24.19*	21.99**	
S.D.	1.095	1.576	3.286	1.635	1.335	
N	6	7	7	7	7	
DAY 7 TO 14						
MEAN	24.75	23.03	20.84**	21.78**	20.87**	
S.D.	0.821	1.668	2.149	1.321	1.674	
N	6	7	7	7	7	
DAY 14 TO 21						
MEAN	26.76	25.60	23.06**	24.16*	22.11**	
S.D.	1.112	1.551	3.160	1.634	1.241	
N	6	7	7	7	7	

* Significantly different from control group (p < .05)
 ** Significantly different from control group (p < .01)
 Data not included for animals with observed food spillage.

TABLE 6
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 SUMMARY OF NECROPSY OBSERVATIONS

ALL PREGNANT FEMALES SACRIFICED AT SCHEDULED LAPAROTOMY
 FEMALES

	GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		7	7	7	7	7
NUMBER OF ANIMALS SACRIFICED		6	7	7	7	7
LIVER						
COLOR CHANGE		0	0	0	1	0
OVARIES						
CYST		1	1	1	0	0
UTERUS						
CONTENTS - COAGULATED BLOOD		1	0	0	0	2
NO IMPLANTS IN ONE HORN		0	0	0	1	0
CONTAINS BLOOD (BY HEMASTIX)		0	0	0	1	0
LUNGS						
COLOR CHANGE		5	5	6	7	6
FOCUS OR FOCI		0	0	1	1	1
KIDNEYS						
HYDRONEPHROSIS		1	0	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 500 PPM, 3 is 1000 PPM, 4 is 1500 PPM, 5 is 2500 PPM

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 SUMMARY OF MATERNAL ORGAN WEIGHTS (GRAMS)

		FEMALES				
GROUP: PPM	0	500	1000	1500	2500	
INITIAL BODY WEIGHT (g)						
MEAN	226.01	226.67	224.68	225.18	226.52	
S.D.	8.518	9.892	10.909	10.867	12.556	
N	6	7	7	7	7	
BODY WEIGHT AT SACRIFICE (g)						
MEAN	389.90	380.65	352.34	360.21**	347.14**	
S.D.	6.863	23.533	57.266	16.721	20.151	
N	6	7	7	7	7	
GRAVID UTERINE WEIGHT (g)						
MEAN	108.390	101.090	90.039	93.165	95.756	
S.D.	9.0443	7.7693	40.5703	16.5047	11.2159	
N	6	7	7	7	7	
CORRECTED BODY WEIGHT (g)^a						
MEAN	281.51	279.56	262.50*	267.05	251.39**	
S.D.	12.348	16.875	22.761	11.536	13.039	
N	6	7	7	7	7	
CORRECTED WEIGHT CHANGE (g)^b						
MEAN	55.50	52.89	37.82*	41.87*	24.87**	
S.D.	8.787	11.848	14.500	6.459	4.800	
N	6	7	7	7	7	
LIVER WEIGHT (g)						
MEAN	13.449	13.099	11.221**	12.216	12.128	
S.D.	1.3877	1.2964	1.4138	1.0767	1.1271	
N	6	7	7	7	7	
RELATIVE LIVER WEIGHT (%)^c						
MEAN	4.772	4.680	4.266**	4.571	4.819	
S.D.	0.3689	0.3050	0.2541	0.2916	0.2758	
N	6	7	7	7	7	

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

^a Corrected body weight = body weight at sacrifice minus gravid uterine weight.

^b Corrected weight change = corrected body weight minus initial body weight.

^c Value is a percentage of corrected body weight.

TABLE 8
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 SUMMARY OF GESTATIONAL PARAMETERS

FEMALES						
GROUP: PPM	0	500	1000	1500	2500	
CORPORA LUTEA						
MEAN	15.8	15.6	16.3	16.4	15.9	
S.D.	0.75	2.07	3.64	3.60	0.69	
N	6	7	7	7	7	
TOTAL IMPLANTS						
MEAN	15.0	14.3	13.4	13.4	15.4	
S.D.	1.10	1.11	5.80	2.30	0.79	
N	6	7	7	7	7	
PERCENT PREIMPLANTATION LOSS^a						
MEAN	5.3	7.5	20.6	14.4	2.7	
S.D.	4.73	7.37	32.14	21.86	3.36	
N	6	7	7	7	7	
VIALE IMPLANTS						
MEAN	14.5	14.0	12.4	12.9	14.6	
S.D.	1.28	1.15	5.80	2.19	1.13	
N	6	7	7	7	7	
NON-VIALE IMPLANTS						
MEAN	0.5	0.3	1.0	0.6	0.9	
S.D.	0.84	0.49	1.15	0.79	1.21	
N	6	7	7	7	7	
EARLY RESORPTIONS						
MEAN	0.5	0.3	0.9	0.6	0.9	
S.D.	0.84	0.49	1.07	0.79	1.21	
N	6	7	7	7	7	
LATE RESORPTIONS						
MEAN	0.0	0.0	0.1	0.0	0.0	
S.D.	0.00	0.00	0.38	0.00	0.00	
N	6	7	7	7	7	
DEAD FETUSES						
MEAN	0.0	0.0	0.0	0.0	0.0	
S.D.	0.00	0.00	0.00	0.00	0.00	
N	6	7	7	7	7	
PERCENT LIVE FETUSES						
MEAN	96.6	98.0	80.3	96.0	94.6	
S.D.	5.85	3.43	36.07	5.58	7.60	
N	6	7	7	7	7	
SEX RATIO (% MALE FETUSES)						
MEAN	47.9	53.5	55.1	44.1	46.3	
S.D.	16.97	15.92	14.75	12.64	13.36	
N	6	7	6	7	7	
FETAL BODY WEIGHTS PER LITTER (GRAMS)						
ALL FETUSES						
MEAN	5.303	5.092*	5.180	5.134	4.708**	
S.D.	0.1509	0.1720	0.4086	0.2416	0.3246	
N	6	7	6	7	7	
MALE FETUSES						
MEAN	5.417	5.254	5.330	5.308	4.890**	
S.D.	0.1843	0.2517	0.3826	0.2661	0.3838	
N	6	7	6	7	7	
FEMALE FETUSES						
MEAN	5.177	4.935*	5.037	5.014	4.557**	
S.D.	0.1831	0.1636	0.4516	0.2597	0.3043	
N	6	7	6	7	7	

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

^a Percent preimplantation loss = [(corpora lutea - total implants)/corpora lutea] X 100.

TABLE 9
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS

SUMMARY OF MALFORMATIONS IN FETUSES AND LITTERS^a

GROUP: PPM	F E T U S E S				L I T T E R S					
	0	500	1000	1500	2500	0	500	1000	1500	2500
NUMBER EXAMINED EXTERNALLY ^b	87	98	87	90	102	6	7	6	7	7

NO EXTERNAL FINDINGS

TOTAL MALFORMATIONS
 NUMBER WITH EXTERNAL MALFORMATIONS
 PERCENT WITH EXTERNAL MALFORMATIONS

0	0	0	0	0	0	0	0	0	0	0
0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

None significantly different from control (0 PPM)

^a For all findings, the number (of fetuses affected or litters with one or more affected fetuses) is presented on top and the percentage of the total (fetuses or litters) examined is presented beneath. A single fetus may be represented more than once in listing individual defects. Only live fetuses were examined.

^b All fetuses were examined externally.

TABLE 10
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 SUMMARY OF VARIATIONS IN FETUSES AND LITTERS^a

	GROUP: PPM	F E T U S E S					L I T T E R S				
		0	500	1000	1500	2500	0	500	1000	1500	2500
NUMBER EXAMINED EXTERNALLY ^b		87	98	87	90	102	6	7	6	7	7
ECCHYMOSIS - TRUNK		4	4	7	3	6	3	3	3	3	4
		4.6	4.1	8.0	3.3	5.9	50.0	42.9	50.0	42.9	57.1
ECCHYMOSIS - EXTREMITIES		1	1	0	0	0	1	1	0	0	0
		1.1	1.0	0.0	0.0	0.0	16.7	14.3	0.0	0.0	0.0
TOTAL VARIATIONS		5	5	7	3	6	4	4	3	3	4
NUMBER WITH EXTERNAL VARIATIONS		5.7	5.1	8.0	3.3	5.9	66.7	57.1	50.0	42.9	57.1
PERCENT WITH EXTERNAL VARIATIONS											

None significantly different from control (0 PPM)

^a For all findings, the number (of fetuses affected or litters with one or more affected fetuses) is presented on top and the percentage of the total (fetuses or litters) examined is presented beneath. A single fetus may be represented more than once in listing individual defects. Only live fetuses were examined.

^b All fetuses were examined externally.

Propionaldehyde: Reproductive/Developmental Toxicity
Range-Finding Study in CD® Rats

Chamber Atmosphere Report

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Chamber Atmosphere Report

SUMMARY

The concentration of propionaldehyde vapor in the exposure chamber was monitored throughout the 23 days of exposure by flame ionization gas chromatography. The concentration in each exposure chamber atmosphere was determined approximately 11 times during each 6-hour exposure. The overall mean (\pm standard deviation) chamber atmosphere concentrations were 490 (\pm 7.7), 1009 (\pm 13.2), 1509 (\pm 9.9), and 2592 (\pm 39.0) ppm, for target concentrations of 500, 1000, 1500, and 2500 ppm, respectively. Propionaldehyde was not detected in the control chamber atmosphere.

The test substance was analyzed before and after the exposure regimen and remained nearly over 99% pure.

MATERIALS AND METHODS

Test Substance

Two 55-gallon containers of propionaldehyde (CAS No. 123-38-6, Lot T-1258, BRRC Sample No. 54-351 A and B) were received from Union Carbide Chemicals and Plastics Company Inc. (UCC&P), S. Charleston, WV, on October 15, 1991. The chemical and physical properties of the test substance are described in Table 1. The compositional analyses were provided by the GLP Analytical Skills Center at the UCC&P South Charleston, WV, Technical Center. A summary of this report is presented in Table 2; the entire report is presented beginning with page 37 of this attachment. The entire report is also presented as Attachment 1 in Appendix 1. The prestudy and poststudy compositional analyses indicated that the test substance was over 99% pure and had remained stable for the duration of the exposure regimen.

Analytical Instrumentation

Perkin-Elmer Sigma 2000 gas chromatograph (GC) equipped with a flame ionization detector was used to analyze the exposure chamber atmospheres for propionaldehyde vapor. The GC operating conditions are presented in Table 3. A Spectra-Physics 4270 Integrator provided a record of the chromatograms and chromatographic analyses as well as peak integration. The data were captured using an IBM PS/2 Computer with Spectra-Physics Chromstation/2 software. In-house software was used to compute daily statistics and also to provide an alarm system which monitored chamber concentrations.

Calibration

Calibration of the gas chromatograph was achieved by injecting gas standards, which were prepared by syringe injection of propionaldehyde test substance into Tedlar[™] gas bags containing UHP nitrogen. These standards were prepared using the mathematical relationship:

$$V = \frac{C \times V_h \times MW \times 298 \times P \times 10^{-6}}{d \times 24.45 \times T \times 760}$$

where: V = required volume of calibration liquid in milliliters at temperature T (degrees K)

C = desired calibration concentration, in ppm

V_h = volume of container, in liters

MW = molecular weight of the calibration liquid

P = barometric pressure, in millimeters of mercury

d = density of the calibration liquid in grams per milliliter at temperature T

24.45 = molecular volume at 298 degrees K and 760 millimeters of mercury, in liters

T = temperature, in degrees Kelvin

The calibration curve (Figure 1) was constructed by plotting peak areas versus the gas standard concentrations. The calibration was checked at least once each week during the exposure regimen.

RESULTS AND DISCUSSION

Chamber Atmosphere Analysis

Each chamber atmosphere was analyzed for propionaldehyde approximately twice each hour during each 6-hour exposure by flame ionization gas chromatography. The daily mean analytical concentrations are listed in Tables 4 through 7. The means of daily mean chamber atmosphere concentrations (± standard deviations) were 490 (± 7.7), 1009 (± 13.2), 1509 (± 9.9), and 2592 (± 39.0) ppm, for the target concentrations of 500, 1000, 1500, and 2500 ppm, respectively. No concentration of propionaldehyde above the estimated minimum detection limit of 5 ppm was detected in the control chamber atmosphere during the study.

Analytical/Nominal Concentration Ratio

The daily analytical/nominal (A/NOM) propionaldehyde concentration ratios are given in Tables 5 through 7, the nominal concentration being an estimate

calculated from the quantity of test substance delivered and the chamber airflow rate. The overall mean A/NOM concentration ratios were 0.97, 1.02, 1.04, and 1.04, for propionaldehyde target concentrations of 500, 1000, 1500, and 2500 ppm, respectively.

Temperature and Relative Humidity

The daily mean temperature and relative humidity values for the exposure chambers are also presented in Tables 4 through 7. The means of daily mean temperature values were 20, 21, 21, 21, and 20°C, for propionaldehyde target concentrations of 0, 500, 1000, 1500, and 2500 ppm, respectively. The means of daily mean relative humidity values were 49, 46, 47, 47, and 48%, respectively.

Analytical Chemist:


Irvin M. Pritts, Ph.D.

4-6-93

Date

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN C57BL/6J MICE

CHEMICAL AND PHYSICAL PROPERTIES¹

Synonyms:	Propenal; Propylaldehyde
Molecular Weight:	58.08
Molecular Formula:	C ₃ H ₅ CHO
Vapor Density (air = 1)	2.0
Appearance and Odor:	Water-white liquid; suffocating odor
Boiling Point, 760 mm Hg:	48°C
Solubility in Water:	22% @ 20°C
Evaporation Rate (but acetate=1):	19.9
Vapor Pressure at 20°C:	approx. 250 mm Hg
Specific Gravity (H ₂ O = 1):	0.7982 @ 20/20°C
Flash Point (Tag Closed Cup):	< -10°C

¹Material Safety Data Sheet, Union Carbide Chemicals and Plastics Company Inc., Revised 8/29/90.

TABLE 2
 PROPIONALDEHYDE: COMBINED PREPARED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS

TEST SUBSTANCE ANALYSIS¹

Component	Prestudy Area ¹	Poststudy Area ¹
Propionaldehyde	99.77 (approx.)	99.42 (approx.)
n-Propanol	0.01	0.02
2-Methyl Butyraldehyde	0.02	0.02
Valeraldehyde	0.06	0.02
Propionic Acid	0.07	0.37
Propionaldehyde Dimers	0.03	0.04
Propionaldehyde Trimers	0.01	0.04
All other Impurities	0.03	0.07

¹The capillary gas chromatographic compositional analyses were provided by the GLP Analytical Skills Center at the UCCSP South Charleston, WV, Technical Center. In addition, gas chromatography-mass spectrometry and nuclear magnetic resonance spectroscopy were independently used to confirm the sample's identity.

TABLE 3
PHOSPHORIC ANHYDRIDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE FINDING STUDY IN CD-1 RATS

GAS CHROMATOGRAPH OPERATING PARAMETERS

Chromatograph:	Perkin-Elmer Sigma 2000
Detector:	Flame Ionization
Column:	10% SP-1000, on 80/100 mesh Supelcoport, 10 ft. x 1/8 in. stainless steel
Column temperature:	170°C
Injector temperature:	100°C gas sample valve
Detector temperature:	250°C
Carrier flow rate:	20 mL/minute nitrogen
Sample size:	0.5 cc
Retention time:	1.4 minutes
GC attenuation:	Range = 100
Integrator attenuation:	128

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN C57 RATS

CHAMBER ATMOSPHERE (FA) 6 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD
1	18.7	50.2	<MDL	---
2	19.8	49.8	<MDL	---
3	20.0	48.8	<MDL	---
4	20.1	49.4	<MDL	---
5	20.8	48.2	<MDL	---
6	20.2	48.4	<MDL	---
7	20.2	52.8	<MDL	---
8	20.7	52.2	<MDL	---
9	20.4	51.3	<MDL	---
10	20.5	50.9	<MDL	---
11	20.0	48.5	<MDL	---
12	20.4	48.1	<MDL	---
13	20.6	48.2	<MDL	---
14	19.9	47.8	<MDL	---
15	20.0	49.0	<MDL	---
16	19.9	48.0	<MDL	---
17	20.0	49.0	<MDL	---
18	19.8	48.4	<MDL	---
19	19.8	48.5	<MDL	---
20	19.0	47.7	<MDL	---
21	20.0	48.6	<MDL	---
22	20.0	49.0	<MDL	---
23	19.5	48.4	<MDL	---
Mean:	20.0	49.2	<MDL	
SD:	0.51	1.40	---	

TEMP = temperature (daily mean)

RH = relative humidity (daily mean)

A = analytical concentration (daily mean)

SD = standard deviation of A

<MDL = less than the minimum estimated detection limit

TABLE 5
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CDF RATS

CHAMBER ATMOSPHERE DATA: 500 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	19.8	47.2	489	6	501	0.98
2	20.8	47.6	488	3	503	0.97
3	20.8	47.2	494	5	506	0.98
4	21.4	47.6	492	6	507	0.97
5	21.7	46.2	512	4	530	0.97
6	21.6	46.7	482	3	503	0.96
7	21.6	47.4	496	6	507	0.98
8	21.8	45.8	500	7	509	0.98
9	21.8	45.5	491	2	507	0.97
10	21.6	46.0	495	2	507	0.98
11	21.8	46.9	483	7	506	0.97
12	21.8	45.7	485	5	512	0.95
13	21.8	44.9	502	22	529	0.95
14	21.6	44.5	494	2	503	0.98
15	21.6	44.9	492	4	505	0.97
16	20.8	45.2	482	4	497	0.97
17	21.6	45.9	484	5	503	0.96
18	21.1	45.7	488	5	505	0.97
19	21.0	45.0	488	7	498	0.98
20	21.2	45.0	482	14	504	0.96
21	20.9	46.0	489	5	507	0.96
22	21.7	46.5	478	4	501	0.95
23	20.8	45.6	487	4	512	0.95
Mean:	21.3	46.0	490	---	507	0.97
SD:	0.51	0.94	7.7	---	8.1	0.011

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration

TABLE 6
 FORMALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS

CHAMBER ATMOSPHERE DATA: 1000 FPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	20.8	46.8	1006	27	985	1.02
2	21.3	46.8	1016	13	991	1.02
3	21.8	47.0	1003	14	988	1.03
4	21.2	47.3	1023	26	989	1.03
5	21.6	46.1	993	15	983	1.01
6	20.8	46.6	1005	16	988	1.02
7	20.8	46.4	1022	10	995	1.03
8	20.8	45.4	1022	14	991	1.03
9	20.8	44.8	986	13	987	1.00
10	20.7	45.8	1011	7	985	1.03
11	20.8	46.2	1002	33	989	1.01
12	20.7	45.3	987	25	979	1.01
13	20.7	46.1	1008	9	986	1.02
14	20.8	46.5	1010	7	983	1.03
15	20.7	47.1	1004	10	985	1.02
16	20.5	47.3	1012	13	993	1.02
17	20.7	47.6	992	13	973	1.02
18	20.3	47.2	1020	6	991	1.03
19	20.0	47.4	1028	7	981	1.05
20	19.7	46.8	1025	22	974	1.05
21	19.9	47.4	985	11	985	1.00
22	20.6	47.2	1027	10	989	1.04
23	19.8	47.2	1010	9	998	1.01
Mean:	20.7	46.6	1009	---	986	1.02
SD:	0.52	0.76	13.2	---	6.0	0.013

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration

TABLE 7
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

CHAMBER ATMOSPHERE DATA: 1500 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	19.5	48.2	1500	17	1446	1.04
2	20.2	48.4	1509	5	1455	1.04
3	20.0	47.5	1505	10	1459	1.03
4	21.1	46.0	1521	19	1457	1.04
5	21.9	47.0	1500	12	1453	1.03
6	22.5	47.2	1502	9	1459	1.03
7	22.2	47.2	1519	6	1452	1.05
8	20.6	47.2	1526	8	1450	1.05
9	21.0	46.7	1501	25	1446	1.04
10	20.7	46.6	1511	8	1447	1.04
11	21.1	47.4	1510	8	1449	1.04
12	18.7	46.7	1500	6	1449	1.04
13	19.5	46.5	1500	4	1456	1.03
14	20.8	47.1	1533	8	1452	1.06
15	20.8	48.1	1511	8	1449	1.04
16	20.5	47.4	1502	18	1444	1.04
17	20.7	47.4	1514	13	1445	1.05
18	20.7	47.3	1494	14	1450	1.03
19	20.6	47.2	1502	14	1434	1.05
20	20.5	46.6	1512	12	1437	1.05
21	19.9	48.8	1507	8	1459	1.03
22	20.7	48.0	1521	12	1452	1.05
23	20.2	47.4	1517	13	1459	1.04
Mean:	20.6	47.4	1509	---	1450	1.04
SD:	0.85	0.60	9.9	---	6.7	0.008

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration

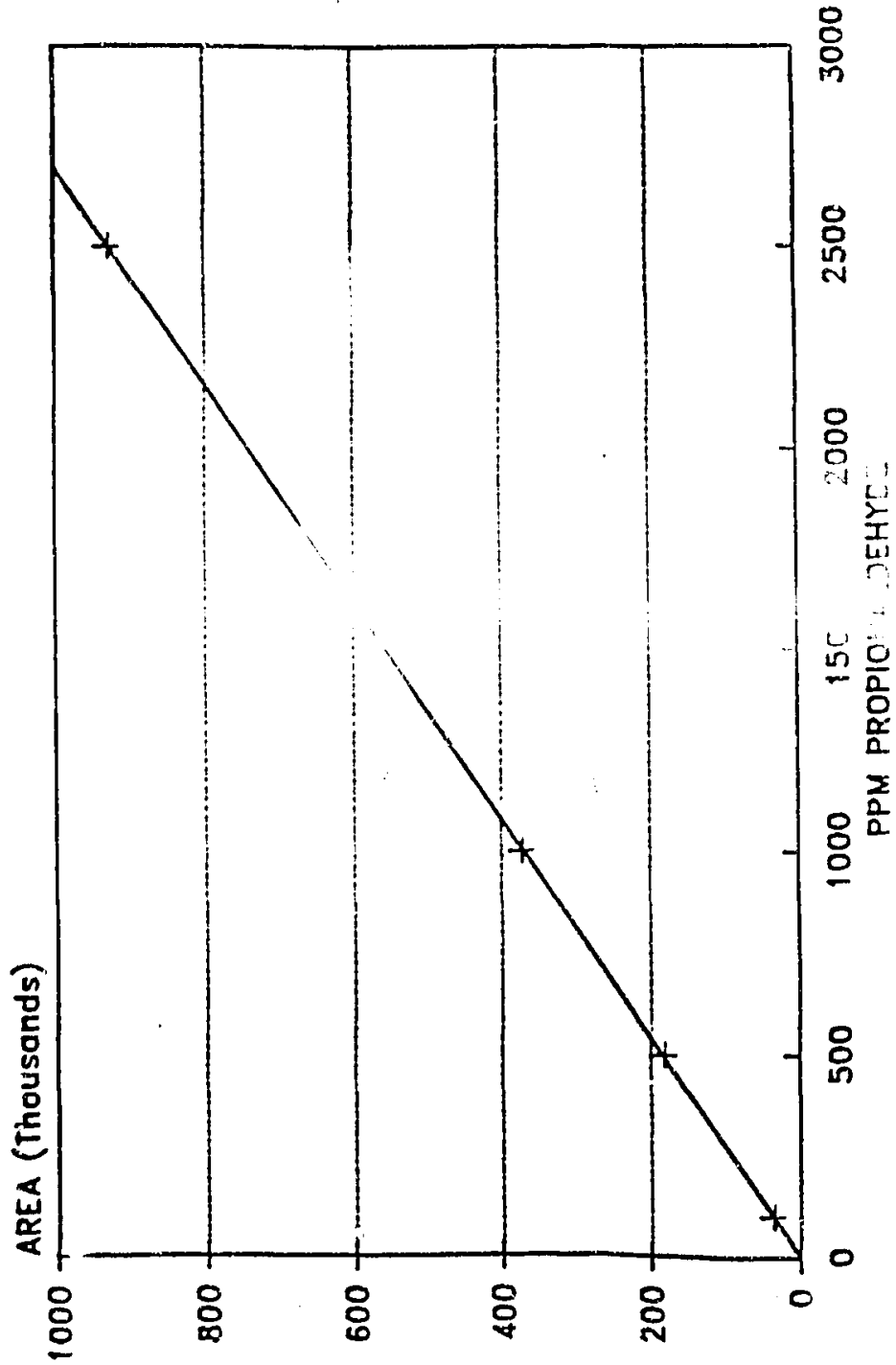
TABLE 8
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

CHAMBER ATMOSPHERE DATA: 2500 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	SD	NOM (ppm)	A/NOM
1	18.5	48.0	2620	27	2556	1.03
2	19.6	48.4	2593	44	2519	1.03
3	19.8	48.6	2541	74	2475	1.03
4	19.8	47.8	2566	63	2436	1.03
5	19.5	47.8	2598	24	2509	1.04
6	20.3	47.4	2639	36	2571	1.03
7	20.8	48.0	2616	92	2513	1.04
8	20.4	48.0	2546	40	2426	1.05
9	19.9	47.4	2517	48	2433	1.03
10	19.9	47.5	2537	37	2455	1.03
11	19.9	48.1	2550	59	2473	1.03
12	20.8	48.0	2579	51	2480	1.04
13	21.3	48.1	2592	57	2490	1.04
14	20.7	48.5	2613	36	2504	1.04
15	20.6	48.1	2599	50	2501	1.04
16	20.5	48.3	2594	12	2506	1.04
17	20.7	48.5	2585	43	2516	1.03
18	20.7	48.4	2580	47	2491	1.04
19	20.6	47.1	2583	263	2481	1.04
20	20.5	46.7	2611	56	2457	1.06
21	19.9	48.9	2638	24	2559	1.02
22	20.7	48.5	2679	27	2577	1.04
23	19.8	47.5	2659	36	2580	1.03
Mean:	20.2	48.0	2592	—	2503	1.04
SD:	0.59	0.53	39.0	—	43.1	0.008

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation of A
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration

FIGURE 1. PROPIONALDEHYDE
CALIBRATION CURVE



and deuteriochloroform were used as received.

Figure 1 shows the ^1H NMR spectrum obtained from the sample 100-SLW-6. The observed chemical shifts, spin-spin coupling patterns, and relative intensities are appropriate for propionaldehyde. The aldehydic proton appears as a triplet at 9.78 ppm; the methyl hydrogens as a triplet at 1.02 ppm; and the methylene hydrogens as a quartet of doublets at 2.48 ppm. The minor peak at 7.57 ppm is probably due to residual protonated solvent. Several very minor peaks are observed but have not been assigned; they probably include spinning side bands, ^{13}C satellites, and minor by-products.

Figure 2 shows the ^{13}C (^1H) spectrum for the same sample. No unusual or unexpected resonances are seen; the three types of carbons present in propionaldehyde are seen: the carbonyl at 202.2 ppm, the methyl at 5.2 ppm, and the methylene at 36.5 ppm. The triplet at 77 ppm is the deuteriochloroform solvent, which was used as a secondary chemical shift reference. Several minor peaks are observed at 101.7, 27.0, 8.3, and 7.1 ppm, which could arise from expected impurities such as the trimer. The NMR spectra are totally consistent with the sample being propionaldehyde which contains no major organic impurities.

GC/MS Analysis Electron ionization (EI) and isobutane chemical ionization (CI) mass spectral data were collected in the UCC&P MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard (HP) 5890 gas chromatograph. The sample, 100-SLW-6, was analyzed by injecting 0.1 μL aliquots onto a DB-1 capillary column held at 30°C for 4 minutes, and then programmed to 250°C at 8°/minute. Figure 3 shows the EI total ion current chromatogram for the sample (scanned from m/z 10 to m/z 310 in the EI mode, and m/z 60-360 in the CI mode). The chromatogram is annotated with identifications based on the components' EI and CI spectra. The propionaldehyde trimers identified by capillary GC were confirmed by GC/CI/MS only.

Capillary GC A HP 5890 gas chromatograph equipped with a flame ionization detector was used to analyze the sample. Aliquots (1 μL) were injected via autoinjector with a 100:1 split ratio onto a DB-1 capillary column started at 60°C and held for 4 minutes, then programmed to 250° at 12°/minute (see Figure 4 for the pre-study sample and Figure 5 for the post-study sample). The averages of triplicate analyses are given below (normalized chromatogram area percent). The slightly lower purity of the post-study sample is due to the increase of propionic acid in the sample.

Component name	100-SLW-6	100-SLW-6R
Propionaldehyde	= 99.77	= 99.42
n propanol	0.01	0.02
2-methyl butyraldehyde	0.02	0.02
valeraldehyde	0.06	0.02
propionic acid	0.07	0.37
propionaldehyde dimers	0.03	0.04
propionaldehyde trimers	0.01	0.04
all other impurities	= 0.03	= 0.07

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC&P Skill Centers show that this sample is propionaldehyde. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purity, measured by capillary GC, is = 99.77% and 99.42%.

ARCHIVES All raw data, records, protocols, samples and final reports are being retained at UCC&P's South Charleston, WV, Technical Center as follows:

- raw data from GC, NMR and GC/MS studies are in 770-127 and 720-151, respectively;
- protocols, notebook and other records are to be kept in the GLP archives;
- the remainder of each sample is being kept in a locked GLP sample box in 770-333.

Final Report, GLP Study # 100-SLW-4

page 2 of 10

ACKNOWLEDGEMENTS We would like to thank Jo Ann Coffey for sample handling, collecting the GC data, and preparing the report, Greg Richards for collecting the GC/MS data, and Kathy Canterbury for collecting the NMR data.

NOTEBOOK REFERENCE: 100-SLW-4 and related pages

Confidentiality No claim of confidentiality is made for any information contained in this study as it pertains to use by any government agency to which it is submitted. This document, however, is proprietary to UCC&P and is confidential and trade secret information in all other countries and for all purposes other than those directly related to the purposes of the reviewing agency. Information contained in these studies should not be reviewed, abstracted or used by persons other than the agency without the expressed written consent of UCC&P except as required to carry out statutory requirements.

GLP Compliance This study was conducted to fully comply with the following GLP standards: FDA, 21 CFR, Part 58;
TSCA, 40 CFR, Part 792;
FIFRA, 40 CFR, Part 160.

Alexander E. Gabany 8/13/92
Alexander E. Gabany, B. S., Study Director date

Arnold M. Harrison 8/13/92
Arnold M. Harrison, Ph. D., NMR Skill Center date

Richard A. McDonie 8/19/92
Richard A. McDonie, B. S. MS Skill Center date

AEG/AMH/AM
Date Study initiated: 10/14/91
Manuscript date (Date Study completed): August 13, 1992
Attachments: 5 Figures;
Sample Protocol;
QAU statement

Figure 3 — Capillary GC/MS RIC of 100-SLW-6 (Propionaldehyde)

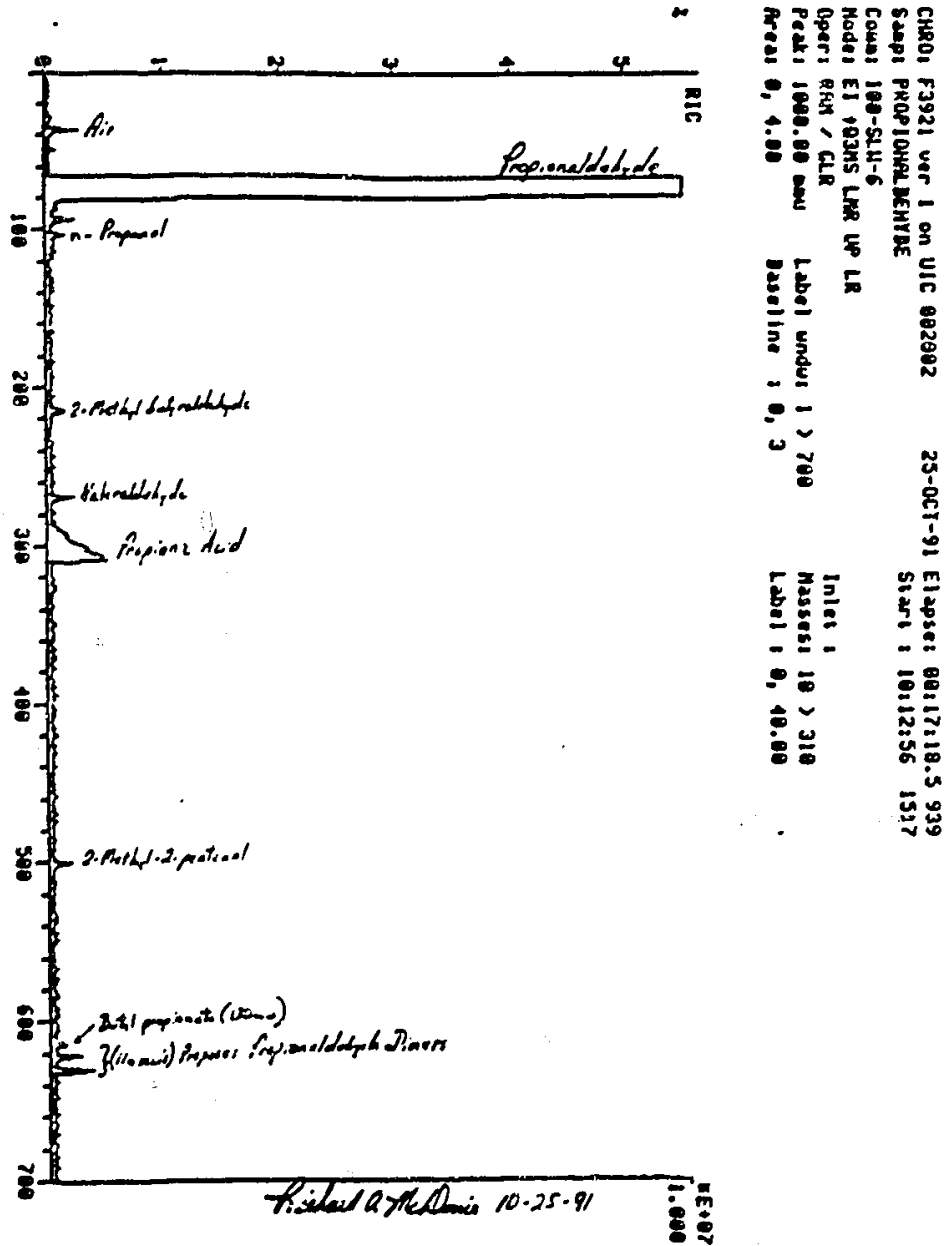


Figure 4 — Capillary Gas Chromatogram of 100-SLW-6 (Propionaldehyde)

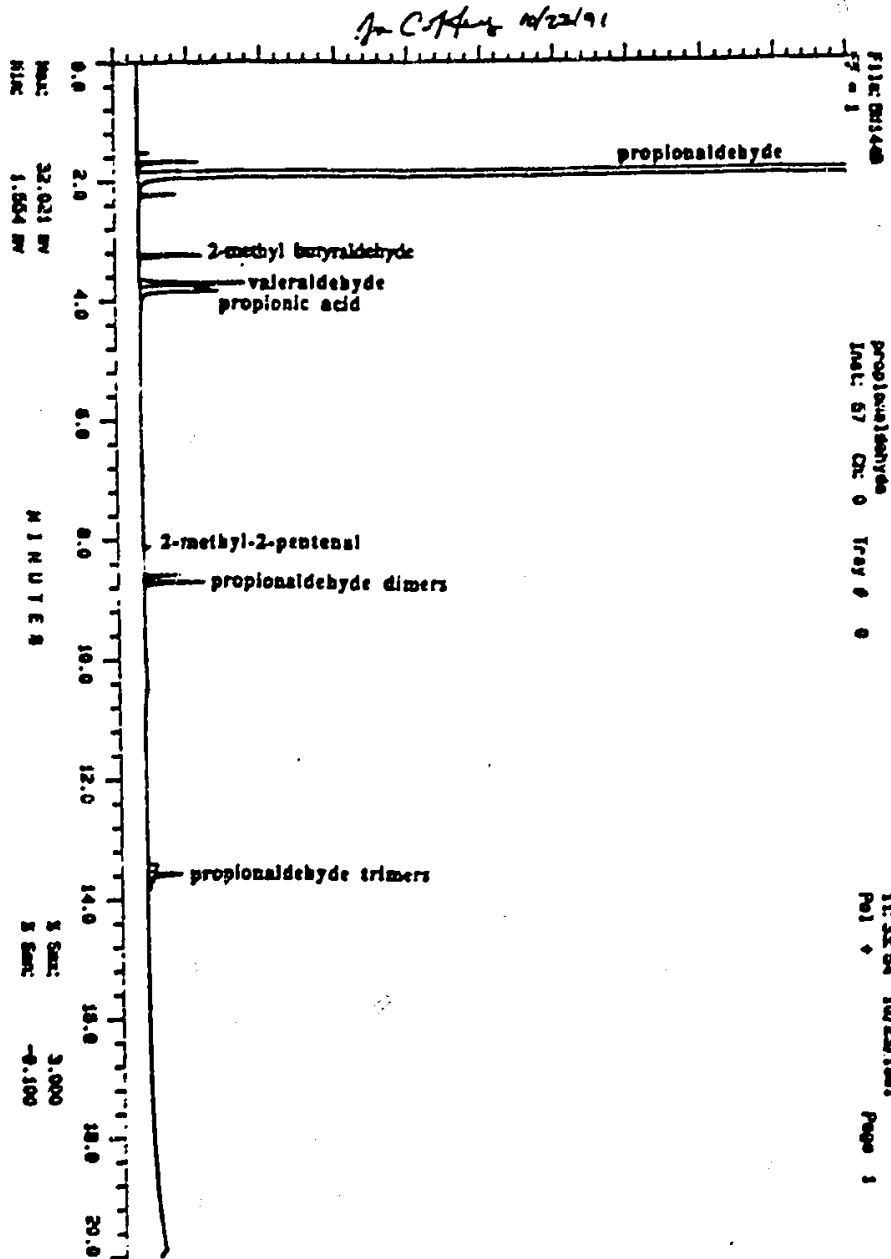
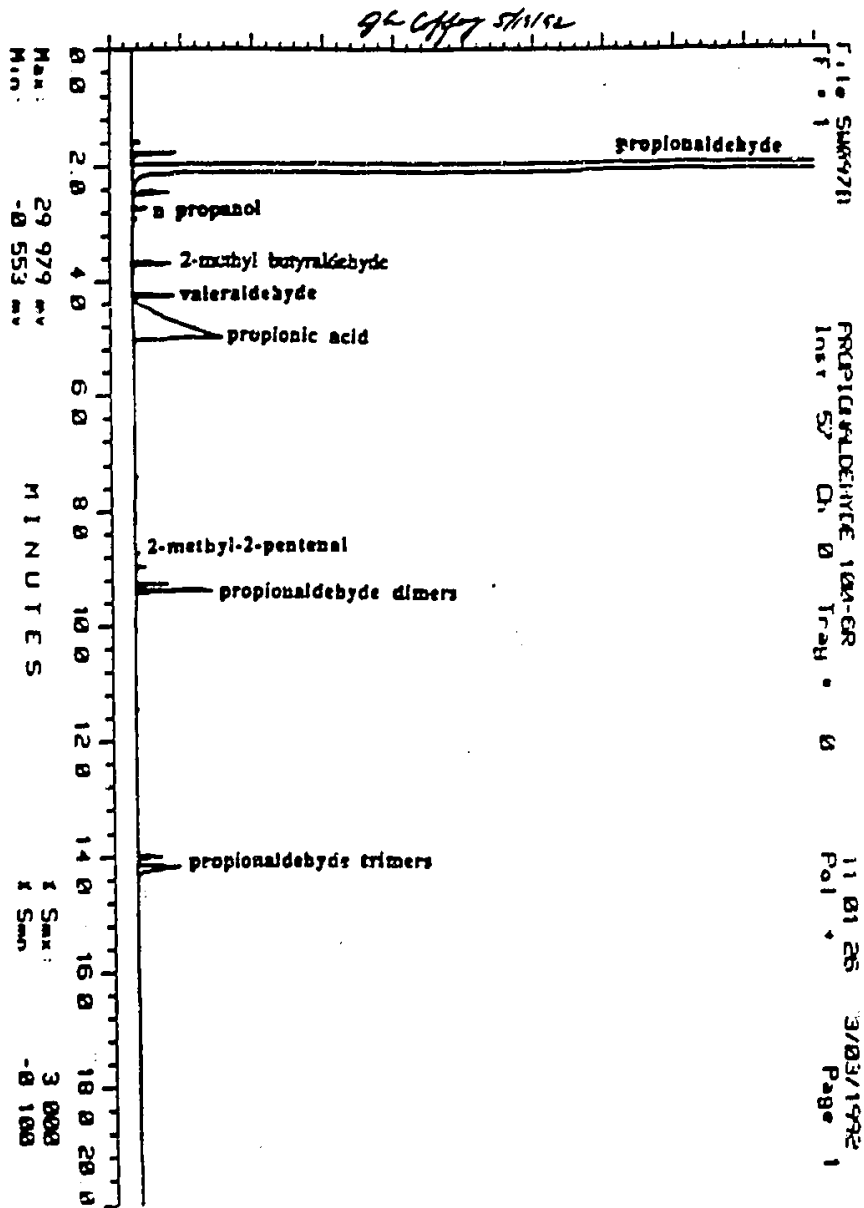


Figure 5 — Capillary Gas Chromatogram of 100-SLW-6R (Propionaldehyde)



APPENDIX 1 100-SLW-4 Protocol



PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

title Propionaldehyde

purpose Analytical Characterization of Sample(s) for Toxicology Studies at Bushy Run Research Center (BRRC)

study number 100-SLW-4

sponsor SOLVENTS AND COATING MATERIALS DIVISION (SCMD)
Union Carbide Chemicals and Plastics Company Inc. (UCC&P)
39 Old Ridgebury Road,
Danbury, Conn. 06817-0001

testing facility UCC&P Technical Center,
South Charleston, WV 25303 (Location 511)

Proposed Starting Date: Monday, October 14, 1991
Proposed Completion Date: December 14, 1991
Estimated Date of Final Report: January 14, 1992



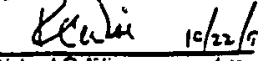
Test Substance(s) 100-SLW-6

Name	Propionaldehyde
Source	TS-2151011; UCC&P, SCMD, Texas City, Texas
CAS Registry No.	123-38-6
Description	Water-white, non-viscous liquid; suffocating odor
Purity	> 99 %
Health/Safety	Stable; highly toxic. MSDS available upon request
Storage Conditions	ambient conditions, away from heat

Study Design

- The test substance(s) will be characterized by:
- Verification of identity by proton- and carbon-NMR.
 - Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥ 0.1 wt. %.
 - Quantitation of the identified impurities by capillary GC.

Reviewed and Approved by:

 10/14/91	 10/14/91	 10/22/91
Stephen L. Wellons GLP Study Director	date Denise L. Johnson GLP Quality Assurance Unit (QAU) Representative	date Richard C. Wise Manager of Product Safety, SCMD, Sponsor

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: PROPIONALDEHYDE

Study No.: 100-SLW-4

Study Director: A.E. Gabany, B.S.

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

<u>Date</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued</u>	
		<u>To Study Director</u>	<u>To Management</u>
Oct. 18, 1991	Protocol Compliance Review	Oct. 18, 1991	Oct. 18, 1991
Feb. 10, 1992	Laboratory Compliance Review	Feb. 10, 1992	May, 1992
Aug. 25, 1992	Final Report Compliance Review	Aug. 25, 1992	Aug 25, 1992


Denise L. Johnson | QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD® Rats

Individual Maternal In-Life Data

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TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD₁ RATS

ABBREVIATIONS

INDIVIDUAL MATERNAL IN-LIFE DATA

Abbreviations for the locations of clinical signs appear in parentheses next to the clinical signs in the following tables. The number included with the abbreviation is the number of times that clinical sign for that location was entered into the computer for that animal during the course of the study. The following is a list of three letter abbreviations for locations of clinical signs that may appear in this appendix.

ABD ABDOMEN	LHL LEG-HIND-LEFT
ANS ANUS	LHR LEG-HIND-RIGHT
AXB AXILLA-BOTH	LNS LOCATION NOT SPECIFIED
AXL AXILLA-LEFT	MTH MOUTH
AXR AXILLA-RIGHT	MUL MULTIPLE AREAS, NOS*
BCK BACK	NCK NECK
BDY ENTIRE BODY	NSE NOSE
CHS CHEST	PAL PAWS-ALL
EAB EAR-BOTH	PFB PAW-FORE-BOTH
EAL EAR-LEFT	PFL PAW-FORE-LEFT
EAR EAR-RIGHT	PFR PAW-FORE-RIGHT
ELB EYELID-BOTH	PHB PAW-HIND-BOTH
ELL EYELID-LEFT	PHL PAW-HIND-LEFT
ELR EYELID-RIGHT	PHR PAW-HIND-RIGHT
EYB EYE-BOTH	PNS PENIS
EYL EYE-LEFT	SCR SCROTUM
EYR EYE-RIGHT	SDB SIDE-BOTH
FAC FACE	SDL SIDE-LEFT
GEN GENITAL	SDR SIDE-RIGHT
HED HEAD	SHB SHOULDER-BOTH
HPB HIP-BOTH	SHL SHOULDER-LEFT
HPL HIP-LEFT	SHR SHOULDER-RIGHT
HPR HIP-RIGHT	TAL TAIL
INB INGUINAL-BOTH	TEE TEETH
INL INGUINAL-LEFT	TRA TREATMENT AREA
INR INGUINAL-RIGHT	TSB TESTIS-BOTH
IAL LEGS-ALL	TSL TESTIS-LEFT
LFB LEG-FORE-BOTH	TSR TESTIS-RIGHT
LFL LEG-FORE-LEFT	VAG VAGINA
LFR LEG-FORE-RIGHT	*NOS NOT OTHERWISE SPECIFIED
LHB LEG-HIND-BOTH	

TABLE 1 (Continued)
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS

ABBREVIATIONS

INDIVIDUAL MATERNAL IN-LIFE DATA

The following is a list of abbreviations or words that may appear in this appendix in reference to individual food consumption values.

- r/s = indicates that the animal was removed from the consumption period due to spillage.
- r/e = indicates that the animal was removed from the consumption period due to excreta in the feeder
- r/o = indicates that the animal was removed from the consumption period for reasons specified in the raw data.
- r/dead = indicates that the animal was removed from the consumption period because it died or was sacrificed during the period in which this abbreviation appears.
- dead = indicates that the animal died prior to the period in which this word appears.
- sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.
- a = Combined interval value removed due to removal of at least one individual interval value (see individual interval footnotes).

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
 FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
0 PPM	25172	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25169	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25171	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25160	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25157	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25163	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25149	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
500 PPM	25152	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25179	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25180	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25155	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25140	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25144	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25129	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
1000 PPM	25156	NORMAL	21	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	14	LACRIMATION (EYR 1)
	25138	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25137	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25134	NORMAL	21	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
		BODY	1	13	UROGENITAL DISCHARGE, RED
	25158	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25132	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
 FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
1000 PPM	25132	FATE	1	21	SCHEDULED SACRIFICE
	25127	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25162	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
1500 PPM		FATE	1	21	SCHEDULED SACRIFICE
	25177	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25165	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25168	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25176	NORMAL	21	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
	FATE	1	21	SCHEDULED SACRIFICE	
2500 PPM		EYES/EARS/NOSE	1	19	PERI OCULAR ENCRUSTATION (EYB 1)
	25136	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25130	NORMAL	21	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	18	PERI OCULAR ENCRUSTATION (EYB 1)
	25164	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
2500 PPM	25167	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25143	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25154	NORMAL	19	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	17-18	PERI OCULAR ENCRUSTATION (EYB 2)
		OTHER	1	12	MISSING EAR TAG
	25151	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
	25128	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	21	SCHEDULED SACRIFICE
25159	NORMAL	22	0-21	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	21	SCHEDULED SACRIFICE	

TABLE 3
 PROPYLALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 GROUP: 0 PPM

PREGNANCY STATUS	DAY 0	7	14	21
25172 P	214.28	257.76	286.63	378.01
25169 NP	224.84	236.13	237.18	250.84
25171 P	229.01	264.45	300.09	392.40
25160 P	236.52	266.96	307.58	394.43
25157 P	227.49	256.10	298.14	397.76
25163 P	216.23	258.01	298.75	389.13
25149 P	232.55	242.06	292.25	387.67
MEAN	226.01	260.89	297.24	389.90
S.D.	8.918	4.288	7.150	6.863
N	6	6	6	6

P=PREGNANT, NP=NOT PREGNANT, RES=REMOVED FROM STUDY, NP AND RES WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 GROUP: 500 PPM

PREGNANCY STATUS	DAY 0	7	14	21
25152 P	216.34	244.73	277.40	371.48
25179 P	217.71	244.47	286.71	371.97
25180 P	235.83	256.55	285.94	379.34
25155 P	241.76	281.94	319.85	422.56
25140 P	231.91	261.86	298.87	382.81
25144 P	219.45	248.93	271.03	344.88
25129 P	223.69	263.14	300.01	391.65
MEAN	226.67	257.37	291.40	380.65
S.D.	9.892	13.262	16.341	23.533
N	7	7	7	7

P=PREGNANT, NP=NOT PREGNANT, RES=REMOVED FROM STUDY, NP AND RES WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 GROUP: 1000 PPM

PREGNANCY STATUS	DAY 0	7	14	21
25156 P	210.10	221.14	229.20	238.77
25138 P	221.95	249.83	286.26	364.67
25137 P	233.05	269.14	306.31	404.73
25134 P	237.38	261.95	297.52	400.02
25158 P	230.05	247.69	278.06	368.83
25132 P	210.32	220.12	247.09	320.48
25127 P	229.93	256.45	285.52	370.27
MEAN	224.68	246.62	275.71	352.54
S.D.	10.909	19.156	27.711	57.266
N	7	7	7	7

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 GROUP: 1500 PPM

PREGNANCY STATUS	DAY 0	7	14	21
25162 P	211.41	236.37	269.26	346.68
25177 P	218.87	234.86	276.64	363.68
25165 P	226.79	248.66	273.61	332.84
25168 P	238.73	259.53	294.47	385.94
25176 P	230.36	247.98	277.31	360.06
25136 P	213.53	246.75	281.66	365.57
25130 P	236.60	264.43	290.22	366.73
MEAN	225.18	248.37	280.45	360.21
S.D.	10.867	10.892	9.036	16.721
N	7	7	7	7

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
 GROUP: 2500 PPM

PREGNANCY STATUS	DAY 0	7	14	21
25164 P	206.14	219.26	251.26	334.50
25167 P	219.87	235.39	263.73	340.87
25143 P	235.73	242.07	263.07	334.71
25154 P	236.89	250.73	280.97	369.76
25151 P	236.58	261.85	289.95	371.08
25128 P	215.47	230.11	253.40	318.53
25159 P	234.93	253.76	289.11	360.54
MEAN	226.52	241.88	270.21	347.14
S.D.	12.556	14.780	16.316	20.151
N	7	7	7	7

P=PREGNANT, NP=NOT PREGNANT, RES=REMOVED FROM STUDY, NF AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 GROUP: 0 PPM

ANIMAL PS	DAY	0-7	7-11	11-14	14-17	17-21	7-14	14-21
25172 P		24.96	25.77	25.39	28.21	27.80	25.60	27.97
25169 NP		18.64	19.52	19.25	22.83	20.41	19.41	21.45
25171 P		21.93	24.15	25.92	27.01	26.44	24.91	26.69
25160 P		20.25	22.77	25.34	26.16	27.35	23.87	26.84
25157 P		20.97	24.43	25.50	27.28	28.42	24.89	27.93
25163 P		21.83	25.42	25.72	25.70	26.35	25.55	26.07
25149 P		21.92	23.76	23.53	24.60	25.42	23.66	25.07
MEAN		21.98	24.38	25.23	26.49	26.96	24.75	26.76
S.D.		1.609	1.099	0.860	1.275	1.095	0.821	1.112
N		6	6	6	6	6	6	6

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
 NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 GROUP: 500 PPM

ANIMAL PS	DAY	0-7	7-11	11-14	14-17	17-21	7-14	14-21
25152 P		20.80	22.57	23.87	25.15	27.18	23.12	26.31
25179 P		19.51	22.16	24.53	26.21	26.65	23.17	26.46
25180 P		19.19	21.19	22.73	24.12	25.36	21.85	24.83
25155 P		22.84	25.82	25.65	28.16	27.54	25.75	27.81
25140 P		20.40	23.41	22.90	26.10	24.06	23.20	24.93
25144 P		21.09	20.18	20.54	22.21	23.46	20.33	22.92
25129 P		22.07	23.63	24.02	25.15	26.52	23.80	25.93
MEAN		20.84	22.71	23.46	25.30	25.62	23.03	25.60
S.D.		1.311	1.828	1.623	1.855	1.576	1.668	1.551
N		7	7	7	7	7	7	7

PS=PREGNANT, P=NOT PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
 NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPRIONALDEHYDR: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 GROUP: 1000 PPM

ANIMAL PS	DAY	0-7	7-11	11-14	14-17	17-21	7-14	14-21
25156 P		16.00	16.33	17.78	17.23	17.09	16.96	17.15
25138 P		18.65	20.50	23.63	22.66	23.37	21.84	23.07
25137 P		21.31	22.36	25.57	26.03	24.39	23.74	25.09
25134 P		20.59	21.85	22.74	26.26	27.48	22.23	26.95
25158 P		18.08	19.23	21.21	23.48	25.14	20.08	24.43
25132 P		16.43	19.73	20.40	21.10	21.24	20.02	21.18
25127 P		19.85	20.88	21.25	23.74	23.39	21.04	23.54
MEAN		18.70	20.13	21.80	22.93	23.16	20.84	23.06
S.D.		2.023	2.000	2.490	3.097	3.286	2.149	3.160
N		7	7	7	7	7	7	7

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
 NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 GROUP: 1500 PPM

ANIMAL PS	DAY	0-7	7-11	11-14	14-17	17-21	7-14	14-21
25162 P		19.44	21.62	24.26	25.08	26.49	22.75	25.89
25177 P		18.30	20.97	23.68	26.09	25.37	22.13	25.68
25165 P		17.67	19.47	20.93	22.08	23.07	20.10	22.65
25168 P		19.49	23.78	23.19	26.80	25.50	23.53	26.06
25176 P		18.08	19.60	20.92	22.67	22.36	20.17	22.49
25136 P		19.61	22.26	22.96	23.56	22.45	22.56	22.93
25130 P		20.40	20.75	21.87	22.52	24.12	21.23	23.43
MEAN		19.00	21.21	22.54	24.12	24.19	21.78	24.16
S.D.		0.988	1.516	1.323	1.878	1.635	1.321	1.634
N		7	7	7	7	7	7	7

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
 NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
 GROUP: 2500 PPH

ANIMAL PS	DAY	0-7	7-11	11-14	14-17	17-21	7-14	14-21
25164 P		16.65	19.59	19.47	21.05	21.57	19.54	21.35
25167 P		17.09	20.07	20.88	21.73	22.19	20.42	21.99
25143 P		17.80	18.63	20.51	21.28	22.21	19.43	21.82
25154 P		18.37	20.42	21.41	23.38	24.02	20.84	23.75
25151 P		20.20	21.96	24.02	24.58	22.52	22.84	23.40
25128 P		18.67	18.70	20.53	20.79	19.54	19.48	20.08
25159 P		20.04	23.66	23.31	23.06	21.88	23.51	22.39
MEAN		18.40	20.43	21.45	22.27	21.99	20.87	22.11
S.D.		1.362	1.817	1.636	1.420	1.335	1.674	1.241
N		7	7	7	7	7	7	7

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
 NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD® Rats

Individual Maternal Necropsy and Laparotomy Data

LIST OF TABLES

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TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CO² RATS

NECROPSY PROTOCOL

FEMALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

ADIPOSE TISSUE	PERITONEAL CAV	THORACIC CAV	PERICARDIAL CAV	ESOPHAGUS
STOMACH	STOMACH GLAND	STOMACH NON-GL	LIVER	PANCREAS
INTESTINES	ADRENAL GL	SPLEEN	DIAPHRAGM	OVARIES
CORPORA LUTEA	OVIDUCT	UTERUS	CERVIX	VAGINA
VULVA	AMNIOTIC SACS	PLACENTAS	NOSE/TURBINATES	LARYNX
TRACHEA	TRACH/BRONC BIF	LUNGS	KIDNEYS	URETER
URINARY BLADDER				

The following organs were weighed at necropsy:

LIVER UTERUS

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 0 PPM FEMALE

ANIMAL 25172 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
KIDNEYS
GROSS: HYDRONEPHROSIS
BILATERAL
MICRO: NOT EXAMINED

ANIMAL 25169 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25171 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

UTERUS
GROSS: CONTENTS - COAGULATED BLOOD
SURROUNDING IMPLANTS #1,#2,#3 AND #4
LUNGS
GROSS: COLOR CHANGE
SOLID DARK RED , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25160 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: NOT EXAMINED

ANIMAL 25157 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

OVARIES
GROSS: CYST
LEFT , CLEAR FLUID FILLED
LUNGS
GROSS: COLOR CHANGE
DARK RED , SOLID , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25163 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 0 PPM FEMALE

ANIMAL 25149 14-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS

GROSS:

COLOR CHANGE

DARK RED AREAS , ALL LOBES

MICRO: N O T

E X A M I N E D

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 500 PPM FEMALE

ANIMAL 25152 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25179 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25180 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
SOLID DARK RED , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25155 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: NOT EXAMINED

ANIMAL 25140 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

OVARIES
GROSS: CYST
RIGHT , CLEAR FLUID FILLED
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25144 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED , SOLID , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25129 14-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 1000 PPM FEMALE

ANIMAL 25156 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25138 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: FOCUS OR FOCI
FEW BLACK , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25137 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25134 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

OVARIES
GROSS: CYST
LEFT , CLEAR FLUID FILLED
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25158 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25132 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25127 14-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 1000 PPM FEMALE

ANIMAL 25127 (CONTINUED)

MICRO: NOT EXAMINED DARK RED AREAS , ALL LOBES

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 1500 PPM FEMALE

ANIMAL 25162 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25177 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25165 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

UTERUS
GROSS: NO IMPLANTS IN ONE HORN
LEFT , NO APPARENT BLOCKAGE
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25168 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25176 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS . ALL LOBES
MICRO: NOT EXAMINED

ANIMAL 25136 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LIVER
GROSS: COLOR CHANGE
DARK BROWN AREAS , RIGHT AND LEFT
MEDIAN LOBES
UTERUS
GROSS: CONTAINS BLOOD (BY HEMASTIX)
RIGHT HORN
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
LUNGS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 1500 PPM FEMALE

ANIMAL 25135 (CONTINUED)

GROSS: FOCUS OR FOCI
FEW BROWN, RIGHT DIAPHRAGMATIC LOBE
MICRO: NOT EXAMINED

ANIMAL 25130 14-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS, ALL LOBES
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD[®] RATS
INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 2500 PPM FEMALE

ANIMAL 25164 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: N O T E X A M I N E D

ANIMAL 25167 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: N O T E X A M I N E D

ANIMAL 25143 12-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

UTERUS
GROSS: CONTENTS - COAGULATED BLOOD
BOTH HORNS
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: N O T E X A M I N E D

ANIMAL 25154 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: N O T E X A M I N E D

ANIMAL 25151 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: N O T E X A M I N E D

ANIMAL 25128 13-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

UTERUS
GROSS: CONTENTS - COAGULATED BLOOD
RIGHT
LUNGS
GROSS: COLOR CHANGE
DARK RED AREAS , ALL LOBES
MICRO: N O T E X A M I N E D

ANIMAL 25159 14-NOV-91
TYPE OF DEATH: SCHEDULED SACRIFICE

LUNGS
GROSS: COLOR CHANGE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 1
PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP: 2500 PPM FEMALE

ANIMAL 25159 (CONTINUED)

LUNGS DARK RED AREAS , ALL LOBES
GROSS: FOCUS OR FOCI
FEW BLACK , ALL LOBES
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL MATERNAL ORGAN WEIGHTS AND NET BODY WEIGHT (GRAMS)
 GROUP: 0 PPM

PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	NET BODY WEIGHT		LIVER
			UTERUS	NET BODY CHANGE	
25172 P	214.28	378.01	112.320	265.69	51.41
25169 NP	224.84	250.84	3.516	247.32	22.48
25171 P	229.01	392.40	118.990	273.41	44.40
25160 P	236.52	394.43	92.180	302.25	65.73
25157 P	227.49	397.76	112.250	285.51	58.02
25163 P	216.23	389.13	108.060	281.07	64.84
25149 P	232.55	387.67	106.540	281.13	48.58
MEAN	226.01	389.90	108.39	281.51	55.50
S.D.	8.92	6.86	9.04	12.35	8.79
N	6	6	6	6	6

P= Pregnant, NP=Not pregnant, RFS=Removed from study, "-"= No data,
 PD= Pregnant, dead before scheduled laparotomy day, NPD= Not pregnant, dead before scheduled laparotomy day.
 NP, NPD, PD and RFS weight(s) not included in calculation of mean.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INDIVIDUAL MATERNAL ORGAN WEIGHTS AND NET BODY WEIGHT (GRAHS)
 GROUP: 500 PPM

PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	UTERUS	NET BODY WEIGHT	NET BODY WEIGHT CHANGE	LIVER
25152 P	216.34	371.48	94.960	276.52	60.18	13.257
25179 P	217.71	371.97	105.020	266.95	49.24	13.276
25180 P	235.83	379.34	102.940	276.40	40.57	13.668
25155 P	241.76	422.56	112.310	310.25	68.49	14.716
25140 P	231.91	382.61	100.990	281.62	49.71	12.449
25144 P	219.45	344.88	87.900	256.98	37.53	10.595
25129 P	223.69	391.69	103.510	288.18	64.49	13.729
MEAN	226.67	380.65	101.09	279.56	52.89	13.10
S.D.	9.89	23.53	7.77	16.87	11.85	1.30
N	7	7	7	7	7	7

P= Pregnant, NP=Not pregnant, RFS=Removed from study, "--"= No data,
 PD= Pregnant, dead before scheduled laparotomy day, NPD= Not pregnant, dead before scheduled laparotomy day.
 NP, NPD, PD and RFS weight(s) not included in calculation of mean.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL MATERNAL ORGAN WEIGHTS AND NET BODY WEIGHT (GRAMS)
 GROUP: 1000 PPM

PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	UTERUS	NET BODY WT. CHANGE		LIVER
				WEIGHT	CHANGE	
25156 P	210.10	238.77	3.012	235.76	25.66	9.066
25138 P	221.95	364.67	87.730	276.94	54.99	11.238
25137 P	232.05	404.73	116.470	288.26	55.21	13.169
25134 P	237.38	400.02	123.100	276.92	39.54	12.529
25158 P	230.05	368.83	95.890	272.94	42.89	11.622
25132 P	210.32	320.48	92.470	228.01	17.69	9.944
25127 P	229.93	370.27	111.600	258.67	28.74	10.974
MEAN	224.68	352.54	90.04	262.50	37.82	11.22
S.D.	10.91	57.27	40.57	22.76	14.50	1.41
N	7	7	7	7	7	7

P= Pregnant, NP=Not pregnant, RFS=Removed from study, "-"= No data,
 PD= Pregnant, dead before scheduled laparotomy day, NPD= Not pregnant, dead before scheduled laparotomy day.
 NP, NPD, PD and RFS weight(s) not included in calculation of mean.

04/01/93

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS
 INDIVIDUAL MATERNAL ORGAN WEIGHTS AND NET BODY WEIGHT (GRAMS)
 GROUP: 1500 PPM

PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	UTERUS	NET BODY WEIGHT	NET BODY WEIGHT CHANGE	LIVER
25162 P	211.41	346.68	90.730	255.95	44.54	12.410
25177 P	216.87	363.68	97.160	266.52	47.65	10.939
25165 P	226.79	332.84	59.572	273.27	46.48	12.717
25168 P	238.73	385.94	100.640	285.30	46.57	13.437
25176 P	230.36	360.06	100.120	259.94	29.58	11.225
25136 P	213.53	365.57	112.570	253.00	39.47	11.273
25130 P	236.60	366.73	91.360	275.37	38.77	13.510
MEAN	225.18	360.21	93.16	267.05	41.87	12.22
S.D.	10.87	16.72	16.50	11.64	6.46	1.08
N	7	7	7	7	7	7

P= Pregnant, NP=Not pregnant, RFS=Removed from study, "-"= No data,
 PD= Pregnant, dead before scheduled laparotomy day, NPD= Not pregnant, dead before scheduled laparotomy day.
 N2, NPD, PD and RFS weight(s) not included in calculation of mean.

TABLE 2
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD-1 RATS
 INDIVIDUAL MATERNAL ORGAN WEIGHTS AND NET BODY WEIGHT (GRAMS)
 GROUP: 2500 PPM

PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	UTERUS	NET BODY WEIGHT	NET BODY CHANGE	LIVER
25164 P	206.14	334.50	99.290	235.21	29.07	10.849
25167 P	219.87	340.87	92.490	248.38	28.51	12.239
25143 P	235.73	334.71	77.750	256.96	21.23	12.343
25154 P	236.89	369.76	110.010	259.75	22.86	12.041
25151 P	236.58	371.08	103.560	267.52	30.94	12.891
25128 P	215.47	318.53	85.410	233.12	17.65	10.637
25159 P	234.93	360.54	101.780	258.76	23.83	13.893
MEAN	226.52	347.14	95.76	251.39	24.87	12.113
S.D.	12.56	20.15	11.22	13.04	4.80	1.13
N	7	7	7	7	7	7

P= Pregnant, NP=Not pregnant, RFS=Removed from study, "-"= No data,
 PD= Pregnant, dead before scheduled laparotomy day, NPD= Not pregnant, dead before scheduled laparotomy day.
 NP, NPD, PD and RFS weight(s) not included in calculation of mean.

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS

ANIMAL #	SEX M F	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA	
		RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT LEFT	TOTAL
		#			#			#			#			#			#	
25172	9	6	10	5	15	0	0	0	0	0	0	0	0	0	0	10	5	15
25169	NOT PREGNANT																	
25171	11	5	7	9	16	0	0	0	0	0	0	0	0	0	0	7	10	17
25160	6	6	7	5	12	0	0	0	0	0	0	0	0	0	0	7	14	21
25157	4	11	8	7	15	0	0	0	0	0	0	0	0	0	0	8	7	15
25163	8	7	8	7	15	0	0	0	0	0	0	0	0	0	0	8	7	15
25149	4	10	7	7	14	0	0	0	0	0	0	0	0	0	0	7	7	14
TOTAL	42	45	47	40	87	0	0	0	0	0	0	0	0	0	0	47	43	90
MEAN	7.0	7.5	7.8	6.7	14.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.8	7.2	15.0
S.D.	2.83	2.43	1.17	1.51	1.38	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.17	1.60	1.10
6 PREGNANT FEMALES																		
25152	4	9	6	6	13	0	0	0	0	0	0	0	0	0	0	6	7	13
25179	8	6	7	7	14	0	0	0	0	0	0	0	0	0	0	7	7	14
25180	10	5	6	9	15	0	0	0	0	0	0	0	0	0	0	6	9	15
25155	6	9	5	10	15	0	0	0	0	0	0	0	0	0	0	5	11	16
25140	10	4	9	5	14	0	0	0	0	0	0	0	0	0	0	9	5	14
25144	5	7	4	8	12	0	0	0	0	0	0	0	0	0	0	4	9	13
25129	10	5	6	9	15	0	0	0	0	0	0	0	0	0	0	6	9	15
TOTAL	53	45	43	55	98	0	0	0	0	0	0	0	0	0	0	43	57	100
MEAN	7.6	6.4	6.1	7.9	14.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.1	8.1	14.3
S.D.	2.57	1.99	1.57	1.68	1.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.57	1.95	1.11
7 PREGNANT FEMALES																		

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS

ANIMAL #	SEX		VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA	
	#	F	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT Ovary	LEFT Ovary
			0	6		0	0		0	0		0	0		0	0			
25156	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	5
25138	6	7	6	7	13	0	0	0	1	1	0	1	6	9	15	7	9	7	9
25137	6	9	7	8	15	0	0	0	2	3	0	0	0	9	18	9	8	9	18
25134	8	10	7	11	18	0	0	0	0	0	0	0	7	11	18	8	15	8	23
25158	10	4	6	8	14	0	0	0	0	0	0	0	0	6	14	6	9	6	15
25132	9	3	5	7	12	0	0	0	0	1	0	0	0	5	8	13	7	9	16
25127	8	7	8	7	15	0	0	0	0	0	0	0	0	8	7	15	8	7	15
TOTAL	47	40	39	48	87	0	0	0	3	3	6	0	1	42	52	94	51	63	114
MEAN	6.7	5.7	5.6	6.9	12.4	0.0	0.0	0.0	0.4	0.4	0.9	0.0	0.1	6.0	7.4	13.4	7.3	9.0	16.3
S.D.	3.30	3.55	2.64	3.34	5.80	0.00	0.00	0.00	0.79	0.53	1.07	0.00	0.38	2.58	3.51	5.80	1.11	3.06	3.64
7 PREGNANT FEMALES																			
FEMALE GROUP: 1500 PPM																			
25162	4	8	5	7	12	0	0	0	1	1	2	0	0	6	8	14	6	8	14
25177	7	7	5	9	14	0	0	0	1	0	1	0	0	6	9	15	7	10	17
25165	3	6	9	0	9	0	0	0	0	0	0	0	0	9	0	9	16	8	24
25168	4	9	6	7	13	0	0	0	1	0	1	0	0	7	7	14	7	8	15
25176	8	6	6	8	14	0	0	0	0	0	0	0	0	6	8	14	6	8	14
25136	10	6	10	6	16	0	0	0	0	0	0	0	0	10	6	16	10	7	17
25130	5	7	7	5	12	0	0	0	0	0	0	0	0	7	5	12	7	7	14
TOTAL	41	49	48	42	90	0	0	0	3	1	4	0	0	51	43	94	59	56	115
MEAN	5.9	7.0	6.9	6.0	12.9	0.0	0.0	0.0	0.4	0.1	0.6	0.0	0.0	7.3	6.1	13.4	8.4	8.0	16.4
S.D.	2.54	1.15	1.95	2.94	2.19	0.00	0.00	0.00	0.53	0.38	0.79	0.00	0.00	1.50	3.02	2.30	3.60	1.00	3.60
7 PREGNANT FEMALES																			

TABLE 3
 PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD RATS

ANIMAL #	SEX	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
		RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL	RIGHT HORN		TOTAL
		F	M		F	M		F	M		F	M		F	M		F	M	
25164	5	11	10	5	15	0	0	0	0	0	0	0	0	0	0	10	10	5	15
25167	5	9	9	5	14	0	0	0	0	0	0	0	0	0	0	9	10	5	15
25143	9	4	6	7	13	0	0	3	0	0	0	0	0	0	0	9	9	7	16
25154	8	8	6	10	16	0	0	0	0	0	0	0	0	0	0	6	10	6	16
25151	7	9	10	6	16	0	0	0	0	0	0	0	0	0	0	10	6	10	16
25128	7	7	10	4	14	0	0	1	1	2	0	0	0	0	0	11	5	12	17
25159	7	7	7	7	14	0	0	0	1	0	0	0	0	0	0	8	7	15	16
TOTAL	47	55	58	44	102	0	0	5	1	6	0	0	0	0	0	63	45	108	111
MEAN	6.7	7.9	8.3	6.3	14.6	0.0	0.0	0.7	0.1	0.9	0.0	0.0	0.0	0.0	0.0	9.0	6.4	15.4	15.9
S.D.	1.70	2.19	1.89	1.98	1.13	0.00	0.00	1.11	0.38	1.21	0.00	0.00	0.00	0.00	0.00	1.63	1.81	0.79	1.89

7 PREGNANT FEMALES

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD® Rats

Incidence of Malformations and Variations by Individual Fetuses
and Litters (Including Individual Fetal Body Weights)

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	
0 PPM					

25172	1 LF# 1	F	5.435	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	M	5.195	NO REMARKABLE OBSERVATIONS	
	3 LF# 3	M	5.189	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	M	5.704	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	M	5.279	NO REMARKABLE OBSERVATIONS	
	6 LF# 6	F	5.447	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	M	5.123	NO REMARKABLE OBSERVATIONS	
	8 LF# 8	M	5.330	NO REMARKABLE OBSERVATIONS	
	9 LF# 9	F	5.160	NO REMARKABLE OBSERVATIONS	
	10 LF#10	M	5.550	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	11 LF#11	M	5.755	NO REMARKABLE OBSERVATIONS	
	12 LF#12	F	5.570	NO REMARKABLE OBSERVATIONS	
	13 LF#13	F	5.018	NO REMARKABLE OBSERVATIONS	
	14 LF#14	M	5.890	NO REMARKABLE OBSERVATIONS	
15 LF#15	F	4.595	NO REMARKABLE OBSERVATIONS		
25171	1 LF# 1	M	5.414	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	M	5.737	NO REMARKABLE OBSERVATIONS	
	3 LF# 3	M	5.677	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	M	5.529	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	F	5.033	NO REMARKABLE OBSERVATIONS	
	6 LF# 6	M	5.484	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	M	5.552	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	8				EARLY(W/PLACENTAL TISSUE)
	9 LF# 8	M	5.280	NO REMARKABLE OBSERVATIONS	
	10 LF# 9	M	5.358	NO REMARKABLE OBSERVATIONS	
	11 LF#10	M	5.325	NO REMARKABLE OBSERVATIONS	
	12 LF#11	F	4.864	NO REMARKABLE OBSERVATIONS	
	13 LF#12	M	5.396	NO REMARKABLE OBSERVATIONS	
	14 LF#13	F	5.229	NO REMARKABLE OBSERVATIONS	
	15 LF#14	M	5.377	NO REMARKABLE OBSERVATIONS	
	16 LF#15	F	5.138	V ECCHYMOSIS - EXTREMITIES	
17 LF#16	F	4.844	RIGHT HIND PAW NO REMARKABLE OBSERVATIONS		
25160	1 LF# 1	M	4.738	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	M	5.071	NO REMARKABLE OBSERVATIONS	
	3 LF# 3	F	5.067	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	F	4.690	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	M	5.397	NO REMARKABLE OBSERVATIONS	
	6 LF# 6	F	5.441	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	F	4.658	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	8				EARLY(W/PLACENTAL TISSUE)
	9 LF# 8	M	5.599	NO REMARKABLE OBSERVATIONS	
	10				EARLY(W/PLACENTAL TISSUE)
	11 LF# 9	M	5.642	NO REMARKABLE OBSERVATIONS	
	12 LF#10	F	5.215	NO REMARKABLE OBSERVATIONS	
	13 LF#11	F	5.411	NO REMARKABLE OBSERVATIONS	
14 LF#12	M	5.340	NO REMARKABLE OBSERVATIONS		
25157	1 LF# 1	F	5.397	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	F	5.577	NO REMARKABLE OBSERVATIONS	
	3 LF# 3	F	5.838	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	F	5.435	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	F	5.314	NO REMARKABLE OBSERVATIONS	
	6 LF# 6	M	5.536	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	F	5.083	NO REMARKABLE OBSERVATIONS	
	8 LF# 8	F	5.373	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
CERVIX POSITION					

M-MALFORMATION, V-VARIATION, LF#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

0 PPM					
FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	
25157	9 LF# 9	F	5.494	NO REMARKABLE OBSERVATIONS	
	10 LF#10	M	5.806	NO REMARKABLE OBSERVATIONS	
	11 LF#11	F	5.380	NO REMARKABLE OBSERVATIONS	
	12 LF#12	F	5.713	NO REMARKABLE OBSERVATIONS	
	13 LF#13	M	5.910	NO REMARKABLE OBSERVATIONS	
	14 LF#14	F	5.273	NO REMARKABLE OBSERVATIONS	
	15 LF#15	M	5.609	NO REMARKABLE OBSERVATIONS	
25163	1 LF# 1	F	5.157	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	F	4.710	NO REMARKABLE OBSERVATIONS	
	3 LF# 3	M	5.305	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	M	5.481	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	F	5.059	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	6 LF# 6	M	5.196	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	M	4.798	NO REMARKABLE OBSERVATIONS	
	8 LF# 8	F	5.059	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	9 LF# 9	M	5.119	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	10 LF#10	M	4.934	NO REMARKABLE OBSERVATIONS	
	11 LF#11	F	4.873	NO REMARKABLE OBSERVATIONS	
	12 LF#12	M	5.361	NO REMARKABLE OBSERVATIONS	
	13 LF#13	M	5.127	NO REMARKABLE OBSERVATIONS	
	14 LF#14	F	5.060	NO REMARKABLE OBSERVATIONS	
15 LF#15	F	4.947	NO REMARKABLE OBSERVATIONS		
25149	1 LF# 1	F	5.147	NO REMARKABLE OBSERVATIONS	
	2 LF# 2	F	5.274	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	3 LF# 3	M	5.625	NO REMARKABLE OBSERVATIONS	
	4 LF# 4	F	5.534	NO REMARKABLE OBSERVATIONS	
	5 LF# 5	F	5.546	NO REMARKABLE OBSERVATIONS	
	6 LF# 6	M	5.690	NO REMARKABLE OBSERVATIONS	
	7 LF# 7	F	5.219	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	8 LF# 8	F	5.280	NO REMARKABLE OBSERVATIONS	
	9 LF# 9	M	5.236	NO REMARKABLE OBSERVATIONS	
	10 LF#10	F	5.314	NO REMARKABLE OBSERVATIONS	
	11 LF#11	F	5.123	NO REMARKABLE OBSERVATIONS	
	12 LF#12	F	5.446	NO REMARKABLE OBSERVATIONS	
	13 LF#13	M	5.108	NO REMARKABLE OBSERVATIONS	
14 LF#14	F	5.431	NO REMARKABLE OBSERVATIONS		

M-MALFORMATION, V-VARIATION, LF#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD¹ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

500 PPM

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDS:
25152	1 LP# 1	F	5.226	NO REMARKABLE OBSERVATIONS
	2 LP# 2	M	5.522	NO REMARKABLE OBSERVATIONS
	3 LP# 3	F	5.146	NO REMARKABLE OBSERVATIONS
	4 LP# 4	F	5.375	NO REMARKABLE OBSERVATIONS
	5 LP# 5	M	5.508	NO REMARKABLE OBSERVATIONS
	6 LP# 6	M	5.522	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	7 LP# 7	F	4.807	NO REMARKABLE OBSERVATIONS
	8 LP# 8	F	5.259	NO REMARKABLE OBSERVATIONS
	9 LP# 9	F	5.236	NO REMARKABLE OBSERVATIONS
	10 LP#10	F	4.541	NO REMARKABLE OBSERVATIONS
	11 LP#11	F	5.265	NO REMARKABLE OBSERVATIONS
	12 LP#12	F	4.622	NO REMARKABLE OBSERVATIONS
13 LP#13	M	4.979	NO REMARKABLE OBSERVATIONS	
25179	1 LP# 1	M	5.071	NO REMARKABLE OBSERVATIONS
	2 LP# 2	F	4.890	NO REMARKABLE OBSERVATIONS
	3 LP# 3	F	4.956	NO REMARKABLE OBSERVATIONS
	4 LP# 4	M	5.205	NO REMARKABLE OBSERVATIONS
	5 LP# 5	F	4.721	NO REMARKABLE OBSERVATIONS
	6 LP# 6	M	5.099	NO REMARKABLE OBSERVATIONS
	7 LP# 7	F	5.208	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	8 LP# 8	M	5.666	NO REMARKABLE OBSERVATIONS
	9 LP# 9	M	5.352	NO REMARKABLE OBSERVATIONS
	10 LP#10	M	5.216	NO REMARKABLE OBSERVATIONS
	11 LP#11	F	4.970	NO REMARKABLE OBSERVATIONS
	12 LP#12	M	5.035	NO REMARKABLE OBSERVATIONS
	13 LP#13	F	5.107	NO REMARKABLE OBSERVATIONS
14 LP#14	M	5.293	NO REMARKABLE OBSERVATIONS	
25180	1 LP# 1	M	4.901	V ECCHYMOSIS - EXTREMITIES LEFT HIND PAW
	2 LP# 2	F	4.748	NO REMARKABLE OBSERVATIONS
	3 LP# 3	M	4.794	NO REMARKABLE OBSERVATIONS
	4 LP# 4	F	4.761	NO REMARKABLE OBSERVATIONS
	5 LP# 5	M	5.225	NO REMARKABLE OBSERVATIONS
	6 LP# 6	M	4.913	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	7 LP# 7	M	5.048	NO REMARKABLE OBSERVATIONS
	8 LP# 8	M	4.769	NO REMARKABLE OBSERVATIONS
	9 LP# 9	M	4.513	NO REMARKABLE OBSERVATIONS
	10 LP#10	M	4.918	NO REMARKABLE OBSERVATIONS
	11 LP#11	F	4.849	NO REMARKABLE OBSERVATIONS
	12 LP#12	F	4.894	NO REMARKABLE OBSERVATIONS
	13 LP#13	M	5.175	NO REMARKABLE OBSERVATIONS
	14 LP#14	M	4.781	NO REMARKABLE OBSERVATIONS
15 LP#15	F	4.176	NO REMARKABLE OBSERVATIONS	
25155	1 LP# 1	M	5.840	NO REMARKABLE OBSERVATIONS
	2 LP# 2	F	5.315	NO REMARKABLE OBSERVATIONS
	3 LP# 3	F	5.198	NO REMARKABLE OBSERVATIONS
	4 LP# 4	F	5.419	NO REMARKABLE OBSERVATIONS
	5 LP# 5	F	5.545	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	6 LP# 6	M	5.463	NO REMARKABLE OBSERVATIONS
	7 LP# 7	M	5.406	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE
	8 LP# 8	F	5.132	NO REMARKABLE OBSERVATIONS
	9			EARLY (W/PLACENTAL TISSUE)
	10 LP# 9	M	5.404	NO REMARKABLE OBSERVATIONS
	11 LP#10	F	5.295	NO REMARKABLE OBSERVATIONS
12 LP#11	F	4.784	NO REMARKABLE OBSERVATIONS	

M-MALFORMATION, V-VARIATION, LP#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

500 PPM					
FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	
25155	13 LP#12	F	4.797	NO REMARKABLE OBSERVATIONS	
	14 LP#13	M	5.731	NO REMARKABLE OBSERVATIONS	
	15 LP#14	M	5.701	NO REMARKABLE OBSERVATIONS	
	16 LP#15	F	5.206	NO REMARKABLE OBSERVATIONS	
25140	1 LP# 1	F	4.792	NO REMARKABLE OBSERVATIONS	
	2 LP# 2	M	5.362	NO REMARKABLE OBSERVATIONS	
	3 LP# 3	M	4.714	NO REMARKABLE OBSERVATIONS	
	4 LP# 4	M	5.712	NO REMARKABLE OBSERVATIONS	
	5 LP# 5	M	5.427	NO REMARKABLE OBSERVATIONS	
	6 LP# 6	F	4.913	NO REMARKABLE OBSERVATIONS	
	7 LP# 7	F	4.788	NO REMARKABLE OBSERVATIONS	
	8 LP# 8	M	5.018	NO REMARKABLE OBSERVATIONS	
	9 LP# 9	M	5.059	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	10 LP#10	M	5.649	NO REMARKABLE OBSERVATIONS	
	11 LP#11	M	5.145	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	12 LP#12	M	5.504	NO REMARKABLE OBSERVATIONS	
	13 LP#13	M	5.435	NO REMARKABLE OBSERVATIONS	
14 LP#14	F	5.234	NO REMARKABLE OBSERVATIONS		
25144	1 LP# 1	F	5.324	NO REMARKABLE OBSERVATIONS	
	2 LP# 2	M	5.587	NO REMARKABLE OBSERVATIONS	
	3 LP# 3	F	5.039	NO REMARKABLE OBSERVATIONS	
	4 LP# 4	M	5.298	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	5 LP# 5	F	4.674	NO REMARKABLE OBSERVATIONS	
	6 LP# 6	F	4.732	NO REMARKABLE OBSERVATIONS	
	7 LP# 7	F	4.724	NO REMARKABLE OBSERVATIONS	
	8 LP# 8	F	5.214	NO REMARKABLE OBSERVATIONS	
	9 LP# 9	M	5.307	NO REMARKABLE OBSERVATIONS	
	10 LP#10	M	5.419	NO REMARKABLE OBSERVATIONS	
	11			EARLY(W/PLACENTAL TISSUE)	
	12 LP#11	M	5.475	NO REMARKABLE OBSERVATIONS	
	13 LP#12	F	3.891	NO REMARKABLE OBSERVATIONS	
25129	1 LP# 1	M	5.060	NO REMARKABLE OBSERVATIONS	
	2 LP# 2	M	4.955	NO REMARKABLE OBSERVATIONS	
	3 LP# 3	M	5.117	NO REMARKABLE OBSERVATIONS	
	4 LP# 4	F	4.825	NO REMARKABLE OBSERVATIONS	
	5 LP# 5	F	4.566	NO REMARKABLE OBSERVATIONS	
	6 LP# 6	M	5.140	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	7 LP# 7	F	5.078	NO REMARKABLE OBSERVATIONS	
	8 LP# 8	M	4.944	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	9 LP# 9	M	4.956	NO REMARKABLE OBSERVATIONS	
	10 LP#10	F	4.996	NO REMARKABLE OBSERVATIONS	
	11 LP#11	M	4.703	NO REMARKABLE OBSERVATIONS	
	12 LP#12	M	5.013	NO REMARKABLE OBSERVATIONS	
	13 LP#13	F	4.991	NO REMARKABLE OBSERVATIONS	
	14 LP#14	M	4.812	NO REMARKABLE OBSERVATIONS	
15 LP#15	M	4.704	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		

M-MALFORMATION, V-VARIATION, LP#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING
1000 PPM				
25138	1 LP# 1	M	4.855	NO REMARKABLE OBSERVATIONS
	2 LP# 2	M	4.881	NO REMARKABLE OBSERVATIONS
	3 LP# 3	F	4.676	NO REMARKABLE OBSERVATIONS
	4 LP# 4	M	4.977	NO REMARKABLE OBSERVATIONS
	5 LP# 5	F	4.411	NO REMARKABLE OBSERVATIONS
	6 LP# 6	F	3.990	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	7 LP# 7	M	4.455	NO REMARKABLE OBSERVATIONS
	8 LP# 8	F	4.193	NO REMARKABLE OBSERVATIONS
	9 LP# 9	F	3.943	NO REMARKABLE OBSERVATIONS
	10 LP#10	M	4.884	NO REMARKABLE OBSERVATIONS
	11 LP#11	F	4.467	NO REMARKABLE OBSERVATIONS
	12			LATE(W/FETAL TISSUE)
	13 LP#12	F	4.363	NO REMARKABLE OBSERVATIONS
	14			EARLY(W/PLACENTAL TISSUE)
	15 LP#13	M	4.821	NO REMARKABLE OBSERVATIONS
25137	1 LP# 1	M	5.414	NO REMARKABLE OBSERVATIONS
	2 LP# 2	F	5.513	NO REMARKABLE OBSERVATIONS
	3 LP# 3	M	6.240	NO REMARKABLE OBSERVATIONS
	4 LP# 4	F	5.464	NO REMARKABLE OBSERVATIONS
	5 LP# 5	F	5.392	NO REMARKABLE OBSERVATIONS
	6 LP# 6	F	5.732	NO REMARKABLE OBSERVATIONS
	7			EARLY(W/PLACENTAL TISSUE)
	8			EARLY(W/PLACENTAL TISSUE)
	9 LP# 7	M	5.920	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	10 LP# 8	M	5.641	NO REMARKABLE OBSERVATIONS
	11 LP# 9	M	5.803	NO REMARKABLE OBSERVATIONS
	12 LP#10	F	5.657	NO REMARKABLE OBSERVATIONS
	13 LP#11	F	5.286	NO REMARKABLE OBSERVATIONS
	14 LP#12	F	5.172	NO REMARKABLE OBSERVATIONS
	15 LP#13	F	5.619	NO REMARKABLE OBSERVATIONS
	16 LP#14	F	5.066	NO REMARKABLE OBSERVATIONS
	17			EARLY(W/PLACENTAL TISSUE)
	18 LP#15	M	5.878	V ECCHYMOSES - TRUNK BETWEEN SCAPULAE
25134	1 LP# 1	M	5.264	NO REMARKABLE OBSERVATIONS
	2 LP# 2	M	5.463	NO REMARKABLE OBSERVATIONS
	3 LP# 3	M	5.609	NO REMARKABLE OBSERVATIONS
	4 LP# 4	F	5.391	NO REMARKABLE OBSERVATIONS
	5 LP# 5	F	4.882	NO REMARKABLE OBSERVATIONS
	6 LP# 6	F	5.051	NO REMARKABLE OBSERVATIONS
	7 LP# 7	M	5.953	V ECCHYMOSES - TRUNK BETWEEN SCAPULAE
	CERVIX POSITION			
	8 LP# 8	F	5.438	NO REMARKABLE OBSERVATIONS
	9 LP# 9	F	5.430	NO REMARKABLE OBSERVATIONS
	10 LP#10	F	4.998	NO REMARKABLE OBSERVATIONS
	11 LP#11	F	5.042	NO REMARKABLE OBSERVATIONS
	12 LP#12	M	5.168	NO REMARKABLE OBSERVATIONS
	13 LP#13	F	4.743	NO REMARKABLE OBSERVATIONS
	14 LP#14	M	4.661	NO REMARKABLE OBSERVATIONS
	15 LP#15	F	4.491	NO REMARKABLE OBSERVATIONS
	16 LP#16	M	5.239	NO REMARKABLE OBSERVATIONS
	17 LP#17	M	4.867	NO REMARKABLE OBSERVATIONS
	18 LP#18	F	3.847	NO REMARKABLE OBSERVATIONS
25158	1 LP# 1	M	4.595	NO REMARKABLE OBSERVATIONS
	2 LP# 2	M	5.242	NO REMARKABLE OBSERVATIONS
	3 LP# 3	M	5.113	NO REMARKABLE OBSERVATIONS
	4 LP# 4	M	5.204	NO REMARKABLE OBSERVATIONS

M-MALFORMATION, V-VARIATION, LP#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	1000 PPM
25158	5 LP# 5	F	4.719	NO REMARKABLE OBSERVATIONS	
	6 LP# 6	F	4.977	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	7 LP# 7	M	4.885	NO REMARKABLE OBSERVATIONS	
	8 LP# 8	F	4.813	NO REMARKABLE OBSERVATIONS	
	9 LP# 9	M	5.070	NO REMARKABLE OBSERVATIONS	
	10 LP#10	M	5.386	NO REMARKABLE OBSERVATIONS	
	11 LP#11	F	4.763	NO REMARKABLE OBSERVATIONS	
	12 LP#12	M	4.665	NO REMARKABLE OBSERVATIONS	
	13 LP#13	M	5.034	NO REMARKABLE OBSERVATIONS	
	14 LP#14	M	4.526	NO REMARKABLE OBSERVATIONS	
25132	1 LP# 1	F	5.370	NO REMARKABLE OBSERVATIONS	
	2 LP# 2	M	5.382	NO REMARKABLE OBSERVATIONS	
	3 LP# 3	M	5.728	NO REMARKABLE OBSERVATIONS	
	4 LP# 4	F	5.713	NO REMARKABLE OBSERVATIONS	
	5 LP# 5	M	5.505	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	6 LP# 6	M	5.807	NO REMARKABLE OBSERVATIONS	
	7 LP# 7	M	5.534	NO REMARKABLE OBSERVATIONS	
	8 LP# 8	M	5.552	NO REMARKABLE OBSERVATIONS	
	9 LP# 9	F	5.347	NO REMARKABLE OBSERVATIONS	
	10			EARLY (W/PLACENTAL TISSUE)	
	11 LP#10	M	5.444	NO REMARKABLE OBSERVATIONS	
	12 LP#11	M	5.346	NO REMARKABLE OBSERVATIONS	
	13 LP#12	M	5.527	NO REMARKABLE OBSERVATIONS	
25127	1 LP# 1	F	5.327	NO REMARKABLE OBSERVATIONS	
	2 LP# 2	M	5.741	NO REMARKABLE OBSERVATIONS	
	3 LP# 3	F	5.164	NO REMARKABLE OBSERVATIONS	
	4 LP# 4	M	5.426	NO REMARKABLE OBSERVATIONS	
	5 LP# 5	F	5.470	NO REMARKABLE OBSERVATIONS	
	6 LP# 6	F	5.264	NO REMARKABLE OBSERVATIONS	
	7 LP# 7	M	5.496	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	8 LP# 8	F	5.210	NO REMARKABLE OBSERVATIONS	
	CERVIX POSITION				
	9 LP# 9	F	5.419	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	10 LP#10	M	5.707	NO REMARKABLE OBSERVATIONS	
	11 LP#11	M	5.567	NO REMARKABLE OBSERVATIONS	
	12 LP#12	M	5.463	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	13 LP#13	F	5.046	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	14 LP#14	M	5.940	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
	15 LP#15	M	5.193	NO REMARKABLE OBSERVATIONS	

M-MALFORMATION, V-VARIATION, LP#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

		1500 PPM		
FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING
25162	1 LF# 1	M	5.343	NO REMARKABLE OBSERVATIONS
	2 LF# 2	F	5.240	NO REMARKABLE OBSERVATIONS
	3 LF# 3	F	5.285	NO REMARKABLE OBSERVATIONS
	4			EARLY(W/PLACENTAL TISSUE)
	5 LF# 4	M	5.755	NO REMARKABLE OBSERVATIONS
	6 LF# 5	F	4.890	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	7 LF# 6	F	5.374	NO REMARKABLE OBSERVATIONS
	8 LF# 7	M	5.993	NO REMARKABLE OBSERVATIONS
	9 LF# 8	F	5.258	NO REMARKABLE OBSERVATIONS
	10 LF# 9	F	5.198	NO REMARKABLE OBSERVATIONS
	11 LF#10	F	5.380	NO REMARKABLE OBSERVATIONS
	12 LF#11	M	5.599	NO REMARKABLE OBSERVATIONS
	13 LF#12	F	5.206	NO REMARKABLE OBSERVATIONS
14			EARLY(W/PLACENTAL TISSUE)	
25177	1 LF# 1	M	5.315	NO REMARKABLE OBSERVATIONS
	2 LF# 2	M	5.254	NO REMARKABLE OBSERVATIONS
	3 LF# 3	M	5.349	NO REMARKABLE OBSERVATIONS
	4 LF# 4	F	5.304	NO REMARKABLE OBSERVATIONS
	5			EARLY(W/PLACENTAL TISSUE)
	6 LF# 5	F	5.281	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	7 LF# 6	F	4.657	NO REMARKABLE OBSERVATIONS
	8 LF# 7	F	4.825	NO REMARKABLE OBSERVATIONS
	9 LF# 8	M	5.134	NO REMARKABLE OBSERVATIONS
	10 LF# 9	M	4.822	NO REMARKABLE OBSERVATIONS
	11 LF#10	F	4.494	NO REMARKABLE OBSERVATIONS
	12 LF#11	F	4.909	NO REMARKABLE OBSERVATIONS
	13 LF#12	M	5.046	NO REMARKABLE OBSERVATIONS
	14 LF#13	F	4.774	NO REMARKABLE OBSERVATIONS
15 LF#14	M	5.025	NO REMARKABLE OBSERVATIONS	
25165	1 LF# 1	F	4.688	NO REMARKABLE OBSERVATIONS
	2 LF# 2	M	4.896	NO REMARKABLE OBSERVATIONS
	3 LF# 3	F	5.040	NO REMARKABLE OBSERVATIONS
	4 LF# 4	F	4.623	NO REMARKABLE OBSERVATIONS
	5 LF# 5	M	5.211	NO REMARKABLE OBSERVATIONS
	6 LF# 6	F	4.278	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE
	7 LF# 7	M	5.112	NO REMARKABLE OBSERVATIONS
	8 LF# 8	F	3.998	NO REMARKABLE OBSERVATIONS
	9 LF# 9	F	5.123	NO REMARKABLE OBSERVATIONS
CERVIX POSITION				
25168	1			EARLY(W/PLACENTAL TISSUE)
	2 LF# 1	M	5.769	NO REMARKABLE OBSERVATIONS
	3 LF# 2	F	5.582	NO REMARKABLE OBSERVATIONS
	4 LF# 3	F	5.567	NO REMARKABLE OBSERVATIONS
	5 LF# 4	F	5.449	NO REMARKABLE OBSERVATIONS
	6 LF# 5	M	5.565	NO REMARKABLE OBSERVATIONS
	7 LF# 6	F	5.478	NO REMARKABLE OBSERVATIONS
	CERVIX POSITION			
	8 LF# 7	F	5.148	NO REMARKABLE OBSERVATIONS
	9 LF# 8	F	5.441	NO REMARKABLE OBSERVATIONS
	10 LF# 9	F	5.094	NO REMARKABLE OBSERVATIONS
	11 LF#10	M	5.732	NO REMARKABLE OBSERVATIONS
	12 LF#11	F	5.566	NO REMARKABLE OBSERVATIONS
	13 LF#12	F	5.203	NO REMARKABLE OBSERVATIONS
14 LF#13	M	5.394	NO REMARKABLE OBSERVATIONS	
25176	1 LF# 1	M	5.026	NO REMARKABLE OBSERVATIONS
	2 LF# 2	M	5.013	NO REMARKABLE OBSERVATIONS

M-MALFORMATION, V-VARIATION, LF#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS
 INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	1500 PPM	
25176	3 LF# 3	F	5.216	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	F	5.160	NO REMARKABLE OBSERVATIONS		
	5 LF# 5	M	5.092	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	M	4.914	NO REMARKABLE OBSERVATIONS		
	CERVIX POSITION					
	7 LF# 7	F	5.173	NO REMARKABLE OBSERVATIONS		
	8 LF# 8	M	4.995	NO REMARKABLE OBSERVATIONS		
	9 LF# 9	F	5.359	NO REMARKABLE OBSERVATIONS		
	10 LF#10	M	5.697	NO REMARKABLE OBSERVATIONS		
	11 LF#11	F	4.903	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	12 LF#12	M	5.136	NO REMARKABLE OBSERVATIONS		
	13 LF#13	F	4.615	NO REMARKABLE OBSERVATIONS		
	14 LF#14	M	5.329	NO REMARKABLE OBSERVATIONS		
	25136	1 LF# 1	F	4.692	NO REMARKABLE OBSERVATIONS	
2 LF# 2		M	4.670	NO REMARKABLE OBSERVATIONS		
3 LF# 3		M	5.482	NO REMARKABLE OBSERVATIONS		
4 LF# 4		F	4.723	NO REMARKABLE OBSERVATIONS		
5 LF# 5		F	4.975	NO REMARKABLE OBSERVATIONS		
6 LF# 6		M	4.830	NO REMARKABLE OBSERVATIONS		
7 LF# 7		M	4.995	NO REMARKABLE OBSERVATIONS		
8 LF# 8		F	4.563	NO REMARKABLE OBSERVATIONS		
9 LF# 9		M	4.972	NO REMARKABLE OBSERVATIONS		
10 LF#10		M	5.230	NO REMARKABLE OBSERVATIONS		
CERVIX POSITION						
11 LF#11		M	4.884	NO REMARKABLE OBSERVATIONS		
12 LF#12		F	4.946	NO REMARKABLE OBSERVATIONS		
13 LF#13		M	5.129	NO REMARKABLE OBSERVATIONS		
14 LF#14		F	4.956	NO REMARKABLE OBSERVATIONS		
15 LF#15		M	5.457	NO REMARKABLE OBSERVATIONS		
16 LF#16	M	4.902	NO REMARKABLE OBSERVATIONS			
25130	1 LF# 1	F	4.361	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	M	5.151	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	M	5.514	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	M	5.535	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	5 LF# 5	F	5.034	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	F	5.202	NO REMARKABLE OBSERVATIONS		
	7 LF# 7	F	5.066	NO REMARKABLE OBSERVATIONS		
	CERVIX POSITION					
	8 LF# 8	F	5.512	NO REMARKABLE OBSERVATIONS		
	9 LF# 9	M	5.530	NO REMARKABLE OBSERVATIONS		
	10 LF#10	F	5.386	NO REMARKABLE OBSERVATIONS		
	11 LF#11	F	4.987	NO REMARKABLE OBSERVATIONS		
12 LF#12	M	5.553	NO REMARKABLE OBSERVATIONS			

M-MALFORMATION, V-VARIATION, LF#- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
 DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING	2500 PPM	
25164	1 LF# 1	F	4.181	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	F	4.725	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	F	4.755	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	F	4.872	NO REMARKABLE OBSERVATIONS		
	5 LF# 5	F	4.874	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	F	4.844	NO REMARKABLE OBSERVATIONS		
	7 LF# 7	M	5.131	NO REMARKABLE OBSERVATIONS		
	8 LF# 8	F	4.757	NO REMARKABLE OBSERVATIONS		
	9 LF# 9	F	4.574	NO REMARKABLE OBSERVATIONS		
	10 LF#10	M	5.072	NO REMARKABLE OBSERVATIONS		
	CERVIX POSITION					
	11 LF#11	F	4.916	NO REMARKABLE OBSERVATIONS		
	12 LF#12	F	5.070	NO REMARKABLE OBSERVATIONS		
	13 LF#13	M	5.468	NO REMARKABLE OBSERVATIONS		
	14 LF#14	F	5.073	NO REMARKABLE OBSERVATIONS		
15 LF#15	M	4.962	NO REMARKABLE OBSERVATIONS			
25167	1 LF# 1	M	4.841	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	F	4.585	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	F	4.531	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	M	4.942	NO REMARKABLE OBSERVATIONS		
	5 LF# 5	F	4.968	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	M	4.956	NO REMARKABLE OBSERVATIONS		
	7 LF# 7	M	4.578	NO REMARKABLE OBSERVATIONS		
	8 LF# 8	F	4.696	NO REMARKABLE OBSERVATIONS		
	9 LF# 9	F	4.534	NO REMARKABLE OBSERVATIONS		
	CERVIX POSITION					
	10 LF#10	M	5.236	NO REMARKABLE OBSERVATIONS		
	11 LF#11	F	4.668	NO REMARKABLE OBSERVATIONS		
	12 LF#12	F	4.746	NO REMARKABLE OBSERVATIONS		
	13 LF#13	F	4.626	NO REMARKABLE OBSERVATIONS		
14 LF#14	F	4.685	NO REMARKABLE OBSERVATIONS			
25143	1 LF# 1	M	4.687	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	F	4.580	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	M	3.570	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	M	4.694	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	5 LF# 5	M	4.735	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	6 LF# 6	F	4.116	NO REMARKABLE OBSERVATIONS		
	7			EARLY(W/PLACENTAL TISSUE)		
	8			EARLY(W/PLACENTAL TISSUE)		
	9			EARLY(W/PLACENTAL TISSUE)		
	CERVIX POSITION					
	10 LF# 7	F	4.235	NO REMARKABLE OBSERVATIONS		
	11 LF# 8	F	3.909	NO REMARKABLE OBSERVATIONS		
	12 LF# 9	M	4.583	NO REMARKABLE OBSERVATIONS		
	13 LF#10	M	3.964	NO REMARKABLE OBSERVATIONS		
	14 LF#11	M	4.410	NO REMARKABLE OBSERVATIONS		
	15 LF#12	M	4.643	NO REMARKABLE OBSERVATIONS		
16 LF#13	M	4.551	NO REMARKABLE OBSERVATIONS			
25154	1 LF# 1	M	5.155	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	F	4.873	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	F	4.648	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	F	5.027	NO REMARKABLE OBSERVATIONS		
	5 LF# 5	F	4.993	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	F	5.043	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
CERVIX POSITION						
7 LF# 7	M	5.160	NO REMARKABLE OBSERVATIONS			
8 LF# 8	F	5.062	NO REMARKABLE OBSERVATIONS			

M-MALFORMATION, V-VARIATION, LFS- LIVE FETUS NUMBER
 SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

PROPIONALDEHYDE: COMBINED REPEATED-EXPOSURE AND REPRODUCTIVE/
DEVELOPMENTAL TOXICITY RANGE-FINDING STUDY IN CD⁰ RATS

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS AT TIME OF LAPAROTOMY

					2500 PPM	
FEMALE	IMPLANT	SEX	WEIGHT(G)	FINDING		
25154	9 LF# 9	F	4.508	NO REMARKABLE OBSERVATIONS		
	10 LF#10	M	5.412	NO REMARKABLE OBSERVATIONS		
	11 LF#11	M	5.355	NO REMARKABLE OBSERVATIONS		
	12 LF#12	F	4.760	NO REMARKABLE OBSERVATIONS		
	13 LF#13	M	5.459	NO REMARKABLE OBSERVATIONS		
	14 LF#14	M	5.032	NO REMARKABLE OBSERVATIONS		
	15 LF#15	M	5.098	NO REMARKABLE OBSERVATIONS		
	16 LF#16	M	4.923	NO REMARKABLE OBSERVATIONS		
25151	1 LF# 1	M	4.796	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	M	4.731	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	M	4.961	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	F	4.478	NO REMARKABLE OBSERVATIONS		
	5 LF# 5	F	4.510	NO REMARKABLE OBSERVATIONS		
	6 LF# 6	M	4.739	NO REMARKABLE OBSERVATIONS		
	7 LF# 7	F	4.549	NO REMARKABLE OBSERVATIONS		
	8 LF# 8	F	4.287	NO REMARKABLE OBSERVATIONS		
	9 LF# 9	M	4.684	NO REMARKABLE OBSERVATIONS		
	10 LF#10	F	4.899	NO REMARKABLE OBSERVATIONS		
	CERVIX POSITION					
	11 LF#11	F	4.100	NO REMARKABLE OBSERVATIONS		
	12 LF#12	F	4.719	NO REMARKABLE OBSERVATIONS		
	13 LF#13	M	4.894	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	14 LF#14	F	4.467	NO REMARKABLE OBSERVATIONS		
	15 LF#15	F	3.100	NO REMARKABLE OBSERVATIONS		
	16 LF#16	M	4.929	NO REMARKABLE OBSERVATIONS		
25128	1 LF# 1	M	3.915	NO REMARKABLE OBSERVATIONS		
	2 LF# 2	F	4.330	NO REMARKABLE OBSERVATIONS		
	3 LF# 3	M	4.290	NO REMARKABLE OBSERVATIONS		
	4 LF# 4	M	4.346	NO REMARKABLE OBSERVATIONS		
	5			EARLY (W/PLACENTAL TISSUE)		
	6 LF# 5	F	4.291	NO REMARKABLE OBSERVATIONS		
	7 LF# 6	M	4.560	NO REMARKABLE OBSERVATIONS		
	8 LF# 7	M	4.310	NO REMARKABLE OBSERVATIONS		
	9 LF# 8	F	4.129	NO REMARKABLE OBSERVATIONS		
	10 LF# 9	F	4.052	NO REMARKABLE OBSERVATIONS		
	11 LF#10	F	3.958	NO REMARKABLE OBSERVATIONS		
		CERVIX POSITION				
		12 LF#11	M	4.594	NO REMARKABLE OBSERVATIONS	
		13 LF#12	F	4.017	NO REMARKABLE OBSERVATIONS	
		14			EARLY (W/PLACENTAL TISSUE)	
		15 LF#13	M	4.521	NO REMARKABLE OBSERVATIONS	
	16 LF#14	F	4.437	NO REMARKABLE OBSERVATIONS		
25159	1 LF# 1	F	4.740	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE		
	2 LF# 2	F	4.657	NO REMARKABLE OBSERVATIONS		
	3			EARLY (W/PLACENTAL TISSUE)		
	4 LF# 3	M	5.478	NO REMARKABLE OBSERVATIONS		
	5 LF# 4	M	5.483	NO REMARKABLE OBSERVATIONS		
	6 LF# 5	F	4.735	NO REMARKABLE OBSERVATIONS		
	7 LF# 6	M	5.192	NO REMARKABLE OBSERVATIONS		
	8 LF# 7	M	5.230	NO REMARKABLE OBSERVATIONS		
		CERVIX POSITION				
		9 LF# 8	M	5.498	NO REMARKABLE OBSERVATIONS	
		10 LF# 9	F	4.798	NO REMARKABLE OBSERVATIONS	
		11 LF#10	M	5.225	V ECCHYMOSIS - TRUNK BETWEEN SCAPULAE	
		12 LF#11	F	5.437	NO REMARKABLE OBSERVATIONS	
		13 LF#12	M	5.386	NO REMARKABLE OBSERVATIONS	
		14 LF#13	F	4.570	NO REMARKABLE OBSERVATIONS	
	15 LF#14	F	4.987	NO REMARKABLE OBSERVATIONS		

M-MALFORMATION, V-VARIATION, LF#- LIVE FETUS NUMBER
SEX: M-MALE, F-FEMALE, U- UNABLE TO DETERMINE SEX

Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD® Rats

Protocol, Protocol Amendment, and Protocol Deviation



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD¹ (Sprague-Dawley)
Rats

BRRC PROJECT NUMBER: 91-13-25601

SPONSOR: Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Chemicals and
Plastics Company Inc.
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center:

Cynthia D. Driscoll 10/15/91
Cynthia D. Driscoll, Ph.D. Date
Study Director

Linda J. Galisti 10/18/91
Linda J. Galisti, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

John P. Van Miller 10/15/91
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Chemicals and
Plastics Company Inc.:

Tipton R. Tyler 10/18/91
Tipton R. Tyler, Ph.D., DABT Date
Associate Director of Applied Toxicology

Division:

Richard C. Wise 10-18-91
Richard C. Wise Date
Manager, Product Safety

Union Carbide Chemicals and Plastics Company Inc.
Excellence Through Quality



OBJECTIVES

The objective of this study is to establish the concentration-response range of propionaldehyde administered by inhalation for maternal and/or developmental toxicity in CD® (Sprague-Dawley) rats. This information will be used to select appropriate exposure concentrations for use in the definitive repeated exposure study which will assess the reproductive and developmental toxicity potential of the test substance.

GENERAL INFORMATION

Sponsor Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics (UCC&P) Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

Project Monitor Tipton R. Tyler, Ph.D., DABT

Testing Facility Bushy Run Research Center, Export, PA 15632-8902

Personnel

Developmental Toxicology and Animal Care	E. R. Altman P. J. Benson, B.S. T. R. Brownfield, B.S. B. L. Butler, A.H.T., AALAS Cert. II M. A. Copeman, A.A., B.S. D. L. Falt, B.S., AALAS Cert. II
Supervisor	L. C. Fisher, B.S., AALAS Cert. III M. F. Kubena, B.S., AALAS Cert. III T. L. Neepser-Bradley, Ph.D. D. J. Tarasi, A.H.T., A.S., AALAS Cert. II
Inhalation Toxicology	I. M. Pritts, Ph. D. L. E. Lipko, AALAS Cert. II
Attending Veterinarian	M. K. Walter, DVM, Diplomate ACVP

All personnel who participate in the conduct of the study will be documented in the raw data.

<u>Starting Date of Acclimation</u>	October 14, 1991
<u>Starting Date of Test Substance Exposure</u>	October 22, 1991
<u>Proposed Date for Completion of In-Life Phase</u>	November 13, 1991
<u>Proposed Date for Submission of the Draft Final Report</u>	To be added by amendment.

Basis for the Study

Pregnant rats, 7/group, will be exposed to the test substance on gestation days (gd) 0 through 20, 6 hours/day. The study will consist of four treatment groups, 2500, 1500, 1000 and 500 ppm, and an air only, 0 ppm, control. Seven pregnant rats will be randomly assigned to each group. On gd 21, females will be euthanized, and the uterine contents will be examined grossly.

This study will be conducted in accordance with the U.S. EPA Good Laboratory Practice Regulations, 40 CFR Part 792 and Annex 2 of the OECD Guidelines for Testing Chemicals (C(81)30 (Final)).

Alteration of Design

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. BRRC reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered in jeopardy. In this event, the Sponsor shall be notified of the alteration as soon as possible, and written verification of the change will be the responsibility of the Study Director. All protocol modifications will be signed by the Study Director and a representative of the Sponsor.

METHODS

Test Substance

Chemical Name	Propionaldehyde
Source	UCC&P Texas City, Texas
CAS Registry Number	123-38-6
Sponsor Identification Number	UCCL70771/UM1275
BRRC Number	54-351A and 54-351B
Percent Active Material	Approximately 98.5% by weight (approximately 1.5% water added to shipping containers as required by DOT regulations).
Description	Water-white liquid; suffocating odor
Solubility	22% at 20°C by weight in water
Boiling Point	760 mm Hg 48°C

Stability of Test Substance	The test substance is considered to be stable under proper storage conditions. Compositional analysis of the test substance will be used as a measure of stability.
Storage Conditions	The test substance will be stored in stainless steel drums, the original containers, in a special enclosure under a nitrogen atmosphere.
Reserve Sample	Due to the nature of the test substance, a reserve sample will not be retained and stored by BRRRC.
Estimated Quantity Needed	Approximately two, 55 gallon drums of the compound will be used throughout all phases of testing. After the assigned studies have been completed, all unused test substance will be returned to the Sponsor.
Test Substance Characterization	Prior to initiation of the range-finding study and following the definitive study, a compositional analysis of the test substance will be performed by the Sponsor.
Safety	A Material Safety Data Sheet (MSDS; Attachment 1) supplied by the Sponsor will be reviewed by all personnel prior to the initiation of the study. This review will be documented. This chemical is extremely flammable; keep away from heat, sparks and flame; reactive with oxygen. Normal precautions for untested chemicals will be used. These procedures include the use of disposable paper or plastic coats or jumpsuits, hats, booties or shoe covers, and butyl or PVC coated gloves while in the animal rooms. Eye protection will include the use of safety glasses.
<u>Test Animals</u>	
Species	CrI:CD®BR rats, commonly referred to as CD® rats
Supplier	Charles River Breeding Laboratories, Portage, Michigan
Rationale	The rat is the preferred species for this type of toxicity testing. The CD® albino rat was selected due to its high fecundity and routine use in rodent reproduction and developmental toxicity studies.
Number and Sex	A total of 60 males and 60 females will be ordered from which 35 successfully mated (plug-positive) females will be selected for the study.
Age and Weight	The male rats will be approximately 70 days of age and will weigh approximately 285-350 g on scheduled animal

receipt date. Female rats will be approximately 63 days of age and 185-225 g upon arrival.

Acclimation and
Pretest
Evaluations

Shortly after their arrival at the laboratory, the animals will be transported to the room selected for the study. Once in the room, the animals will be removed from the shipping cartons and examined. All animals with evidence of disease or physical abnormalities will be discarded and their rejection from the shipment will be recorded. If an unusually large number of rats show evidence of disease or physical abnormalities, the shipment of rats will be rejected for use in the study. A total of 10 rats (5 male and 5 female) will be randomly selected for a health screen as discussed below.

All remaining rats will be housed two per cage for an acclimatization period of approximately one week. At least 24 hours prior to mating, males will be transferred to their mating cages and housed individually.

During the acclimation period, animals will be fed the same diet which will be used during the study. Animals will be observed twice daily for any overt clinical signs of disease or abnormality. Individual detailed physical examinations will be conducted twice prior to the mating period. Animals showing abnormalities deemed by the Study Director or other appropriate supervisory personnel to render the animal unacceptable for placement on the study will be sacrificed and discarded on the day observed. If an unusually large number of rats show signs of disease, the shipment of rats will be rejected for use in the study.

Rats will be weighed twice during the acclimation period. Any rat whose weight gain during this period is not considered normal for this age and strain of rats, or whose absolute body weight at the second weighing is outside 20% of the population mean for each sex, will not be considered for use in the study.

Quality
Control

Quality control will be performed within two days after the receipt of the animals. The pretest health screen will consist of a viral screen, examinations for fecal parasites, necropsy examinations, and histopathological evaluations of selected tissues. The screen will be performed on 5 animals/sex selected directly from the shipping cartons with as many cartons as possible being represented. The gross examinations will be conducted on all 10 rats selected

for the health screen. The viral screen will be conducted on five animals/sex selected from the 10 rats designated for the health screen.

The following viruses will be included in the viral screen:

Pneumonia virus of mice (PVM)
 Reovirus type 3 (Rao3)
 Kilham rat virus
 Toolen H-1
 Sendai
 Lymphocytic choriomeningitis (LCM)
 Rat coronavirus
 SDA
 Minute virus of mice (MVM)
 Mycoplasma pulmonis
 Polyoma virus
 Encephalomyelitis (CDVII)
 Mouse adenovirus FL/K87 (MAD)

Fecal examination for parasites will be conducted using a cellophane tape test on 5 animals/sex from the 10 animals selected for the prestudy screen, and by zinc sulfate flotation from cecal contents obtained at necropsy on 5 animals/sex.

Histopathology will be performed on three sacrificed animals/sex. At least the following tissues will be examined: liver, kidneys, trachea, lungs, heart, spleen, salivary glands, submandibular lymph nodes, and nasal cavities.

The purpose of this screen is to determine the suitability of the population of animals proposed for this study. Therefore, the results of this screen will be available before the study begins.

Identification

Animals shall be uniquely identified prior to initiation of the study by cage identification and ear tags. The individual animal numbers will be documented in the study records.

Colled Animals

Animals received with the initial shipment but not used in the study will be euthanized or used for training or methods development. Records will be kept documenting the fate of all animals received for the study.

Husbandry

The experiment will be carried out under standard laboratory conditions in the Chemical Hygiene Fellowship Building of BRRC. Stainless steel cages with wire mesh floors will be used throughout the study.

Stainless steel cages will be changed at least once every two weeks. Paperboard kept under each cage will be changed regularly. During the mating period, paperboard will be changed daily.

For exposures, animals will be transferred, one per cage to stainless steel wire-mesh cages. Stainless steel shelf pans will be placed under each row of cages to prevent urinary and fecal contamination of animals at lower levels.

Animal room temperature and humidity will be recorded continuously using an automatic recorder. Temperature will be maintained at 66-77°F and relative humidity will be maintained at 40-70%. The temperature and humidity will be checked by a technician at each room check and a record will be kept indicating that it was done. Appropriate corrective action will be taken whenever readings outside the specified limits are observed. If the temperature or humidity remains outside the prescribed range for more than 24 hours, the Sponsor's representative will be notified.

The accuracy of the temperature and humidity recording devices will be checked periodically and calibrated when necessary. The verification and calibration data will be recorded. Any time the continuous recording equipment is found to be malfunctioning, the temperature and humidity of the animal room will be manually measured and recorded at each room check.

Fluorescent lighting will provide illumination 12 hours per day using an automatic timer. There will be at least ten air changes per hour.

Diet

Certified Ground Rodent Chow® (#5002, Ralston Purina Company) will be available ad libitum except during exposures. The analyses of chemical composition and possible contaminants of each batch of diet will be performed by Ralston Purina Company (St. Louis, MO) and the results of their analysis will be checked by the Study Director.

Water

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum, except during exposures, by automatic watering system with demand control valves mounted on each rack. Water pressure and function of the individual cage rack systems will be checked at each room check and a record will be kept indicating it was done. Drinking water contaminant levels will be measured at regular

intervals per EPA specifications, to include the 129 "priority" pollutants, identified in the Federal Register 45 (98), Appendix D, Part 122, and shall comply with human requirements.

Study Design

Number of Groups

The study will consist of a control and four exposure groups.

Number of Animals per Group

The study will begin with 7 females/group in order to yield at least 3 pregnant females per group.

Organization

Group	Number of Female Animals	Concentration of Propionaldehyde Vapor (ppm)
Control	7	0
Low	7	500
Mid-1	7	1000
Mid-2	7	1500
High	7	2500

Mating

At approximately 10 weeks of age, virgin female rats considered to be in good health (as noted by the Study Veterinarian) will be randomly mated on a 1:1 basis to virgin male rats approximately 11 weeks of age. The observation of a copulation plug in the morning beneath the mating cage will be considered evidence of successful mating. Females observed with copulation plugs when checked in the afternoon will be removed from the study. The day the copulation plug is observed will be designated gestation day (gd) 0.

Plug-positive females will be transferred to individual study carriers for conducting exposures and individually housed for the remainder of the study. The males will be used for a single mating and then removed from the study room at the completion of the mating portion of the study.

Group Assignment

On each designated gd 0, when there are at least five successfully mated females, they will be assigned to one of five groups, using a weight stratified randomization procedure. On a day when there are less than five successfully mated females, the females for that day will not be assigned to the study.

The stratified randomization procedure will assign animals to groups such that the body weights of all groups are homogenous by statistical analysis at study initiation.

Animals not assigned to the study will be euthanized and discarded, used for training of BRRC staff or used for methods development. The fate of all animals not selected for use in this study will be documented in the raw data.

Duration of Exposures Successfully mated females will be exposed on gestation day (gd) 0 through 20, 6 hours/day.

Administration of Test Substance and Inhalation Chamber Operation

Route and Justification Animals will be administered the test substance as a vapor. The inhalation route of administration is considered to be a meaningful way to evaluate the toxicity of chemicals with the use pattern of propionaldehyde. Inhalation is a potential route of human exposure.

Exposure Chambers Five stainless steel chambers (approximately 4.3 cubic meters) with glass doors and windows for animal observations will be used. The chamber size is adequate to ensure that the total "volume" of test animals shall not exceed 5% of the volume of the test chamber. The exposure chambers are located in room 138.

Chambers will be provided with air at a flowrate of approximately 1000 liters/minute (13-14 air changes per hour) to ensure an adequate oxygen content of 19%. The rate of airflow will be monitored continuously and recorded approximately every 30 minutes. All chambers will be maintained at a slightly negative pressure to prevent any vapor from entering the room containing the chambers.

The temperature and relative humidity of the exposure chambers will be monitored continuously and recorded approximately 12 times during each exposure. Temperature will be maintained at 68-75°F (22 ± 2°C) and relative humidity will be maintained between 40 and 60%.

To compensate for any (undetected) differences in environment or test substance concentration within the chamber, all exposure cage positions will be rotated weekly. A description of the rotation will be provided in the raw data.

**Target Exposure
Concentration
Selection**

Four graduated concentration levels of the test substance as a vapor will be selected by the Sponsor, for evaluation in four groups of rats. An additional group, a concurrent control, will be placed in an inhalation chamber and exposed to air only.

**Test Vapor
Generation**

The test liquid will be metered from a piston pump into a heated glass evaporator similar in design to that described by Snellings and Dodd (1990). Temperatures in the evaporator will be maintained at the lowest level sufficient to vaporize the liquid, and will be recorded.

Test Vapor Analysis

Chamber concentration of the test substance will be determined approximately once each hour by a gas chromatographic (GC) technique. The details of the GC method will be described in the study report. The analytical monitoring system will be set to alarm at concentrations < or > 10% of the target chamber concentrations. The chamber sampling probes will be placed in the breathing zone of the animals. The daily nominal (estimated) chamber concentrations will also be determined.

**Chamber
Concentration
Distribution**

The uniformity of propionaldehyde vapor in each of the exposure chambers will be examined prior to initiating the definitive study.

At termination of the definitive study, the last container used to generate the test vapors will be returned to the Sponsor for compositional (stability) analysis.

Experimental Evaluations**Mortality
Checks and
Clinical Signs**

All females assigned to the study will be observed for mortality twice daily, 7 days/week. During the 5-day work week, the first daily mortality check will be conducted prior to exposures or before 9:00 a.m., and the second one will generally be conducted following exposures or after 2:00 p.m. On weekends, the first daily mortality check will be conducted prior to exposures or before 9:00 a.m. and the second mortality check will be conducted following exposure or, if exposures are not conducted, after noon.

Study animals will be given detailed examinations for clinical signs of toxicity once daily following exposure. Overt signs of toxicity will be monitored visually in the morning while transferring animals to the exposure cages.

Overt signs of toxicity will be monitored visually in conjunction with the afternoon mortality checks.

Observed mortality and/or clinical signs will be recorded on the day observed. Lack of clinical signs during daily detailed physical examinations will also be recorded.

Body Weight

Individual maternal body weights will be measured on gd 0, 7, 14 and 21. Body weight gains will be computed.

Food Consumption

Individual food consumption measurements will be collected for intervals gd 0-7, 7-14 and 14-21. During the course of the study, the area under the cage will be examined for food spillage during each daily room check and significant food spilled will be noted in the raw data. Significant food spillage will be defined as any amount that can be easily discerned. No effort will be made to measure spilled food. Food consumption data for animals with recorded spills will not be used in summarization of results within a particular interval.

**Dead or Moribund
Animals**

Necropsies will be performed seven days per week on all females not surviving to scheduled sacrifice in an attempt to determine the cause of death. If possible, the uterus will be examined and the status of implantation sites will be recorded. For apparently nonpregnant uteri, pregnancy status will be determined by staining with 10% ammonium sulfide (Salewski, 1964). Maternal organ weights will not be measured for animals which are found dead.

Any animal showing signs of severe debilitation or toxicity, particularly if death appears imminent, will be humanely sacrificed by carbon dioxide asphyxiation to prevent loss of tissues through autolysis. The uterus will be examined and the status of implantation sites will be recorded. For apparently nonpregnant uteri, pregnancy status will be determined by staining with 10% ammonium sulfide. Maternal organ weights (as specified for animals surviving to scheduled sacrifice) will be collected for animals which are sacrificed in extremis.

**Abortion or
Premature
Delivery**

If signs of abortion or premature delivery are observed, the animal will be euthanized by injection of pentobarbital and a complete necropsy will be performed. The uterus will be opened and examined, and site descriptions will be identified and recorded. Ovarian corpora lutea of pregnancy will be counted. Maternal organs (as specified for animals surviving to scheduled sacrifice) will be weighed. Maternal tissues will be retained in fixative only as deemed necessary by the gross findings.

**Maternal Sacrifice
and Laparotomy**

On gd 21, all surviving dams will be sacrificed by carbon dioxide asphyxiation. The order of sacrifice will be random. The maternal body cavities be opened by a midline thoracotomy. The gravid uterus, ovaries (including corpora lutea), cervix, vagina and abdominal and thoracic cavities will be examined grossly. The uterus with ovaries and oviducts attached will be externally examined for signs of hemorrhage and then removed from the peritoneal cavity and weighed. Ovaries will then be removed and corpora lutea will be counted. The liver will be removed, weighed and discarded.

The uterus will be dissected longitudinally to expose the contents. All live and dead fetuses and resorptions and their locations within the uterus will be recorded. Uteri from females that appear nonpregnant will be placed in 10% ammonium sulfide solution for confirmation of pregnancy status (Salewski, 1964).

**Fetal
Evaluations**

All fetuses designated as live will be weighed, sexed and examined for external malformations (including cleft palate) and variations and then anesthetized by hypothermia, sacrificed by decapitation and discarded. All fetuses designated as dead will be weighed, examined externally and discarded.

**Statistical
Evaluation**

The unit of comparison will be the pregnant female or the litter. Data collected for nonpregnant females and females which abort or deliver early, will not be included in the statistical analyses.

The data for continuous, parametric variables will be intercompared for the exposure and control groups by use of Levene's test for homogeneity of variance, by analysis of variance and by t-tests. The t-tests will be used, if the analysis of variance is significant, to delineate which groups differ from the control group. If Levene's test indicates homogeneous variances, the groups will be compared by an analysis of variance for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicates heterogeneous variances, the groups will be compared by an analysis of variance for unequal variances followed, when appropriate, by separate variance t-tests. For discontinuous data, the Kruskal-Wallis test followed, when appropriate, by Mann-Whitney U tests. Frequency data will be compared using Fisher's exact test. All statistical tests, except the frequency comparisons, will be performed using BMDP Statistical Software (Dixon, 1990). The frequency data tests are described in Biometry (Sokal,

R. R. and Rohlf, P. J., W. H. Freeman and Company: San Francisco, 1969). The probability value of $p < 0.05$ (two-tailed) will be used as the critical level of significance for all tests.

RECORDS

All raw data and reports from this study will be retained by BRRC for at least 10 years after completion of the study. Tissues preserved in fixative will be retained for at least five years. Paraffin blocks and tissue slides, if any, will be retained indefinitely.

Prior to discarding any of the above data or materials, the Sponsor will be contacted and given the option of obtaining it or arranging for continued storage. All data and materials mentioned above will remain the sole property of the Sponsor and can be removed from BRRC at the Sponsor's discretion.

REPORT

Draft Data Summary

An unaudited draft data summary covering all parameters evaluated in the study will be prepared and issued approximately one week after the completion of the terminal sacrifice. Data on continuous variables will be summarized on tables as means and standard deviations while data on discrete variables will be summarized on incidence tables. Narratives will be included where necessary. The purpose of this report will be to provide statistically evaluated draft summary data for use in selection of exposure concentrations for use in a definitive repeated-exposure and reproductive/developmental toxicity screen with this compound.

Draft Final Report

A draft of the final report will be submitted to the Sponsor within four months after the completion of the terminal sacrifice. This report will be a comprehensive report which will include all information necessary to provide a complete and accurate description and evaluation of the test procedures and results. It will include: a summary; appropriate text discussions of the experimental design, materials and methods and results; and summary mean or incidence tables of maternal in-life and necropsy data and fetal evaluations.

Final Report

The draft final report will be reviewed by the Sponsor, and comments on the report will be provided to BRRC within six weeks from the date of submission of the draft version. BRRC will consider these comments in preparing the final report. Assuming the Sponsor's comments are received at the specified time and no major revisions are required, BRRC will submit a final report within twelve weeks of issuance of the draft report.

The final report will be audited by the QA department and contain a signed quality assurance statement. In addition, it will contain appendices with individual animal data and other pertinent information. Two copies of the final report will be submitted to the Sponsor.

ANIMAL USE POLICY

It is the goal of BRRRC, through the establishment and activities of the Institutional Animal Care and Use Committee (IACUC), to comply with the U.S. Animal Welfare Act and the subsequent rules promulgated by the U.S. Department of Agriculture and in effect on the date of this protocol. It has been determined that the work described herein minimizes the number of animals used, is necessary, and uses the most appropriate species and strain in order to provide meaningful results and the most useful information for comparative purposes relative to previous studies. Furthermore, this study will be conducted humanely, and to the best of our knowledge, neither unnecessarily duplicates any previous work, nor can it be accomplished using currently available, validated non-animal models.

GOOD LABORATORY PRACTICE COMPLIANCE

The Bushy Run Research Center, through the administration of a quality assurance program by the Good Laboratory Practices Committee and Quality Assurance Unit, assures compliance of all phases of toxicological studies conducted at the Bushy Run Research Center with existing regulations and generally accepted good laboratory practices.

The study will be subjected to periodic inspections and the final report will be reviewed by the BRRRC Quality Assurance Unit. All quality assurance inspection records and the Master Schedule will be made available to the Sponsor during Sponsor visits.

REFERENCES

Organization for Economic Cooperation and Development (OECD) (1981). OECD Principles of Good Laboratory Practice, C(81)30(Final).

Proposed OECD Guidelines for Testing of Chemicals (1990). Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test.

Salewski, E. (1964). Fabermethode Zum Macroscopischen Nachweis Von Implantation-Stellen am Uterus der Ratte. Naunyn-Schmeidebergs, Arch. Exp. Pathol. Pharmacol. 247, 367.

Bokal, R. R. and F. J. Rohlf (1969). Biometry, W. H. Freeman and Co., San Francisco, pp 369-371, 299-340, 370-372, 589-595.

ATTACHMENT 1

PAGE 1

FOR INTERNAL USE ONLY

UNION CARBIDE CORPORATION
Solvents and Coatings Materials Division

MATERIAL SAFETY DATA SHEET

EFFECTIVE DATE: 08/24/90

Union Carbide urges each customer or recipient of this MSDS to study it carefully to become aware of and understand the hazards associated with the product. The reader should consider consulting reference works or individuals who are experts in ventilation, toxicology, and fire prevention, as necessary or appropriate to use and understand the data contained in this MSDS.

To promote safe handling, each customer or recipient should: (1) notify its employees, agents, contractors and others whom it knows or believes will use this material of the information in this MSDS and any other information regarding hazards or safety; (2) furnish this same information to each of its customers for the product; and (3) request its customers to notify their employees, customers, and other users of the product of this information.

I. IDENTIFICATION

PRODUCT NAME: PROPIONALDEHYDE
 CHEMICAL NAME:
 Propionaldehyde
 CHEMICAL FAMILY: Aldehydes
 FORMULA: C₃H₆O
 MOLECULAR WEIGHT: 58.08
 SYNONYMS: Propanal; Propylaldehyde
 CAS # AND 123-38-6
 CAS NAME: Propanal

II. PHYSICAL DATA

BOILING POINT, 760 mm Hg: 48 C (113.4 F)
 SPECIFIC GRAVITY(H₂O = 1): 0.7982
 FREEZING POINT: -80 C (-112 F)
 VAPOR PRESSURE (T 20°C): 258 mm Hg
 VAPOR DENSITY (air = 1): 2.0
 EVAPORATION RATE
 (Butyl Acetate = 1): 19.9
 SOLUBILITY IN WATER by wt: 22X @ 20 C
 APPEARANCE AND ODOR: Water-white liquid; suffocating odor
 PERCENT VOLATILES (by volume): 100

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 EMERGENCY PHONE NUMBER: 1-800-UCC-HELP (Number available at all times)

UNION CARBIDE CORPORATION
 Solvents and Coatings Materials Division
 39 Old Ridgebury Road, Danbury, Ct. 06817-0001

ATTACHMENT 1 (Continued)

PAGE 2 FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

III. INGREDIENTS

MATERIAL	%	TLV (Units)	Hazard
Propionaldehyde (CAS #123-38-6)	100	None established	Harmful if inhaled; eye irritant, flca

IV. FIRE AND EXPLOSION HAZARD DATA**FLASH POINT**

<0 F (<-18 C) Tag Closed Cup; <0 F (<-18 C) Tag Open Cup

FLAMMABLE LIMITS IN AIR, by volume:

LOWER: 2.6
UPPER: 17.0

EXTINGUISHING MEDIA:

Apply alcohol-type or all-purpose-type foams by manufacturer's recommended techniques for large fires. Use CO2 or dry chemical media for small fires.

SPECIAL FIRE FIGHTING PROCEDURES:

Use water spray to cool fire-exposed containers and structures. Use water spray to disperse vapors; reignition is possible. Use self-contained breathing apparatus and protective clothing. Use remote spray monitors or fight fire from behind shields.

UNUSUAL FIRE AND EXPLOSION HAZARDS:

Vapors form from this product and may travel or be moved by air currents and ignited by pilot lights, other flames, sparks, heaters, electrical equipment, static discharges or other ignition sources at locations distant from product handling point.

Vapors may settle in low or confined areas, or travel a long distance to an ignition source and flash back explosively.

This material may produce a floating fire hazard.

ATTACHMENT 1 (Continued)

PAGE 3

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

V. HEALTH HAZARD DATA**EXPOSURE LIMIT(S):**

None established by ACGIH or OSHA.

EFFECTS OF SINGLE OVEREXPOSURE**SWALLOWING:**

Moderately toxic. Severely irritating to the gastrointestinal tract causing a burning sensation in the mouth and throat, nausea, headache, dizziness, abdominal discomfort, vomiting and diarrhea.

SKIN ABSORPTION:

No evidence of adverse effects from available information.

INHALATION:

Vapors may be irritating to the respiratory tract. High concentrations may cause headache, nausea, vomiting, coughing, and difficulty breathing, narcosis, and may result in the inhalation of potentially lethal amounts of acetic acid.

SKIN CONTACT:

May cause slight irritation, seen as mild local redness.

EYE CONTACT:

Causes severe irritation, seen as marked excess redness and swelling of the conjunctiva.

EFFECTS OF REPEATED OVEREXPOSURE:

Repeated or prolonged exposure may result in the development of dermatitis.

MEDICAL CONDITIONS AGGRAVATED BY OVEREXPOSURE:

Breathing of vapor and/or mist may aggravate asthma and inflammatory or fibrotic pulmonary disease.

SIGNIFICANT LABORATORY DATA WITH POSSIBLE RELEVANCE TO HUMAN**HEALTH HAZARD EVALUATION:**

Rats exposed to 1300 ppm for six days experienced liver damage.

OTHER EFFECTS OF OVEREXPOSURE:

None currently known.

EMERGENCY AND FIRST AID PROCEDURES:**SWALLOWING:**

If patient is conscious and has a gag reflex, give two glasses of water and induce vomiting. Call a physician immediately.

SKIN:

Immediately flush skin with plenty of water while removing contaminated clothing and shoes. Obtain medical attention. Wash clothing before wearing again. Discard shoes.

INHALATION:

Remove to fresh air. Give artificial respiration if not breathing. Oxygen may be given by qualified personnel if breathing is difficult.

ATTACHMENT 1 (Continued)

PAGE 4

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONAL DEHYDE

Obtain medical attention.

EYES:

Immediately flush eyes thoroughly with water and continue washing for at least 15 minutes. Obtain medical attention, preferably from an ophthalmologist, urgently.

NOTES TO PHYSICIAN:

There is no specific antidote. Treatment of overexposure should be directed at the control of symptoms and the clinical condition of the patient.

VI. REACTIVITY DATA**STABILITY:** Stable**CONDITIONS TO AVOID:**

Avoid contamination with basic materials. Contamination with basic materials (examples: sodium hydroxide, caustic soda, amines, ammonia, etc.) can result in a rapid exothermic reaction.

Avoid contamination with strong mineral acids:

Contamination with strong mineral acids can result in a rapid exothermic reaction.

Avoid air (oxygen):

Contact with air results in carboxylic acid formation. Oxidation can also cause formation of hazardous peroxides or peracids.

INCOMPATIBILITY (MATERIALS TO AVOID):

Alcohols, alkalies, amines, ammonia, caustics, halogen-containing compounds, oxygen, strong mineral acids.

HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS:

Burning will produce carbon monoxide and/or carbon dioxide.

Carbon monoxide is highly toxic if inhaled; carbon dioxide in sufficient concentrations can act as an asphyxiant.

HAZARDOUS POLYMERIZATION: MAY OCCUR**CONDITIONS TO AVOID:**

May react with evolution of heat in the presence of alkalies, amines, and acids.

VII. SPILL OR LEAK PROCEDURES**STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED**

Eliminate sources of ignition. Wear suitable, protective equipment; avoid contact with liquid and vapors. Collect for disposal. Highly toxic to aquatic life. Avoid discharge to sewers or waterways.

HABYDISPOSAL METHOD:

Incinerate in a furnace where permitted under appropriate Federal, State and local regulations. This product can be toxic to the microorganisms in a

ATTACHMENT 1 (Continued)

PAGE 5

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

wastewater treatment plant; however, a solution of about 10 ppm concentration was found to be biodegradable in laboratory studies.

VIII. SPECIAL PROTECTION INFORMATIONRESPIRATORY PROTECTION (SPECIFY TYPE):

Self-contained breathing apparatus in high vapor concentrations.

VENTILATION:

This product should be stored and handled in vapor-tight equipment, under an atmosphere of oxygen-free nitrogen. When this is done, general (mechanical) room ventilation should be satisfactory. Special, local ventilation is needed at points where vapors can be expected to escape to the workplace air.

PROTECTIVE GLOVES:

Butyl or PVC coated

EYE PROTECTION:

Monogoggles

OTHER PROTECTIVE EQUIPMENT:

Eye bath, safety shower

IX. SPECIAL PRECAUTIONSPRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE:

DANGER! Extremely Flammable.
Harmful if inhaled.
Causes eye irritation.

Keep away from heat, sparks, and flame.
Avoid breathing vapor.
Avoid contact with eyes.
Keep container closed.
Use with adequate ventilation.
Wash thoroughly after handling.

FOR INDUSTRY USE ONLYOTHER PRECAUTIONS:

STORAGE: Reacts with oxygen; store under oxygen-free nitrogen.
(See Incompatibility).

ATTACHMENT 1 (Continued)

PAGE 4

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

PROCESS HAZARD: Sudden release of hot organic chemical vapors or mists from process equipment operating at elevated temperature and pressure, or sudden ingress of air into vacuum equipment, may result in ignitions without the presence of obvious ignition sources. Published "autoignition" or "ignition" temperature values cannot be treated as safe operating temperatures in chemical processes without analysis of the actual process conditions.

Any use of this product in elevated-temperature processes should be thoroughly evaluated to establish and maintain safe operating conditions. Further information is available in a technical bulletin entitled "Ignition Hazards of Organic Chemical Vapors."

TRANSFER HAZARD: Vapors of this product may be ignited by static sparks. Use proper bonding and grounding during liquid transfer as described in National Fire Protection Association document NFPA 77.

X. REGULATORY INFORMATIONSTATUS ON SUBSTANCE LISTS:

THE CONCENTRATIONS SHOWN ARE MAXIMUM OR CEILING LEVELS (WEIGHT %) TO BE USED FOR CALCULATIONS FOR REGULATIONS. TRADE SECRETS ARE INDICATED BY "TS".

FEDERAL EPA

COMPREHENSIVE ENVIRONMENTAL RESPONSE, COMPENSATION, AND LIABILITY ACT OF 1980 (CERCLA) REQUIRES NOTIFICATION OF THE NATIONAL RESPONSE CENTER OF RELEASE OF QUANTITIES OF HAZARDOUS SUBSTANCES EQUAL TO OR GREATER THAN THE REPORTABLE QUANTITIES (RQs) IN 40 CFR 302.4.

COMPONENTS PRESENT IN THIS PRODUCT AT A LEVEL WHICH COULD REQUIRE REPORTING UNDER THE STATUTE ARE:
None

Superfund Amendments and Reauthorization Act of 1986 (SARA) Title III requires Emergency Planning Based on Threshold Planning Quantities (TPQs) and release Reporting Based on Reportable Quantities (RQs) in 40 CFR 233 (Used for SARA 302, 311 AND 312).

Components Present in this Product at a level which could require Reporting under the statute are:
None

SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT OF 1986 (SARA) TITLE III REQUIRES SUBMISSION OF ANNUAL REPORTS OF RELEASE OF TOXIC CHEMICALS THAT APPEAR IN 40 CFR 372 (FOR SARA 312). THIS INFORMATION MUST BE INCLUDED IN ALL MSDS THAT ARE COPIED AND DISTRIBUTED FOR THIS MATERIAL.

COMPONENTS PRESENT IN THIS PRODUCT AT A LEVEL WHICH COULD REQUIRE REPORTING UNDER THE STATUTE ARE:

CHEMICAL	CAS NUMBER	UPPER BOUND CONCENTRATION %
Propionaldehyde	123-24-6	100

ATTACHMENT 1 (Continued)

PAGE 7 FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONALDEHYDE

STATE RIGHT-TO-KNOW

CALIFORNIA PROPOSITION 65

This product does not contain materials which the State of California has found to cause cancer, birth defects, or other reproductive harm.

Massachusetts 105 CMR 670.000 Right-to-know, Substance List (MSL) Hazardous Substances and Extraordinarily Hazardous Substances on the MSL must be identified when present in products.

Components present in this product at a level which could require reporting under the statute are:

HAZARDOUS SUBSTANCES (=) 12)

CHEMICAL	CAS NUMBER	UPPER BOUND CONCENTRATION %
Propionaldehyde	123-38-6	100

Pennsylvania Right-to-know, Hazardous Substance List Hazardous Substances and Special Hazardous Substances on the List must be identified when present in products.

Components present in this product at a level which could require reporting under the statute are:

HAZARDOUS SUBSTANCES (=) 12)

CHEMICAL	CAS NUMBER	UPPER BOUND CONCENTRATION %
Propionaldehyde	123-38-6	100

TSCA INVENTORY STATUS

The ingredients of this product are on the TSCA inventory.

CALIFORNIA RULE 443.1 VOC'S:

VOC 797 g/l; Vapor pressure 258 mm Hg @ 20 C

OTHER REGULATORY INFORMATION:

None

NOTE

The opinions expressed are those of qualified experts within Union Carbide. We believe that the information contained is current as of the date of this Material Safety Data Sheet. Since the use of this information and of these opinions and the conditions of the use of the product are not within the control of Union Carbide, it is the user's obligation to determine the conditions of safe use of the product.

ATTACHMENT 1 (Continued)

PAGE 8

FOR INTERNAL USE ONLY

PRODUCT NAME: PROPIONYL DEHYDRATE

DATE: 08/29/90

REVISION DATE: 08/29/90

REVISED SECTION:

Section III: INGREDIENTS CORRECTION

PRODUCT: 70771

F NUMBER: C02220

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BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4801

PROTOCOL AMENDMENT 1

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD¹ Rats


BRRC PROJECT NUMBER: 91-13-25601


SPONSOR: Solvents and Coatings Materials Division
Union Carbide Chemicals and
Plastics Company Inc.
39 Old Ridgebury Road
Danbury, CT 06817-0001

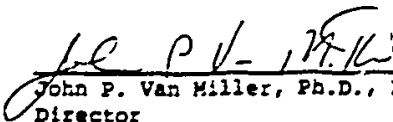
TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Chemicals and
Plastics Company Inc.
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

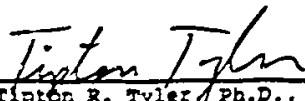
Bushy Run Research Center:


Cynthia D. Driscoll, Ph.D. 7/14/92
Study Director Date



Linda J. Calista, B.S. 7/21/92
Manager, Good Laboratory Date
Practices/Quality Assurance


John P. Van Miller, Ph.D., DABT 7/21/92
Director Date

Union Carbide Chemicals
and Plastics Company Inc.:


Tipton R. Tyler, Ph.D., DABT 7/31/92
Associate Director of Applied Toxicology Date

Division:


Richard C. Wise 8-3-92
Manager, Product Safety Date

Union Carbide Chemicals and Plastics Company Inc.
Excellence Through Quality



The protocol is amended as follows:

Item 1

Location of Protocol Deletion Page 1, Title

Description of Protocol Deletion (Sprague-Dawley)

Rationale The parenthetical designation of (Sprague-Dawley) in reference to Charles River CD® rats has been removed in order to accurately reflect the strain designation as provided by the supplier.

Item 2

Location of Protocol Deletion Page 2, Objectives

Description of Protocol Deletion (Sprague-Dawley)

Rationale See rationale for Item 1.

Item 3

Location of Protocol Change Page 3, Sponsor Identification Number

Description of Protocol Change Change DCC70771/UN1275 to T-1258

Rationale The incorrect number was listed in the range-finder protocol.

Item 4

Location of Protocol Deletion Page 4, Supplier

Description of Protocol Deletion Breeding

Rationale The correct name of the supplier is Charles River Laboratories.

reprotos\protocol\APPROVED
July 14, 1992

PROTOCOL DEVIATION

TITLE: Propionaldehyde: Combined Repeated-Exposure and Reproductive/
Developmental Toxicity Range-Finding Study in CD² Rats

BRRC PROJECT NUMBER: 91-13-25601

The following deviations from the written protocol for this study or from BRRC Standard Operating Procedures occurred during this study:

1. In the protocol, it was stated that the date for submission of the Draft Final Report would be added to the protocol by amendment. The Draft Final Report was issued on June 17, 1992, but an amendment was not written.

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