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Re: For Your Information Submission:

The enclosed information is submitted on behalf of Dow Corning Corporation, Midland, Michigan, 48686-0994, on a For-Your-Information (FYI) basis as a follow-up to submissions made concerning decamethylcyclopentasiloxane (DMCPS), which chemical substance was the subject of a health and safety data rule issued under Section 8(d) of the Toxic Substances Control Act (TSCA) and with an effective date of June 14, 1993 (sunset date June 30, 1998), as codified at 40 CFR 716 (Health and Safety Data Reporting). The information presented in this submission was generated as part of our Siloxane Research Program. This program was the subject of a memorandum of understanding, dated April 9, 1996 between Dow Corning and EPA.

Listed Chemical Substance:

541-02-6 Decamethylcyclopentasiloxane (DMCPS, D₅)

Final Study Report:

Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study

Dow Corning Corporation
2004-I0000-54669
December 21, 2004

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Manufacturer:

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For purposes of this TSCA For-Your-Information (FYI) submission, the general INTERNAL designation on the attached health and safety report is waived by Dow Corning.

If you require further information regarding this submission, please contact Michael Thelen, Manager of U.S. EPA Regulatory Affairs, at 989-496-4168 or at the address provided herein.

Sincerely,

A handwritten signature in black ink, appearing to read "Kathleen P. Plotzke". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

Kathleen P. Plotzke
Director, Health and Environmental Sciences
(989) 496-8046

**DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT**

Report No.: 2004-10000-54669

Title: **Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study**

Study No.: 8631

Test Article: Decamethylcyclopentasiloxane

Study Director: Paul A. Jean, Ph.D.
Senior Toxicology Specialist

Sponsor: Dow Corning Corporation
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Sponsor Representative: Steven D. Crofoot, M.S.
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Study Completion Date: December 21, 2004

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ABSTRACT

Decamethylcyclopentasiloxane (D₅) is a low molecular weight cyclic siloxane with both industrial and commercial applications. Repeated exposure to D₅ vapor has been shown to induce a reversible increase in liver weight and a modest induction of cytochrome P450 enzymes in rats. The primary objective of this study was to evaluate liver and thyroid cell proliferation and liver hypertrophy in rats after repeated exposure to 160 ppm D₅ vapor. Female Fischer 344 rats were exposed to D₅ vapor by whole body inhalation for 6 hr/day; 5 days/week for up to 4 weeks. A separate group of female Fischer 344 rats served as a positive control group and were provided drinking water containing phenobarbital (PB; 0.05% w:v). Cell proliferation was evaluated by immunohistochemical analysis of 5'-bromo-2-deoxyuridine (BrdU) incorporation. Liver hypertrophy was determined by evaluating the number of hepatocellular nuclei present in a fixed microscopic field size relative to controls. Alza® osmotic mini pumps (2ml, 10µl/hr) containing BrdU (20 mg/ml) were implanted (subcutaneous) 6 days prior to necropsy. Animals from each treatment group (0 and 160 ppm D₅, 0.05% PB) were euthanized on study days 6, 13, and 27. Liver and thyroid tissues were collected, weighed, sectioned, and processed for subsequent immunohistochemical analysis.

Exposure to 160 ppm D₅ produced a transient increase in liver weight, hepatocellular hyperplasia, and hepatocellular hypertrophy. Liver weight (liver-to-body weight ratio) was increased 12%(11%) and 11%(9%) after 1 and 2 five-day exposure periods, respectively. Liver weight was not different from control after 4 five-day exposure periods. Similarly, exposure to 160 ppm D₅ for 1 five-day period produced a 3.5-fold increase in hepatocellular hyperplasia and significant hepatocellular hypertrophy in the centrilobular region. Hepatocellular hyperplasia and hypertrophy were at or near control levels after 2 and 4 five-day exposure periods.

Exposure to 160 ppm D₅ for 1, 2, and 4 five-day periods had no effect on thyroid weight. Thyroid cell hyperplasia was slightly increased relative to controls (1.7 to 1.9-fold) after each of the exposure periods. Statistical significance was achieved only for increases after 2 and 4 five-day exposure periods.

The effects of administration of the positive control agent, phenobarbital, were as expected. Liver weight was increased approximately 30% after 1, 2 and 4 weeks of treatment. The increase in liver weight was accompanied by a burst of hepatocellular hyperplasia during the first five-day exposure period. Hepatocellular hyperplasia was not different from control with continued PB administration. Centrilobular hepatocellular hypertrophy was significantly increased at each of the time points.

Phenobarbital administration produced a significant increase in thyroid weight that, at four weeks, is greater than can be accounted for by increased body weight. The increase in thyroid weight at four weeks was accompanied by a statistically significant increase in thyroid cell hyperplasia.

This study has demonstrated that repeated inhalation exposure to 160 ppm D₅ vapor can cause a modest and non-sustained increase in liver weight, a burst of hepatocellular proliferation and centrilobular hypertrophy in female Fischer 344 rats. Exposure to D₅ had no effect on thyroid weight even though there was a slight increase in thyroid cell proliferation observed after 2 and 4 five-day exposure periods.

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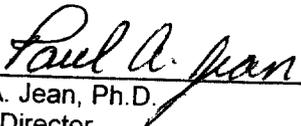
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GLP COMPLIANCE STATEMENT

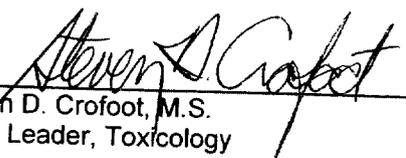
The work described in this report entitled "**Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) On Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study**" (Dow Corning Corporation study number: 8631) was carried out using the best available scientific methodology, and procedures were followed to assure accurate, high quality results. However, this non-regulated study was *not* conducted to meet all of the requirements described in Good Laboratory Practices Regulations such as those documented in the Federal Register 40 CFR Part 792.



Paul A. Jean, Ph.D.
Study Director



Date



Steven D. Crofoot, M.S.
Team Leader, Toxicology



Date

STUDY INFORMATION

Study Initiation Date:	31 October 1995
Experimental Start Date:	7 November 1995
Experimental Termination Date:	14 June 2004
Study Completion Date:	December 21, 2004
Study Director:	Paul A. Jean, Ph.D.
Sponsor:	Dow Corning Corporation 2200 West Salzburg Rd. Midland, Michigan 48686
Sponsor Representative:	Steven D. Crofoot, M.S. Team Leader, Toxicology

OBJECTIVE

The principle objective of this study was to evaluate the effects of repeated whole-body vapor inhalation exposure of female Fischer 344 rats to decamethylcyclopentasiloxane (D₅) on liver and thyroid cell proliferation and liver hypertrophy.

TEST, CONTROL, REFERENCE ARTICLE INFORMATION

1. Test Article

- Identification: Decamethylcyclopentasiloxane
Supplied as Dow Corning® 1693 Fluid
- Lot Number: WCO15338
- CAS Number: 541-02-6
- Source: Dow Corning Corporation
- Physical Description: Liquid
- Stability: Chemically Stable
- Purity: 99.3%
- Solubility: Tetrahydrofuran, Hexane, Toluene
- Chemical Characterization: Dow Corning Report: 1997-I0000-43682
- Expiration Date: 6 June 1999
- Storage: Room Temperature
- Archive Requirements: A sample was collected and archived within Dow Corning Corporation's HES Archive Facility

2. Positive Control Article

- Identification: Phenobarbital, sodium salt
- Lot Number: 122HO143
- CAS Number: 50-06-6
- Source: Sigma Chemical Company
St. Louis, MO
- Physical Description: White powder
- Stability: Chemically Stable
- Purity: As supplied
- Solubility: Not applicable
- Chemical Characterization: Material was used as supplied
- Expiration Date: 1 June 1999
- Storage: Room Temperature
- Archive Requirements: A sample was collected and archived within Dow Corning Corporation's HES Archive Facility

ROUTE OF EXPOSURE

During this study, D₅ was administered via whole-body vapor inhalation exposure. Exposures were for 6 hr/day, 5 days/week for up to 4-weeks. Five-day exposure periods were separated by two-day non-exposure periods.

Phenobarbital was administered as a drinking water additive at a known tumor-promoting dose (0.05% w/v). Administration was continuous over the course of the study in contrast to the 5 day per week D₅ exposure periods. Water consumption was monitored each time water bottles were changed in order to estimate the amount of phenobarbital consumed and to ensure that the presence of phenobarbital in the drinking water would not make the water less palatable.

TEST SYSTEM

1. Species: Rattus norvegicus
2. Strain: Fischer 344
3. Source: Charles River Breeding Laboratories, Inc.
Raleigh, North Carolina
4. Age at experimental start: ≈8 weeks
5. Body Weight at experimental start: 150 – 170 g
6. Sex and number placed on study: Female; 10 rats/group; 9 groups
7. Identification Method: Each animal received a Q# upon receipt. After randomization animals selected for use were uniquely identified by a Monel® metal ear tag displaying the animal number. Individual cage labels were used to display the animal number, group number, study number, exposure level, sex, species, strain, Study Director, exposure initiation date, and in-life phase termination date.

METHOD OF EUTHANASIA

All animals were anesthetized with CO₂ (approximately 20-30 seconds) and then exsanguinated.

JUSTIFICATION FOR SELECTION OF TEST SYSTEM

The Fischer 344 rat is recognized as an appropriate animal model for toxicity studies and represents a widely used strain for which significant historical data are available. In addition, the Fischer 344 rat has been used in previous studies of D₅. Therefore, it was appropriate to use this strain to maintain consistency and allow for cross study-comparisons. Females were chosen rather than males because they have historically demonstrated greater degrees of liver enlargement following repeated inhalation exposure to D₅. Ten animals (N=10) per group were determined to be sufficient based on power analysis and observations made in previous studies.

METHOD OF RANDOMIZATION

Upon release from quarantine, animals were weighed and then randomized by weight stratification into test groups using a table of random numbers generated by Microsoft® Excel Version 5.0. Animals outside ± 20 percent of the mean body weight for the group being randomized were excluded. After randomization, test animals were ear tagged and cage labels with group assignments and other pertinent data were placed on the outside of each cage.

HOUSING AND MAINTENANCE (HUSBANDRY)

1. Housing Requirement:
All animals were individually housed in clean suspended wire-mesh cages (7" X 10" X 7") during the quarantine and in-life phase of the study. Before each exposure, animals were transferred into cages designed for placement within the exposure chambers. Following the exposure period, the animals were returned to their original cages. Cages used during non-exposure periods were elevated above Bed-O'Cobs® bedding. The bedding was changed at least twice a week. The cages were subjected to routine cleaning at a frequency consistent with the Animal Resource Department SOPs. During the in-life portion of the study the animals were located in animal room 217 within Dow Corning Corporation's Health and Environmental Sciences building.
2. Environmental Conditions:
Environmental controls were set to maintain room temperature between 64-79°F and relative humidity at 30-70 percent. Air handling units were set to provide approximately 10-15 air changes per hour. Fluorescent lighting controlled by light timers provided illumination for a 12-hour light/dark cycle (~6:00 a.m.-6:00 p.m.). Temperature and relative humidity were monitored continuously and the light cycle was checked at least once a week.

3. Basal Diet:

Purina® Certified Rodent Chow® #5002 was offered *ad libitum* (except during chamber exposures) during the study. Analysis of the certified feed for the presence of nutritional components, heavy metals, and pesticides was performed and provided by the manufacturer. The low levels of contaminants detected were typical of laboratory animal feed and deemed acceptable.

4. Drinking Water:

Reverse osmosis purified water was available *ad libitum* (except during chamber exposure) upon arrival at the testing facility and throughout conduct of the study. Water bottles were changed at least twice a week. Animals in groups 3A-3C were administered phenobarbital in their drinking water. Water consumption was monitored to ensure that the animals receiving phenobarbital in their water found it to be palatable and were drinking normally.

ANIMAL RECEIPT AND QUARANTINE

Upon receipt, each animal was given a general health exam as it was transferred from the shipping carton to the quarantine cages. All study animals were quarantined for seven days. During the quarantine period each animal was observed twice daily during the week, and once a day on weekends, for changes in general appearance and behavior.

ANIMAL WELFARE ACT COMPLIANCE

Animal use in this study was in compliance with all applicable sections of the final rules of the Animal Welfare Act regulations (9 CFR): parts 1, 2, and 3.

EXPERIMENTAL DESIGN

Animals were randomized into three groups, each with three subgroups as follows, group 1A-1C (controls), group 2A-2C (160 ppm D₅), and group 3A-3C (0.05% PB). On study day 0, 7 and 21 animals in subgroups "A", "B" and "C", respectively, were anesthetized with isoflurane, prepped for aseptic surgery, and fitted with a mini osmotic pump. Each pump was filled with 20 mg/ml of 5'-bromo-2-deoxyuridine (BrdU) and surgically placed under the skin for continuous subcutaneous administration of BrdU. Exposure to filtered room air (groups 1A-1C), D₅ (groups 2A-2C), and PB (groups 3A-3C) began for all animals on study day 1. Animals in groups 3A-3C were placed in the inhalation chamber and exposed to filtered room air in the same manner as the control animals. On study day 6, 13, and 27 subgroup "A", "B", and "C" animals were euthanized, respectively. Liver, lungs, brain, thyroid and a section of duodenum were collected from each animal. Organ weights were determined for the liver, lungs, brain and thyroid (after fixation). The thyroid/parathyroid, lungs, duodenum section and one section from the median, left and right lateral lobes of the liver were placed in 10% formalin for histological evaluation. An assessment of cell proliferation was then conducted on the fixed tissues (liver (medial lobe only) and thyroid) following standardized immunohistochemical methodologies (BrdU staining and analysis). Liver hypertrophy was evaluated microscopically. Body weight and consumption of food and water were monitored weekly. Clinical observations were conducted daily. The lungs collected from each animal at necropsy were processed into slides and stained for BrdU analysis. No staining was observed in the preliminary evaluation of these slides. Lung tissue was not evaluated further.

Group/subgroup	Treatment	Route	N
1A	Air	Inhalation	10
1B	Air	Inhalation	10
1C	Air	Inhalation	10
2A	160 ppm D ₅	Inhalation	10
2B	160 ppm D ₅	Inhalation	10
2C	160 ppm D ₅	Inhalation	10
3A	Phenobarbital	Inhalation	10
3B	Phenobarbital	Drinking Water	10
3C	Phenobarbital	Drinking Water	10
		Drinking Water	10

TEST ARTICLE PREPARATION AND ANALYSIS

Decamethylcyclopentasiloxane vapor generation was performed following standard methodologies. Test article was metered into a heated glass J-tube for vaporization. Carrier gas (filtered air) was passed at a controlled rate through the J-tubes. The air/vapor mixture exiting the J-tube was directed into the inlet port at the top of the 450-Liter Rochester style chambers where it mixed with chamber make-up air to achieve target chamber vapor concentrations. Animal positions within the exposure caging were rotated on a daily basis to minimize the potential effect of any concentration variations in the chambers. Further details regarding inhalation exposure methodology are provided in Appendix B.

Phenobarbital drinking water solutions (0.05% w/v) were prepared based on weights and volumes of sufficient quantity to provide for the duration of the experimental phase. Fresh solutions were prepared weekly. The solutions were prepared using reverse osmosis purified water and stored in an appropriate container at $5^{\circ} \pm 3^{\circ}\text{C}$. Phenobarbital was used as provided and dosing solutions were not evaluated for stability or confirmation of nominal concentration.

PROCEDURES

1. Preparation of 5'-bromo-2-deoxyuridine (BrdU) Stock Solution: BrdU was purchased from Sigma Chemical Company (catalog number: B-5002). BrdU is light sensitive and was protected from fluorescent light exposure. All work was performed under incandescent lighting. Storage of stock BrdU powder was kept in a desiccator at a temperature of $5^{\circ} \pm 3^{\circ}\text{C}$. To prepare the working stock, BrdU powder was removed from the refrigerator and allowed to warm to room temperature. BrdU powder was weighed and dissolved in sterile phosphate buffered saline (pH 7.6 ± 0.1) in an amount that would yield a final concentration of approximately 20 mg/ml. The PBS solution was pre-warmed to $37\text{-}40^{\circ}\text{C}$ in some instances to facilitate the solubilization of BrdU. Stirring or shaking the mixture also helped facilitate the process.
2. Surgical Placement of Mini Osmotic Pumps: Osmotic pumps (model 2ML1, 7 day) were obtained from Alza Corporation, Palo Alto, CA. The pumps for a given experiment were all of the same type and lot. Individuals trained in aseptic techniques performed the subcutaneous implantation of the mini pumps. All surgical procedures as well as loading of pumps were done under aseptic conditions. The animal was anesthetized (isoflurane vapor) and the skin was prepared at the site of implantation by shaving an area on the upper back close to the neck and then washing the area with betadine and/or alcohol swabs. An incision was made perpendicular to the spine and the pump inserted just under the skin with the BrdU delivery end nearest the head. The skin around the incision was carefully pulled back together and closed with wound clips and/or sutures.
3. Tissue Processing: When all samples were collected and placed in fixative, the fixation containers were placed on a shaker for at least 4 hours. Note that the total time for fixation (shaker time plus non-shaker time) did not exceed 45-55 hours. Following formalin fixation, the tissues were processed as follows: 2 changes of 30% ethanol, 1 change of 70% ethanol, 2 changes of 80% ethanol, 2 changes of 95% ethanol, 2 changes of 100% ethanol, and 2 changes of xylene. Actual times and subsequent processing steps were done according to standard operating procedures. Samples were embedded in paraffin blocks as soon as possible. Low melt paraffin was used.

Paraffin-embedded tissues were sectioned and placed on glass slides for immunostaining or staining with hematoxylin and eosin.

4. Immunohistochemical Staining Procedures: Visualization of BrdU antigen was accomplished with the DAKO EnVision® System Peroxidase according to the manufacturer's procedures. This detection method uses a horseradish peroxidase (HRP) labeled polymer attached to secondary antibody that recognizes primary antibodies produced in the mouse. Tissue sections were deparaffinized in xylene and taken to water via graded alcohols.

For detection of BrdU, tissue DNA must be denatured to facilitate antigen interaction with the primary antibody. Thus, sections were incubated in 4N HCl at 37°C for 20-25 minutes and then rinsed with

reverse osmosis purified water. The tissues were then rinsed two times (5-10 minutes each change) with phosphate buffered saline containing 0.1% Tween-20 (PBSt). Peroxidase blocking agent was added for 5 minutes followed by two rinses with PBSt. Primary antibody for BrdU was diluted 1:200 in phosphate buffered saline with 1% bovine serum albumin (BSA) and incubated with tissue sections for 10 minutes (in the dark). Following two more rinses with PBSt the HRP-labeled polymer was applied and allowed to incubate for 10 minutes. This was followed with two washes of PBSt (3-6 minutes each) prior to incubating with substrate-chromagen (in the dark) for 8 minutes. Two more PBSt washes (3-6 minutes) prepared the tissues for the DAB enhancer, which was applied for 5 minutes (in the dark). The sections were then rinsed with two changes of reverse osmosis purified water (3-6 minutes each change) prior to being counterstained in aqueous hematoxylin (Innovex Biosciences, Richmond, CA). The sections were then dehydrated by incubations with 50%, 95%, and 100% (absolute) ethanol. The slides were cleared with two rinses in xylene (5-10 minutes each) and coverslipped. After poor preliminary results due to contaminated absolute ethanol, a pepsin digestion step was added and a second complete set of slides (all animals represented) were processed. The protocol was carried out exactly as above, except that slides were placed in a pepsin solution for 5 minutes at 37 °C immediately after the HCl denaturing step and washed twice with PBSt.

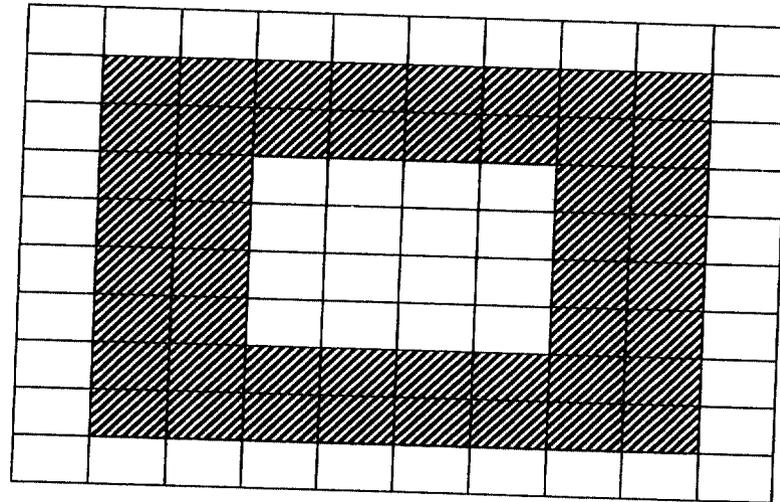
Cell replication was determined by counting the number of positively stained hepatocytes with the BioQuant® Image analysis system (Bioquant-R & M Biometrics, Inc., Nashville, TN) under 40X magnification. Portions counted were randomly selected and at least 1000 hepatocytes were counted per slide. The labeling index (LI %) was calculated by dividing the number of positive nuclei by the total number counted and then multiplying by 100.

Cellular hypertrophy was initially quantitated with the Bioquant system, by counting nuclei in a fixed field. However, as a contaminated lot of ethanol caused unacceptable cell shrinkage, the process was re-run. In the second attempt, nuclei were counted manually, using an eyepiece grid in the objective lens. For panlobular counting, random sections of liver were chosen that did not contain any features (veins, arteries...) that would interfere with the count. Also, a centrilobular count was performed in a similar manner. In this case, central veins were identified that would fit into a 4x4 box in the center of the 10x10 grid. The nuclei in the 2 rows of squares surrounding the 4x4 box were then counted (Figure 1.).

IN-LIFE TEST SYSTEM OBSERVATIONS AND PROCEDURES

1. **Food Consumption:** Food consumption was monitored once per week. The difference in feeder weights represents the amount of food in grams consumed for each animal over the experimental period.
2. **Water Consumption:** Water consumption was determined twice weekly. Water bottles from animals subject to necropsy were also weighed on the day of necropsy.
3. **Body Weights:** Individual body weights were taken prior to the start of the study for randomization into groups. During the in-life portion of the study, animals had body weights taken on days 0, 7, 14, 21 and 27. Terminal body weights were taken on days 6, 13 and 27 and were adjusted by subtraction of the loaded pump weight.
4. **Mortality/ Morbidity Checks:** Animals were observed twice a day during the week and once a day on weekends and holidays for signs of mortality/morbidity by animal care personnel.
5. **Clinical Observations:** Clinical observations were made on each animal daily, including Saturdays and Sundays.

Figure 1. Representation of Counting Grid Used to Evaluate Centrilobular Hypertrophy



Center clear cell = maximal area that a central vein can occupy.

 = grids where nuclei are counted

STATISTICAL METHODS

Analysis of all data was carried out using SAS® v. 8.2. For each endpoint, a two-step process was followed. First the data were analyzed with a full model including treatment, day and all possible interactions. The purpose of this analysis was to determine if there were significant day*treatment interactions (i.e., did the response vary across days). The second step was to determine if there were treatment-related effects within an individual exposure period. This was evaluated using a model with treatment as the only term. Mean responses in animals exposed to either phenobarbital or D₅ were compared to control using Dunnett's test for multiple comparisons against a control. The log₁₀ transformation was applied to the BrdU labeling index data in order to stabilize variance across groups. The family wise error rate for all tests was held at 5% ($\alpha = 0.05$). If the data was not both normally distributed with equal variances among the groups, the nonparametric Kruskal Wallis test was used, followed by individual Wilcoxon tests if the Kruskal Wallis test was significant. Food and water consumption were analyzed using nonparametric techniques because the data was not normally distributed.

The statistical analysis results are summarized in Appendix A.

RESULTS

Results from the initial analysis of liver and thyroid tissues for hyperplasia suggested that the tissues collected from rats following 1 and 2 five-day exposure periods had not been optimally processed. Investigation of this anomaly revealed that a poor quality lot of absolute ethanol was utilized in the tissue dehydration step and likely contributed to the markedly reduced BrdU signal. A pepsin digestion step was added to the process of slide preparation for BrdU analysis to ensure that potentially masked signal, a likely outcome for poorly dehydrated tissue samples, would become unmasked. Pepsin digestion had the desired effect of increasing the BrdU signal in tissue suspected of having been compromised by poor dehydration and yet had no impact on tissue not compromised by poor dehydration. The tissue hyperplasia data presented in this report were derived from tissues prepared utilizing the pepsin digestion step as detailed in the methods section.

Similarly, liver hypertrophy was considered suspect when the initial slide evaluation showed no hypertrophy at any time point for the positive control, phenobarbital. A second set of slides was prepared from fixed tissues and evaluated (panlobular). No increase in hypertrophy was detected in the positive control, a finding inconsistent with the historical data. A second evaluation was performed with these slides and focused only on the centrilobular region. This evaluation revealed statistically significant hypertrophy for the positive control. It remains unknown why the positive control gave rise to only centrilobular hypertrophy. The effect of D₅ on liver hypertrophy will focus only on the results obtained from the centrilobular evaluation.

This study was conducted to evaluate the effect(s) of exposure to 160 ppm D₅ vapor on cell proliferation (liver and thyroid) and hypertrophy (liver) in the rat as a function of exposure duration. Female Fischer 344 rats were exposed to 157.4 ± 1.3ppm, 158.0 ± 3.6ppm and 160.2 ± 3.7ppm D₅ vapor (mean concentration ± standard deviation) for 1, 2, or 4 five-day exposure periods, respectively. Control (air exposed) and PB-treated rats (positive control group) were placed into inhalation chambers to mimic the exposure routine of the D₅ exposed animals. However, D₅ vapor was not directed into these chambers. Summary data detailing the inhalation exposure is provided in Appendix B.

Exposure to 160 ppm D₅ was well tolerated. There were no treatment-related clinical signs of toxicity (Table 1), no effect on food or water consumption (Table 2), and no effect on body weight (Table 3).

Exposure to 160 ppm D₅ gave rise to an increase in absolute liver weight, liver-to-body weight and liver-to-brain weight ratios following 1 and 2 five-day exposure periods (Table 4). The increases in absolute liver weight were 12%, 11%, and 6%, relative to controls, after 1, 2 and 4 five-day exposure periods, respectively. The increases in liver:body weight ratio were 11%, 11%, and 7%, relative to controls, after 1, 2 and 4 five-day exposure periods, respectively. The increases in liver:brain weight ratio were 14%, 12%, and 4%, relative to controls, after 1, 2 and 4 five-day exposure periods, respectively. The slight increase in mean values after 4 five-day exposure periods did not achieve statistical significance. Accompanying the D₅-induced increase in liver weight was an increase in hepatocellular hyperplasia as demonstrated by increases in the BrdU LI (Table 5). The BrdU LI was increased approximately 3.5-fold after 1 five-day exposure period. Continued exposure to 160 ppm D₅ for 2 and 4 five-day exposure periods gave rise to a 1.5- and 1.6-fold increase in BrdU LI, respectively. The 1.5-fold increase after 2 five-day periods of exposure to 160 ppm D₅ was not statistically different from control. Centrilobular hypertrophy was evident in D₅ treated rats only at the end of the first five-day exposure period (Table 6).

Absolute thyroid weight, thyroid-to-body weight and thyroid-to-brain weight ratios were unaffected by D₅ exposure (Table 7). Thyroid cell hyperplasia was increased following D₅ exposures (Table 5). Exposure to 160 ppm D₅ for 2 and 4 five-day exposure periods was shown to cause a statistically significant 1.9- and 1.7-fold increase in BrdU LI, respectively. The BrdU LI after 1 five-day D₅ exposure period was also 1.7-fold greater than control, however it did not achieve statistical significance.

The administration of PB to a separate group of rats provided for a concurrent positive control group. As anticipated for this control agent and administration regimen, PB-treatment gave rise to a variety of effects. Treatment with PB resulted in an increased incidence of porphyrin staining around the eyes (Table 1) and a 13% increase in food consumption during the first week of treatment (Table 2). Body weight was not affected by PB-treatment (Table 3).

Administration of PB resulted in statistically significant increases in liver weight following 1, 2, and 4 weeks of treatment (Table 4). The increases were 31%, 28%, and 35% percent relative to control values for absolute liver weight after 1, 2, and 4 weeks of treatment, respectively. The increases were 28%, 26%, and 35% relative to control values for liver:body weight ratio after 1, 2, and 4 weeks of treatment, respectively. The increases were 32%, 31%, and 38% relative to control values for liver:brain weight ratio after 1, 2, and 4 weeks of treatment, respectively. Accompanying the PB-induced increase in liver weight was a transient increase in hepatocellular hyperplasia as demonstrated by increased BrdU LI (Table 5). The BrdU LI was increased 5-fold after the first week of treatment. The BrdU LI after 2 and 4 weeks of treatment was not statistically different from control. Liver hypertrophy, as measured by a reduction in the number of hepatocellular nuclei within a fixed microscopic field size, was significantly different for PB exposed rats when the examination was focused on the centrilobular region. The mean number of hepatocellular nuclei per field were significantly reduced by 21%, 15.3%, and 14.9% in rats following 1, 2, and 4 weeks of treatment, respectively.

Administration of PB resulted in increased thyroid weight after 1, 2 and 4 weeks of treatment (Table 8). Absolute thyroid weight (thyroid-to-brain weight) increases were 15%(16%), 14%(17%) and 31%(36%) after 1, 2, and 4 weeks of treatment, respectively. Thyroid-to-body weight ratio was increased 13%, 11%, and 30% after 1, 2, and 4 weeks of treatment, respectively. However the increases after 1 and 2 weeks of treatment did not achieve statistical significance. Thyroid cell hyperplasia was increased 1.3-fold after one week of treatment, 3.3-fold after 2 weeks and 9.6-fold after 4 weeks of treatment. The increase at 1 and 2 weeks did not attain statistical significance. The temporal affects on thyroid weight and hyperplasia are generally consistent with the historical data.

Group mean lung weight in the D₅ and PB treatment groups were not different from the control values at any of the time points evaluated (summary data not shown). Individual animal organ weight data for lung, liver, thyroid and brain is provided in Appendix D.

DISCUSSION

Repeated exposure to D₅ has been shown to produce a reversible liver weight increase and a cytochrome P450 enzyme induction profile similar to that induced by PB in rats (McKim *et al.*, 1999). As a result, D₅ has been described as "a weak phenobarbital-like inducer of rat liver xenobiotic-metabolizing enzymes." In order to extend our understanding of the biochemical effects of repeated inhalation exposure to D₅ vapor in the rat, the present study has examined the effects of whole-body vapor inhalation exposure to 160 ppm D₅ on liver and thyroid hyperplasia and liver hypertrophy in female Fischer 344 rats with respect to exposure duration.

Repeated vapor inhalation exposure of female Fischer 344 rats to 160 ppm D₅ produced a transient increase in liver weight of approximately 11% relative to control. The liver weight increase was present after 1 and 2 five-day exposure periods with a return to control levels by the end of the 4th five-day exposure period. The transient nature of the D₅-induced increase in liver weight could be representative of an adaptive change in response to the D₅ challenge that was sufficient to allow the organ to return to a "normal" weight status under conditions of continued exposure. The "burst" in hepatocellular hyperplasia and hypertrophy observed after the first five-day exposure period with return to near control levels after 2 and 4 five-day exposure periods is consistent with the early organ weight change. This pattern of response is typical of many xenobiotics and is considered to represent an adaptive change involving upregulation of biochemical pathways/processes involved in their metabolism/elimination (Williams & Iatropoulos, 2002).

In contrast to the effect of D₅ exposure on the liver, thyroid weight was unaffected by D₅ exposure. Thyroid hyperplasia was elevated only slightly (<2-fold) and was without temporal differentiation. These results suggest minimal response of the thyroid in female Fischer 344 rats to the applied repeated-exposure design employed in this study for the endpoints evaluated.

Administration of PB produced an early and sustained increase in liver weight and an early burst of hepatocellular proliferation. A sustained increase in hepatocellular hypertrophy was expected but not observed in panlobular evaluations. However a focused evaluation of the centrilobular region

demonstrated a significant increase in hepatocellular hypertrophy at each time point. Thyroid weight and thyroid cell proliferation were increased with peak responses observed after 4 five-day exposure periods. In general these results were consistent with that anticipated for this positive control agent.

CONCLUSION

The results of this study have demonstrated that repeated-exposure of female Fischer 344 rats to D₅ can induce an early non-sustained increase in liver weight and an early burst of hepatocellular hyperplasia and centrilobular hypertrophy. Thyroid weight was unaffected by D₅ exposure however exposure did give rise to a slight increase (<2-fold) in thyroid cell hyperplasia without regard for exposure duration.

The response to D₅ exposure by the liver and thyroid was generally similar to that observed with PB. Differences may represent dose/potency inequities such that effects elicited by exposure to 160 ppm D₅ may be more comparable to a much lower (non-tumor promoting) dose of PB.

REFERENCES

McKim, James M.; Choudhuri, Supratim; Wilga, Paul C.; Burns, Leigh A.; Breen, John G.; Mast, Richard W.; Alworth, William L., *Induction of Hepatic Xenobiotic Metabolizing Enzymes in Female Fischer-344 Rats Following Repeated Inhalation Exposure to Decamethylcyclopentasiloxane (D₅)*. Toxicological Sciences, 50, pp.10-19, 1999.

Williams, Gary M., & Iatropoulos, Michael J., *Alteration of Liver Cell Function and Proliferation: Differentiation Between Adaptation and Toxicity*. Toxicologic Pathology, 30, pp 41-53, 2002.

Table 1.
Clinical Observations Summary

Clinical Observation	Incidence ¹		
	Control	160 ppm D ₅	0.05% PB ²
Normal	11 / 30	11 / 30	7 / 30
Urine Staining, perineal region	18 / 30	19 / 30	15 / 30
Porphyrin Staining, eye(s)	1 / 30	1 / 30	11 / 30
Dried Fluid, eye(s)	0 / 30	1 / 30	6 / 30

¹Summary incidence is the number of animals expressing the finding at least once during the study period by the total number of animals in the treatment group.

²PB was administered as a drinking water additive 7 days/week.

*Significantly different from control, $p < 0.05$

Table 2.

Effect of D₅ and PB Exposure of Female Fischer 344 Rats on Food and Water Consumption

Treatment ¹	Measure ²	Exposure Periods ³ :		
		1	2	4
Control 160 ppm D ₅ PB (0.05%)	Food Consumption	66.4 (5.5)	153.8 (6.7)	320.2 (22.1)
	Food Consumption	69.9 (2.6)	155.0 (10.1)	306.8 (13.9)
	Food Consumption	75.1* (3.4)	164.6 (13.1)	339.3 (16.8)
Control 160 ppm D ₅ PB (0.05%)	Water Consumption	72.8 (6.3)	172.8 (12.4)	380.5 (6.03)
	Water Consumption	82.3 (9.1)	188.3 (15.4)	391.4 (23.1)
	Water Consumption	75.3 (9.7)	177.4 (10.8)	368.0 (16.6)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/week.

²Values represent consumption expressed as mean grams/day/exposure period (standard deviation)

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

Table 3.
Effect of D₅ and PB Exposure of Female Fischer 344 Rats on Body Weight

Treatment ¹	Measure ²	Exposure Period ³ :		
		1	2	4
Control 160 ppm D ₅ PB (0.05%)	Body Weight	156.2 (5.4)	159.0 (4.2)	165.6 (5.0)
	Body Weight	158.8 (4.4)	161.7 (4.7)	163.5 (2.3)
	Body Weight	159.4 (5.1)	161.7 (3.6)	165.9 (4.9)
Control 160 ppm D ₅ PB (0.05%)	Brain Weight	1.644 (0.037)	1.661 (0.0226)	1.680 (0.0388)
	Brain Weight	1.613 (0.050)	1.644 (0.0483)	1.697 (0.0297)
	Brain Weight	1.624 (0.044)	1.622* (0.0325)	1.642* (0.0259)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/week.

²Values represent mean terminal body weight expressed in grams (standard deviation).

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

*Significantly different from control at p<0.05; N = 10

Table 4.
Effect of D₅ and PB Exposure of Female Fischer 344 Rats on Liver Weight and Liver Weight Ratios

Treatment ¹	Measure ²	Exposure Period ³ :		
		1	2	4
Control 160 ppm D ₅ PB (0.05%)	Liver Weight	5.499 (0.340)	5.673 (0.239)	5.613 (0.231)
	Liver Weight	6.176* (0.238)	6.274* (0.444)	5.925 (0.542)
	Liver Weight	7.189* (0.278)	7.265* (0.303)	7.574* (0.453)
Control 160 ppm D ₅ PB (0.05%)	Liver:Body Weight	0.0352 (0.0015)	0.0357 (0.0017)	0.0339 (0.0015)
	Liver:Body Weight	0.0389* (0.0016)	0.0388* (0.0021)	0.0362 (0.0031)
	Liver:Body Weight	0.0451* (0.0022)	0.0450* (0.0020)	0.0457* (0.0025)
Control 160 ppm D ₅ PB (0.05%)	Liver:Brain Weight	3.347 (0.2229)	3.416 (0.1505)	3.344 (0.1894)
	Liver:Brain Weight	3.833* (0.2211)	3.818* (0.2611)	3.493 (0.3454)
	Liver:Brain Weight	4.431* (0.2252)	4.481* (0.2069)	4.613* (0.2682)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/ week.

²Values represent mean liver weight expressed in grams or the weight ratio (standard deviation).

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

*Significantly different from control at p<0.05; N = 10

Table 5.
Effect of D₅ and PB Exposure of Female Fischer 344 Rat Liver and Thyroid Hyperplasia

Treatment ¹	Measure ²	Exposure Period ³ :		
		1	2	4
Control	Liver BrdU LI	5.58 (1.91)	9.08 (2.80)	7.63 (1.89)
160 ppm D ₅	Liver BrdU LI	19.71* (8.52)	13.72 (5.34)	12.28* (4.41)
PB (0.05%)	Liver BrdU LI	27.66* (7.85)	11.71 (6.67)	8.29 (4.23)
Control	Thyroid BrdU LI	2.39 (1.26)	1.51 (0.51)	2.22 (1.02)
160 ppm D ₅	Thyroid BrdU LI	4.05 (2.62)	2.90* (0.92)	3.87* (1.38)
PB (0.05%)	Thyroid BrdU LI	3.15 (2.66)	5.00 (3.43)	21.30* (7.71)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/week.

²Values represent the mean percent labeling indices (standard deviation).

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

*Significantly different from control at p<0.05; N = 10

Table 6.
Effect of D₅ and PB Exposure of Female Fischer 344 Centrilobular Rat Liver Hypertrophy

Treatment ¹	Measure ²	Exposure Period ³ :		
		1	2	4
Control	Hypertrophy	25.73 (2.17)	23.61(4.28)	23.03(3.38)
160 ppm D ₅	Hypertrophy	23.26* (2.47)	23.05 (2.56)	23.93(2.55)
PB (0.05%)	Hypertrophy	20.17* (4.74)	20*(4.43)	19.61*(3.64)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/week.

²Values represent mean number of nuclei per fixed microscopic field (standard deviation).

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

*Significantly different from control at p<0.05; N = 10

Table 7.
Effect of D₅ and PB Exposure of Female Fischer 344 Rats on Thyroid Weight and Thyroid Weight Ratios

Treatment ¹	Measure ²	Exposure Period ³ :		
		1	2	4
Control 160 ppm D ₅ PB (0.05%)	Thyroid Weight	0.0108 (0.0016)	0.0111 (0.0018)	0.0114 (0.0018)
	Thyroid Weight	0.0120 (0.0007)	0.0106 (0.0011)	0.0123 (0.0012)
	Thyroid Weight	0.0124* (0.0014)	0.0126* (0.0014)	0.0150* (0.0023)
Control 160 ppm D ₅ PB (0.05%)	Thyroid:Body Weight	0.000069 (0.000011)	0.000070 (0.000011)	0.000069 (0.000010)
	Thyroid:Body Weight	0.000076 (0.000004)	0.000066 (0.000006)	0.000075 (0.000007)
	Thyroid:Body Weight	0.000078 (0.000009)	0.000078 (0.000008)	0.000090* (0.000014)
Control 160 ppm D ₅ PB (0.05%)	Thyroid:Brain Weight	0.00656 (0.00089)	0.00668 (0.00109)	0.00678 (0.00109)
	Thyroid:Brain Weight	0.00749 (0.00046)	0.00644 (0.00057)	0.00724 (0.00079)
	Thyroid:Brain Weight	0.00761* (0.00082)	0.00779* (0.00088)	0.00912* (0.00150)

¹Control (air) and D₅ vapor was administered by whole-body inhalation (6 hours/day). PB was administered as a drinking water additive 7 days/week.

²Values represent mean liver weight expressed in grams or the weight ratio (standard deviation).

³1 = 1 five-day period (days 1-6); 2 = 2 five-day periods (days 1-13); 4 = 4 five-day periods (days 1 - 27)

*Significantly different from control at p<0.05; N = 10

APPENDIX A

Contributing Scientist Report: Statistics for Study 8631

Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study

Dow Corning Corp.
Study 8631

MEMORANDUM

To: Paul Jean

From: Trevor Newhook

Subject: Analysis of the data from study 8631

This study was carried out to evaluate the effects of Decamethylcyclopentasiloxane (D₅, 160ppm by inhalation) on liver and thyroid cell hyperplasia and liver hypertrophy in female Fischer 344 (F344) rats following 1, 2, or 4 five-day exposure periods. Statistical analysis indicates that both D₅ and phenobarbital significantly increased liver BrdU labeling index relative to control after 1 five-day exposure period and D₅ significantly increased liver BrdU labeling index relative to control at 4 weeks. There was no difference in the mean thyroid BrdU labeling index among treatment groups after 1 five-day exposure period. After 2 five-day exposure periods, there was a significant increase in the mean thyroid BrdU labeling index in animals treated with D₅ but not phenobarbital. Both D₅ and phenobarbital significantly increased the mean thyroid BrdU labeling index after 4 five-day exposure periods. Phenobarbital significantly reduced the number of nuclei per field in the liver relative to control after 1 five-day exposure period, but not after 2 or 4 five-day exposure periods. D₅ had no significant effect on the number of nuclei per field on any of the days tested when compared to controls. Animals treated with phenobarbital had significantly heavier livers than controls after each of the five-day exposure periods whether expressed as gross weight, liver to body weight ratio or liver to brain weight ratio. Animals exposed to D₅ showed significant increases in mean liver weight, liver-to-body weight ratio, and liver-to-brain weight ratio relative to control after 1 and 2 five-day exposure periods. Phenobarbital increased thyroid weight relative to control after 1, 2 and 4 five-day exposure periods. Phenobarbital significantly increased the thyroid to body weight ratio relative to control at the end of the final exposure period and significantly increased the mean thyroid-to-brain weight after each period of exposure. Animals exposed to phenobarbital had significantly greater mean levels of food consumption than controls after 1 five-day exposure period. Water consumption was not different from control values in the D₅ and phenobarbital treatment groups.

Introduction

This study was carried out to evaluate the effects of D₅ (160ppm by inhalation) on liver and thyroid hyperplasia and liver hypertrophy in female Fischer 344 (F344) rats following 1, 2, and 4 five-day exposure periods.

Methods

Analysis of all data was carried out using SAS[®] v. 8.2. For each endpoint, a two-step process was followed. First the data were analyzed with a full model including treatment, day and all possible interactions. The purpose of this analysis was to determine if there were significant day*treatment interactions (i.e., did the response vary across days). The second step was to determine if there were treatment related effects within an individual exposure period. This was evaluated using a model with treatment as the only term. Mean responses in animals exposed to either phenobarbital or D₅ were compared to

Dow Corning Corp.
Study 8631

control using Dunnett's test for multiple comparisons against a control. The \log_{10} transformation was applied to the BrdU labeling index data in order to stabilize variance across groups. The family wise error rate for all tests was held at 5 % ($\alpha = 0.05$). If the data was not both normally distributed with equal variances among the groups, the nonparametric Kruskal Wallis test was used, followed by individual Wilcoxon tests if the Kruskal Wallis test was significant. Food and water consumption were analyzed using nonparametric techniques because the data was not normally distributed.

Results

Hyperplasia:

Liver: The analysis indicates that both D₅ and phenobarbital significantly increased the liver BrdU labeling index relative to control after 1 five-day exposure period. There was no difference among treatment groups after 2 five-day exposure periods. There was a significant increase in the mean labeling index in animals treated with D₅, but not phenobarbital for 4 five-day exposure periods.

Thyroid: There was no difference among treatment groups after 1 five-day exposure period. After 2 five-day exposure periods, there was a significant increase in the mean labeling index in animals treated with D₅ but not phenobarbital. Both D₅ and Phenobarbital significantly increased the mean BrdU labeling index after 4 five-day exposure periods.

Hypertrophy: D₅ had no significant effect on the number of nuclei per field relative to control. Phenobarbital significantly decreased the number of nuclei per field relative to control after 1 five-day exposure period, but not after 2 or 4 five-day exposure periods.

Body/Organ Weights:

Body weight – no significant differences in body weight were observed among groups in this study

Brain weight – phenobarbital significantly decreased brain weight relative to control after 2 and 4 five-day exposure periods.

Liver weight – phenobarbital significantly increased absolute liver weight, liver to body weight ratio, and liver to brain weight ratio relative to control after 1, 2, and 4 five-day exposure periods. D₅ significantly increased absolute liver weight, liver to body weight ratio, and liver to brain weight ratio relative to control after 1 and 2 five-day exposure periods.

Lung weight – There were no significant differences in the mean lung weight in the treated groups compared to the control using nonparametric techniques.

Thyroid weight – phenobarbital significantly increased thyroid weight and the thyroid to brain weight ratio relative to control after 1, 2, and 4 five-day exposure periods. The thyroid to body weight ratio in animals exposed to phenobarbital for 4 five-day exposure periods was also significantly different from control. D₅ had no effect on thyroid weight.

Feed Consumption: Animals treated with phenobarbital had mean total feed consumption values that were significantly greater than control after 1 five-day exposure period. D₅ had no effect on food consumption.

Dow Corning Corp.
Study 8631

Water Consumption: Animals exposed to D₅ and phenobarbital did not have mean total water consumption values that were significantly greater than control.

Documentation

The SAS® Log and Output for this analysis are stored in the study file.

References

¹ SAS Institute Inc., SAS/STAT® User's Guide, Version 8, Cary, NC: SAS Institute Inc., 1999, p 1546.

Signature: 
Trevor Newhook
Biostatistician

Date: 1-30-03

DC Study Number: 8631

MEMORANDUM

To: Paul Jean
From: Cynthia Van Landingham

This document contains the statistical analysis of the data from Study 8631, which was completed on 13th of July, 2004.

Signature Cynthia Van Landingham Date 10/17/2004

Methods

This is an assessment of in-vitro data to evaluate the potential for D₅ and Phenobarbital to affect the mean number of cell nuclei per microscope field. Data was provided for 3 specific time points (1 week, 2 weeks and 4 weeks) for controls, animals exposed to 160 ppm of D₅ and animals treated with phenobarbital. The determination of nuclei/field was done two ways – centrilobular and panlobular. Analysis of all data was carried out using SAS v. 8.2. For each endpoint, a two-step process was followed. First the data were analyzed in an ANCOVA with a full model including agent, week and all possible interactions. The purpose of this analysis was to determine if there were significant week by agent interactions (i.e., did the response vary across days). The second step was to determine if there were agent-related effects within an individual exposure period. This was evaluated separately for each week of data using an ANOVA with agent as the independent variable. For the ANOVA, the assumptions of normality of the residuals and the homogeneity of the data were tested using a Shapiro-Wilk test for the normality ($\alpha = 0.01$) and Levene's test for homogeneity ($\alpha = 0.01$). For data that did not satisfy the assumptions of normality of the residuals and homogeneity of the variances, a Kruskal-Wallis test would be used. Mean responses in animals exposed to either phenobarbital or D₅ were compared to control using Dunnett's test for multiple comparisons against a control if the ANOVA was used and Wilcoxon test if the Kruskal-Wallis test was used.

Results

All data was analyzed using the ANCOVA and ANOVA. There were no significant differences across weeks, agents or the interaction of weeks and agent when the D₅ data was compared to control for either the centrilobular or panlobular data. However, when compared by week, the mean D₅ nuclei/field was significantly lower than control in the week 1 centrilobular data (p=0.0344) and the week 2 panlobular data (p=0.0469).

There was a significant difference between the phenobarbital centrilobular data when compared to control over the entire interaction model (p=0.0003) due to the agent (p<0.0001). The weeks and week by agent interaction were not significant. In addition, at each week the mean phenobarbital centrilobular nuclei/field were statistically significantly lower than the mean control nuclei/field (week 1 p = 0.0013, week 2 p = 0.0466, and week 4 p = 0.0114). However, there were no statistically significant differences in any of the comparisons of the phenobarbital panlobular nuclei/field data to control.

APPENDIX B

Inhalation Methods Summary Report for Study 8631

Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study

SUMMARY

Female Fischer 344 rats were exposed to decamethylcyclopentasiloxane (D₅) vapor for 1, 2 or 4 five-day exposure periods. Each successive five-day exposure period was separated by a two-day non-exposure period. Daily exposures consisted of a 6 hr exposure to a target vapor concentration of 160 ppm D₅ sandwiched between T₉₉ periods of approximately 20 minutes each. Mean exposure concentrations (standard deviation) for animals in each of the three exposure subgroups were 157.4±1.3ppm, 158.0±3.6ppm and 160.2±3.7ppm D₅ vapor (mean concentration ± standard deviation) for 1, 2 and 4 five-day exposure periods, respectively. Animals in the control and phenobarbital (PB) treatment groups were placed in inhalation chambers daily for the same duration as the D₅ exposed animals but they were not exposed to D₅ vapor. The range of mean daily chamber temperatures and relative humidity for all exposure chambers were 22.5-24.5°C and 35.1-41.1%, respectively.

MATERIALS AND METHODS

A. Inhalation Exposure Methods

Exposures were conducted in 450-liter Rochester style stainless steel and glass whole body chambers (Figure 1) operated under dynamic conditions (chamber pressure: ~ -0.6 in. H₂O). The air supplied to the inlet of the chambers was room air that had been passed through activated carbon and HEPA filters. Chamber airflow rates were measured using sharp-edged orifice plates (Doebelin, 1983) and differential pressure transducers (Validyne model DP 851C-P10) equipped with digital displays. The pressure transducers were calibrated prior to study initiation using an NIST traceable Modus[®] digital manometer (Model MA2-0021). Chamber airflow was maintained at 12-15 air changes per hour resulting in a T₉₉ of approximately 20 minutes (Silver, 1946). Each chamber was leak tested under normal operating parameters prior to the start of the study. As an extra precaution, chambers were operated under slightly negative pressures (~ -0.6" H₂O) during exposures. Chamber temperature and relative humidity were monitored using Omega[®] Engineering, Inc. sensors (Model HX11-C) equipped with digital displays. Each sensor was calibrated prior to start of the study using an NIST traceable thermal coupler (Omega[®] HH11 for temperature) and NIST traceable Hygrometer (Fisher Scientific Digital Humidity/ Temperature meter for humidity). Airflow, temperature, and humidity were monitored continuously and manually recorded every thirty minutes during each exposure period. Prior to the first day of exposure chamber test article homogeneity was evaluated for all chambers in which test article was generated. During this evaluation, test article was introduced into each exposure chamber at or near the appropriate target concentration. The chamber atmosphere was then sampled three times each at six different locations from within the chamber. The average area count response for each location was calculated and compared to results from the reference location. A difference between the reference and other sample locations of less than or equal to ten percent was considered acceptable. Homogeneity evaluations for all chambers were within acceptable limits.

Decamethylcyclopentasiloxane vaporization was conducted using glass J-tubes (Miller *et al.*, 1980) containing 6 mm soda lime glass beads. J-tubes were wrapped with heat tape and insulation and operated at a temperature of between 70-80°C to promote efficient vaporization of D₅ (Figure 2). Fluid Metering[®], Inc. (FMI) pumps were used to meter D₅ at a constant flow rate from glass reservoirs into the J-tubes. Grade D breathable air, supplied from a NASH[®] compressor, was passed as the carrier gas through the J-tubes at a controlled rate. The air/D₅ vapor exiting the J-tube was then introduced into the inlet port at the top of the chambers for dilution into the make-up air stream.

B. Test Article Monitoring

1. Nominal:

The amount of test article used during each daily exposure period was determined by measuring the difference between the pre- and post-exposure weight of the test article reservoirs. The vapor generation time (one T_{99} plus the six hour exposure period), test article consumption, and total volume of air through the chambers was used to calculate nominal concentration values (Silver, 1946).

2. Measured:

A Varian® 3400 gas chromatograph (G.C. conditions are presented in Table 1) operated by a Varian Star® Workstation was used for analytical determination of chamber concentrations (Figure 3). The instrument was equipped with a flame ionization detector (FID), a Valco® stream selector valve, and a heated Valco® injector valve. Five point calibrations were performed prior to the start of the study by preparing samples in Tedlar® gas sampling bags. Two bag standards of known concentration were prepared for each of five calibration levels by injecting a known volume of D_5 into a measured volume of air. A heat gun was then used to completely vaporize the D_5 inside the bag. Each bag was sampled twice for a total of twenty sample points. The Varian Star® software (Version 4.5), was then used to generate a calibration curve (origin was not used as a sample point) for each G.C. method. Multiple calibration curves were used to span the large range of exposure concentrations. Before each exposure a bag standard was prepared for each calibration curve and analyzed using the appropriate method for verification of the performance of the G.C. During the daily G.C. verification, the bag standards were attached to the sample lines at the chambers. If the response for the bag standard was not within ten percent of the expected area count response, a second standard was prepared. If the result was still not within acceptable limits, the GC was re-calibrated following the exposure and the daily results recalculated. During conduct of an exposure, each chamber was analyzed a minimum of once an hour for the duration of the exposure period.

3. Sampling System:

Samples of the chamber test atmosphere were drawn from the exposure chambers through ¼" O.D. Teflon® tubing and a Valco® stream selector valve using Thomas vacuum pumps (Model 917CA18). One pump was used for the sample line and the second pump was used to for continuous purge of the other sample lines. The samples were drawn under negative pressure through a 229µL stainless steel sample loop and injected onto the column using an air actuated Valco® injector valve. Prior to initiation of the study, sample line flow rates and sample line loss were measured to confirm the integrity of the air sampling system. Flow rates and sample line loss rates were within acceptable tolerances.

C. Exposure Procedures

Before each exposure, animals were transferred from their housing caging into exposure caging (individual compartments approximately 6" W x 6" H x 7" L). Animal positions in these exposure cages were rotated front to back, and top to bottom, on a daily basis to eliminate any bias related to potential differences in concentrations among positions within the chamber. Animals were caged individually in both the housing and exposure caging. To avoid confusion during transfer, the exposure cages and the chambers were labeled with color-coded tags. Following each exposure period, the animals were returned to their housing caging. Food and water were not available to the animals during the exposure periods.

RESULTS

Daily mean chamber temperature and relative humidity for all of the exposure chambers combined ranged between 22.5-24.5°C and 35.1-41.1%, respectively. The daily mean individual chamber temperature and humidity values are summarized in table 2 (this appendix). The mean chamber D₅ vapor concentrations for the D₅ exposure group were 157.4±1.3ppm, 158.0±3.6ppm and 160.2±3.7ppm D₅ vapor (mean concentration ± standard deviation) for 1, 2 and 4 five-day exposure periods, respectively. The individual chamber daily mean exposure concentrations are summarized in table 3 (this appendix).

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Figure 1

Diagram of Exposure Chamber and Sampling System

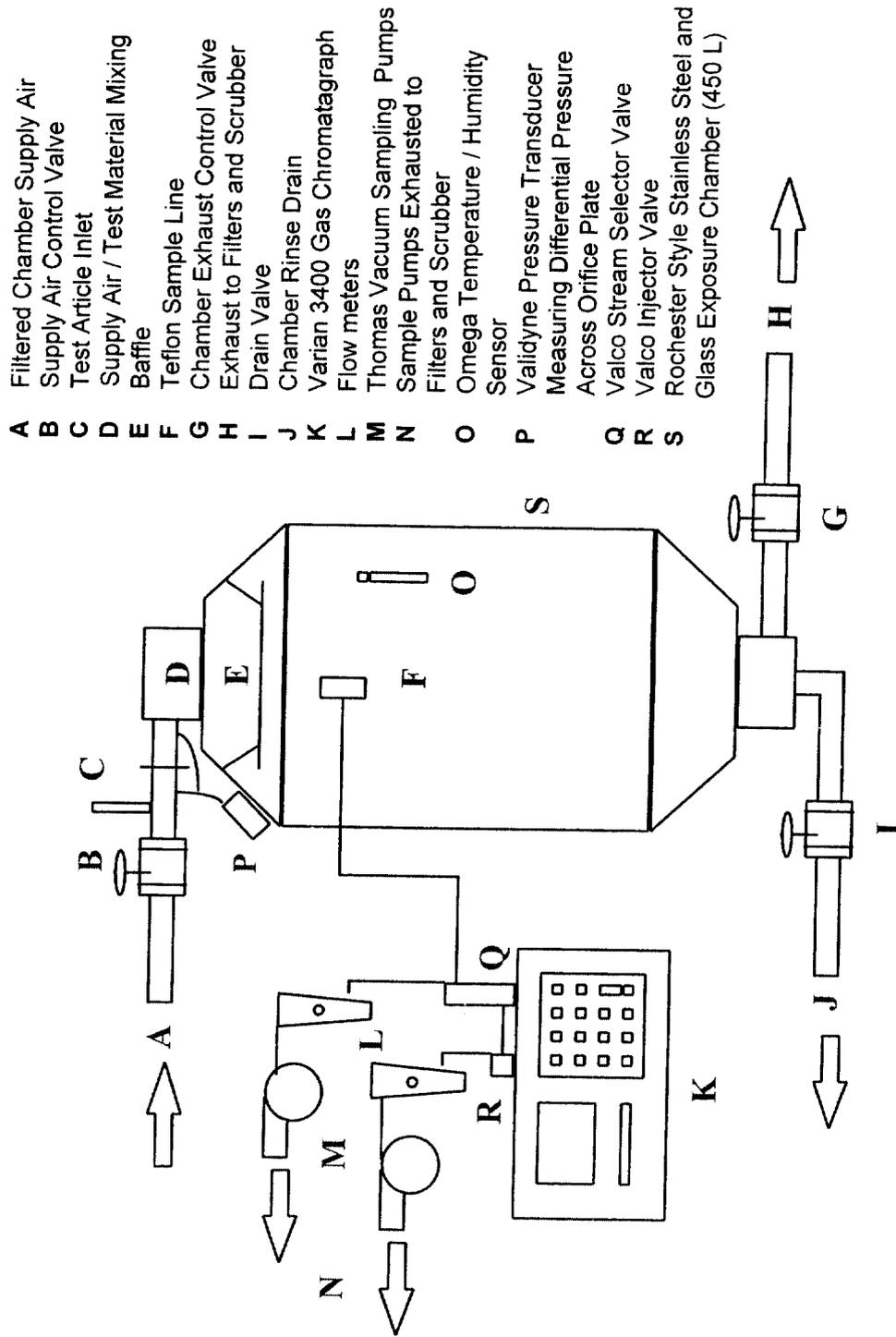


Figure 2

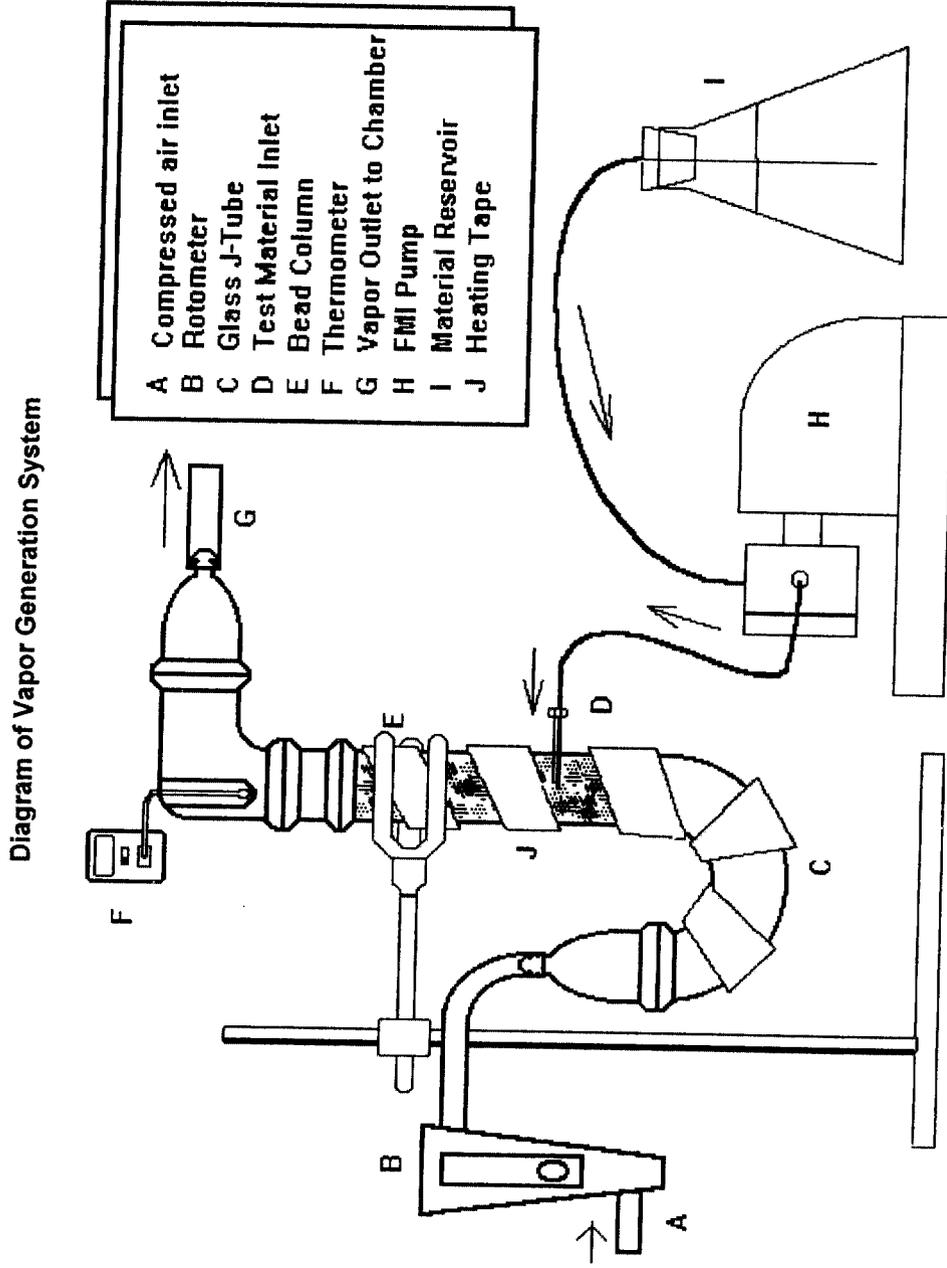
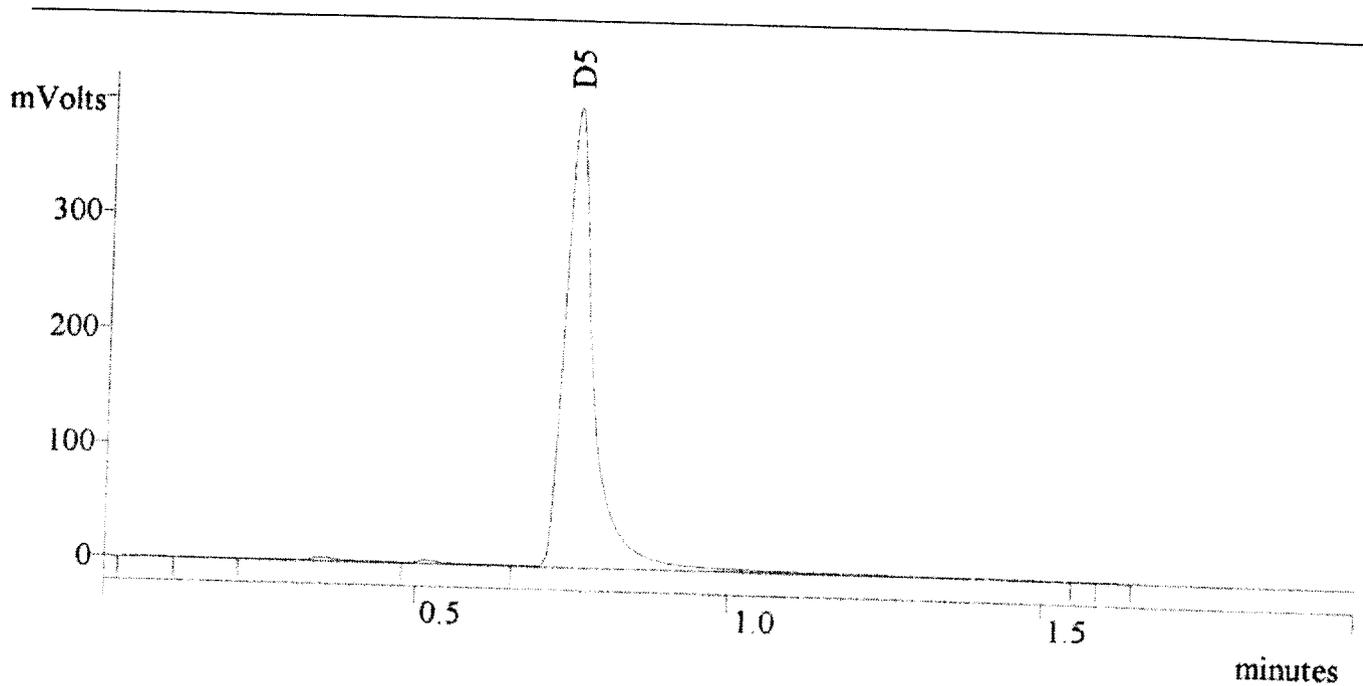


Figure 3

Typical Gas Chromatography Chromatogram



Peak No	Ret. Time (min)	Peak Name	Concentration (ppm)	Time Offset (min)	Area (counts)	Rel Ret Time	Sep. Code	Status Codes
1	0.084		0	0.000	125	0.00	BV	
2	0.195		0	0.000	133	0.00	VV	
3	0.354		0	0.000	1140	0.00	VV	
4	0.519		0	0.000	843	0.00	VV	
5	0.748	D5	153	-0.012	132315	0.00	VB	
Totals			153	-0.012	134556			

Table 1

Gas Chromatography Conditions for Decamethylcyclopentasiloxane Analysis

Gas Chromatograph (GC)

Model:	Varian® 3400
Identification:	13440
Software:	Varian® Star version 4.5 for Windows® 95

GC Injector

Initial temperature:	225 degrees C (Isothermal)
----------------------	----------------------------

GC Column

Model:	J & W DB-5
Serial number:	1277624a
Length:	15 meter
Film thickness:	1.5 µm
Carrier gas:	Helium
Temperature:	150 degrees C (Isothermal)
Hold time:	6 minutes

GC Detector

Type:	FID
Temperature:	250 degrees C

Flow Rates

Air:	288 ml/min.
Helium:	10.7 ml/min.
Helium + make-up:	28.9 ml/min.
Hydrogen:	60.2 ml/min.

Autosampler

Type:	Valco stream selector valve
Sample loop volume:	229 µL

Table 2

Chamber Temperature and Humidity Summary

0ppm D ₅ Exposure Group								
Five-day Exposure Period	Study Day	Mean Daily Temperature (oC)			Mean Daily Humidity (%)			
		Chamber 1	Chamber 2	Mean	Chamber 1	Chamber 2	Mean	
First	1	23.9	23.2	23.6	37.7	38.5	38.1	
	2	23.8	22.7	23.3	37.9	37.5	37.7	
	3	22.7	22.0	22.4	38.6	38.5	38.6	
	4	22.9	22.4	22.7	39.4	38.8	39.1	
	5	22.8	21.7	22.3	38.7	40.0	39.4	
				Mean =	22.8		Mean =	38.6
				Std dev =	0.6		Std dev =	0.7
Second	8	22.7	22.0	22.4	38.9	39.4	39.2	
	9	22.5	21.9	22.2	40.3	41.0	40.7	
	10	23.0	22.3	22.7	40.8	40.0	40.4	
	11	23.1	22.4	22.8	40.9	40.6	40.8	
	12	23.1	22.6	22.9	42.9	41.7	42.3	
				Mean ¹ =	22.7		Mean ¹ =	39.6
			Std dev ¹ =	0.4		Std dev ¹ =	1.4	
Third	15	22.4	21.5	22.0	41.7	42.2	42.0	
	16	22.4	22.0	22.2	42.2	41.7	42.0	
	17	22.8	22.2	22.5	42.6	42.2	42.4	
	18	22.3	21.5	21.9	40.7	41.2	41.0	
	19	22.5	22.3	22.4	43.5	42.5	43.0	
Fourth	22	23.0	22.4	22.7	42.7	42.7	42.7	
	23	22.0	22.0	22.0	46.0	43.0	44.5	
	24	22.4	22.0	22.2	45.0	44.7	44.9	
	25	23.4	22.9	23.2	43.6	42.9	43.3	
	26	23.1	22.9	23.0	41.2	40.5	40.9	
				Mean ² =	22.5		Mean ² =	41.1
			Std dev ² =	0.5		Std dev ² =	2.0	

¹Mean and standard deviation of values for the entire period (1 and 2 five-day exposures)

²Mean and standard deviation of values for the entire period (1-4 five-day exposures)

Table 2

Chamber Temperature and Humidity Summary
 (Continued)

160ppm D ₅ Exposure Group							
Five-day Exposure Period	Study Day	Mean Daily Temperature (°C)			Mean Daily Humidity (%)		
		Chamber 1	Chamber 2	Mean	Chamber 1	Chamber 2	Mean
First	1	25.2	24.8	25.0	34.4	35.2	34.8
	2	24.9	25.1	25.0	34.1	35.8	35.0
	3	24.2	24.2	24.2	34.6	33.7	34.2
	4	24.6	24.7	24.7	34.9	36.5	35.7
	5	23.7	24.0	23.9	36.4	34.9	35.7
				Mean =	24.5		Mean =
			Std dev =	0.5		Std dev =	0.6
Second	8	24.2	24.1	24.2	35.3	35.8	35.6
	9	23.9	23.5	23.7	36.2	37.2	36.7
	10	24.6	24.2	24.4	35.0	36.8	35.9
	11	23.8	24.0	23.9	35.6	35.1	35.4
	12	24.2	24.1	24.2	36.3	37.8	37.1
			Mean ¹ =	24.3		Mean ¹ =	35.6
			Std dev ¹ =	0.5		Std dev ¹ =	0.9
Third	15	23.6	23.6	23.6	35.6	35.8	35.7
	16	23.4	23.5	23.5	37.0	36.3	36.7
	17	23.8	23.9	23.9	36.6	36.7	36.7
	18	23.1	23.4	23.3	35.2	35.6	35.4
	19	23.6	23.7	23.7	37.2	37.8	37.5
Fourth	22	23.5	23.6	23.6	38.3	38.4	38.4
	23	23.9	23.9	23.9	37.3	38.5	37.9
	24	23.7	23.5	23.6	38.7	39.6	39.2
	25	24.4	24.5	24.5	38.0	38.8	38.4
	26	24.0	23.7	23.9	36.9	37.6	37.3
			Mean ² =	24.0		Mean ² =	36.4
			Std dev ² =	0.5		Std dev ² =	1.3

¹Mean and standard deviation of values for the entire period (1 and 2 five-day exposures)

²Mean and standard deviation of values for the entire period (1-4 five-day exposures)

Table 2

Chamber Temperature and Humidity Summary
 (Continued)

Phenobarbital Exposure Group								
Five-day Exposure Period	Study Day	Mean Daily Temperature (oC)			Mean Daily Humidity (%)			
		Chamber 1	Chamber 2	Mean	Chamber 1	Chamber 2	Mean	
First	1	25.0	24.3	24.7	33.5	38.3	35.9	
	2	25.3	23.7	24.5	31.8	38.3	35.1	
	3	24.5	22.5	23.5	31.6	39.1	35.4	
	4	24.9	23.3	24.1	32.3	39.1	35.7	
	5	24.2	22.3	23.3	32.8	40.3	36.6	
			Mean =		24.0	Mean =		35.7
			Std dev =		0.6	Std dev =		0.6
Second	8	24.3	22.9	23.6	33.3	39.9	36.6	
	9	23.9	22.7	23.3	35.0	41.0	38.0	
	10	24.6	23.2	23.9	33.4	40.6	37.0	
	11	24.3	23.1	23.7	34.4	41.4	37.9	
	12	24.4	23.4	23.9	35.6	43.4	39.5	
			Mean ¹ =		23.8	Mean ¹ =		36.8
		Std dev ¹ =		0.5	Std dev ¹ =		1.4	
Third	15	23.9	22.1	23.0	35.7	43.2	39.5	
	16	23.8	23.0	23.4	36.9	42.2	39.6	
	17	24.3	22.2	23.3	37.0	45.7	41.4	
	18	23.9	21.6	22.8	36.0	44.2	40.1	
	19	24.2	22.5	23.4	37.8	45.8	41.8	
Fourth	22	24.0	22.0	23.0	38.7	47.7	43.2	
	23	24.2	22.0	23.1	38.1	47.2	42.7	
	24	23.8	22.9	23.4	40.3	45.2	42.8	
	25	24.8	22.5	23.7	39.0	47.4	43.2	
	26	24.3	23.1	23.7	38.3	43.1	40.7	
			Mean ² =		23.5	Mean ² =		39.1
		Std dev ² =		0.5	Std dev ² =		2.8	

¹Mean and standard deviation of values for the entire period (1 and 2 five-day exposures)

²Mean and standard deviation of values for the entire period (1-4 five-day exposures)

Table 3

Chamber D ₅ Vapor Concentration Summary					
160ppm D ₅ Exposure Group					
Five-day Exposure Period	Study Day	Mean Daily Chamber Concentrations (ppm D ₅)			
		Chamber 1	Chamber 2	Mean	
First	1	157	161	159.0	
	2	155	159	157.0	
	3	156	159	157.5	
	4	157	159	158.0	
	5	154	157	155.5	
				Mean =	157.4
				Std dev =	1.3
Second	8	155	159	157.0	
	9	153	156	154.5	
	10	152	155	153.5	
	11	160	163	161.5	
	12	166	166	166.0	
				Mean ¹ =	158.0
			Std dev ¹ =	3.6	
Third	15	160	162	161.0	
	16	157	159	158.0	
	17	159	161	160.0	
	18	163	163	163.0	
	19	165	165	165.0	
Fourth	22	161	162	161.5	
	23	165	165	165.0	
	24	163	163	163.0	
	25	162	163	162.5	
	26	166	164	165.0	
				Mean ² =	160.2
			Std dev ² =	3.7	

¹Mean and standard deviation of values for the entire period (1 and 2 five-day exposures)

²Mean and standard deviation of values for the entire period (1-4 five-day exposures)

APPENDIX C

Individual Animal Clinical Observations for Study 8631

Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study

Individual Animal Clinical Observations – Group 1-A

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day						
				1	2	3	4	5	6	
Control	1-A	C7205	Normal	P	P	P	P	P	P	NP
			Urine staining, perineal region	NP	NP	NP	NP	NP	P	
Control	1-A	C7206	Normal	P	P	P	P	P	P	
Control	1-A	C7207	Normal	NP	P	P	P	P	P	
Control	1-A	C7208	Urine staining, perineal region	P	NP	NP	NP	NP	NP	NP
Control	1-A	C7209	Normal	P	P	P	P	P	P	
Control	1-A	C7210	Normal	P	P	P	P	NP	NP	
Control	1-A	C7211	Porphyrin staining, eye(s)	NP	NP	NP	P	P	P	
Control	1-A	C7212	Normal	P	NP	NP	NP	NP	NP	
Control	1-A	C7213	Urine staining, perineal region	NP	P	P	P	P	P	
Control	1-A	C7214	Normal	P	P	P	P	P	P	

Individual Animal Clinical Observations – Group 1-B

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day														
				1	2	3	4	5	6	7	8	9	10	11	12	13		
Control	1-B	C7215	Normal	P	NP													
			Urine staining, perineal region	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-B	C7216	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-B	C7217	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-B	C7218	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-B	C7219	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-B	C7220	Normal	P	NP													
			Urine staining, perineal region	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-B	C7221	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-B	C7222	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-B	C7223	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-B	C7224	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 1-C

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day														
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Control	1-C	C7225	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7226	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7227	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7228	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7229	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7230	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7231	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7232	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7233	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7234	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 1-C (continued)

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day													
				15	16	17	18	19	20	21	22	23	24	25	26	27	
Control	1-C	C7225	Normal	P	NP	NP	NP	NP	NP	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	P	P	P	P	NP								
Control	1-C	C7226	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	P	P	NP	NP	NP	NP	NP
Control	1-C	C7227	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7228	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7229	Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Urine staining, perineal region	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7230	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7231	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7232	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
Control	1-C	C7233	Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Urine staining, perineal region	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Control	1-C	C7234	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 2-A

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day					
				1	2	3	4	5	6
160 ppm D ₅	2-A	C7235	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7236	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7237	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7238	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7239	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7240	Normal	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-A	C7241	Urine staining, perineal region	P	P	P	P	P	P
160 ppm D ₅	2-A	C7242	Normal	P	P	P	P	P	P
160 ppm D ₅	2-A	C7243	Normal	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-A	C7244	Urine staining, perineal region	P	P	P	P	P	P
160 ppm D ₅	2-A	C7244	Normal	P	P	P	P	P	P

Individual Animal Clinical Observations – Group 2-B

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day																					
				1	2	3	4	5	6	7	8	9	10	11	12	13									
160 ppm D ₅	2-B	C7245	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P								
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP						
160 ppm D ₅	2-B	C7246	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P							
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP					
160 ppm D ₅	2-B	C7247	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P						
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP				
160 ppm D ₅	2-B	C7248	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P					
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP			
160 ppm D ₅	2-B	C7249	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P				
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP		
160 ppm D ₅	2-B	C7250	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	
160 ppm D ₅	2-B	C7251	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-B	C7252	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-B	C7253	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-B	C7254	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 2-C

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day															
				1	2	3	4	5	6	7	8	9	10	11	12	13	14		
160 ppm D ₅	2-C	C7255	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7256	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7257	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7258	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7259	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7260	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7261	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7262	Dried fluid, eye(s)	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7263	Porphyrin staining, eye(s)	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7264	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 2-C (continued)

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day													
				15	16	17	18	19	20	21	22	23	24	25	26	27	
160 ppm D ₅	2-C	C7255	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Normal	NP	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7256	Urine staining, perineal region	P	NP												
			Normal	NP	NP	P	NP	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7257	Urine staining, perineal region	P	P	NP	NP	P	NP	NP	NP	NP	P	NP	NP	P	NP
160 ppm D ₅	2-C	C7258	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7259	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7260	Normal	P	P	NP	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7261	Urine staining, perineal region	NP	NP	P	NP										
160 ppm D ₅	2-C	C7262	Dried fluid, eye(s)	P	NP												
			Urine staining, perineal region	NP	P	P	P	NP	NP	P	NP						
			Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
160 ppm D ₅	2-C	C7263	Porphyryn staining, eye(s)	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
160 ppm D ₅	2-C	C7264	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

Individual Animal Clinical Observations – Group 3-A

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day					
				1	2	3	4	5	6
0.05% PB	3-A	C7265	Normal	P	P	P	P	P	P
				P	P	P	P	P	P
0.05% PB	3-A	C7266	Normal	P	P	P	P	P	P
				P	P	P	P	P	P
0.05% PB	3-A	C7267	Porphyrin staining, eye(s)	NP	NP	P	P	NP	NP
				P	P	P	P	NP	P
0.05% PB	3-A	C7268	Urine staining, perineal region	NP	NP	NP	NP	P	NP
				P	P	P	P	NP	P
0.05% PB	3-A	C7269	Porphyrin staining, eye(s)	P	P	P	P	NP	NP
				NP	NP	NP	NP	P	P
0.05% PB	3-A	C7270	Porphyrin staining, eye(s)	P	P	NP	NP	NP	P
				NP	NP	P	P	P	NP
0.05% PB	3-A	C7271	Normal	P	P	P	P	P	P
				P	P	P	P	P	P
0.05% PB	3-A	C7272	Normal	P	P	P	P	P	P
				P	P	P	P	P	P
0.05% PB	3-A	C7273	Normal	P	P	P	P	P	P
				P	P	P	P	P	P
Control	3-A	C7274	Porphyrin staining, eye(s)	P	P	NP	NP	NP	NP
				NP	NP	P	P	P	P

Individual Animal Clinical Observations – Group 3-C

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day																
				1	2	3	4	5	6	7	8	9	10	11	12	13	14			
0.05% PB	3-C	C7285	Normal	P	P	NP	P	P	P	P	P	P	P	P	P	P	P	P		
			Pophryin staining, eye(s)	NP	F	NP														
0.05% PB	3-C	C7286	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7287	Normal	P	NP	P														
			Urine staining, perineal region	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
0.05% PB	3-C	C7288	Pophryin staining, eye(s)	NP	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	P	NP															
0.05% PB	3-C	C7289	Urine staining, perineal region	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7290	Urine staining, perineal region	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7291	Urine staining, perineal region	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	P	NP															
0.05% PB	3-C	C7292	Urine staining, perineal region	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7293	Urine staining, perineal region	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
0.05% PB	3-C	C7294	Urine staining, perineal region	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	P	NP
			Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

Individual Animal Clinical Observations – Group 3-C (continued)

Treatment Group	Sub-Group	Animal Number	Clinical Sign	Study Day															
				15	16	17	18	19	20	21	22	23	24	25	26	27			
0.05% PB	3-C	C7285	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Pophyryn staining, eye(s)	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7286	Normal	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7287	Normal	NP	NP	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Urine staining, perineal region	P	P	NP	NP	NP	P	P	P	P	P	P	P	P	P	P	P
0.05% PB	3-C	C7288	Pophyryn staining, eye(s)	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	P	NP	P	NP												
0.05% PB	3-C	C7289	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7290	Urine staining, perineal region	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7291	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	P	NP	P	NP												
0.05% PB	3-C	C7292	Urine staining, perineal region	NP	P	NP													
			Normal	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
0.05% PB	3-C	C7293	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	P	P	NP	P	P	P	P	P	P	P	P	P	P	P	P	P
0.05% PB	3-C	C7294	Urine staining, perineal region	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP
			Normal	P	NP	P	NP												

APPENDIX D

Individual Animal and Organ Weights for Study 8631

Non-Regulated Study: Effects of Decamethylcyclopentasiloxane (D₅) on Cell Proliferation in the Liver of Female Fischer 344 Rats: A 28-Day Inhalation Study

Individual Animal and Organ Weights – Group A

Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7205	Control	F	153.5	5.6303	1.6414	1.0400	0.00820
C7206	Control	F	150.0	5.4558	1.5977	0.9102	0.01048
C7207	Control	F	156.4	5.8074	1.7267	0.8737	0.01220
C7208	Control	F	149.7	4.9106	1.6400	0.7566	0.01159
C7209	Control	F	156.3	5.4885	1.6453	0.8285	0.01019
C7210	Control	F	157.3	5.4965	1.6278	0.7798	0.00857
C7211	Control	F	162.3	5.8249	1.6342	0.8107	0.01194
C7212	Control	F	158.3	5.2410	1.6792	0.7974	0.01270
C7213	Control	F	151.2	5.1241	1.6409	0.7437	0.01203
C7214	Control	F	166.6	6.0132	1.6041	0.8360	0.00985
MEAN =			156.2	5.4992	1.6437	0.8377	0.0108
STDEV =			5.4	0.3397	0.0368	0.0874	0.0016
Animal #	Dose (D5)	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7235	160 ppm	F	154.8	6.4085	1.6025	0.7820	0.01274
C7236	160 ppm	F	154.3	6.2574	1.5863	0.9150	0.01135
C7237	160 ppm	F	156.8	6.2418	1.5017	0.9548	0.01200
C7238	160 ppm	F	157.2	6.0029	1.6307	0.8509	0.01220
C7239	160 ppm	F	154.5	6.0211	1.6217	0.8191	0.01145
C7240	160 ppm	F	164.2	6.6114	1.6329	0.8310	0.01138
C7241	160 ppm	F	156.6	5.8207	1.6997	0.7830	0.01217
C7242	160 ppm	F	160.1	6.0833	1.6005	0.8821	0.01120
C7243	160 ppm	F	166.1	6.3350	1.6160	0.8901	0.01244
C7244	160 ppm	F	163.4	5.9750	1.6395	0.8534	0.01347
MEAN =			158.8	6.1757	1.6132	0.8561	0.0120
STDEV =			4.4	0.2378	0.0499	0.0557	0.0007
Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7265	PB	F	158.0	7.3000	1.5429	0.7483	0.00925
C7266	PB	F	157.6	7.3758	1.5822	0.8206	0.01335
C7267	PB	F	157.1	7.6330	1.6225	0.8081	0.01454
C7268	PB	F	157.4	7.3474	1.6513	0.8104	0.01204
C7269	PB	F	165.8	7.0514	1.6051	0.8871	0.01172
C7270	PB	F	154.1	6.9805	1.6053	0.7645	0.01162
C7271	PB	F	163.4	7.3967	1.6608	0.7877	0.01270
C7272	PB	F	162.6	7.2210	1.6579	0.8248	0.01233
C7273	PB	F	151.4	6.7523	1.6177	0.7730	0.01339
C7274	PB	F	166.9	6.8319	1.6934	0.8987	0.01280
MEAN =			159.4	7.1890	1.6239	0.8123	0.0124
STDEV =			5.1	0.2777	0.0436	0.0493	0.0014

Individual Animal and Organ Weights - Group B

Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7215	Control	F	154.8	5.6757	1.6414	0.8381	0.01004
C7216	Control	F	162.0	5.9269	1.6715	0.7861	0.00992
C7217	Control	F	157.2	5.8950	1.6827	0.8395	0.01237
C7218	Control	F	153.1	5.5495	1.6430	0.7302	0.01034
C7219	Control	F	155.5	5.7214	1.6591	0.8215	0.01308
C7220	Control	F	156.8	5.2901	1.6300	0.7961	0.00933
C7221	Control	F	163.9	5.9950	1.6434	0.8632	0.01165
C7222	Control	F	159.4	5.7954	1.6542	0.8293	0.01458
C7223	Control	F	162.5	5.4963	1.6832	0.7714	0.00897
C7224	Control	F	165.4	5.3824	1.6994	0.7963	0.01078
MEAN =			159.1	5.6728	1.6608	0.8072	0.0111
STDEV =			4.2	0.2386	0.0226	0.0391	0.0018
Animal #	Dose (D5)	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7245	160 ppm	F	164.8	6.6149	1.6966	0.8132	0.01027
C7246	160 ppm	F	158.9	6.0230	1.6198	0.8185	0.00927
C7247	160 ppm	F	156.5	5.9533	1.5451	0.7566	0.00965
C7248	160 ppm	F	156.6	6.4765	1.6644	0.7823	0.00983
C7249	160 ppm	F	158.8	5.9924	1.6638	0.8013	0.01186
C7250	160 ppm	F	163.7	6.3161	1.5766	0.8290	0.00914
C7251	160 ppm	F	172.1	7.1182	1.6634	0.8950	0.01162
C7252	160 ppm	F	160.9	6.3938	1.6754	0.7954	0.01187
C7253	160 ppm	F	164.7	6.3735	1.6616	0.8427	0.01157
C7254	160 ppm	F	160.3	5.4808	1.6737	0.8255	0.01085
MEAN =			161.7	6.2743	1.6440	0.8160	0.0106
STDEV =			4.7	0.4435	0.0483	0.0373	0.0011
Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7275	PB	F	158.7	7.3000	1.6051	0.7632	0.01195
C7276	PB	F	157.8	7.4617	1.5960	0.7811	0.01395
C7277	PB	F	162.1	7.7254	1.6384	0.7932	0.01166
C7278	PB	F	166.4	7.1061	1.6296	0.8060	0.01231
C7279	PB	F	162.2	7.7321	1.5875	0.8002	0.01497
C7280	PB	F	156.1	6.8480	1.5997	0.7595	0.00997
C7281	PB	F	160.2	7.1475	1.6482	0.7876	0.01250
C7282	PB	F	162.0	6.8938	1.5805	0.7505	0.01257
C7283	PB	F	164.7	7.2314	1.6552	0.8161	0.01378
C7284	PB	F	166.9	7.2057	1.6771	N/D	0.01273
MEAN =			161.7	7.2652	1.6217	0.7842	0.0126
STDEV =			3.6	0.3028	0.0325	0.0225	0.0014

Individual Animal and Organ Weights – Group C

Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7225	Control	F	163.0	5.7587	1.7514	0.7826	0.00966
C7226	Control	F	165.5	5.6440	1.6987	0.8147	0.00901
C7227	Control	F	158.7	5.3866	1.6863	0.7721	0.01162
C7228	Control	F	158.7	5.5107	1.6803	0.7612	0.01024
C7229	Control	F	167.8	6.1275	1.5970	0.8173	0.01064
C7230	Control	F	166.7	5.3883	1.6724	0.7750	0.01226
C7231	Control	F	163.9	5.4020	1.6649	0.7997	0.01079
C7232	Control	F	168.8	5.7395	1.6592	0.7831	0.01414
C7233	Control	F	167.6	5.6767	1.6934	0.7843	0.01106
C7234	Control	F	175.7	5.492	1.6971	0.8091	0.01440
MEAN =			165.6	5.6126	1.6801	0.7899	0.0114
STDEV =			5.0	0.2305	0.0388	0.0192	0.0018
Animal #	Dose (D5)	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7255	160 ppm	F	161.1	5.9117	1.6983	0.8189	0.01051
C7256	160 ppm	F	164.4	6.2589	1.6883	0.7582	0.01266
C7257	160 ppm	F	163.6	6.8233	1.6424	0.8275	0.01304
C7258	160 ppm	F	166.4	6.5449	1.7328	0.8194	0.01154
C7259	160 ppm	F	164.6	6.1081	1.6605	0.7702	0.01388
C7260	160 ppm	F	162.2	5.4223	1.6986	0.7942	0.01166
C7261	160 ppm	F	167.4	6.0365	1.7382	0.8225	0.01271
C7262	160 ppm	F	159.7	5.5046	1.6976	0.7827	0.01224
C7263	160 ppm	F	162.4	5.0657	1.6965	0.7935	0.01393
C7264	160 ppm	F	163.0	5.5747	1.7209	0.8307	0.01043
MEAN =			163.5	5.9251	1.6974	0.8018	0.0123
STDEV =			2.3	0.5415	0.0297	0.0256	0.0012
Animal #	Dose	Sex	Body Weight (g)	Liver Weight (g)	Brain Weight (g)	Lung Weight (g)	Thyroid Weight (g)
C7285	PB	F	164.6	7.9021	1.6565	0.7606	0.01566
C7286	PB	F	157.8	7.4983	1.6511	0.7342	0.01289
C7287	PB	F	175.2	8.0975	1.6781	0.8709	0.01172
C7288	PB	F	161.0	7.1336	1.6048	0.7738	0.01430
C7289	PB	F	166.4	7.9450	1.6244	0.8443	0.01782
C7290	PB	F	164.4	7.6594	1.6607	0.8086	0.01399
C7291	PB	F	168.3	7.5719	1.6416	0.7902	0.01465
C7292	PB	F	170.2	8.0162	1.6363	0.8207	0.01462
C7293	PB	F	167.6	6.6677	1.6679	0.7940	0.01438
C7294	PB	F	163.4	7.2521	1.6006	0.8200	0.01953
MEAN =			165.9	7.5744	1.6422	0.8017	0.0150
STDEV =			4.9	0.4530	0.0259	0.0402	0.0023