Protocol No. HLS Study No. 00-6128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate

١.

ITI Study No. ITI 801 Security: Industrial

# GLP COMPLIANCE STATEMENT

This study was conducted in compliance with EPA Good Laboratory Practices as set forth in 79.60, CFR Vol. 59, No. 122, 27 June 1994 with the following exceptions:

The identity, strength, purity and composition or other characteristics to define the positive control article have not been determined by the Testing Facility. The positive control article has been characterized as per the Certificate of Analysis on file with the Testing Facility. The stability of the positive control article has not been determined by the Testing Facility. Analyses to determine the uniformity (as applicable) or concentration of the positive control article mixture were not performed by the Testing Facility. The stability of the positive control article mixture has not been determined by the Testing Facility.

The method used for antibody-forming cell assay has not been formally validated.

Kinber L. White, Jr., Ph.D

Principal Investigator ImmunoTox®, Inc.

Gary M. Hoffman, B.A., DABT Study Director Huntingdon Life Sciences

#### Page 2 of 27

Protocol No. HLS Study No. 00-8128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate ITI Study No. ITI 801 Security: Industrial Page 1213

# II. QUALITY ASSURANCE STATEMENT

Test Substance: Gasoline TAME Vapor Condensate

Report Title: Immunological Evaluation of Gasoline TAME Vapor Condensate in Female Sprague Dawley Rats Using the Plaque-Forming Cell Assay

Protocol Title: Gasoline TAME Vapor Condensate: A 13-Week Whole-Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments And 4-Week *In Vivo* Genotoxicity and Immunotoxicity Assessments

Protocol No.: HLS Study No. 00-6128

The final report for the indicated protocol has been reviewed by the Quality Assurance Unit of Virginia Commonwealth University. Furthermore, the Quality Assurance Unit has conducted the following inspections and reported to the Immuno $Tox^{\Phi}$ , inc. Principal Investigator, and then has submitted written reports of said inspections to the Study Director and Management.

Inspection/Audits were performed and reported on the following dates:

Performed	Reported	Activity
25 July 2001	25 July 2001	AFC Assay
24-25 January 2002	28 January 2002	Data Audit
24-25 January 2002	28 January 2002	1st Draft Report Audit

Approved and submitted by: Quality Assurance Manager

Ωdii Date

Office of Research \* Quality Assurance Unit \* Box 980568 \* Richmond, Virginia 23298 0568 \* (804) 828-5587 \* Fax (804) 828-5604

Page 3 of 27

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management. This report reflects the raw data as far as can be reasonably established.

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
Facility Inspection	26 Sep 00	5 Dec 00
GLP Protocol Review	20,24 Apr 01	24 Apr 01
Exposure, Monitoring & Equipment Records	26 Jun 01	26 Jun 01
Positive Control Dosing	20 Jul 01	20 Jul 01
Immunotoxicity Necropsy and Training Records	24 Jul 01	24 Jul 01
Subcontractor Final Report	22-25 Feb 02	26 Feb 02
Final Report Review and Protocol Amendments 1-5	5-7 Jan 09	9 Jan 09
Protocol Amendment 6	11 Aug 11	11 Aug 11

rove

Fran Jannone B.A., RQAP-GLP Quality Assurance Group Leader

18 Aug. 11 Date ()

4 of 27

Protocol No. HLS Study No. 00-6128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate ITI Study No. ITI 801 Security: Industrial Page 1215

# III. SIGNATURE OF PRINCIPALS

This report describes the results used to evaluate the relative immunotoxicological potential of the test substance, Gasoline TAME Vapor Condensate, which was administered by inhalation via whole-body exposure to female Sprague Dawley rats.

Kimber L. White, Jr., Ph.D., Principal Investigator, was responsible for the overall conduct of the immunotoxicity evaluations in this study. Vanessa L. Peachee, Ph.D., served as the Assistant Principal Investigator and was responsible for the day-to-day activities of the immunotoxicity evaluations in this study.

Kimber L. White, Jr., Ph.D. Principal Investigator ImmunoTox®, Inc.

1. En Date <u>38 Apr 11</u> All Date <u>28 Apr 11</u>

Vanessa L. Peachee, Ph.D. Assistant Principal Investigato ImmunoTox<sup>®</sup>, Inc.

Approved:

Gary M. Hoffman, B.A., DABT

Study Director Huntingdon Life Sciences

6000 Date

#### Page 5 of 27

ITI Study No. ITI 801 Security: Industrial

# TABLE OF CONTENTS

Ι.	GLP	Compliance Statement2
11.	Qual	ity Assurance Statements
	Imm	unoTox®, Inc
	Hunt	ingdon Life Sciences4
III.	Sign	ature of Principals5
IV.	Exec	utive Summary8
V.	Intro	duction 10
VI.	Meth	ods of Procedure 12
	Ex	perimental Design
	Va	riables Assessed
	7	Ferminal Body and Organ Weights12
	5	plenocyte Preparation
	S	pleen IgM Antibody Response to the T-dependent Antigen, sRBC. Day 4 Response 13
	Da	ta14
	ĩ	Data Handling and Statistical Analysis14
	Ι	Data Retention
VII.	Resu	lts
	Te	rminal Body and Organ Weights15
	Sp	leen IgM Antibody Response to the T-dependent Antigen, sRBC. Day 4 Response 17
VIII.	Cond	20 clusion
IX.	Refe	rences
х.	List	of Figures
	1.	Absolute (mg) and Relative (%) Spleen Weight in Female Sprague Dawley Rats
		Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for
		4 Weeks
	2.	Absolute (mg) and Relative (%) Thymus Weight in Female Sprague Dawley Rats
		Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for
		4 Weeks
	3.	Spleen Cell Number in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor
		Condensate via Inhalation for 5 Days per Week for 4 Weeks

Page 6 of 27

# APPENDICES

XI.

A Individual Animal Data

B Contracting Sponsor's Exposure and Animal Data

# IV. EXECUTIVE SUMMARY

The study was conducted as part of Huntingdon Life Sciences (HLS) Study No. 00-6128 at ImmunoTox<sup>®</sup>, Inc., Richmond, Virginia. The Principal Investigator was Kimber L. White, Jr., Ph.D., and Vanessa L. Peachee, M.S., served as the Assistant Principal Investigator. The study was conducted to provide evaluation of immunological parameters for Huntingdon Life Sciences.

The objective of the study was to determine the potential effects of Gasoline TAME Vapor Condensate for its ability to affect the humoral immune component of the immune system, when evaluated in the antibody-forming cell response to the T-dependent antigen, sheep erythrocytes. Female Sprague Dawley rats were administered Gasoline TAME Vapor Condensate for 5 days per week for 4 weeks by inhalation via whole body exposure by Huntingdon Life Sciences (HLS) Princeton Research Center (PRC) personnel. Three exposure levels of 2,000, 10,000 and 20,000 mg/m<sup>3</sup> of the test substance were used in the study. The in-life phase of the study was conducted by HLS, East Millstone, NJ; and the immunological evaluation was conducted by ImmunoTox<sup>®</sup>, Inc., Richmond, VA. On the day of sacrifice, spleens were placed in tubes containing media, placed on ice, and shipped to ImmunoTox<sup>®</sup>, Inc. in Richmond, VA, for assay evaluation on the following day.

Executive Summary Table ES-1 shows a summary of the selected toxicology and immunology parameters evaluated. Exposure to Gasoline TAME Vapor Condensate resulted in no statistically significant changes in terminal body weight for any exposure level. Furthermore, there were no statistically significant effects observed in either thymus or spleen weight following exposure to Gasoline TAME Vapor Condensate, when evaluated as either absolute or relative weight (% body weight), as compared to the air control.

Exposure to Gasoline TAME Vapor Condensate did not result in statistically significant changes in the IgM antibody-forming cell (AFC) response to the T-dependent antigen, sheep erythrocytes, when evaluated as either specific activity (AFC/10<sup>6</sup> spleen cells) or as total spleen activity (AFC/spleen). The positive control, CPS, produced the anticipated results in the various parameters evaluated.

In conclusion, the results of this immunotoxicological evaluation demonstrate that, under the experimental conditions used, exposure to the Gasoline TAME Vapor Condensate test substance did not adversely affect the functional ability of the humoral immune component of the immune system.

Page 8 of 27

ITI Study No. ITI 801 Security: Industrial

# Table ES-1

# SUMMARY TABLE FOR TOXICOLOGY AND IMMUNOLOGY STUDIES

Parameter	Result	Maximum Effect	Exposure Level (mg/m <sup>3</sup> )
Terminal Body Weight			***************************************
Day 28	No Effect		
Organ Weights (Absolute	and Relative)		
Spleen	No Effect		
Thymus	No Effect		
Spleen IgM Antibody-Forr	ning Cell Respons	se to Sheep Erythrocy	tes
IgM AFC/10 <sup>6</sup> Spleen Cells	No Effect		
IgM AFC/Spleen (x103)	No Effect		

Page 9 of 27

ITI Study No. ITI 801 Security: Industrial

# V. INTRODUCTION

The purpose of this study was to provide evaluation of immunological parameters for Huntingdon Life Sciences (HLS) Study No. 00-6128. In this study, the ability of the test substance, Gasoline TAME Vapor Condensate, was evaluated for its ability to affect the humoral immune component of the immune system, when evaluated in the antibody-forming cell response to the T-dependent antigen sheep erythrocytes. The study was conducted in female animals because female rats have a more robust immune response than do the male animal of the species. Accordingly, female rats have a greater sensitivity for detecting an adverse effect of a compound should one occur. Routinely, immunotoxicology evaluations conducted by the National Toxicology Program (NTP) evaluate compounds only in female animals. Four days prior to sacrifice, ImmunoTox<sup>®</sup>, Inc. personnel sensitized the rats by intravenous administration of sheep erythrocytes at the HLS facility. On the day of sacrifice, HLS Princeton Research Center (PRC) personnel aseptically removed the spleen from each animal. The spleens were weighed, placed in tubes containing media, and sent to ImmunoTox®, Inc. in Richmond, VA, on ice for evaluation the following day. Spleens were received on 25 July 2001 and the immunological evaluation was conducted on the same day. The IgM antibody-forming cell (AFC) response to the T-dependent antigen sheep erythrocytes, also referred to as the plaque assay, was the immunological assay conducted to evaluate the effect of Gasoline TAME Vapor Condensate on the immune response. This assay has been shown to be the most predictive functional assay for determining the immunotoxicological potential of a compound (Luster et al.<sup>1</sup>).

As background, sheep erythrocytes (sRBC) are a T-dependent antigen and, thus, T cells, B cells, and macrophages are required to function properly in order to obtain an antibody-forming cell (AFC) response. If the test article affects any of these cell types to a significant degree, an altered response will be observed. As a result, the T-dependent IgM response to sRBC is one of the most sensitive immunotoxicological assays currently in use. A significant modulation in the IgM AFC response, when appropriately compared to vehicle controls, indicates that the test agent is capable of modifying the humoral immune response in the whole animal and, thus, has the potential for immunotoxicity. This assay is one of the Tier I assays used by the NTP<sup>2</sup>.

Kimber L. White, Jr., Ph.D., was the Principal Investigator for the immunological evaluation conducted by ImmunoTox<sup>®</sup>, Inc., and Gary M. Hoffman, B.A., DABT, was the HLS Study Director. Vanessa L. Peachee, M.S., served as the Assistant Principal Investigator for ImmunoTox<sup>®</sup>, Inc. and was responsible for carrying out the IgM antibody-forming cell assay.

: .

· ··.

·.. ·

ι.

ITI Study No. ITI 801 Security: Industrial

In evaluating the effects of Gasoline TAME Vapor Condensate on the immune system, the immunologic and toxicologic parameters evaluated were spleen and thymus weights, and the spleen IgM antibody response to the T-dependent antigen (sheep erythrocytes, sRBC).

To the best of our knowledge, no significant protocol or standard operating procedure deviations occurred during the study, which affected the quality of the data and the ability to interpret the data with respect to the immunotoxicology of Gasoline TAME Vapor Condensate.

....

1

Page 11 of 27

# VI. METHODS OF PROCEDURE

# EXPERIMENTAL DESIGN

The immunotoxicological satellite study consisted of a vehicle group, three exposure levels of Gasoline TAME Vapor Condensate, and a positive control group. There were 10 female Sprague Dawley rats in each of the groups. Animals were exposed by Huntingdon Life Sciences Princeton Research Center (PRC) personnel to either vehicle (air only) or Gasoline TAME Vapor Condensate at exposure levels of 2,000, 10,000 or 20,000 mg/m<sup>3</sup> via inhalation for 4 weeks (5 days per week). Cyclophosphamide (CPS) was given as the positive control. Cyclophosphamide was obtained from the Sigma Chemical Company (responsible for its characterization), and was dissolved and diluted in phosphate buffered saline at Huntingdon Life Sciences to stock concentrations of 5.0 mg/ml for use as the positive control for this study. Positive control animals received CPS, a known immunosuppressive agent, by intraperitoneal (i.p.) administration at a dose of 50 mg/kg body weight, as a 10 ml/kg solution on the last 4 days of exposure. These animals were not chamber exposed. On the day of sacrifice, one day after the last exposure, PRC personnel aseptically removed the spleen from each animal, weighed it, placed it in a collecting tube containing Earle's Balanced Salt Solution (EBSS) with HEPES and Gentamicin solution (prepared at PRC), and shipped the spleens on ice in individual shipping containers at 2-8°C by carrier to ImmunoTox®, Inc. for overnight delivery. Upon receipt, spleens were further processed for determination of IgM antibody response.

# VARIABLES ASSESSED

<u>Terminal Body and Organ Weights</u>. Huntingdon Life Sciences PRC personnel collected blood (serum) samples (orbital collection anesthetized via carbon dioxide/oxygen inhalation) and then sacrificed (carbon dioxide inhalation) the animals on the day after the final exposure. The serum samples were frozen ( $\leq$ -20°C). The thymuses were removed, weighed and preserved (formalin) for possible histopathology. Spleens were removed, weighed, and shipped at the time of sacrifice by PRC personnel to ImmunoTox<sup>®</sup>, Inc. for immunotoxicological evaluation.

<u>Splenocyte Preparation</u>. Upon arrival at the ImmunoTox<sup>®</sup>, Inc. testing facility, spleens were accessioned in accordance with the SOP for receipt of biological samples. Single-cell suspensions were prepared from each spleen using a Stomacher<sup>®</sup> 80 Lab Blender in accordance with the SOP

Page 12 of 27

for rat spleens. Cell suspensions were then centrifuged and resuspended in Earle's Balanced Salt Solution with HEPES. Viability of splenocytes was determined using propidium iodide (PI) and the Coulter® EPICS® XL-MCL<sup>™</sup> Flow Cytometer.

Spleen IgM Antibody Response to the T-dependent Antigen, sRBC. Day 4 Response. The primary IgM response to sheep erythrocytes was measured using a modified hemolytic plague assay of Jerne<sup>2</sup>. Rats were exposed to the test article for 5 days per week for 4 weeks. Rats were sensitized by ImmunoTox®, Inc. personnel with 2x108 sRBC i.v. four days prior to sacrifice and, on the day after the last exposure, animals were sacrificed by PRC personnel. Spleen cell suspensions were prepared as described above. The cells were centrifuged and resuspended in a 6-ml volume, and 1:50 and 1:150 dilutions were prepared. An 0.1-ml aliquot of spleen cells from each suspension was added to separate test tubes, each containing 25 µl guinea pig complement, 25  $\mu$ l sRBC, and 0.5 ml of warm agar (0.5%). After thoroughly mixing, each test tube mixture was plated onto a separate petri dish, covered with a microscope cover slip, and incubated at approximately 36-38°C for 3 hours. One dilution per animal was evaluated. Spleen cell counts were performed on the 6-ml samples using a Model Z1 Coulter Counter. The spleen weight, cells/spleen, AFC/10<sup>6</sup> Spleen Cells, and AFC/Spleen were determined. The plaques, which developed, were counted using a Belico plaque viewer. A plaque, occurring from the lysis of sRBC, is elicited as a result of the interaction of complement and antibodies (produced in response to the i.v. sensitization) directed against sRBC. Each plaque is generated from a single IgM antibody-producing B cell, permitting the number of AFC present in the whole spleen to be calculated. The data are expressed as Specific Activity (AFC/10<sup>6</sup> Spleen Cells) and Total Spleen Activity (AFC/Spleen).

DATA

Data Handling and Statistical Analysis. The data obtained in this study were analyzed in accordance with standard operating procedure. Data were first tested for homogeneity of variances using the Bartlett's Chi Square Test<sup>3</sup>. Homogeneous data were evaluated by a parametric one-way analysis of variance<sup>4</sup>. When significant differences occur, exposed groups were compared to the vehicle control group using the Dunnett's t Test<sup>5</sup>. Non-homogeneous data were evaluated using a non-parametric analysis of variance<sup>6</sup>. When significant differences occur, exposed groups were compared to vehicle control group using the Gehan-Wilcoxon Test<sup>7</sup> when appropriate. The Jonckheere's Test<sup>8</sup> was used to test for exposure level-related trends across the vehicle and exposed groups. The positive control was compared to the vehicle control group using the Student t Test<sup>9</sup>. The criteria for accepting the results of the positive control in the assay was a statistically significant ( $p \le 0.05$ ) decrease in the response as compared to the vehicle control group.

P values of 0.05 or less, as compared to the vehicle control group, were considered statistically significant and are indicated in the tables and in the figures with a single asterisk (\*). A double asterisk (\*\*) was used to indicate a p value of 0.01 or less. In the text, the word significant indicates that the response was statistically significant at  $p \le 0.05$ . In the tables, the abbreviation NS is used to indicate "Not Significant" for p values greater than 0.05.

<u>Data Retention</u>. All data and records were returned to the Contracting Sponsor following acceptance of the final report. Upon completion of this study, the report and raw data for this study will be maintained in the archives of Huntingdon Life Sciences.

:

ITI Study No. ITI 801 Security: Industrial

# VII. RESULTS

TERMINAL BODY AND ORGAN WEIGHTS

The terminal body weight data from the study are shown in Table 1 for the control and Test Substance-exposed groups. The terminal body weights were obtained by Huntingdon Life Sciences PRC personnel. The mean ending weight for the vehicle-exposed rats was 255.7 grams. No statistically significant differences were observed in terminal body weights of the Gasoline TAME Vapor Condensate-exposed animals at any exposure level as compared to the vehicle (air only) controls.

The organ weights of the control and Test Substance-exposed rats are shown in Table 1. No effect was observed, following exposure to Gasoline TAME Vapor Condensate, on spleen or thymus weights when evaluated either as absolute or relative weight. Treatment with the positive control, cyclophosphamide, had a significant decrease of 50% on absolute spleen weight and a significant decrease of 77% on absolute thymus weight, compared to the vehicle control. In addition, the positive control, cyclophosphamide had a significant decrease of 47% on relative spleen weight and a 75% decrease on relative thymus weight, compared to the vehicle control. Shown graphically in Figures 1 and 2 is the lack of effect on spleen and thymus weights following exposure to Gasoline TAME Vapor Condensate.

ITI Study No. ITI 801 Security: Industrial

# Figure 1

Absolute (mg) and Relative (%) Spleen Weight in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks



Absolute (mg) and Relative (%) Thymus Weight in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks



. .



Page 16 of 27

ITI Study No. ITI 801 Security: Industrial

# SPLEEN IGM ANTIBODY RESPONSE TO THE T-DEPENDENT ANTIGEN, SRBC. DAY 4 RESPONSE

The spleen IgM antibody-forming cell response, i.e. plaque assay, was evaluated on spleens removed 1 day after the last exposure, which was Day 4 after antigen sensitization. Day 4 after antigen sensitization is the peak day for the sRBC IgM AFC response in rats. Viabilities were conducted on all cell suspensions using propidium iodide (PI) and the Coulter<sup>®</sup> EPICS<sup>®</sup> XL-MCL<sup>™</sup> Flow Cytometer. The viabilities from all samples were greater than 84%.

In the plaque-forming cell (PFC) assays conducted by our laboratory and at the National Toxicology Program (NTP) Immunotoxicology Laboratory of the National Institute of Environmental Health Sciences, the PFC assay results are not adjusted for spleen cell viability. The reasons for this are as follows. In *in vitro* studies, which utilize a single population of cells, e.g. YAC-1 cells, correcting for viability is biologically meaningful. These cells, being of identical type, respond to stimuli in a similar manner and will die off at a similar rate. When spleens are utilized as the source of cells, this represents a heterogeneous mixture of cells, including neutrophils, lymphocytes, and macrophages. Each of these cell types will respond differently to stimuli under in vitro conditions, i.e., neutrophils will die off at a faster rate than lymphocytes. Accordingly, conducting viability determinations on total spleen cells is of little biological value when one is evaluating antigen specific antibody production by plasma cells. More specifically, once the structural integrity of the spleen is compromised, as occurs in preparing a single cell suspension, the cells now in an in vitro environment begin to die with the polymorphonuclear cells dying off at a much faster rate than will either lymphocytes or macrophages. The procedure utilized in our laboratory, and by the NTP Immunotoxicology Laboratory, minimizes the time it takes from preparing the single cell suspension of spleen cells to having them incubating in the assay petri dishes. By minimizing this preparation time, we also minimize the loss of viability, which occurs the longer the cells sit in the *in vitro* cell culture conditions. The decrease in viability, which does occur during this time, is predominately due to the dying off of the more fragile polymorphonuclear cells and not the lymphocytes, particularly those antibodyforming cells (plasma cells) making antibody to sheep erythrocytes. This is due in part to the fact that cells undergoing high metabolic activities, such as rapidly proliferating cells or cells synthesizing antibody, are less susceptible to compounds that produce cell death than are quiescent cells. It is for these reasons that there is no correlation between viability of individual spleen cell preparations and their ability to produce antibodies to sheep erythrocytes. Correcting for viability for a homogenous population in *in vitro* cultures is scientifically sound;

Page 17 of 27

Elen 1

however, as indicated above, using this procedure for mixed cell populations such as those present in the spleen, will result in artificially inflated PFC values.

The results of the AFC response are shown in Table 2 and in Figures 3 and 4. As indicated above, exposure to Gasoline TAME Vapor Condensate did not result in spleen weights that were significantly different from the vehicle control group. Furthermore, as shown graphically in Figure 3, there were no significant differences in spleen cell number following exposure to Gasoline TAME Vapor Condensate as compared to the vehicle control group. As expected, the positive control, cyclophosphamide (CPS), produced an 83% decrease in spleen cell number when compared to the vehicle control group.

# Figure 3

Spleen Cell Number in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks



Shown in Table 2 and Figure 4 are the functional results from the IgM antibody-forming cell (AFC) assay. Shown in the left panel are the results when the data are expressed as specific activity and the results of the total spleen activity are shown in the right panel. In the IgM antibody-forming cell response, there were no statistically significant differences between the Gasoline TAME Vapor Condensate-exposed animals and the vehicle control group when evaluated either as Specific Activity (AFC/10<sup>6</sup> Spleen Cells) or as Total Spleen Activity (AFC/Spleen). As anticipated, the positive control, CPS, significantly decreased the AFC response when evaluated as either specific activity or total spleen cell activity.

# Figure 4

IgM Antibody-Forming Cell Response to Sheep Erythrocytes in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks



Page 20 of 27

ITI Study No. ITI 801 · Security: Industrial

# VIII. CONCLUSION

Exposure of female Sprague Dawley rats to Gasoline TAME Vapor Condensate for a period of 5 days per week for 4 weeks did not result in alterations of the humoral immune response as evaluated in the IgM antibody-forming cell response to the T-dependent antigen sheep erythrocytes. There was no statistically significant effect on thymus weight, spleen weight, spleen cell number, or IgM antibody production when evaluated as either specific activity or as total spleen activity. Based on the immunological parameters evaluated, under the experimental conditions of the study, Gasoline TAME Vapor Condensate did not adversely affect the immune response of female Sprague Dawley rats.

# IX. REFERENCES

- 1. Luster MI, Munson AE, Thomas P, Holsapple MP, Fenters J, White KL, Jr., Lauer LD, and Dean JD (1988). Development of a testing battery to assess chemical-induced immunotoxicity. *Fund. Appl. Toxicol.* 10:2-19.
- 2. Jerne NK, Henry C, Nordin AA, Fun H, Koros MC, and Lefkovits I (1974). Plaque-forming cells: Methodology and theory. *Trnspl. Rev.* 18:130-191.
- 3. Bartlett MS (1937). Sub-sampling for attributes. J. Roy. Stat. Soc. Suppl. 4:131-135.
- 4. Kruskall WH and Wallis WA (1952). Use of ranks in one-criterion variance analysis. *J. Amer. Stat. Assoc.* 47:583-621.
- 5. Dunnett CW (1955). A multiple comparison procedure for comparing several treatments with a control. *J. Amer. Stat. Assoc.* 50:1096-1121.
- 6. Wilson, KV (1956). A distribution free test of analysis of variance. *Psychol. Bull.* 53:96-101.
- 7. Gross AJ and Clark VA (1975). Gehan-Wilcoxon Test. In *Survival Distribution: Reliability Applications in Biomedical Sciences*. AJ Gross and VA Clark, eds. John Wiley and Sons, New York, p. 120-123.
- 8. Hollander M and Wolfe DA (1975). Jonckheere's Test: Non-parametric Statistics Methods, eds. M. Hollander and D.A. Wolfe, John Wiley and Sons, New York, p. 124-129.
- 9. Sokal RR and Rohlf FJ (1981). *Biometry*. Freeman, San Francisco, p. 226-231.

Parameter	Vehicle	Gasoli	Gasoline TAME Vapor (mg/m <sup>3</sup> )			H/NH Trend	d
	(10)	2000 (10)	10000 (10)	20000 (10)	50 mg/kg (10)	Analys	is
Body Wgt (g)	255.7 ± 5.1	252.0 ± 5.8	261.9 ± 8.2	255.8 ± 6.3	238.5 ± 8.9	H NS	
Spleen (mg) % Body Wgt	587 ± 24 0.230 ± 0.008	623 ± 39 0.247 ± 0.013	676 ± 27 0.259 ± 0.008	618 ± 25 0.242 ± 0.01	291 ± 16** 1 0.122 ± 0.004**	H NS H NS	
Thymus (mg) % Body Wgt	452 ± 34 0.176 ± 0.012	497 ± 47 0.196 ± 0.016	502 ± 44 0.194 ± 0.018	468 ± 17 0.182 ± 0.00	106 ± 8** 8 0.044 ± 0.003**	NH NS H NS	

Female Sprague Dawley rats were administered vehicle control (air only) or gasoline TAME vapor condensate by inhalation via whole-body exposure for 5 days per week for 4 weeks. The positive control, cyclophosphamide, was administered i.p. on the last 4 days of exposure. On the day of sacrifice, spleens were placed in tubes containing media and sent to Richmond, VA, on ice for next day cell preparation. The rats were necropsied and indicated organs weighed. Values represent the mean  $\pm$  SE derived from the number of animals indicated in parentheses. H = homogeneous data and NH = non-homogeneous data using the Bartlett's Test for homogeneity. Homogeneous data were evaluated using a parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Dunnett's t Test. Non-homogeneous data were evaluated using a non-parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Wilcoxon Rank Test. The positive control was compared to the vehicle control using the Student's t Test. Values significantly different from vehicle control at  $p \le 0.05$  are indicated by an asterisk, while those significant at  $p \le 0.01$  are noted by a double asterisk. The Jonckheere's Test was used to test for dose-related trends among the vehicle and exposed groups.

Key:  $mg = milligrams; m^3 = cubic meter of air; kg = kilograms; Wgt = weight; NS = not significant for p values greater than 0.05.$ 

Body Weight (g) and Organ Weights (mg) in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks

# Table 2

Exposure	Body Wgt (g)	Spleen Wgt (mg)	Spleen Cells (x10 <sup>7</sup> )	IgM AFC/ 10 <sup>6</sup> Spleen Cells	IgM AFC/Spleen (x 10 <sup>3</sup> )
Vehicle	255.7 ± 5.1	587 ± 24	60.71 ± 3.45	1560 ± 342	928 ± 184
	(10)	(10)	(10)	(10)	(10)
Gasoline TAME Va	apor Condensate				
2000 mg/m <sup>3</sup>	252.0 ± 5.8	623 ± 39	64.78 ± 5.15	1250 ± 194	785 ± 114
-	(10)	(10)	(10)	(10)	(10)
$10000 \text{ mg/m}^3$	261.9 ± 8.2	676 ± 27	68.09 ± 5.01	$1384 \pm 208$	908 ± 132
<b>_</b>	(10)	(10)	(10)	(10)	(10)
$20000 \text{ mg/m}^3$	$255.8 \pm 6.3$	$618 \pm 25$	55.34 ± 3.00	$1514 \pm 289$	874 ± 177
<b>_</b> ,	(10)	(10)	(10)	(10)	(10)
Cyclophosphamide	e (1217)	()	<b>v</b> = - <b>v</b>	( = - )	( )
50 mg/kg	238.5 ± 8.9	291 ± 16**	10.41 ± 0.52**	0 ± 0**	0 ± 0**
	(10)	(10)	(10)	(10)	(10)
H/NH	н	н	H	Н	H
Trend Analysis	NS	NS	. NS	NS	NS

Spleen Antibody-Forming Cell Response to T-dependent Antigen Sheep Erythrocytes in Female Sprague Dawley Rats Exposed to Gasoline TAME Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks - Day 4 Response

Female Sprague Dawley rats were administered vehicle control (air only) or gasoline TAME vapor condensate by inhalation via whole-body exposure for 5 days per week for 4 weeks. The positive control, cyclophosphamide, was administered i.p. the last 4 days of exposure. Four days prior to sacrifice, the rats were immunized (iv) with  $2x10^8$  sRBC. On the day of sacrifice, spleens were placed in tubes containing media and sent to Richmond, VA, on ice for next day cell preparation. Spleens were prepared into single cell suspensions and the number of IgM sRBC antibody-forming cells was determined. Values represent the mean  $\pm$  SE derived from the number of animals indicated in parentheses. H = homogeneous data and NH = non-homogeneous data using the Bartlett's Test for homogeneity. Homogeneous data were evaluated using a parametric analysis of variance. When significant differences occurred, exposed groups were compared to the vehicle control group using the Dunnett's t Test. The positive control was compared to the vehicle control using the Student's t Test. Values significantly different from vehicle control at  $p \le 0.05$  are indicated by an asterisk, while those significant at  $p \le 0.01$  are noted by a double asterisk. The Jonckheere's Test was used to test for dose-related trends among the vehicle and exposed groups.

Key: g = grams; mg = milligrams;  $m^3 = cubic$  meter of air; kg = kilograms; Wgt = weight; NS = not significant for p values greater than 0.05

. . · ·

Protocol No. HLS Study No. 00-6128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate ITI Study No. ITI 801 Security: Industrial

# APPENDIX A

# INDIVIDUAL ANIMAL DATA

. .

Page 24 of 27

INDIVIDUAL ANIMAL DATA ORGAN WEIGHTS GASOLINE TAME VAPOR CONDENSATE HLS STUDY NO: 00-6128 SPONSOR STUDY NO.: 221-TAME-S

ANIMAL NO	GROUP	DOSE	SEX	BODY WGT (G)	SPLEEN (MG)	THYMUS (MG)	SPLEEN /%BODY WT	THYMUS /% BODY WT
1531	GI	AIR ONLY	F	284.5	681	400	0.240	0.140
1532	GI	AIR ONLY	F	260.2	495	551	0.190	0.210
1533	GI	AIR ONLY	F	254.5	587	596	0.230	0.230
1534	GI	AIR ONLY	F	254.8	554	349	0.220	0.140
1535	GI	AIR ONLY	F	273.2	714	573	0.260	0.210
1536	GI	AIR ONLY	F	237.3	653	381	0.280	0.160
1537	GI	AIR ONLY	F	264.0	597	527	0.230	0.200
1538	GI	AIR ONLY	۲	256.3	574	485	0.220	0.190 .
1539	G	AIR ONLY	r -	239.9	509	3/3	0.210	0.160
1340	GI		5	231.9	502	201	0.220	0.120
2521	Gil	2,000 MG/M° GASOLINE TAME VAPOR	-	243.6	632	527	0.260	0.220
2522	GII	2,000 MG/Mª GASOLINE TAME VAPOR	4	265.9	786	796	0.300	0.300
2523	GII	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	234.5	450	413	0.190	0.180
2524	Gil	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	245.2	465	366	0.190	0.150
2525	GII	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	۶	232.3	505	257	0.220	0.110
2526	Gli	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	279.3	633	624	0.230	0.220
2527	GII	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	269.6	807	543	0.300	0.200
2528	Gil	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	250.4	704	537	0.280	0.210
2529	GI	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	271.2	655	459	0.240	0.170
2530	GI	2 000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	, F	227.6	591	448	0.260	0,200
3521	611	10 000 MG/M <sup>3</sup> GASOLINE TAME VAPOR		275 3	664	587	0.240	0.210
2522	GIII	10,000 MOVEL CASOLINE TAKE VAPOR	5	273.3	676	301	0.240	0.270
3322	Gill	10,000 MO/M GASOLINE TAME VAPOR		231.3	6/6	434	0.270	0.180
3523	GII	TU, OUU MG/Mª GASOLINE TAME VAPUR	r	241.4	641	555	0.270	0.230
3524	GII	10,000 MG/M° GASOLINE TAME VAPOR		260.5	655	144	0.250	0.060
3525	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	238.7	669	522	0.280	0.220
3526	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	242.5	63,1	580	0.260	0.240
3527	GII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	248.7	741	620	0.300	0.250
3528	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	247,2	503	509	0.200	0.210
3529	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	310,4	827	603	0.270	0.190
3530	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	302.9	750	449	0.250	0.150
4531	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	292.2	756	462	0.260	0.160
4532	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	229.7	588	504	0.260	0.220
4533	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	263.8	618	381	0.230	0.140
4534	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	244.1	627	473	0.260	0.190
4535	GIV	20 000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	250.7	511	456	0.200	0.180
4536	GIV	20 000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	, F	264 1	714	484	0.270	0.180
4537	GIV	20,000 MC/M <sup>3</sup> GASOLINE TAME VAPOR	-	245.5	590	404	0.240	0.160
4539	GIV	20,000 MG/M <sup>3</sup> CASOLINE TAME VAPOR	È	229.2	530	403	0.260	0.180
4000	GIV	20,000 MG/M GASOLINE TAME VAPOR	- F	200.2	404	7.73	0.200	0.100
4539	GIV	20,000 MG/Mº GASULINE TAME VAPOR	-	284.1	494	556	0.170	0.190
4540	GIV	20,000 MG/M° GASOLINE TAME VAPOK	-	245.5	051	550	0.270	0.220
5551	GV		Ē	240.0	295	. 104	0.120	0.060
2222	GV		F	230.0	308	116	0.130	0.040
5534	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	235.3	328	108	0.140	0.050
5535	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	199.0	238	48	0.120	0.020
5536	ĞV	50 MG/KG CYCLOPHOSPHAMIDE	Ē	264.6	292	113	0.110	0.040
5537	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	253.0	352	124	0.140	0.050
5538	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	184.0	179	101	0.100	0.050
5539	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	233.2	284	82	0.120	0.040
5540	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	261.3	330	129	0.130	0.050

Page 25 of 27

G=GRAMS, MG=MILLIGRAMS, M3=CUBIC METER OF AIR, KG=KILOGRAMS, WT=WEIGHT

# Page 1235

INDIVIDUAL ANIMAL DATA AFC GASOLINE TAME VAPOR CONDENSATE HLS STUDY NO.: 00-6128 SPONSOR STUDY NO.: 211-TAME-S

·									
·····	ANIMAL NO	GROUP	DOSE	<u>SEX</u>	IGM AFC/10° SPLEEN CELLS	IGM AFC/SPLEEN x 10°	CELLS/SPLEEN x 10'	SPLEEN WEIGHT (MG)	BODY WEIGHT (G)
	1001	G		۲ ۲	. 1471	1044	70.98	661	285
	1332	G		Ē	7822	1881	56.74	493	255
	1534	G	AIR ONLY	É	595	381	64.02	554	255
	1535	GI	AIR ONLY	F	1129	888	78.66	714	273
	1536	G	AIR ONLY	F	1823	1179	64.68	653	237
	1537	Gi	AIR ONLY	Ē	604	378	62.58	597	264
	1538	GI	AIR ONLY	۴	3967	1890	47.64	574	256
	1539	Gl	AIR ONLY	F	610	282	46.20	509	240
	1540	Gl	AIR ONLY	F	1349	633	46.92	502	232
	2521	Gli	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	1511	990	65.52	632	244
	2522	GI	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	1326	1314	99.1Z	786	266
	2523	GII	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	2374	1044	43.98	450	235
	2524	GII	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	1106	456	41.22	465	245
	2525	GI	2,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	2132	1287	60.36	505	232
	2526	GII	2.000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	682	468	68.58	633	279
	2527	GII	2.000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	967	750	77.58	807	270
	2528	GI	2.000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	965	603	62.46	704	250
	2529	GI	2.000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	414	255	61.62	655	271
	2530	GR	2 000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	1020	687	67.38	591	228
	3521	GII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	Ē	814	597	73.38	664	275
	3522	GII	10 000 MG/M <sup>3</sup> GASOLINE TAME VAROR	Ē	1644	1080	65 70	676	251
	3522	GIII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	È	1292	792	61 32	641	241
	3524	GII	10,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	5	1400	819	58.50	655	261
	3525	CIII	10,000 MG/M <sup>3</sup> CASOLINE TAME VAPOR	5	1121	747	55.55	669	239
	3323	Gill	10,000 MG/M GASOLINE TAME VAPOR	Ē	3700	1602	60.00	621	2/3
	3320	Gill	10,000 MG/M GASOLINE TAME VAPOR	- F	2730	675	70.22	741	243
	3321	GIII	10,000 MG/Mª GASOLINE TAME VAPOR	5	980	073	12.14	502	243
	3340	GM	10,000 MG/M <sup>2</sup> GASOLINE TAME VAPOR	-	1928	1520	45.14	202	24/
	3529	GIII	10,000 MG/Mª GASOLINE TAME VAPOR		1466	1000	77.10	750	202
	3530	GHI	10,000 MG/Mº GASOLINE TAME VAPOR	۲ -	416	321	77.10	750	303
	4531	GIV	20,000 MG/MP GASOLINE TAME VAPUR	-	2052	1341	65.34	736	292
	4532	GIV	20,000 MG/M <sup>o</sup> GASOLINE TAME VAPOR	-	2414	1341	55.56	588	230
	4533	GIV	20,000 MG/M <sup>o</sup> GASOLINE TAME VAPOR	F	633	315	49.80	618	264
	4534	GIV	20,000 MG/M° GASOLINE TAME VAPOR	F	1816	1035	57.00	627	244
	4535	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	433	189	43.68	511	251
	4536	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	F	1785	1287	72.12	714	264
	4537	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	۶	1426	741	51.96	590	246
	4538	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	۴	3217	1791	55.68	. 627	238
	4539	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	۴	654	267	40.80	494	284
	4540	GIV	20,000 MG/M <sup>3</sup> GASOLINE TAME VAPOR	۴	707	435	61.50	651	246
	5531	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	. 0	12.12	295	247
	5532	GV	SO MG/KG CYCLOPHOSPHAMIDE	5	0	0	10.44	308	237
	5553	6V GV		۲ ۲	0	0	12.00	305	235
	5535	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	ő	õ	8.10	238	199
	5536	Ğv	SO MG/KG CYCLOPHOSPHAMIDE	F	ŏ	õ	10.92	292	265
	5537	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	ō	ō	9.06	352	253
	5538	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	Ō	Ô,	9.30	179	184
	5539	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	8.34	284	233
	5540	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	10.98	330	261

.

.

. .

••

. •• P ag Protocol No. HLS Study No. 00-6128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate

ITI Study No. ITI 801 Security: Industrial

KEY: G=GRAMS, MG=MILLIGRAMS, M<sup>3</sup>=CUBIC METER OF AIR, KG=KILOGRAMS

.

. .

Protocol No. HLS Study No. 00-6128 Abbreviated Title: Immunological Evaluation of Gasoline TAME Vapor Condensate ITI Study No. ITI 801 Security: Industrial

# APPENDIX B

# CONTRACTING SPONSOR'S EXPOSURE AND ANIMAL DATA

Page 27 of 27

Huntingdon Life Sciences	00-6128	Page 1238
	211-TAME-S	Final Report

Animal Exposure and Animal Data	
Preface	Appendix B

**INTRODUCTION:** The following is data generated at Huntingdon Life Sciences, East Millstone, NJ. The separately issued main study report should be referenced for details of the procedures used for test atmosphere generation/characterization and animal evaluations.

STUDY DATES:	Date of Animal Receipt:	7 June 2001
	Experimental Initiation Date:	26 June 2001 (in-life)
	Experimental Completion Date:	24 July 2001 (in-life)
	Draft Report Date:	28 February 2002

**EXPOSURES AND IN-LIFE SUMMARY:** The actual measured results during the exposures were comparable to the targeted exposure levels. There were no exposure-related effects seen in the test animals with regards to body weights and feed consumption.

# TABLE OF CONTENTS

# **TABLES**

A.	Chamber Monitoring Results	1239
B.	Summary of Clinical Observations (pretest only)	1247
C.	Mean Body Weights (grams)	1248
D.	Mean Body Weight Change (grams)	1249
E.	Mean Feed Consumption Values (grams/kg/day)	1250
F.	Individual Clinical Observations (pretest only)	1251
G.	Individual Body Weights (grams)	1256
H.	Individual Body Weight Change (grams)	1261
I.	Individual Feed Consumption Values (grams/kg/day)	1266
J.	Animal Termination History	1271

00-6128

Table A

				Chamber Monitoring Results									
					Cum	ulative E	xposure F	lecord					
					Group	IA - 0 mg	/m <sup>3</sup> (Air	Control)					
												Chamber E	nvironment
									P	article S	Size	Me	an
Day	Date	Exposure	Nominal	Ana	lytical Ch	amber Cor	centrati	on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indivi	dual.		MMAD	GSD	TMC	·	
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
0	26-Jun-01	1	0	0	0	0	0	0				25	48
1	27-Jun-01	2	0	0	0	0	0	0				25	- 50
2	28-Jun-01	3	0	0	0	0	0	0				25	49
3	29-Jun-01	4	0	0	0	0	0	0				25	48
6	2-Jul-01	5	0	0	0	0	0	0	2.809	1.858	3.49E-03	26	48
7	3-Jul-01	6	0	0	0	0	0	0				24	47
8	4-Jul-01	7	0	Q	0	0	0	0				24	49
9	5-Jul-01	8	0	0	0	0	0	0				24	52
10	6-Jul-01	9	0	0	0	0	0	0				24	47
13	9-Jul-01	10	0	0	0	0	0	0	1.023	2.369	2.30E-02	24	47
14	10-Jul-01	11	0	0	Ο.	0	0	0				25	46
15	11-Jul-01	12	0	0	0	0	0	0				25	48
16	12-Jul-01	13	0	0	· 0	0	0	0				25	50
17	13-Jul-01	14	0	0	0	0	0	0	2.799	2.189	3.66E-03	25	52
20	16-Jul-01	15	0	0	0	0	0	0				25	47
21	17-Jul-01	16	0	0	0	0	0	0	3.519	2.858	1.24E-02	24	49
22	18-Jul-01	17	0	0	0 0 0 0						24	50	
23	19-Jul-01	18	0	0	0 0 0 0						24	51	
24	20-Jul-01	19	0	0	0 0 0 0						24	48	
27	23-Jul-01	20	0	0	0 0 0 0						24	48	
		Mean	0		0			2.538	2,319	1.06E-02	24.6	48.7	
		S.D.	0			0			1.064	0.417	9.23E-03	0.6	1.7

Table A

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE BODY INHALATION TOXICITY STUDY IN RATS

00-6128

				Chamber Monitoring Results									
					c	Cumulative	Exposure	Record					
					Gro	ир IB - Оп	mg/m³ (Ai	r Contro	1)				
												Chamber Er	vironment
										Particle	Size	Mea	in
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	on	E	Determina	tions	Temperature	Humidity
	1	Number		Mean		Indivi	idual		MMAD .	GSD	TMC		
L			(mg/m³)	(mg/m³)		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
0	26-Jun-01	1	0	0	0	0	0	0				24	50
1	27-Jun-01	2	0	0	0	0	0	0				24	52
2	28-Jun-01	3	0	0	0	0	0	0				24	50
3	29-Jun-01	4	0	0	0	0	0	0				24	51
6	2-Jul-01	5	0	0	0	0	0	0	4.591	1.924	1.19E-02	25	50
7	3-Jul-01	6	0	0	0	0	0	0				25	50
8	4-Jul-01	7	0	0	0	0	0	0				24	56
9	5-Jul-01	8	0	0	0	0	0	0				24	57
10	6-Jul-01	9	0	0	0	0	0	0				24	50
13	9-Jul-01	10	0	0	0	0	0	0	0.9107	1.949	1.96E-02	25	50
14	10-Jul-01	11	0	0	0	0	0	0				24	50
15	11-Jul-01	12	0	0	0	0	0	0				24	50
16	12-Jul-01	13	0	0	0	0	0	0				24	51
17	13-Jul-01	14	0	0	O	0	0	0	3.456	1.961	2.88E-03	24	54
20	16-Jul-01	15	0	0	0	0	0	0				24	49
21	17-Jul-01	16	0	0	0	0	0	0	1.980	2.424	1.24E-02	24	51
22	18-Jul-01	17	0	0	0	0	0	0				24	54
23	19-Jul-01	18	0	0	0	0	0	0				24	54
24	20-Jul-01	19	0	0	0	0	0	0				24	50
27	23-Jul-01	20	0	0	0	0	0	0				25	51
		Mean	0		0		2.734	2.065	1.17E-02	24.2	51.5		
		S.D.	0			o		1.619	0.240	6.85E-03	0.4	2.3	

Chamber Environment

Mean

(°C)

23.5

0.5

Humidity

(8)

45.8

1.4

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE BODY INHALATION TOXICITY STUDY IN RATS

00-6128

Chamber Monitoring Results Cumulative Exposure Record Group IIA - 2,000  $mg/m^3$ Particle Size Date Exposure Nominal Analytical Chamber Concentration Determinations Temperature Number Mean Individual MMAD GSD TMC  $(mg/m^3)$  $(mg/m^3)$  $(mg/m^3)$  $(mq/m^3)$ (µm) 26-Jun-01 27-Jun-01 28-Jun-01 29-Jun-01 2-Jul-01 2.943 1.989 1.98E-03 3-Jul-01 4-Jul-01 5-Jul-01 6-Jul-01 9-Jul-01 0.9020 1.89E-02 1.764 10-Jul-01 11-Jul-01 

2.021

0.8582

1.681

0.999

2.043

1.737

1.883

0.155

2.44E-03

4.80E-03

7.03E-03

8.01E-03

Table A

Day

12-Jul-01

13-Jul-01

16-Jul-01

17-Jul-01

18-Jul-01

19-Jul-01

20-Jul-01

23-Jul-01

Mean

S.D.

00-6128

	Chamber Monitoring Results												
					(	Cumulative	Exposure	Record					
						Group IIE	3 - 2,000	mg/m <sup>3</sup>					
												Chamber	Environment
								i	Pa	article S	lize	М	ean
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Co	ncentrati	on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indiv	idual		MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	'm <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
0	26-Jun-01	1	2540	1903	1750	1870	2050	1940				23	49
1	27-Jun-01	2	2520	2130	2060	2270	2030	2160				23	50
2	28-Jun-01	· 3	2480	2143	2540	2080	1940	2010				23	49
3	29-Jun-01	4	2520	2033	2010	2090	2080	1950				23	49
6	2-Jul-01	5	2450	2095	2150	2180	1940	2110	3.662	2.163	2.35E-03	24	48
7	3-Jul-01	6	2310	1938	1700	2040	2010	2000				23	46
8	4-Jul-01	7	2300	2103	2080	1930	1810	2590				23	48
9	5-Jul-01	8	2420	1998	2050	2210	2050	1680				23	51
10	6-Jul-01	9	2250	1858	1680	2090	1910	1750				23	46
13	9-Jul-01	10	2530	1885	1940	1630	2030	1940	0.9443	2,426	2.12E-02	23	47
14	10-Jul-01	11	2440	2028	1900	2040	1980	2190				23	48
15	11-Jul-01	12	2260	1883	1610	2170	2010	1740				23	47
16	12-Jul-01	13	2310	1938	1760	2060	2120	1810				23	47
17	13-Ju1-01	14	2390	1885	1610	1890	1980	2060	3.122	2.100	5.53E-03	23	50
20	16-Jul-01	15	2350	2013	1860	2280	1930	1980				23	47
21	17-Jul-01	16	2270	1905	1820	1880	1910	2010	0.8414	1.609	4.19E-03	22	48
22	18-Jul-01	17	2440	1985	1850	1950	2190	1950		1		22	49
23	19-Jul-01	18	2760	1985	2010	2080	1980	1870				22	48
24	20-Jul-01	19	2430	1963	1860	1860	2080	2050				22	46
27	23-Jul-01	20	2480	2173	2220	2250	2030	2190				23	47
		Mean	2423			1992		2.142	2.075	8.32E-03	22.9	48.0	
		S.D.	124	1		180	)		1.460	0.341	8.69E-03	0.5	1.4

00-6128

						Thompson Ma		Descilte	·····			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
						manber Mo	-	Results					
					C	Cumulative	Exposure	Record					
		<del>γ</del>		<u>, , , , , , , , , , , , , , , , , ,</u>	·· <i>·</i> · · · ·	Group IIIA	<u> </u>	0 mg/m <sup>3</sup>	r				
												Chamber En	vironment
									P	article &	Size	Mea	n
Day	Date	Exposure	Nominal	Ana	lytical (	hamber Con	ncentrati	on	De	eterminat	ions	Temperature	Humidity
		Number		Mean		Indivi	idual		MMAD	GSD	TMC		
			(mg/m³)	(mg/m³)		(mg/	m <sup>3</sup> )		(µm)		$(mg/m^3)$	(°C)	(%)
0	26-Jun-01	1	10400	10560	10100	9950	11300	10900				24	47
1	27-Jun-01	2	10000	10500	9810	10600	10100	11500				24	48
2	28-Jun-01	3	9970	10300	12000	8740	9950	10500				24	48
3	29-Jun-01	4	9170	10560	9140	12000	11000	10100				24	47
6	2-Jul-01	5	9580	9983	8900	9880	9950	11200	5.574	2.285	2.90E-03	25	45
7	3-Jul-01	6	9240	10120	9450	10700	10400	9910				25	47
8	4-Jul-01	7	10100	10690	11700	10900	9660	10500				24	50
9	5-Jul-01	8	9950	9908	9770	10600	9630	9630				24	54
10	6-Jul-01	9	9930	10750	9910	11500	10900	10700				24	47
13	9-Jul-01	10	9870	9815	10900	11100	8600	8660	0.9057	1.859	1.85E-02	24	48
14	10-Jul-01	11	10300	10730	10400	10400	10700	11400				24	47
15	11-Jul-01	12	9660	9438	8540	10900	9370	8940				24	47
16	12-Jul-01	13	10800	11750	11600	12800	11700	10900				24	46
17	13-Jul-01	14	10000	11250	10500	11500	11400	11600	9.339	2.648	4.18E-03	24	48
20	16-Jul-01	15	10200	10190	9810	8530	10900	11500				24	45
21	17-Jul-01	16	10500	11180	9810	11800	11900	11200	0.9086	2.148	5.08E-03	23	50
22	18-Jul-01	17	9930	10340	10600	10600	11400	8760				23	53
23	19-Jul-01	18	9480	11380	11500	10900	11400	11700			ļ	23	51
24	20-Jul-01	19	9810	10200	10100	11000	9730	9950				24	47
27	23-Jul-01	20	9900	10330	10400	10300	10100	10500				24	49
		Mean	9940		10497		4.182	2.235	7.67E-03	24.0	48.2		
		s n	399			944			4.082	0.328	7.28E-03	0.5	2.4

00-6128

.

					c	hamber Mor	itoring	Results					
					C	umulative	Exposure	Record					
						Group IIIB	- 10,000	) mg/m <sup>3</sup>					
												Chamber E	nvironment
									Pa	article S	Size	Me	an
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Co	ncentrati	.on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indiv	ldual		MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(୫)
0	26-Jun-01	1	10400	11400	11500	11500	11700	10900				24	43
1	27-Jun-01	2	10000	10680	10800	10900	11400	9630				24	46
2	28-Jun-01	3	9970	10140	9660	9910	10100	10900				24	45
3	29-Jun-01	4	9170	9940	10300	10200	9450	9810				24	45
6	2-Jul-01	5	9580	9148	8060	10200	8700	9630	2.528	1.914	1.30E-03	25	44
7	3-Ju1-01	6	9240	10310	10800	11100	9590	9730				24	43
8	4-Ju1-01	7	10100	10950	11200	10100	11000	11500				24	45
9	5-Jul-01	8	9950	10400	10200	11100	10200	10100				24	48
10	6-Jul-01	9	9930	10220	11700	9990	9590	9590				24	42
13	9-Jul-01	10	9870	10150	9590	9700	10900	10400	0.9015	1.780	1.61E-02	24	44
14	10-Jul-01	11	10300	10850	11000	11600	10300	10500				24	44
15	11-Jul-01	12	9660	9888	9630	10600	9840	9480				23	45
16	12-Jul-01	13	10800	10960	9840	11800	11400	10800				24	44
17	13-Jul-01	14	10000	10540	10600	12000	10800	8760	3.139	2.249	3.16E-03	24	45
20	16-Jul-01	15	10200	10070	8960	9700	10100	11500				24	43
21	17-Jul-01	16	10500	11280	12100	11400	11100	10500	0.8798	1.913	4.37E-03	23	45
22	18-Jul-01	17	9930	10020	10900 9810 10200 9180					23	46		
23	19-Jul-01	18	9480	11680	12000 11900 11400 11400					23	46		
24	20-Jul-01	19	9810	9598	9480 9100 10000 9810					23	43		
27	23-Jul-01	20	9900	10680	10300 11000 10800 10600					24	44		
1		Mean	9940		10444			1.862	1.964	6.23E-03	23.8	44.5	
1		S.D.	399	1		10444 873			1.149	0.200	6.70E-03	0.5	1.4

Table A

. -

00-6128

Chamber Monitoring Results									·				
					C.	umulative :	Exposure	Record					
						Group IVA	- 20,000	mg/m <sup>3</sup>					
												Chamber H	Invironment
									Pa	article S	Size	Ме	an
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indivi	idual		MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
0	26-Jun-01	1	17600	20150	20000	20600	20900	19100				25	49
1	27-Jun-01	2	19100	21100	19200	22900	19900	22400				25	51
2	28-Jun-01	3	20100	20680	21400	19400	21300	20600				25	50
3	29-Jun-01	4	18900	20950	21500     21500     19600     21200       21400     20000     19700     22800     2						25	50	
6	2-Jul-01	5	18000	20980	21400	20000	19700	22800	2.988	2.234	2.03E-03	26	49
7	3-Jul-01	б	19800	20400	20200	18500	22700	20200				25	48
8	4-Jul-01	7	18900	20380	20300	20400	19700	21100				25	. 52
9	5-Jul-01	8	19800	20850	21500	20800	19800	21300				25	54
10	6-Jul-01	9	19200	19650	18600	19100	19600	21300				25	49
13	9-Jul-01	10	19000	19880	20300	21200	18700	19300	0.9082	1.748	1.72E-02	25	50
14	10-Jul-01	11	18600	19630	19400	20000	19600	19500				26	50
15	11-Jul-01	12	19100	20780	17600	22500	23000	20000				26	49
16	12-Jul-01	13	18800	19600	18600	20000	19700	20100				26	49
17	13-Jul-01	14	17400	20100	18700	21700	20100	19900	1.920	1.859	1.96E-03	26	50
20	16-Jul-01	15	. 19000	20200	20300	20700	20600	19200				26	49
21	17-Jul-01	16	18200	19650	19100	19300	20000	20200	0.8551	1,671	4.38E-03	24	51
22	18-Jul-01	17	18800	21380	21600 20400 22000 21500					24	53		
23	19-Jul-01	18	18900	21200	22000 22900 21000 18900						24	51	
24	20-Jul-01	19	18700	19650	20300 20800 18400 19100					24	46		
27	23-Jul-01	20	17800	20580	21300 20500 20700 19800					25	51		
	•	Mean	18785		20388			1.668	1.878	6.39E-03	25.1	50.1	
1.1		S.D.	710			20388 1184			1.007	0.250	7.29E-03	0.7	1.8

.

-

Table A

# GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE BODY INHALATION TOXICITY STUDY IN RATS

00-6128

					(	Chamber Mo	nitoring	Results		······································			
					. (	Cumulative	Exposure	Record					
						Group IVB	- 20,000	) mg/m <sup>3</sup>					
				· · · · · · · · · · · · · · · · · · ·								Chamber 1	Environment
									Pa	rticle S	ize	M	ean
Day	Date	Exposure	Nominal	Ana	lytical C	Chamber Con	ncentrati	on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indivi	ldual		MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
0	26-Jun-01	1	17600	19380	19000	19100	19400	20000				24	49
1	27-Jun-01	2	19100	20630	19400	19200	22300	21600				24	51
2	28-Jun-01	3	20100	20830	22100	20600	20600	20000				25	51
3	29-Jun-01	4	18900	18530	18100	17100	19000	19900				24	51
6	2-Jul-01	5	18000	19530	18700	19700	19400	20300	3.133	2.363	2.02E-03	25	50
7	3-Jul-01	6	19800	21030	20400	21700	20100	21900				26	48
8	4-Jul-01	7	18900	20380	19500 20700 20000 21300						25	54	
9	5-Jul-01	8	19800	21180	19500     20700     20000     21300       21600     22300     20400     20400						25	55	
10	6-Jul-01	9	19200	21080	20700	21100	22200	20300				.25	50
13	9-Jul-01	10	19000	19550	19400	18800	20200	19800	0.8877	1.583	1.61E-02	25	52
14	10-Ju1-01	11	18600	20030	19600	20200	20100	20200				24	49
15	11-Jul-01	12	19100	20180	21500	19300	18600	21300				24	50
16	12-Jul-01	13	18800	20630	21400	21000	20800	19300				24	55
17	13-Jul-01	14	17400	19430	18300	20600	19400	19400	0,9560	2.242	7.88E-03	24	52
20	16-Jul-01	15	19000	20430	21000	20800	20500	19400				25	50
21	17-Jul-01	16	18200	19800	21400	18500	18900	20400	0.8593	1.735	4.90E-03	25	50
22	18-Jul-01	17	18800	19980	21100	19800	19600	19400			1	25	53
23	19-Jul-01	18	18900	19950	20800	21400	19100	18500				25	51
24	20-Jul-01	19	18700	20000	19600 21000 20000 19400				ļ	25	46		
27	23-Jul-01	20	17800	21330	20600 21400 22200 21100					25	51		
		Mean	1.8785			20190			1.459	1.981	7.73E-03	24.7	50.9
		S.D.	710			1092			1.117	0.380	6.07E-03	0.6	2.2

9-JAN-2009 12:54

Huntingdon Life Sciences 00-61281 Immunotoxicity Sub-Group

Page 1247

#### TABLE B

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES				SUMMARY C	OF CLINICA	L OBSERV	ATIONS			
	GROUP#	DAY OF -11 TOTAL	STUDY						 	 
# OF ANIMALS EXAMINED	1 2 3 4 5	10 10 10 10 10								

#### NORMAL

WITHIN	NORMAL	LIMITS	1	10	10
			2	10	10
			3	10	10
			4	10	10
			5	10	10

Page 1248

TABLE C

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES			ME	AN BODY WEIGHTS (	GRAMS)		T 17 T7			
	EXPOSURE LEV	DOSE GROUP: VEL (mg/m3);	I O	II 2,000	III 10,000	IV 20,000	V POSITIVE CONTROL			
WEEK	-1	MEAN	158	156	157	156	156			
		S.D.	7.1	8.8	6.1	12.8	9.8			
		N	10	10	10	10	10			
WEEK	0	MEAN	205	200	207	205	202			
		S.D.	13.1	11.7	15.3	14.4	18.5			
		N	10	10	10	10	10			
WEEK	l	MEAN	223	217	222	223	225			
		S.D.	13.1	12.3	16.3	15.6	20.4			
		N	10	10	10	10	10			
WEEK	2	MEAN	237	232	239	236	243			
	-	S.D.	14.4	15.1	20.3	15.7	26.4			
		N	10	10	10	10	10			
WEEK	3	MEAN	250	247	250	245	251			
	5	S.D.	11.0	17.9	19.8	15.6	26.5			
		N	10	10	10	10	10			
WEEK	4	MEAN	256	252	262	256	239			
	-	S.D.	16.3	18.3	25.9	20.1	28.1			
		N	10	10	10	10	10			
			~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~							

No statistically significant differences

Page 1249

TABLE D

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES				ME	AN BODY WEIGHT CH	ANGE (GRAMS)	GRAMS)					
	EXPOSU	DO RE LEVEL	SE GROUP: (mg/m3):	I 0	II 2,000	III 10,000	IV 20,000	V POSITIVE CONTROL				
WEEK	0 TO	1	MEAN S.D. N	18 8.6 10	17 7.6 10	15 4.6 10	17 9.1 10	23 7.1 10				
WEEK	0 TO	2	MEAN S.D. N	32 10.7 10	32 9.0 10	32 9.8 10	30 8.9 10	42 11.6 10				
WEEK	0 TO	3	MEAN S.D. N	45 8.5 10	48 10.2 10	43 10.6 10	39 10.4 10	50 14.1 10				
WEEK	0 TO	4	MEAN S.D. N	51 11.8 10	52 10.3 10	55 13.6 10	50 10.1 10	37 15.7 10				

No statistically significant differences

.

Page 1250

#### TABLE E

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

LUES (GRAMS/KG/DAY)	NSUMPTION VALUES	MEAN FEED			FEMALES		
V	IV	III	II	I	DOSE GROUP:		
POSITIVE CONTROL	20,000	10,000	2,000	0	EVEL (mg/m3):	EXPOSURE LEV	
101	100	0.0	05	07	MEDN	0	WEEV
101	100	98 E E	55	21	MEAN 9 D	v	MBBK
10	10	10	10	2.5	N N		
91**	84	84	86	83	MEAN	1	WEEK
5.6	4.0	4.0	5.9	3.7	S.D.		
10	10	10	10	10	N		
85	82	81	83	80	MEAN	2	WEEK
4.4	3.3	4.3	5.4	5.3	S.D.		
10	10	10	10	10	N		
78	77	77	81	76	MEAN	3	WEEK
5.1	5.2	3.6	б.О	3.2	S.D.		
10	10	10	9	10	N		
62*	74	73	77**	69	MEAN	4	WEEK
6.7	5.1	4.2	6.3	2.2	S.D.		
9	10	10	10	10	N		
	10 82 3.3 10 77 5.2 10 74 5.1 10	10 81 4.3 10 77 3.6 10 73 4.2 10	10 83 5.4 10 81 6.0 9 77** 6.3 10	10 80 5.3 10 76 3.2 10 69 2.2 10	N MEAN S.D. N MEAN S.D. N MEAN S.D. N	2 3 4	WEEK WEEK WEEK

Statistical key: \* = p<0.05 \*\* = p<0.01

9-JAN-2009 12:57

Huntingdon Life Sciences 00-6128I Immunotoxicity Sub-Group

FEMALES GROUP I 0 mg/m3

Page 1251

TABLE F

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL CLINICAL OBSERVATIONS

\_\_\_\_\_ DAY OF l ANIMAL# OBSERVATIONS STUDY 1 \_\_\_\_\_ 1531 WITHIN NORMAL LIMITS Ρ 1532 WITHIN NORMAL LIMITS Ρ 1533 WITHIN NORMAL LIMITS Ρ 1534 WITHIN NORMAL LIMITS Ρ 1535 WITHIN NORMAL LIMITS P WITHIN NORMAL LIMITS 1536 ₽ 1537 WITHIN NORMAL LIMITS Ρ WITHIN NORMAL LIMITS 1538 Ρ 1539 WITHIN NORMAL LIMITS Ρ 1540 WITHIN NORMAL LIMITS Ρ - --

Page 1252

TABLE F

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP II 2,000 mg/m3 DAY OF 1 ANIMAL# OBSERVATIONS STUDY 1 2521 WITHIN NORMAL LIMITS р 2522 WITHIN NORMAL LIMITS ₽ WITHIN NORMAL LIMITS 2523 ₽ 2524 WITHIN NORMAL LIMITS Ρ WITHIN NORMAL LIMITS 2525 Ρ 2526 WITHIN NORMAL LIMITS ₽ 2527 WITHIN NORMAL LIMITS Ρ 2528 WITHIN NORMAL LIMITS Р 2529 WITHIN NORMAL LIMITS Р 2530 WITHIN NORMAL LIMITS ₽ CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

Page 1253

#### TABLE F

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP III 10,000 mg/m3 DAY OF 1 ANIMAL# OBSERVATIONS STUDY 1 ------3521 WITHIN NORMAL LIMITS P 3522 WITHIN NORMAL LIMITS Ρ 3523 WITHIN NORMAL LIMITS Ρ 3524 WITHIN NORMAL LIMITS Р 3525 WITHIN NORMAL LIMITS Ρ WITHIN NORMAL LIMITS 3526 Ρ 3527 WITHIN NORMAL LIMITS Ρ WITHIN NORMAL LIMITS 3528 Ρ 3529 WITHIN NORMAL LIMITS ₽ 3530 WITHIN NORMAL LIMITS ₽ 

9-JAN-2009 12:57

Huntingdon Life Sciences 00-61281 Immunotoxicity Sub-Group

Page 1254

TABLE F

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP IV 20,000 mg/m3 DAY OF 1 STUDY ANIMAL# OBSERVATIONS 1 4531 WITHIN NORMAL LIMITS ₽ WITHIN NORMAL LIMITS Ρ 4532 4533 WITHIN NORMAL LIMITS Ρ WITHIN NORMAL LIMITS 4534 Ρ WITHIN NORMAL LIMITS 4535 P WITHIN NORMAL LIMITS Ρ 4536 WITHIN NORMAL LIMITS 4537 P 4538 WITHIN NORMAL LIMITS ₽ WITHIN NORMAL LIMITS Ρ 4539 4540 WITHIN NORMAL LIMITS Ρ - - -

Page 1255

TABLE F

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES	GROUP V POSITIVE CONTROL		
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1 1
5531	WITHIN NORMAL LIMITS	•	P
5532	WITHIN NORMAL LIMITS	•	P
5533	WITHIN NORMAL LIMITS		P
5534	WITHIN NORMAL LIMITS		P
5535	WITHIN NORMAL LIMITS		P
5536	WITHIN NORMAL LIMITS		P
5537	WITHIN NORMAL LIMITS		Ð
5538	WITHIN NORMAL LIMITS		P
5539	WITHIN NORMAL LIMITS		P
5540	WITHIN NORMAL LIMITS		P

Page 1256

TABLE G

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

						:	INDIVIDU	AL BODY WEIGHTS (GRAMS)
FEMALES	GROUP I	0 n	ng/m3					
		WEEF	OF STU	JDY				
ANIMAL#		-1	0	1	2	3	4	
1531		162	218	235	256	263	285	
1532		155	206	235	237	244	260	
1533		156	198	208	228	245	255	
1534		160	210	219	223	246	255	
1535		172	224	244	262	270	273	
1536		153	184	204	218	242	237	
1537		166	204	233	248	258	264	
1538		150	200	219	225	251	256	
1539		158	217	221	236	246	240	
1540		148	187	212	235	233	232	
MEAN		158	205	223	237	250	256	
S.D.		7.1	13.1	13.1	14.4	11.0	16.3	
N		10	10	10	10	10	10	· · · · · · · · · · · · · · · · · · ·

Page 1257

TABLE G

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP I	I 2,	,000 mg,	/m3				
		WEEI	K OF ST	JDY				
ANIMAL#		-1	0	1	2	З	4	
2521		164	204	220	233	242	244	
2522		158	209	226	237	258	266	
2523		156	185	211	226	236	235	
2524		154	198	206	223	235	245	
2525		152	192	204	216	231	232	
2526		162	205	237	258	276	279	
2527		166	217	224	250	270	270	
2528		153	198	216	235	249	250	
2529		161	209	225	236	257	271	
2530		135	179	196	206	220	228	
MEAN		156	200	217	232	247	252	
S.D.		8.8	11.7	12.3	15.1	17.9	18.3	
N		10	10	10	10	10	10	

Page 1258

TABLE G

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES	GROUP	III :	10,000 T	mg/m3				
		WEEI	K OF STU	UDY				
ANIMAL#		-1	0	1	2	3	4	
3521		162	222	236	253	260	275	
3522		146	191	209	233	246	251	•
3523		159	198	210	217	231	241	
3524		154	200	214	228	246	261	
3525		152	195	204	222	228	239	
3526		160	208	215	222	236	243	
3527		157	196	216	234	247	249	
3528		153	197	216	233	241	247	
3529		167	233	252	274	275	310	
3530		164	228	244	272	291	303	
MEAN		157	207	222	239	250	262	
S.D.		6.1	15.3	16.3	20.3	19.8	25.9	
N		10	10	10	10	10	10	

.

Page 1259

-----

## TABLE G

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

# INDIVIDUAL BODY WEIGHTS (GRAMS) FEMALES GROUP IV 20,000 mg/m3 WEEK OF STUDY ANIMAL# -1 0 1 2 3 4

ANIMAL#	-1	0	1	2	3	4
4531	165	230	247	263	281	292
4532	156	201	205	221	229	230
4533	. 152	204	241	245	249	264
4534	155	204	218	221	234	244
4535	153	207	216	227	236	251
4536	161	214	225	239	244	264
4537	160	190	214	229	244	246
4538	162	188	213	229	241	238
4539	172	227	243	260	259	284
4540	124	191	206	223	230	246
MEAN	156	205	223	236	245	256
S.D.	12.8	14.4	15.6	15.7	15.6	20.1
N	10	10	10	10	10	10

.

Page 1260

## TABLE G

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP V	PO	SITIVE (	CONTROL			
		WEE	K OF ST	UDY		•••	
ANIMAL#		-1	0	l	2	3	4
5531		163	203	230	250	266	247
5532		153	205	231	238	245	237
5533		158	213	244	272	286	271
5534		157	189	216	230	237	235
5535		152	191	208	220	226	199
5536		161	207	239	258	275	265
5537		166	223	242	278	259	253
5538		133	164	178	189	198	184
5539		155	195	220	238	246	233
5540		167	228	239	260	274	261
MEAN		156	202	225	243	251	239
S.D.		9,8	18.5	20.4	26.4	26.5	28.1
N		10	10	10	10	10	10

Page 1261

•

TABLE H

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP I	0 1	ng/m3			TRATTERN PORT WITCHT CHARGE (GRAND)
		WEEK	OF STUE	Y		
ANIMAL#		0-1	0-2	0-3	0-4	
1531		16	37	44	66	
1532		29	31	39	54	
1533		10	30	46	56	
1534		9	13	36	45	
1535		19	38	45	49	
1536		20	34	57	53	
1537		30	44	55	60	
1538		19	25	52	57	
1539		4	19	29	23	
1540		25	48	46	45	
MEAN		18	32	45	51	
S.D.		8.6	10,7	8.5	11.8	
N		10	10	10	10	

9-JAN-2009 12:59

Huntingdon Life Sciences 00-61281 Immunotoxicity Sub-Group

.

Page 1262

TABLE H

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

Females Groui	?II 2,	000 mg,	/m3		
	WEEK	OF STU	DY		
ANIMAL#	0-1	0-2	0-3	0 - 4	
2521	16	29	38	40	
2522	18	28	49	57	
2523	26	41	51	50	
2524	8	25	37	48	
2525	12	24	39	40	
2526	32	53	71	74	
2527	7	33	53	53	
2528	18	37	52	53	
2529	16	26	48	62	
2530	17	27	41	49	
MEAN	17	32	48	52	
S.D.	7.6	9.0	10.2	10.3	
N	10	10	10	10	

Page 1263

TABLE H

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP III	1	.0,000 r	mg/m3								
	WEEK OF STUDY											
ANIMAL#		0-1	0-2	0-3	0 - 4							
3521		14	31	38	53							
3522		18	42	54	б0							
3523		13	20	33	44							
3524		15	28	47	61							
3525		9	27	33	43							
3526		7	14	28	35							
3527		21	39	51	53							
3528		19	36	43	50							
3529		19	41	42	78							
3530		16	43	62	75							
MEAN		15	32	43	55							
S.D.		4.6	9.8	10.6	13.6							
N		10	10	10	10							

.

Huntingdon Life Sciences 00-6128I Immunotoxicity Sub-Group

Page 1264

## TABLE H

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP IN	V 20	0,000 mg	g/m3		
		WEEK	OF STU	 2Y		
ANIMAL#		0-1	0-2	0-3	0-4	
4531		18	34	51	63	
4532		4	21	29	29	
4533		37	41	45	60	
4534		14	17	30	40	
4535		10	21	29	44	
4536		11	25	30	51	
4537		24	39	53	55	
4538		25	41	53	51	
4539		17	34	33	58	
4540		15	32	39	54	
MEAN		17	30	39	50	
S.D.		9.1	8.9	10.4	10.1	
N		10	10	10	10	

Page 1265

#### TABLE H

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP V	POS	SITIVE (	CONTROL		
		WEEK	OF STU	DY		
ANIMAL#	1	0-1	0-2	0 - 3	0 - 4	
5531		27	46	63	44	· · · · · · · · · · · · · · · · · · ·
5532	1	26	33	39	31	
5533		31	59	73	58	
5534	:	27	41	48	47	
5535		18	29	36	8	
5536		33	52	69	58	
5537	,	19	55	37	30	
5538	1	14	26	34	21	
5539	•	25	43	51	38	
5540	I	12	32	46	34	
MEAN		23	42	50	37	
S.D.		7.1	11.6	14.1	15.7	
N		10	10	10	10	

9-JAN-2009 13:00

Huntingdon Life Sciences 00-6128I Immunotoxicity Sub-Group

Page 1266

TABLE I

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL FEED CONSUMPTION VALU	UES (GRAMS/KG/DAY)
----------------------------------	--------------------

FEMALES	GROUP I	0 m	ıg∕m3				
		WEEK	OF STU	DY			
ANIMAL#		0	1	2	3	4	
1531		95	79	81	72	72	
1532		SF	88	79	78	72	
1.533		95	81	81	73	71	
1534		99	79	78	78	68	
1535		98	87	79	71	70	
1536		93	81	76	75	67	· · · · · · · · · · · · · · · · · · ·
1537		98	85	76	77	68	
1538		98	83	80	82	69	
1539		97	79	76	74	70	
1540		101	88	94	75	65	
MEAN		97	83	80	76	69	
S.D.		2.5	3.7	5.3	3.2	2.2	
N		9	10	10	10	10	

SF=Spilled Feeder

.

Page 1267

TABLE I

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GF	ROUP II 2	,000 mg/	/m3		
	WEE	K OF STU	JDY		
ANIMAL#	0	1	2	3	4
2521	89	88	79	77	75
2522	95	96	89	SF	91
2523	91	92	86	82	76
2524	97	87	84	84	74
2525	95	83	78	83	73
2526	92	87	77	70	70
2527	98	87	93	90	85
2528	98	84	81	75	74
2529	94	76	77	79	73
2530	99	79	83	87	75
MEAN	95	86	83	81	77
S.D.	3.3	5.9	5.4	6.0	6.3
N	10	10	1.0	9	10

•

SF=Spilled Feeder

.

Page 1268

# TABLE I

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES	GROUP III	10,000	mg/m3		
	WEE	K OF S	TUDY		
ANIMAL#	0	1	2	3	4
3521	99	81	77	76	76
3522	108	92	92	85	81
3523	93	79	76	77	68
3524	90	83	80	79	72
3525	98	88	85	77	75
3526	101	83	82	80	73
3527	91	86	80	73	69
3528	100	87	80	76	74
3529	102	82	82	74	74
3530	94	81	79	73	66
MEAN	98	84	81	77	73
S.D.	5.5	4.0	4.3	3.6	4.2
N	10	1.0	10	10	10

Page 1269

#### TABLE I

## GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

# INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES	GROUP IV	20	,000 mg	r/m3	1101	VIDOAD FI	CONSUMPTION VALUES (GRAMS/RG/DA	(1)
		WEEK	OF STU	DY				
ANIMAL#		0	1	2	3	4		
4531	*********	104	84	82	80	76		
4532		99	80	83	76	70		`
4533		103	92	80	65	70		
4534		94	81	76	79	70		
4535		102	83	83	75	73		
4536		104	86	87	86	83		
4537		95	81	80	77	71		
4538		89	88	84	78	75		
4539		99	83	88	81	84		
4540		110	78	81	77	73		
MEAN		100	84	82	77	74		
S.D.		6.0	4.0	3.3	5.2	5.1		
N		10	10	10	10	10		

Page 1270

TABLE I

#### GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

#### INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES	GROUP V	POS	SITIVE C	ONTROL		
		WEEI	OF STU	DY		
ANIMAL#		0	1	2	3	4
5531		107	93	88	76	56
5532		104	92	81	79	63
5533		112	95	89	77	61
5534		91	90	81	82	73
5535		97	89	84	80	SF
5536	•	94	90	82	77	57
5537		100	83	88	69	58
5538		109	104	93	89	71
5539		96	89	80	77	65
5540		97	86	84	74	53
MEAN		101	91	85	78	62
S.D.		7.0	5.6	4.4	5.1	6.7
N		10	10	10	10	9

SF=Spilled Feeder

9-JAN-2009 13:00

Huntingdon Life Sciences 00-6128I Immunotoxicity Sub-Group

Page 1271

## TABLE J

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES G	ROUP I 0 mg/m	3				
ANIMAL#	TYPE DEAT	of Th	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
1531	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1532	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1533	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1534	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1535	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1536	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1537	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1538	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1539	TERMINAL	SACRIFICE	24-JUL-01	4	28	
1540	TERMINAL	SACRIFICE	24-JUL-01	4	28	

# Huntingdon Life Sciences 00-61281 Immunotoxicity Sub-Group

Page 1272

#### TABLE J

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP II 2,000 mg/m3				
ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	 
2521	TERMINAL SACRIFICE	24-JUL-01	4	28	 
2522	TERMINAL SACRIFICE	24-JUL-01	4	28	
2523	TERMINAL SACRIFICE	24-JUL-01	4	28	
2524	TERMINAL SACRIFICE	24-JUL-01	4	28	
2525	TERMINAL SACRIFICE	24-JUL-01	4	28	
2526	TERMINAL SACRIFICE	24-JUL-01	4	28	
2527	TERMINAL SACRIFICE	24-JUL-01	4	28	
2528	TERMINAL SACRIFICE	24-JUL-01	4	28	
2529	TERMINAL SACRIFICE	24-JUL-01	4	28	
2530	TERMINAL SACRIFICE	24-JUL-01	4	28	
				• • • • • • • • • • • • • • • • • • •	 

9-JAN-2009 13:00

Huntingdon Life Sciences 00-6128I Immunotoxicity Sub-Group

Page 1273

#### TABLE J

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

TYPE OF ANIMAL#DATE OF DEATHWEEK OF STUDY DBATHSTUDY DAY3521TERMINAL SACRIFICE24-JUL-014283522TERMINAL SACRIFICE24-JUL-014283523TERMINAL SACRIFICE24-JUL-014283524TERMINAL SACRIFICE24-JUL-014283525TERMINAL SACRIFICE24-JUL-014283526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	FEMALES	GROUP III 10,000 mg/m3				
3521   TERMINAL SACRIFICE   24-JUL-01   4   28     3522   TERMINAL SACRIFICE   24-JUL-01   4   28     3523   TERMINAL SACRIFICE   24-JUL-01   4   28     3524   TERMINAL SACRIFICE   24-JUL-01   4   28     3525   TERMINAL SACRIFICE   24-JUL-01   4   28     3526   TERMINAL SACRIFICE   24-JUL-01   4   28     3527   TERMINAL SACRIFICE   24-JUL-01   4   28     3528   TERMINAL SACRIFICE   24-JUL-01   4   28     3529   TERMINAL SACRIFICE   24-JUL-01   4   28     3530   TERMINAL SACRIFICE   24-JUL-01   4   28	ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	 
3522TERMINAL SACRIFICE24-JUL-014283523TERMINAL SACRIFICE24-JUL-014283524TERMINAL SACRIFICE24-JUL-014283525TERMINAL SACRIFICE24-JUL-014283526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	3521	TERMINAL SACRIFICE	24-JUL-01	4	28	 
3523TERMINAL SACRIFICE24-JUL-014283524TERMINAL SACRIFICE24-JUL-014283525TERMINAL SACRIFICE24-JUL-014283526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	3522	TERMINAL SACRIFICE	24-JUL-01	4	28	
3524TERMINAL SACRIFICE24-JUL-014283525TERMINAL SACRIFICE24-JUL-014283526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	3523	TERMINAL SACRIFICE	24-JUL-01	4	28	
3525TERMINAL SACRIFICE24-JUL-014283526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	3524	TERMINAL SACRIFICE	24-JUL-01	4	28	
3526TERMINAL SACRIFICE24-JUL-014283527TERMINAL SACRIFICE24-JUL-014283528TERMINAL SACRIFICE24-JUL-014283529TERMINAL SACRIFICE24-JUL-014283530TERMINAL SACRIFICE24-JUL-01428	3525	TERMINAL SACRIFICE	24-JUL-01	4	28	
3527   TERMINAL SACRIFICE   24-JUL-01   4   28     3528   TERMINAL SACRIFICE   24-JUL-01   4   28     3529   TERMINAL SACRIFICE   24-JUL-01   4   28     3530   TERMINAL SACRIFICE   24-JUL-01   4   28	3526	TERMINAL SACRIFICE	24-JUL-01	4	28	
3528 TERMINAL SACRIFICE 24-JUL-01 4 28   3529 TERMINAL SACRIFICE 24-JUL-01 4 28   3530 TERMINAL SACRIFICE 24-JUL-01 4 28	3527	TERMINAL SACRIFICE	24-JUL-01	4	28	
3529     TERMINAL SACRIFICE     24-JUL-01     4     28       3530     TERMINAL SACRIFICE     24-JUL-01     4     28	3528	TERMINAL SACRIFICE	24-JUL-01	4	28	
3530 TERMINAL SACRIFICE 24-JUL-01 4 28	3529	TERMINAL SACRIFICE	24-JUL-01	4	28	
	3530	TERMINAL SACRIFICE	24-JUL-01	4	28	 

Page 1274

## TABLE J

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP IV 20,000 mg/m3				
ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
4531	TERMINAL SACRIFICE	24-JUL-01	4	28	
4532	TERMINAL SACRIFICE	24-JUL-01	4	28	
4533	TERMINAL SACRIFICE	24-JUL-01	4	28	
4534	TERMINAL SACRIFICE	24-JUL-01	4	28	
4535	TERMINAL SACRIFICE	24-JUL-01	4	28	
4536	TERMINAL SACRIFICE	24-JUL-01	4	28	
4537	TERMINAL SACRIFICE	24-JUL-01	4	28	
4538	TERMINAL SACRIFICE	24-JUL-01	4	28	
4539	TERMINAL SACRIFICE	24-JUL-01	4	28	
4540	TERMINAL SACRIFICE	24-JUL-01	4	28	

Page 1275

.

TABLE J

GASOLINE TAME VAPOR CONDENSATE: A 13-WEEK WHOLE-BODY INHALATION TOXICITY STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES	GROUP V POSITIVE CONTROL			
ANTMAL#	TYPE OF DEATH	DATE OF	WEEK OF	STUDY
		DBAIN		UA1
5531	TERMINAL SACRIFICE	24-JUL-01	4	28
5532	TERMINAL SACRIFICE	24-JUL-01	4	28
5533	TERMINAL SACRIFICE	24-JUL-01	4	28
5534	TERMINAL SACRIFICE	24-JUL-01	4	28
5535	TERMINAL SACRIFICE	24-JUL-01	4	28
5536	TERMINAL SACRIFICE	24-JUL-01	4	28
5537	TERMINAL SACRIFICE	24-JUL-01	4	28
5538	TERMINAL SACRIFICE	24-JUL-01	4	28
5539	TERMINAL SACRIFICE	24-JUL-01	4	28
5540	TERMINAL SACRIFICE	24-JUL-01	4	28
		24.000		