FINAL REPORT

Immunological Evaluation of Gasoline MTBE Vapor Condensate in Female Sprague Dawley Rats Using the Plaque Forming Cell Assay

Test Substance:	Gasoline MTBE Vapor Condensate
Protocol No:	HLS 00-6126
Subcontractor's Sponsor:	Huntingdon Life Sciences Mettlers Road East Millstone, NJ 08875 (732) 873-2550 *Phone* (732) 873-3992 *Fax*
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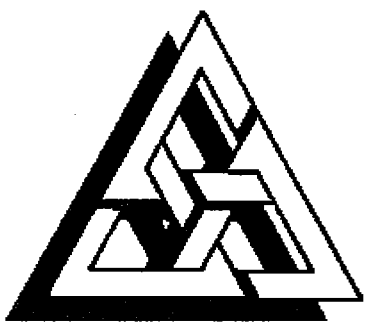
Sponsor's Representative:	Thomas M. Gray, M.S., DABT
ImmunoTox's Project Number:	ITI 601
Date:	27 April 2007
Principal Investigator:	Kimber L. White, Jr., Ph.D.
Studies Conducted at:	ImmunoTox, Inc. Virginia Bio•Technology Research Park 800 East Leigh Street, Suite 209 Richmond, VA 23219-1534 (804) 828-6880 *Phone* (804) 828-6881 *Fax*



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I. GLP COMPLIANCE STATEMENT

This study was conducted in compliance with the United States Environmental Protection Agency's (EPA) Good Laboratory Practice Standards 79.60, CFR Vol. 59, No. 122, 27 June 1994 with the following exceptions:

1. It was the Sponsor's responsibility to maintain the methods of synthesis, fabrication, or derivation of the test fuel. This had not been completed when the study initiated but is currently with the Sponsor.

2. 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 not 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 mixture were not performed by the Testing Facility. The stability of the positive control article mixture has not been determined by the Testing Facility.

Gary M. Hoffman, B.A., D.AB.T.
Study Director

28 Jun 02
Date

Thomas M. Gray, M.S., D.A.B.T.
Sponsor Representative

Date

II. QUALITY ASSURANCE STATEMENTS

Test Substance: Gasoline MTBE Vapor Condensate

Report Title: Immunotoxicological Evaluation of Gasoline MTBE Vapor Condensate in Female Sprague Dawley Rats Using the Plaque Forming Cell Assay

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

Huntingdon Life Sciences, Inc. Study No. 00-6126
Sponsor Study No. 211-MTBE-S

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 ImmunoTox, Inc. Principal Investigator, and then has submitted written reports of said inspections to the Study Director and Management via the Principal Investigator.

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

Performed	Reported	Activity
March 7, 2001	March 15, 2001	AFC Assay
August 30, 2001	September 7, 2001	AFC Assay (2nd Repeat)
October 19-22, 2001	October 24, 2001	Data Audit
October 22-24, 2001	October 24, 2001	1st Draft Report Audit
April 21, 2007	April 23, 2007	Final Report Audit

Approved and submitted by: _____ 27 April 07
Quality Assurance Manager — Date

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HUNTINGDON LIFE SCIENCES QUALITY ASSURANCE STATEMENT

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
GLP Protocol Review	8 – 9 Jan 01	12 Jan 01
Positive Control Immunotoxicity Animals Dose Administration	2 Mar 01	2 Mar 01
Immunotoxicity Necropsy and Training Records	6 Mar 01	8 Mar 01
Immunotoxicity Blood Collection and Necropsy	2 May 01	2 May 01
Positive Control Dose Administration	27 Aug 01	29 Aug 01
Immunotoxicity Necropsy and Training Records	29 Aug 01	29 Aug 01
Final Immunotox Report	6 – 8 Aug 01	8 Nov 01
Sponsor's Comments & Report Verification	22 – 24 Aug 05	24 Aug 05

Sonya Gray
Senior Quality Assurance Auditor

27 Jun 07
Date

III. SIGNATURE OF PRINCIPALS

This report describes the results used to evaluate the relative immunotoxicological potential of the test substance, Gasoline MTBE 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, M.S., 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.

Date 27 Apr 07

Vanessa L. Peachee, M.S.
Assistant Principal Investigator
ImmunoTox, Inc.

Date 27 Apr. 07

Approved:

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

28 Jun 07
Date

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IV. EXECUTIVE SUMMARY

The study was conducted as part of Huntingdon Life Sciences (HLS) Study No. 00-6126 at ImmunoTox, 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 MTBE 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 MTBE 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^3 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, Inc., Richmond, VA. Huntingdon Life Sceinces 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 (≤-20°C). The thymuses were removed and weighed by PRC personnel, and preserved (formalin) for possible histopathology. On the day of sacrifice, spleens were placed in tubes containing media, placed on ice, and shipped to ImmunoTox, Inc. in Richmond, VA, for assay evaluation on the following day.

In evaluating the effect of Gasoline MTBE Vapor Condensate on the humoral immune response, three studies were conducted. In the first study, cyclophosphamide (CPS) the positive control produced the anticipated suppression in the functional assay. However, treatment with CPS did not result in a significant decrease in spleen cell number as is routinely observed. The lack of effect on spleen cell number, was a concern to the Principal Investigator. After discussions among the Principal Investigator, Study Director, and the Sponsor, the decision was made to repeat the study. A repeat study was carried out. However, due to oversight, the spleens were collected but not sent by overnight delivery. After discussions between the Principal Investigator and the Study Director, the decision was made to run the assay when the samples arrived at ImmunoTox Inc., which was two days after sacrifice. On a previous study conducted by ImmunoTox, Inc., for a different sponsor, a similar situation had occurred. The results from that study, when the spleens were evaluated two days after sacrifice, were usable being consistent with results from studies conducted on samples received the day after sacrifice.

In the repeat Gasoline MTBE Vapor Condensate, this was not the case. The Principal Investigator considered the results obtained from the functional assays unusable for a proper immunotoxicological evaluation of Gasoline MTBE Vapor Condensate. Accordingly, the study was then conducted for a third time, referred to as the 2nd Repeat Study, and it is the results from this third study which are reported in this report. The results from the first study and the repeat study are included in the Appendix of the report and are referred to on occasion.

Executive Summary Table ES-1 shows a summary of the selected toxicology and immunology parameters evaluated. Exposure to Gasoline MTBE 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 MTBE Vapor Condensate, when evaluated as either absolute or relative weight (% body weight), as compared to the air control.

Exposure to Gasoline MTBE 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/10^6 spleen cells) or as total spleen activity (AFC/spleen). In the 2nd Repeat Study, 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 MTBE Vapor Condensate test substance did not adversely affect the functional ability of the humoral immune component of the immune system.

Table ES-1

SUMMARY TABLE FOR TOXICOLOGY AND IMMUNOLOGY STUDIES

Parameter	Result	Maximum Effect	Dose	Comment
Body Weight				
Day 29	No Effect			
Organ Weights Absolute				
Spleen	No Effect			
Thymus	No Effect			
Organ Weights Relative				
Spleen	No Effect			
Thymus	No Effect			
Spleen IgM Antibody-Forming Cell Response to Sheep Erythrocytes				
IgM AFC to sRBC	No Effect			

V. INTRODUCTION

The purpose of this study was to provide evaluation of immunological parameters for Huntingdon Life Sciences (HLS) Study No. 00-6126. In this study (2nd Repeat Study), the test substance, Gasoline MTBE 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, 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 on ice to ImmunoTox, Inc. in Richmond, VA, for evaluation the following 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 MTBE Vapor Condensate on the immune response. This assay has been shown to be the most predictive assay for determining the immunotoxicological potential of a compound (Luster *et al.*[1]).

In evaluating the effect of Gasoline MTBE Vapor Condensate on the humoral immune response, three studies were conducted. In the first study, spleens were received on 07 March 2001 and the immunological evaluation was conducted on this day. In this first study, cyclophosphamide (CPS) the positive control produced the anticipated suppression in the functional assay. However, treatment with CPS did not result in a significant decrease in spleen cell number as is routinely observed. The lack of effect on spleen cell number, was a concern to the Principal Investigator. After discussions among the Principal Investigator, Study Director, and the Sponsor, the decision was made to repeat the study.

A repeat study was carried out; however, due to oversight, the spleens were collected but not sent by overnight delivery. After discussions between the Principal Investigator and the Study Director, the decision was made to run the assay when the samples arrived at ImmunoTox Inc. Spleens arrived on 04 May 2001, two days after sacrifice. In a previous study conducted by ImmunoTox, Inc., for a different sponsor, a similar situation had occurred. The results from that study, when the spleens were evaluated two days after sacrifice, were usable being consistent

with results from studies conducted on sample received the day after sacrifice. In the repeat Gasoline MTBE Vapor Condensate, this was not the case. The Principal Investigator considered the results obtained from the functional assays unusable for a proper immunotoxicological evaluation of Gasoline MTBE Vapor Condensate since the response of the control animals was so low. Accordingly, the study was then conducted for a third time; this third study is referred to as the 2nd Repeat Study. The spleens for the 2nd Repeat Study arrived on 30 August 2001, one day after sacrifice, and were evaluated the same day. The results from the 2nd Repeat Study are reported in this report. The data tables from the first study and the repeat study are included in the Appendix of the report and are referred to on occasion.

Kimber L. White, Jr., Ph.D., was the Principal Investigator for the immunological evaluation conducted by ImmunoTox, 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, Inc. and was responsible for carrying out the IgM antibody-forming cell assay.

In evaluating the effects of Gasoline MTBE 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 2nd Repeat Study, which affected the quality of the data and the ability to interpret the data with respect to the immunotoxicology of Gasoline MTBE Vapor Condensate.

VI. METHODS OF PROCEDURE

EXPERIMENTAL DESIGN

The immunotoxicological satellite study consisted of a vehicle group, three exposure levels of Gasoline MTBE 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 MTBE Vapor Condensate at exposure levels of 2,000, 10,000 or 20,000 mg/m^3 via inhalation for 4 weeks (5 days per week). Cyclophosphamide (CPS; Sigma Chemical Co., Lot No. 108H0568), was given as the positive control. The positive control animals received 50 mg/kg of CPS, a known immunosuppressive agent, administered intraperitoneally (i.p.) on the last 4 days of exposure by PRC personnel. CPS, a white powder, was prepared in phosphate buffered saline at a concentration of 5 mg/ml and stored in aliquots at -10 to -30°C. On each day of exposure an aliquot was thawed and used. The expiration date of each thawed aliquot was the day of use. Purity and stability information on cyclophosphamide is on file with the manufacturer. These animals were not chamber exposed. Four days prior to sacrifice, animals were sensitized by ImmunoTox personnel in the morning with sRBC by i.v. injection. On the morning of 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, and shipped the spleens in individual shipping containers at 2-8°C on ice packs by carrier to ImmunoTox for overnight delivery. Upon receipt the next day, spleens were further processed for determination of IgM antibody response

VARIABLES ASSESSED

Terminal Body and Organ Weights. The terminal body weights were obtained by Huntingdon Life Sciences PRC personnel. 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 (≤-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, Inc. for immunotoxicological evaluation.

Splenocyte Preparation. Upon arrival at the ImmunoTox 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® 80 Lab Blender in accordance with the SOP for rat spleens. Cell suspensions were then centrifuged and resuspended in Earle's Balanced Salt Solution with HEPES. Viability of splenocytes were determined using propidium iodide (PI) and the Coulter EPICS XL-MCL Flow Cytometer.

Spleen IgM Antibody Response to the T-dependent Antigen, sRBC. Day 4 Response. 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[2].

The primary IgM response to sheep erythrocytes was measured using a modified hemolytic plaque assay of Jerne[3]. Rats were exposed to the test article for 5 days per week for 4 weeks. Rats were sensitized by ImmunoTox, Inc. personnel with $2x10^8$ 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 µl 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 number, following lysis of RBC, was performed on the 6-ml samples using a Model Z1 Coulter Counter. The spleen weight, cells/spleen, AFC/10^6 spleen cells, and AFC/spleen were determined. The plaques that developed were counted using a Bellco plaque viewer. For each spleen, 2 dilutions (1:50 and 1:150) were prepared. At the time of counting, each plate was examined. Routinely, the plate that had between 100-300 plaques was counted. When the

number of plaques are in excess of 350 plaques per plate, it becomes difficult to obtain an accurate count using the Bellco 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/10^6 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 procedures. Data were first tested for homogeneity of variances using the Bartlett's Chi Square Test[4]. Homogeneous data were evaluated by a parametric one-way analysis of variance[5]. When significant differences occur, exposed groups were compared to the vehicle control group using the Dunnett's t Test[6]. Non-homogeneous data were evaluated using a non-parametric analysis of variance[5]. When significant differences occur, exposed groups were compared to vehicle control group using the Gehan-Wilcoxon Test[7] when appropriate. The Jonckheere's Test[8] 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[9]. The criteria for accepting the results of the positive control in the assay was a statistically significant ($p \leq 0.05$) 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 $p \leq 0.05$. In the tables the abbreviation NS is used to indicate "Not Significant" for p values greater than 0.05.

Data Retention. All data and records were returned to the Contracting Sponsor following acceptance of the final report. Records maintained for this protocol include: study sheet, chemical preparation form, and authorized signatures and initials forms. Upon completion of this study, the report and raw data for this study will be maintained in the archives of Huntingdon Life Sciences.

VII. RESULTS

TERMINAL BODY AND ORGAN WEIGHTS

The terminal body weight data for the 2nd Repeat Study are shown in Table 1 for the control and Test Substance-exposed groups. No statistically significant differences were observed in terminal body between the vehicle control and the animals exposed to Gasoline MTBE Vapor Condensate. A similar lack of effect on terminal body weight was observed in the first and repeat studies (Appendix A).

The organ weights of the control and Test Substance-exposed rats for the 2nd Repeat Study are shown in Table 1. No effect was observed, following exposure to Gasoline MTBE Vapor Condensate, on spleen or thymus weight when evaluated either as absolute or relative weight. A similar lack of effect on organ weights was observed in the first and repeat studies (Appendix A).

Shown graphically in Figures 1 and 2 is the lack of effect on spleen and thymus weights following exposure to Gasoline MTBE Vapor Condensate.

Figure 1
Absolute (mg) and Relative (%) Spleen Weight in Female Sprague Dawley Rats Exposed to Gasoline MTBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks
(2nd Repeat Study)

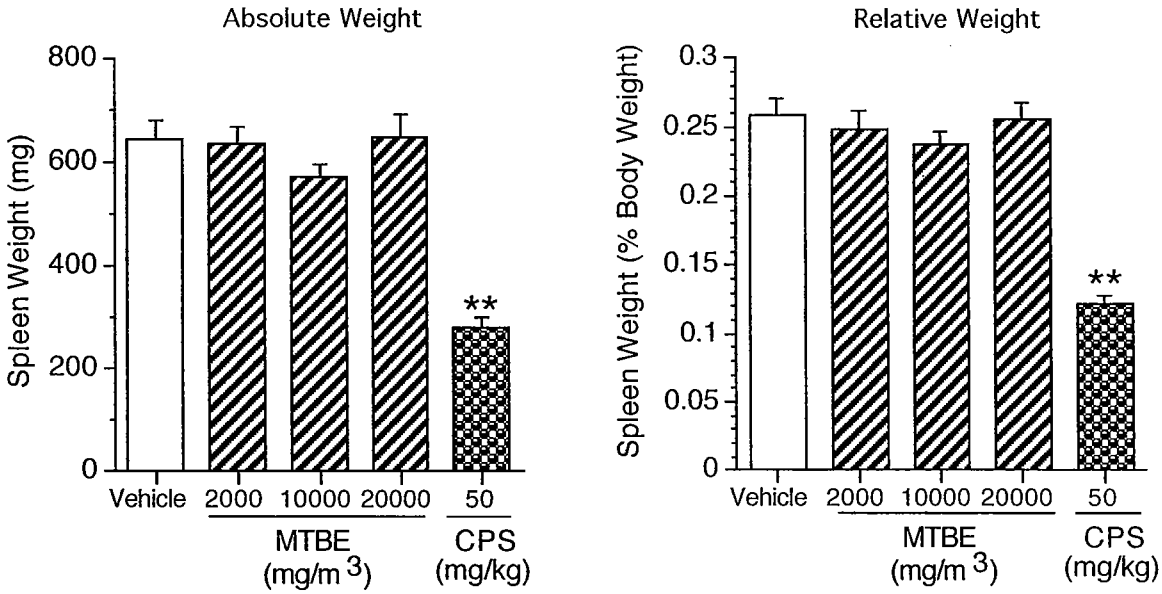
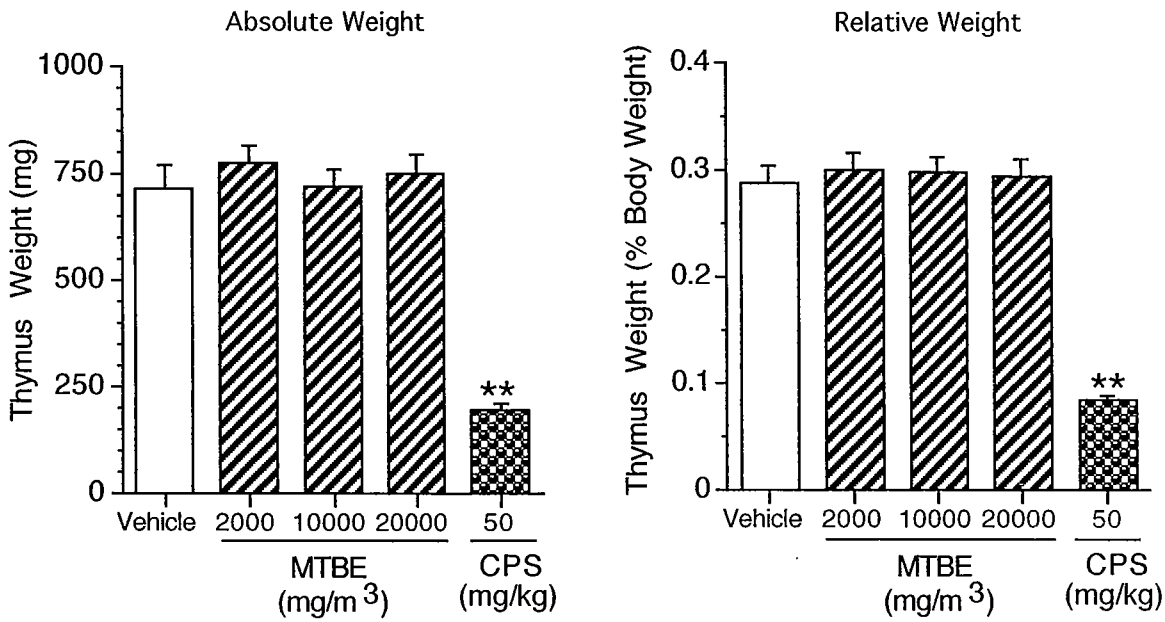


Figure 2
Absolute (mg) and Relative (%) Thymus Weight in Female Sprague Dawley Rats Exposed to Gasoline MTBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks
(2nd Repeat Study)



In the 2nd Repeat Study, treatment with the positive control, cyclophosphamide, produced a significant decrease of 56% on absolute spleen weight and a 73% decrease on absolute thymus weight, compared to the vehicle control. When evaluated as relative weight, cyclophosphamide, produced a 53% decrease in spleen weight and a 71% decrease on thymus weight.

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 EPICS XL-MCL Flow Cytometer. The viabilities from all samples were greater than 87%.

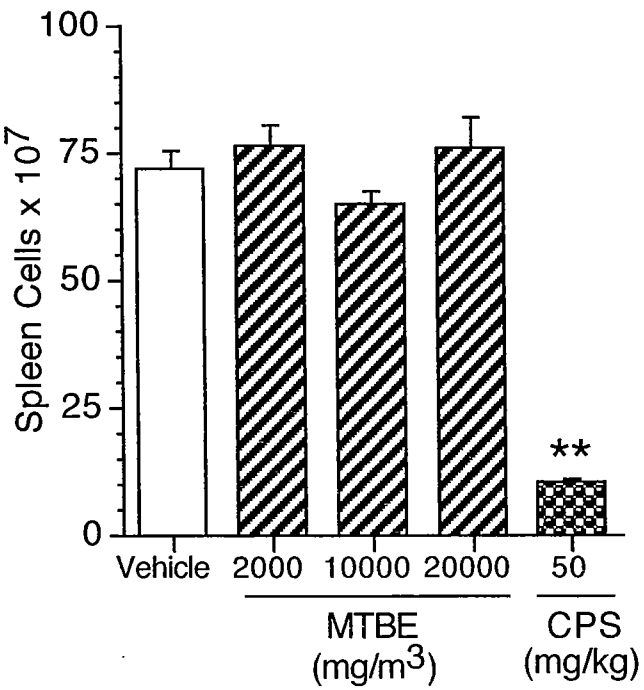
In the plaque-forming cell (PFC) assays conducted by our laboratory and at the National Toxicology Program (NTP) Immunotoxicology Laboratory of the National Institute of Environmental Health Sciences, the PFC assay results are not adjusted for spleen cell viability. The reasons for this are as follows. 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 antibody-forming 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 which 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; 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 2nd Repeat Study AFC response are shown in Table 2 and in Figures 3 and 4. As was shown in Table 1 and Figure 1 above, exposure to Gasoline MTBE Vapor Condensate did not result in spleen weights significantly different from the vehicle control group. Furthermore, as shown in Figure 3, there was no significant difference in the spleen cell number following exposure to Gasoline MTBE Vapor Condensate. A similar lack of effect on spleen cell numbers was observed in the first and repeat studies (Appendix A). As expected, in the 2nd Repeat Study, the positive control, cyclophosphamide (CPS), produced an 85% decrease in spleen cell number when compared to the vehicle control group.

Figure 3

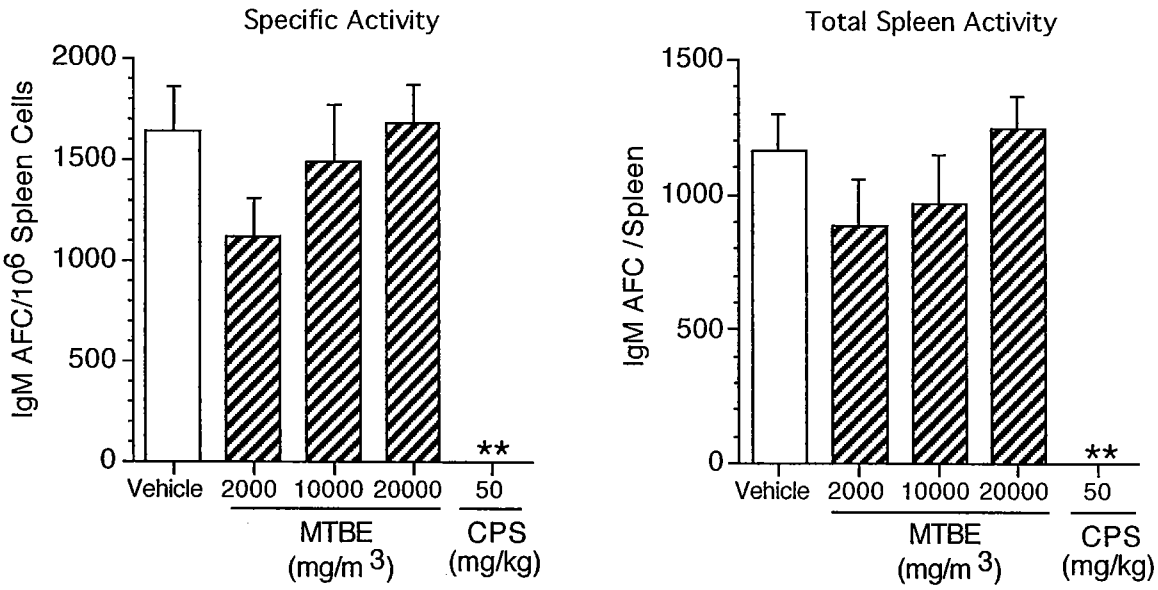
Spleen Cell Number in Female Sprague Dawley Rats Exposed to Gasoline MTBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks
(2nd Repeat Study)



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. While the AFC response of the low dose animals was less than those of the vehicle air controls, the decrease did not reach the level of statistical significance. In the IgM antibody-forming cell response, there were no statistically significant differences between the Gasoline MTBE Vapor Condensate-exposed animals and the vehicle control group when evaluated either as specific activity (AFC/10^6 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 MTBE Vapor Condensate via Inhalation for 5 Days per Week for 4 Weeks (2^{nd} Repeat Study)



VIII. CONCLUSION

Exposure of female Sprague Dawley rats to Gasoline MTBE 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 MTBE Vapor Condensate did not adversely affect the immune response of female Sprague Dawley rats.

IX. REFERENCES

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Table 1

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

2nd Repeat Study

Parameter	Vehicle	Gasoline MTBE Vapor (mg/m^3)			Cyclophosphamide	H/NH	Trend Analysis
		2000	10000	20000	50 mg/kg		
	(10)	(10)	(10)	(10)	(10)		
Body Wgt (g)	248.3 ± 6.1	256.9 ± 3.3	242.5 ± 6.5	254.8 ± 7.2	231.3 ± 9.2	H	NS
Spleen (mg)	646 ± 35	637 ± 34	574 ± 25	651 ± 43	283 ± 18**	H	NS
% Body Wgt	0.259 ± 0.012	0.248 ± 0.013	0.237 ± 0.009	0.255 ± 0.012	0.122 ± 0.006**	H	NS
Thymus (mg)	719 ± 53	775 ± 40	722 ± 38	753 ± 43	196 ± 15**	H	NS
% Body Wgt	0.288 ± 0.016	0.301 ± 0.015	0.298 ± 0.015	0.295 ± 0.016	0.084 ± 0.005**	H	NS

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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 ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

Table 2

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

2nd Repeat Study

Exposure	Body Wgt (g)	Spleen Wgt (mg)	Spleen Cells ($x10^7$)	IgM AFC/ 10^6 Spleen Cells	IgM AFC/Spleen ($x 10^3$)
Vehicle	248.3 ± 6.1 (10)	646 ± 35 (10)	72.09 ± 3.82 (10)	1646 ± 218 (10)	1162 ± 137 (10)
Gasoline MTBE Vapor					
2000 mg/m^3	256.9 ± 3.3 (10)	637 ± 34 (10)	76.52 ± 4.07 (10)	1128 ± 190 (10)	887 ± 171 (10)
10000 mg/m^3	242.5 ± 6.5 (10)	574 ± 25 (10)	65.13 ± 2.81 (10)	1490 ± 282 (10)	966 ± 185 (10)
20000 mg/m^3	254.8 ± 7.2 (10)	651 ± 43 (10)	76.28 ± 5.97 (10)	1680 ± 199 (10)	1245 ± 122 (10)
Cyclophosphamide 50 mg/kg	231.3 ± 9.2 (10)	283 ± 18** (10)	10.65 ± 0.74** (10)	0 ± 0** (10)	0 ± 0** (10)
H/NH	H	H	H	H	H
Trend Analysis	NS	NS	NS	NS	NS

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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. Spleens were sent to Richmond, VA, on ice the following day. Spleens were prepared into single cell suspensions and the number of IgM sRBC antibody-forming cells was determined. Values represent the mean ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

APPENDIX A - FIRST AND REPEAT STUDY TABLES

Appendix A - Table 1

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

Parameter	Vehicle	Gasoline MTBE Vapor (mg/m^3)			Cyclophosphamide	H/NH	Trend Analysis
		2000	10000	20000	50 mg/kg		
	(10)	(10)	(10)	(10)	(10)		
Body Wgt (g)	251.5 ± 6.8	261.9 ± 5.7	257.3 ± 3.7	245.9 ± 4.5	234.3 ± 4.7	H	NS
Spleen (mg)	612 ± 36	596 ± 24	623 ± 21	574 ± 23	274 ± 10**	H	NS
% Body Wgt	0.243 ± 0.012	0.229 ± 0.011	0.242 ± 0.007	0.233 ± 0.008	0.117 ± 0.003**	H	NS
Thymus (mg)	614 ± 36	555 ± 30	544 ± 20	514 ± 23	129 ± 8**	H	$p \leq 0.01$
% Body Wgt	0.245 + 0.013	0.213 ± 0.011	0.211 ± 0.007	0.211 ± 0.011	0.055 ± 0.004**	H	$p \leq 0.05$

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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 ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

Appendix A - Table 2

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

Repeat Study

Parameter	Vehicle	Gasoline MTBE Vapor (mg/m^3)			Cyclophosphamide	H/NH	Trend
		2000	10000	20000	50 mg/kg		Analysis
	(10)	(10)	(10)	(10)	(10)		
Body Wgt (g)	234.1 ± 3.3	228.5 ± 5.0	235.2 ± 3.7	234.2 ± 3.7	208.8 ± 5.3**	H	NS
Spleen (mg)	589 ± 23	563 ± 29	544 ± 18	587 ± 26	236 ± 12**	H	NS
% Body Wgt	0.252 ± 0.012	0.245 ± 0.009	0.230 ± 0.007	0.249 ± 0.010	0.113 ± 0.005**	H	NS
Thymus (mg)	589 ± 30	599 ± 15	532 ± 22	594 ± 54	120 ± 9**	NH	NS
% Body Wgt	0.251 ± 0.013	0.264 ± 0.005	0.227 ± 0.010	0.254 ± 0.021	0.057 ± 0.003**	NH	$p \leq 0.05$

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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 ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

Appendix A - Table 3

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

Day 4 Response

Exposure	Body Wgt (g)	Spleen Wgt (mg)	Spleen Cells ($x10^7$)	IgM AFC/ 10^6 Spleen Cells	IgM AFC/Spleen ($x\ 10^3$)
Vehicle	251.5 ± 6.8 (10)	612 ± 36 (10)	67.33 ± 4.99 (10)	786 ± 199 (10)	510 ± 121 (10)
Gasoline MTBE Vapor					
2000 mg/m^3	261.9 ± 5.7 (10)	596 ± 24 (10)	66.37 ± 3.71 (10)	316 ± 85 (10)	202 ± 50 (10)
10000 mg/m^3	257.3 ± 3.7 (10)	623 ± 21 (10)	63.62 ± 2.76 (10)	784 ± 223 (10)	488 ± 137 (10)
20000 mg/m^3	245.9 ± 4.5 (10)	574 ± 23 (10)	63.89 ± 2.67 (10)	898 ± 264 (10)	581 ± 173 (10)
Cyclophosphamide 50 mg/kg	234.3 ± 4.7 (10)	274 ± 10** (10)	69.42 ± 4.17 (10)	0 ± 0** (10)	0 ± 0** (10)
H/NH	H	H	H	NH	NH
Trend Analysis	NS	NS	NS	NS	NS

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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 ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

Appendix A - Table 4

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

Repeat Study

Exposure	Body Wgt (g)	Spleen Wgt (mg)	Spleen Cells ($x10^7$)	IgM AFC/ 10^6 Spleen Cells	IgM AFC/Spleen ($x\ 10^3$)
Vehicle	234.1 ± 3.3 (10)	589 ± 23 (10)	74.62 ± 4.09 (10)	363 ± 60 (10)	284 ± 57 (10)
Gasoline MTBE Vapor					
2000 mg/m^3	228.5 ± 5.0 (10)	563 ± 29 (10)	66.49 ± 4.12 (10)	275 ± 77 (10)	179 ± 48 (10)
10000 mg/m^3	235.2 ± 3.7 (10)	544 ± 18 (10)	64.38 ± 3.14 (10)	266 ± 92 (10)	185 ± 71 (10)
20000 mg/m3	234.2 ± 3.7 (10)	587 ± 26 (10)	64.82 ± 3.11 (10)	386 ± 212 (10)	224 ± 107 (10)
Cyclophosphamide 50 mg/kg	208.8 ± 5.3** (10)	236 ± 12** (10)	13.39 ± 1.00** (10)	18 ± 16** (10)	2 ± 1** (10)
H/NH	H	H	H	NH	H
Trend Analysis	NS	NS	NS	$p \leq 0.05$	$p \leq 0.05$

Female Sprague Dawley rats were administered vehicle control (air only) or Gasoline MTBE 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. Spleens were sent to Richmond, VA, on ice the following day. Spleens were prepared into single cell suspensions and the number of IgM sRBC antibody-forming cells was determined 2 days after sacrifice. Values represent the mean ± 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 $p \leq 0.05$ are indicated by an asterisk, while those significant at $p \leq 0.01$ are noted by a double asterisk. The Jonckheere's Test was used to test for exposure level-related trends among the vehicle and exposed groups.

APPENDIX B – INDIVIDUAL ANIMAL DATA

INDIVIDUAL ANIMAL DATA
ORGAN WEIGHTS
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126
SPONSOR STUDY NO.: 211-MTBE-S

ANIMAL NO	GROUP	DOSE	SEX	BODY WGT (G)	SPLEEN (MG)	THYMUS (MG)	SPLEEN /% BODY WT	THYMUS /% BODY WT	COMMENTS
1531	GI	AIR ONLY	F	284.5	550	504	0.190	0.180	
1532	GI	AIR ONLY	F	258.5	592	596	0.230	0.230	
1533	GI	AIR ONLY	F	250.0	521	675	0.210	0.270	
1534	GI	AIR ONLY	F	219.6	585	444	0.270	0.200	
1535	GI	AIR ONLY	F	263.9	577	620	0.220	0.230	
1536	GI	AIR ONLY	F	233.7	548	597	0.230	0.260	
1537	GI	AIR ONLY	F	224.7	584	534	0.260	0.240	
1538	GI	AIR ONLY	F	270.2	759	641	0.280	0.240	
1539	GI	AIR ONLY	F	270.1	877	863	0.320	0.320	
1540	GI	AIR ONLY	F	239.6	530	670	0.220	0.280	
2521	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	249.9	741	692	0.300	0.280	
2522	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	244.7	580	390	0.240	0.160	
2523	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	269.7	523	583	0.190	0.220	
2524	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	257.6	512	533	0.200	0.210	
2525	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	278.2	544	506	0.200	0.180	
2526	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	257.3	699	640	0.270	0.250	
2527	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	281.7	577	638	0.200	0.230	
2528	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	226.6	544	444	0.240	0.200	
2529	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	279.3	640	513	0.230	0.180	
2530	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	274.4	604	610	0.220	0.220	
3521	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	254.7	622	486	0.240	0.190	
3522	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	241.4	655	553	0.270	0.230	
3523	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	266.0	677	674	0.250	0.250	
3524	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	257.7	571	469	0.220	0.180	
3525	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	241.4	499	591	0.210	0.240	
3526	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	268.5	578	602	0.220	0.220	
3527	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	274.9	734	548	0.270	0.200	
3528	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	256.2	658	503	0.260	0.200	
3529	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	246.7	644	507	0.260	0.210	
3530	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	265.2	594	505	0.220	0.190	
4531	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	244.8	556	490	0.230	0.200	
4532	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	238.6	488	358	0.200	0.150	
4533	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	246.8	649	589	0.260	0.240	
4534	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	249.2	534	462	0.210	0.190	
4535	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	251.3	480	520	0.190	0.210	
4536	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	223.3	552	593	0.250	0.270	
4537	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	248.4	594	484	0.240	0.190	
4538	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	259.0	664	578	0.260	0.220	
4539	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	270.9	682	508	0.250	0.190	
4540	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	226.4	536	557	0.240	0.250	
5531	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	231.3	221	174	0.100	0.080	
5532	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	235.5	290	136	0.120	0.060	
5533	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	221.1	249	95	0.110	0.040	
5534	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	256.6	285	120	0.110	0.050	
5535	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	219.6	260	157	0.120	0.070	
5536	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	255.9	333	135	0.130	0.050	
5537	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	217.0	266	112	0.120	0.050	
5538	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	224.3	268	118	0.120	0.050	
5539	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	233.5	260	106	0.110	0.050	
5540	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	247.9	311	132	0.130	0.050	

INDIVIDUAL ANIMAL DATA
ORGAN WEIGHTS
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126 (REPEAT)
SPONSOR STUDY NO.: 211-MTBE-S

RAT NO	GROUP	DOSE	SEX	BODY WGT (G)	SPLEEN (MG)	THYMUS (MG)	SPLEEN /% BODY WT	THYMUS /% BODY WT	COMMENTS
1546	GI	AIR ONLY	F	227.9	705	592	0.310	0.260	
1547	GI	AIR ONLY	F	239.2	615	509	0.260	0.210	
1548	GI	AIR ONLY	F	227.2	669	567	0.290	0.250	
1549	GI	AIR ONLY	F	244.0	516	696	0.210	0.290	
1550	GI	AIR ONLY	F	221.7	613	733	0.280	0.330	
1551	GI	AIR ONLY	F	237.4	568	572	0.240	0.240	
1552	GI	AIR ONLY	F	226.4	640	404	0.280	0.180	
1553	GI	AIR ONLY	F	220.9	493	530	0.220	0.240	
1554	GI	AIR ONLY	F	249.1	574	632	0.230	0.250	
1555	GI	AIR ONLY	F	246.9	494	650	0.200	0.260	
2536	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	219.2	598	656	0.270	0.300	
2537	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	237.9	699	584	0.290	0.250	
2538	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	233.4	489	634	0.210	0.270	
2539	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	214.0	444	533	0.210	0.250	
2540	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	246.8	681	607	0.280	0.250	
2541	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	250.1	647	641	0.260	0.260	
2542	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	222.0	490	575	0.220	0.260	
2543	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	232.5	535	605	0.230	0.260	
2544	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	230.9	577	640	0.250	0.280	
2545	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	197.9	465	519	0.230	0.260	
3536	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	235.5	546	618	0.230	0.260	
3537	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	228.6	602	679	0.260	0.300	
3538	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	219.9	461	507	0.210	0.230	
3539	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	237.5	483	457	0.200	0.190	
3540	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	241.0	642	546	0.270	0.230	
3541	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	238.9	536	548	0.220	0.230	
3542	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	215.7	528	452	0.240	0.210	
3543	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	246.6	524	489	0.210	0.200	
3544	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	234.5	521	494	0.220	0.210	
3545	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	254.2	601	534	0.240	0.210	
4546	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	247.6	677	546	0.270	0.220	
4547	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	235.7	591	513	0.250	0.220	
4548	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	236.3	502	635	0.210	0.270	
4549	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	242.2	684	946	0.280	0.390	
4550	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	233.7	524	498	0.220	0.210	
4551	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	242.9	542	526	0.220	0.220	
4552	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	229.2	613	430	0.270	0.190	
4553	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	204.9	508	467	0.250	0.230	
4554	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	232.8	511	529	0.220	0.230	
4555	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	236.6	716	850	0.300	0.360	
5546	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	184.3	190	107	0.100	0.060	
5547	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	235.8	223	142	0.090	0.060	
5548	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	211.8	286	151	0.140	0.070	
5549	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	209.8	252	112	0.120	0.050	
5550	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	208.2	219	105	0.110	0.050	
5551	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	190.2	183	73	0.100	0.040	
5552	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	199.0	239	94	0.120	0.050	
5553	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	229.8	252	172	0.110	0.070	
5554	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	221.6	294	111	0.130	0.050	
5555	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	197.1	222	136	0.110	0.070	

INDIVIDUAL ANIMAL DATA
ORGAN WEIGHTS
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126 (2ND REPEAT)
SPONSOR STUDY NO.: 211-MTBE-S

ANIMAL NO	GROUP	DOSE	SEX	BODY WGT (G)	SPLEEN (MG)	THYMUS (MG)	SPLEEN /% BODY WT	THYMUS /% BODY WT	COMMENTS
1581	GI	AIR ONLY	F	246.5	732	667	0.300	0.270	
1582	GI	AIR ONLY	F	217.9	516	466	0.240	0.210	
1583	GI	AIR ONLY	F	266.0	708	847	0.270	0.320	
1584	GI	AIR ONLY	F	252.0	633	607	0.250	0.240	
1585	GI	AIR ONLY	F	257.6	749	812	0.290	0.320	
1586	GI	AIR ONLY	F	240.1	780	799	0.320	0.330	
1587	GI	AIR ONLY	F	282.6	692	1065	0.240	0.380	
1588	GI	AIR ONLY	F	239.8	538	638	0.220	0.270	
1589	GI	AIR ONLY	F	256.6	670	681	0.260	0.270	
1590	GI	AIR ONLY	F	223.6	445	607	0.200	0.270	
2581	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	240.7	674	780	0.280	0.320	
2582	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	262.3	538	805	0.210	0.310	
2583	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	264.3	759	966	0.290	0.370	
2584	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	262.2	505	717	0.190	0.270	
2585	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	263.3	690	658	0.260	0.250	
2586	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	244.4	657	517	0.270	0.210	
2587	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	247.8	462	749	0.190	0.300	
2588	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	248.3	604	900	0.240	0.360	
2589	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	267.1	799	823	0.300	0.310	
2590	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	268.3	677	835	0.250	0.310	
3581	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	277.0	722	650	0.260	0.230	
3582	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	229.5	565	835	0.250	0.360	
3583	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	226.4	537	639	0.240	0.280	
3584	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	236.7	484	652	0.200	0.280	
3585	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	228.3	557	813	0.240	0.360	
3586	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	217.4	501	482	0.230	0.220	
3587	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	269.4	559	893	0.210	0.330	
3588	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	261.9	521	730	0.200	0.280	
3589	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	247.8	708	795	0.290	0.320	
3590	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	231.0	588	730	0.250	0.320	
4581	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	237.0	544	676	0.230	0.290	
4582	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	213.0	494	655	0.230	0.310	
4583	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	271.6	568	689	0.210	0.250	
4584	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	263.6	626	669	0.240	0.250	
4585	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	265.6	584	728	0.220	0.270	
4586	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	289.7	922	870	0.320	0.300	
4587	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	227.0	589	712	0.260	0.310	
4588	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	255.6	722	796	0.280	0.310	
4589	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	265.9	625	648	0.240	0.240	
4590	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	259.3	833	1083	0.320	0.420	
5581	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	203.0	216	159	0.110	0.080	
5582	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	210.0	198	157	0.090	0.070	
5583	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	238.0	243	214	0.100	0.090	
5584	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	202.5	282	168	0.140	0.080	
5585	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	234.5	342	161	0.150	0.070	
5586	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	219.5	294	181	0.130	0.080	
5587	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	249.7	264	304	0.110	0.120	
5588	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	203.4	272	165	0.130	0.080	
5589	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	264.3	345	230	0.130	0.090	
5590	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	288.0	374	224	0.130	0.080	

INDIVIDUAL ANIMAL DATA
AFC
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126
SPONSOR STUDY NO.: 211-MTBE-S

ANIMAL NO	GROUP	DOSE	SEX	IGM AFC/10^6 SP.C.	IGM AFC/SPLEEN 10^3	CELLS/SPLEEN x 10^7	SPLEEN WEIGHT (MG)	BODY WEIGHT (G)	COMMENTS
1531	GI	AIR ONLY	F	50	30	59.82	550	284.5	
1532	GI	AIR ONLY	F	169	108	63.96	592	258.5	
1533	GI	AIR ONLY	F	738	411	55.68	521	250.0	
1534	GI	AIR ONLY	F	1014	576	56.82	585	219.6	
1535	GI	AIR ONLY	F	1126	720	63.96	577	263.9	
1536	GI	AIR ONLY	F	2275	1413	62.10	548	233.7	
1537	GI	AIR ONLY	F	802	477	59.46	584	224.7	
1538	GI	AIR ONLY	F	395	288	72.84	759	270.2	
1539	GI	AIR ONLY	F	457	501	109.62	877	270.1	
1540	GI	AIR ONLY	F	830	573	69.06	530	239.6	
2521	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	159	150	94.44	741	249.9	
2522	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	581	345	59.34	580	244.7	
2523	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	938	567	60.42	523	269.7	
2524	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	457	303	66.30	512	257.6	
2525	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	169	120	71.04	544	278.2	
2526	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	146	111	76.08	699	257.3	
2527	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	249	153	61.44	577	281.7	
2528	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	105	57	54.42	544	226.6	
2529	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	234	144	61.56	640	279.3	
2530	GII	2,000 MG/M^3 GASOLINE MTBE VAPOR	F	123	72	58.62	604	274.4	
3521	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	401	282	70.26	622	254.7	
3522	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	436	300	68.88	655	241.4	
3523	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	267	189	70.68	677	266.0	
3524	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	1710	993	58.08	571	257.7	
3525	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	496	234	47.16	499	241.4	
3526	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	63	39	62.22	578	268.5	
3527	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	395	306	77.40	734	274.9	
3528	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	1918	1221	63.66	658	256.2	
3529	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	1734	1086	62.64	644	246.7	
3530	GIII	10,000 MG/M^3 GASOLINE MTBE VAPOR	F	418	231	55.20	594	265.2	
4531	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	570	357	62.58	556	244.8	
4532	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	1036	627	60.54	488	238.6	
4533	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	517	396	76.56	649	246.8	
4534	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	343	210	61.20	534	249.2	
4535	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	519	258	49.68	480	251.3	
4536	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	297	165	55.56	552	223.3	
4537	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	2865	1800	62.82	594	248.4	
4538	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	1884	1341	71.16	664	259.0	
4539	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	481	363	75.54	682	270.9	
4540	GIV	20,000 MG/M^3 GASOLINE MTBE VAPOR	F	470	297	63.24	536	226.4	
5531	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	62.64	221	231.3	
5532	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	59.04	290	235.5	
5533	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	61.02	249	221.1	
5534	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	60.66	285	256.6	
5535	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	59.76	260	219.6	
5536	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	88.32	333	255.9	
5537	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	77.04	266	217.0	
5538	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	62.34	268	224.3	
5539	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	67.44	260	233.5	
5540	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	95.94	311	247.9	

INDIVIDUAL ANIMAL DATA
AFC
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126 (REPEAT)
SPONSOR STUDY NO.: 211-MTBE-S

ANIMAL NO	GROUP	DOSE	SEX	IGM AFC/10^6 SP.C.	IGM AFC/SPLEEN 10^3	CELLS/SPLEEN 10^7	SPLEEN WEIGHT (MG)	BODY WEIGHT (G)
1546	GI	AIR ONLY	F	597	573	96.00	705	227.9
1547	GI	AIR ONLY	F	498	387	77.76	615	239.2
1548	GI	AIR ONLY	F	571	528	92.52	669	227.2
1549	GI	AIR ONLY	F	279	168	60.12	516	244.0
1550	GI	AIR ONLY	F	291	225	77.34	613	221.7
1551	GI	AIR ONLY	F	282	213	75.42	568	237.4
1552	GI	AIR ONLY	F	623	432	69.30	640	226.4
1553	GI	AIR ONLY	F	170	96	56.58	493	220.9
1554	GI	AIR ONLY	F	131	102	78.06	574	249.1
1555	GI	AIR ONLY	F	190	120	63.12	494	246.9
2536	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	387	300	77.58	598	219.2
2537	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	785	471	60.00	699	237.9
2538	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	525	330	62.88	489	233.4
2539	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	290	165	56.88	444	214.0
2540	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	164	153	93.54	681	246.8
2541	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	337	213	63.12	647	250.1
2542	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	145	90	61.92	490	222.0
2543	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	24	15	62.76	535	232.5
2544	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	38	30	78.18	577	230.9
2545	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	56	27	48.06	465	197.9
3536	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	589	399	67.74	546	235.5
3537	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	104	75	71.94	602	228.6
3538	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	140	66	47.10	461	219.9
3539	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	120	78	65.22	483	237.5
3540	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	252	201	79.74	642	241.0
3541	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	31	18	58.92	536	238.9
3542	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	82	48	58.86	528	215.7
3543	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	248	144	58.08	524	246.6
3544	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	132	78	59.28	521	234.5
3545	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	959	738	76.92	601	254.2
4546	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	926	717	77.46	677	247.6
4547	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	227	150	66.12	591	235.7
4548	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	2136	978	45.78	502	236.3
4549	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	89	60	67.38	684	242.2
4550	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	142	93	65.40	524	233.7
4551	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	53	30	57.06	542	242.9
4552	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	56	36	63.96	613	229.2
4553	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	41	27	65.34	508	204.9
4554	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	15	9	59.16	511	232.8
4555	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	171	138	80.52	716	236.6
5546	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	20.82	190	184.3
5547	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	21	3	14.58	223	235.8
5548	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	14.34	286	211.8
5549	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	13.98	252	209.8
5550	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	11.58	219	208.2
5551	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	162	15	9.24	183	190.2
5552	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	11.58	239	199.0
5553	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	11.82	252	229.8
5554	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	16.68	294	221.6
5555	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	11.34	222	197.1

INDIVIDUAL ANIMAL DATA
AFC
GASOLINE MTBE VAPOR CONDENSATE
HLS STUDY NO.: 00-6126 (2ND REPEAT)
SPONSOR STUDY NO.: 211-MTBE-S

ANIMAL NO	GROUP	DOSE	SEX	IGM AFC/10^6 SP.C.	IGM AFC/SPLEEN 10^3	CELLS/SPLEEN x10^7	SPLEEN WEIGHT (MG)	BODY WEIGHT (G)	COMMENTS
1581	GI	AIR ONLY	F	2149	1701	79.14	732	246.5	
1582	GI	AIR ONLY	F	2949	1755	59.52	516	217.9	
1583	GI	AIR ONLY	F	604	393	65.10	708	266.0	
1584	GI	AIR ONLY	F	1150	918	79.86	633	252.0	
1585	GI	AIR ONLY	F	1366	1134	83.04	749	257.6	
1586	GI	AIR ONLY	F	1014	882	86.94	780	240.1	
1587	GI	AIR ONLY	F	1714	1341	78.24	692	282.6	
1588	GI	AIR ONLY	F	2271	1296	57.06	538	239.8	
1589	GI	AIR ONLY	F	1855	1458	78.60	670	256.6	
1590	GI	AIR ONLY	F	1388	741	53.40	445	223.6	
2581	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	745	633	85.02	674	240.7	
2582	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	678	420	61.98	538	262.3	
2583	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	496	381	76.80	759	264.3	
2584	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	462	306	66.30	505	262.2	
2585	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	1634	1332	81.54	690	263.3	
2586	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	1442	1350	93.60	657	244.4	
2587	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	1262	729	57.78	462	247.8	
2588	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	1989	1359	68.34	604	248.3	
2589	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	1950	1863	95.52	799	267.1	
2590	GII	2,000 MG/M3 GASOLINE MTBE VAPOR	F	628	492	78.30	677	268.3	
3581	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	1083	858	79.20	722	277.0	
3582	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	3140	1899	60.48	565	229.5	
3583	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	1554	1035	66.60	537	226.4	
3584	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	912	549	60.18	484	236.7	
3585	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	2248	1404	62.46	557	228.3	
3586	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	1814	963	53.10	501	217.4	
3587	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	861	471	54.72	559	269.4	
3588	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	621	444	71.52	521	261.9	
3589	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	2348	1827	77.82	708	247.8	
3590	GIII	10,000 MG/M3 GASOLINE MTBE VAPOR	F	317	207	65.22	588	231.0	
4581	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	2091	1503	71.88	544	237.0	
4582	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	3174	1809	57.00	494	213.0	
4583	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1896	1242	65.52	568	271.6	
4584	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1297	972	74.94	626	263.6	
4585	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1489	981	65.88	584	265.6	
4586	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1311	1566	119.46	922	289.7	
4587	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1598	1089	68.16	589	227.0	
4588	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1463	1125	76.92	722	255.6	
4589	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	824	528	64.08	625	265.9	
4590	GIV	20,000 MG/M3 GASOLINE MTBE VAPOR	F	1656	1638	98.94	833	259.3	
5581	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	9.18	216	203.0	
5582	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	6.66	198	210.0	
5583	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	9.06	243	238.0	
5584	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	11.40	282	202.5	
5585	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	10.92	342	234.5	
5586	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	12.24	294	219.5	
5587	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	10.50	264	249.7	
5588	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	8.70	272	203.4	
5589	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	14.10	345	264.3	
5590	GV	50 MG/KG CYCLOPHOSPHAMIDE	F	0	0	13.74	374	288.0	

APPENDIX C - CONTRACTING SPONSOR'S EXPOSURE AND ANIMAL DATA

	Animal Exposure and Animal Data Preface	Appendix C

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. Note that for brevity and relevance, only the data from the 2nd Repeat Study (exposed concurrent with study 00-4208) is presented. The data for the Original and 1st Repeat Study are available in the study file.

STUDY DATES:

Date of Animal Receipt:	19 July 2001
Experimental Initiation Date:	2 August 2001 (in-life)
Experimental Completion Date:	29 August 2001 (in-life)

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.

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TABLES

Table A Gasoline MTBE Vapor Condensate: A 13-Week Whole-Body Inhalation Toxicity Study in Rats

Chamber Monitoring Results
Cumulative Exposure Record
Group I - 0 mg/m^3 (Air Control)

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
			Nominal	Mean	Individual				MMAD	GSD	TMC	Mean Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)				(µm)		(mg/m^3)	(°C)	(%)
51	2-Aug-01	52	0	0	0	0	0	0				24	52
52	3-Aug-01	53	0	0	0	0	0	0				24	66
55	6-Aug-01	56	0	0	0	0	0	0				24	45
56	7-Aug-01	57	0	0	0	0	0	0				24	50
57	8-Aug-01	58	0	0	0	0	0	0	0.847	1.920	1.09E-02	24	46
58	9-Aug-01	59	0	0	0	0	0	0				25	48
59	10-Aug-01	60	0	0	0	0	0	0				24	52
60	11-Aug-01	61	0	0	0	0	0	0				23	47
62	13-Aug-01	63	0	0	0	0	0	0				24	42
63	14-Aug-01	64	0	0	0	0	0	0				23	54
64	15-Aug-01	65	0	0	0	0	0	0	0.832	1.444	2.82E-03	24	41
65	16-Aug-01	66	0	0	0	0	0	0				23	51
66	17-Aug-01	67	0	0	0	0	0	0				24	42
69	20-Aug-01	70	0	0	0	0	0	0				24	45
70	21-Aug-01	71	0	0	0	0	0	0				24	42
71	22-Aug-01	72	0	0	0	0	0	0	11.36	3.068	5.34E-03	24	48
72	23-Aug-01	73	0	0	0	0	0	0				24	50
73	24-Aug-01	74	0	0	0	0	0	0				22	71
76	27-Aug-01	77	0	0	0	0	0	0				24	43
77	28-Aug-01	78	0	0	0	0	0	0				24	42
		Mean	**0**		**0**				**4.346**	**2.144**	**6.35E-03**	**23.8**	**48.9**
		S.D.	**0**		**0**				**6.074**	**0.835**	**4.13E-03**	**0.6**	**7.8**

Table A Gasoline MTBE Vapor Condensate: A 13-Week Whole-Body Inhalation Toxicity Study in Rats

Chamber Monitoring Results
Cumulative Exposure Record
Group II - 2000 mg/m^3

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
			Nominal	Mean	Individual				MMAD	GSD	TMC	Mean Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)				(µm)		(mg/m^3)	(°C)	(%)
51	2-Aug-01	52	2130	2038	2070	2040	2010	2030				24	56
52	3-Aug-01	53	2110	2023	2100	1820	2190	1980				25	63
55	6-Aug-01	56	1950	2013	1920	1990	2080	2060				25	44
56	7-Aug-01	57	2070	2023	1900	2130	2060	2000				24	50
57	8-Aug-01	58	2050	2023	1970	2120	2020	1980	0.814	1.374	6.71E-03	25	44
58	9-Aug-01	59	2020	2000	1950	2000	2000	2050				25	48
59	10-Aug-01	60	2030	2000	1930	1900	2060	2110				25	53
60	11-Aug-01	61	2060	2035	2170	1980	2020	1970				24	43
62	13-Aug-01	63	2090	2095	2030	2000	2150	2200				25	40
63	14-Aug-01	64	2140	2053	2060	2010	2090	2050				24	48
64	15-Aug-01	65	2050	2045	2060	2080	2000	2040	1.156	2.940	8.00E-03	25	39
65	16-Aug-01	66	1930	2000	2000	1810	2240	1950				24	45
66	17-Aug-01	67	2020	2045	2000	2000	2050	2130				25	39
69	20-Aug-01	70	2200	1990	2070	1720	2140	2030				25	43
70	21-Aug-01	71	2060	2020	2020	2030	2030	2000				25	38
71	22-Aug-01	72	2020	2050	2000	2130	2010	2060	0.910	1.693	1.67E-03	25	44
72	23-Aug-01	73	2060	1978	2040	2000	1950	1920				24	50
73	24-Aug-01	74	2270	1985	2010	2000	2000	1930				24	62
76	27-Aug-01	77	2070	2155	2030	2130	2450	2010				25	39
77	28-Aug-01	78	2050	2028	2060	2000	2120	1930				25	38
		Mean	**2069**		**2030**				**0.960**	**2.002**	**5.46E-03**	**24.7**	**46.3**
		S.D.	**77**		**96**				**0.177**	**0.828**	**3.35E-03**	**0.5**	**7.5**

Table A Gasoline MTBE Vapor Condensate: A 13-Week Whole-Body Inhalation Toxicity Study in Rats

Chamber Monitoring Results
Cumulative Exposure Record
Group III - 10000 mg/m^3

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
				Mean	Individual					MMAD	GSD	TMC	Mean Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)					(µm)		(mg/m^3)	(°C)	(%)
51	2-Aug-01	52	10200	10430	10100	10300	10200	11100					24	58
52	3-Aug-01	53	10000	10360	10100	10900	10500	9920					25	64
55	6-Aug-01	56	9950	10300	11100	10100	10000	10000					25	43
56	7-Aug-01	57	9990	10400	9900	10600	10900	10200					25	45
57	8-Aug-01	58	10300	10180	10100	9800	10100	10700		0.825	1.462	7.14E-03	25	44
58	9-Aug-01	59	10000	10220	9770	10700	10000	10400					25	46
59	10-Aug-01	60	9650	10130	10000	10000	10800	9700					25	54
60	11-Aug-01	61	10000	10170	10000	9770	10200	10700					24	43
62	13-Aug-01	63	10100	10380	10300	10400	10400	10400					25	40
63	14-Aug-01	64	9660	10230	10000	10000	10400	10500					25	42
64	15-Aug-01	65	9550	10280	9920	10100	10000	11100		0.841	1.913	3.74E-03	25	39
65	16-Aug-01	66	9600	9953	10200	10600	10000	9010					24	49
66	17-Aug-01	67	9870	10340	10000	10800	9940	10600					25	39
69	20-Aug-01	70	10300	10180	10000	10300	10100	10300					24	49
70	21-Aug-01	71	10400	10310	9230	10600	11000	10400					26	38
71	22-Aug-01	72	9480	10150	10100	10000	9910	10600		0.946	2.321	1.83E-03	25	42
72	23-Aug-01	73	10000	10300	10500	10500	10000	10300					25	48
73	24-Aug-01	74	10100	10180	11100	9420	9390	10800					24	55
76	27-Aug-01	77	10400	10880	10400	10600	11300	11200					26	40
77	28-Aug-01	78	10000	10260	10200	9950	10300	10600					26	39
		Mean	**9978**		**10280**					**0.871**	**1.899**	**4.24E-03**	**24.9**	**45.9**
		S.D.	**275**		**446**					**0.065**	**0.430**	**2.69E-03**	**0.6**	**7.2**

Table A Gasoline MTBE Vapor Condensate: A 13-Week Whole-Body Inhalation Toxicity Study in Rats

Chamber Monitoring Results
Cumulative Exposure Record
Group IV - 20000 mg/m^3

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment Mean	
				Mean	Individual					MMAD	GSD	TMC	Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)					(µm)		(mg/m^3)	(°C)	(%)
51	2-Aug-01	52	21300	20280	20000	20400	20600	20100					24	60
52	3-Aug-01	53	21300	20400	20100	19300	21400	20800					25	55
55	6-Aug-01	56	21000	20300	20400	20000	20200	20600					25	42
56	7-Aug-01	57	20000	20230	20300	20400	20200	20000					25	44
57	8-Aug-01	58	20800	20000	20000	20500	20000	19500		0.814	1.354	7.83E-03	25	44
58	9-Aug-01	59	21100	20180	19800	20700	20000	20200					25	46
59	10-Aug-01	60	21200	20450	19900	20500	21000	20400					25	50
60	11-Aug-01	61	19900	18530	19200	18500	20300	16100					25	41
62	13-Aug-01	63	21300	20030	20000	19600	20400	20100					25	41
63	14-Aug-01	64	21500	20050	20100	20000	20100	20000					24	40
64	15-Aug-01	65	21500	20450	20000	20800	20600	20400		0.891	2.023	3.28E-03	25	39
65	16-Aug-01	66	21000	20200	20200	20000	20400	20200					25	41
66	17-Aug-01	67	21400	20200	20000	20100	20000	20700					25	38
69	20-Aug-01	70	21400	20000	19600	20400	20000	20000					24	46
70	21-Aug-01	71	21300	20180	19700	20300	20700	20000					25	37
71	22-Aug-01	72	21000	20350	19800	20800	20000	20800		0.898	1.811	1.60E-03	25	41
72	23-Aug-01	73	21300	20030	19800	20400	19700	20200					25	44
73	24-Aug-01	74	21700	20180	19800	20200	20200	20500					24	52
76	27-Aug-01	77	22000	20630	19900	21100	20800	20700					25	39
77	28-Aug-01	78	21200	20000	20000	20000	20000	20000					25	38
		Mean	**21160**		**20131**					**0.867**	**1.729**	**4.24E-03**	**24.8**	**43.9**
		S.D.	**491**		**630**					**0.047**	**0.342**	**3.22E-03**	**0.4**	**6.1**

TABLE B

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY -7	TOTAL
# OF ANIMALS EXAMINED	1	10	
	2	10	
	3	10	
	4	10	
	5	10	
NORMAL			
WITHIN NORMAL LIMITS	1	10	10
	2	9	9
	3	10	10
	4	10	10
	5	10	10
APPEARANCE			
SOFT PROTRUSION - MID ABDOMEN	1	0	0
	2	1	1
	3	0	0
	4	0	0
	5	0	0

TABLE C

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES — MEAN BODY WEIGHTS (GRAMS)

DOSE GROUP:		I	II	III	IV	V
EXPOSURE LEVEL (mg/m3):		0	2,000	10,000	20,000	POSITIVE CONTROL
WEEK -1	MEAN	128	129	129	128	128
	S.D.	9.1	8.3	9.3	8.8	9.1
	N	10	10	10	10	10
WEEK 0	MEAN	161	164	162	163	162
	S.D.	8.7	7.7	10.7	13.4	14.4
	N	10	10	10	10	10
WEEK 1	MEAN	193	199	193	199	196
	S.D.	9.6	10.4	15.3	15.3	21.1
	N	10	10	10	10	10
WEEK 2	MEAN	217	224	216	225	218
	S.D.	14.3	9.8	18.8	17.7	21.9
	N	10	10	10	10	10
WEEK 3	MEAN	232	240	231	240	237
	S.D.	18.5	14.2	17.9	20.6	31.0
	N	10	10	10	10	10
WEEK 4	MEAN	237	249	237	248	230
	S.D.	20.1	13.0	20.7	21.4	28.4
	N	10	10	10	10	10

No statistically significant differences

TABLE D

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES — MEAN BODY WEIGHT CHANGE (GRAMS)

DOSE GROUP:		I	II	III	IV	V
EXPOSURE LEVEL (mg/m3):		0	2,000	10,000	20,000	POSITIVE CONTROL
WEEK 0 TO 1	MEAN	32	35	32	36	34
	S.D.	5.8	5.9	6.2	11.8	8.5
	N	10	10	10	10	10
WEEK 0 TO 2	MEAN	56	60	54	63	56
	S.D.	10.2	6.2	9.2	15.2	10.2
	N	10	10	10	10	10
WEEK 0 TO 3	MEAN	72	76	69	78	75
	S.D.	14.3	12.4	9.8	15.8	18.3
	N	10	10	10	10	10
WEEK 0 TO 4	MEAN	76	85	75	86	68
	S.D.	15.5	11.6	12.0	16.9	16.1
	N	10	10	10	10	10

No statistically significant differences

TABLE E

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

FEMALES — MEAN FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

	DOSE GROUP:	I	II	III	IV	V
	EXPOSURE LEVEL (mg/m3):	0	2,000	10,000	20,000	POSITIVE CONTROL
WEEK 0	MEAN	133	133	132	135	133
	S.D.	7.0	8.0	5.8	6.7	7.2
	N	9	10	10	9	9
WEEK 1	MEAN	97	98	96	99	103
	S.D.	5.7	7.1	4.9	7.8	6.2
	N	10	10	10	10	10
WEEK 2	MEAN	86	89	86	89	91
	S.D.	3.6	7.7	5.2	4.3	5.9
	N	10	10	10	10	10
WEEK 3	MEAN	82	84	83	84	86
	S.D.	3.7	7.2	6.4	1.8	3.5
	N	9	8	9	10	10
WEEK 4	MEAN	85	85	83	85	77*
	S.D.	4.2	7.2	6.4	1.9	5.2
	N	10	10	10	10	9

Statistical key: * = p<0.05

TABLE F

G MTBE VC: 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 I 0 mg/m3

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7
1581	WITHIN NORMAL LIMITS	P
1582	WITHIN NORMAL LIMITS	P
1583	WITHIN NORMAL LIMITS	P
1584	WITHIN NORMAL LIMITS	P
1585	WITHIN NORMAL LIMITS	P
1586	WITHIN NORMAL LIMITS	P
1587	WITHIN NORMAL LIMITS	P
1588	WITHIN NORMAL LIMITS	P
1589	WITHIN NORMAL LIMITS	P
1590	WITHIN NORMAL LIMITS	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

TABLE F

G MTBE VC: 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

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7
2581	WITHIN NORMAL LIMITS	P
2582	WITHIN NORMAL LIMITS	P
2583	WITHIN NORMAL LIMITS	P
2584	WITHIN NORMAL LIMITS	P
2585	APPEARANCE: SOFT PROTRUSION - MID ABDOMEN	P
2586	WITHIN NORMAL LIMITS	P
2587	WITHIN NORMAL LIMITS	P
2588	WITHIN NORMAL LIMITS	P
2589	WITHIN NORMAL LIMITS	P
2590	WITHIN NORMAL LIMITS	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

TABLE F

G MTBE VC: 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

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7
3581	WITHIN NORMAL LIMITS	P
3582	WITHIN NORMAL LIMITS	P
3583	WITHIN NORMAL LIMITS	P
3584	WITHIN NORMAL LIMITS	P
3585	WITHIN NORMAL LIMITS	P
3586	WITHIN NORMAL LIMITS	P
3587	WITHIN NORMAL LIMITS	P
3588	WITHIN NORMAL LIMITS	P
3589	WITHIN NORMAL LIMITS	P
3590	WITHIN NORMAL LIMITS	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

TABLE F

G MTBE VC: 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

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7
4581	WITHIN NORMAL LIMITS	P
4582	WITHIN NORMAL LIMITS	P
4583	WITHIN NORMAL LIMITS	P
4584	WITHIN NORMAL LIMITS	P
4585	WITHIN NORMAL LIMITS	P
4586	WITHIN NORMAL LIMITS	P
4587	WITHIN NORMAL LIMITS	P
4588	WITHIN NORMAL LIMITS	P
4589	WITHIN NORMAL LIMITS	P
4590	WITHIN NORMAL LIMITS	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

TABLE F

G MTBE VC: 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 - 7
5581	WITHIN NORMAL LIMITS	P
5582	WITHIN NORMAL LIMITS	P
5583	WITHIN NORMAL LIMITS	P
5584	WITHIN NORMAL LIMITS	P
5585	WITHIN NORMAL LIMITS	P
5586	WITHIN NORMAL LIMITS	P
5587	WITHIN NORMAL LIMITS	P
5588	WITHIN NORMAL LIMITS	P
5589	WITHIN NORMAL LIMITS	P
5590	WITHIN NORMAL LIMITS	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

TABLE G

G MTBE VC: 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 I 0 mg/m3

	WEEK OF STUDY					
ANIMAL#	-1	0	1	2	3	4
1581	121	170	191	213	228	237
1582	130	151	182	197	209	207
1583	119	157	198	222	256	254
1584	137	167	195	222	237	239
1585	116	156	188	224	233	249
1586	128	156	192	220	225	230
1587	143	175	211	239	265	274
1588	139	165	195	215	224	227
1589	127	164	199	231	240	245
1590	124	148	176	191	206	210
MEAN	128	161	193	217	232	237
S.D.	9.1	8.7	9.6	14.3	18.5	20.1
N	10	10	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE G

G MTBE VC: 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 II 2,000 mg/m3

	WEEK OF STUDY					
ANIMAL#	-1	0	1	2	3	4
2581	118	152	176	206	210	230
2582	139	171	207	233	241	256
2583	118	158	195	214	248	258
2584	126	166	205	231	246	255
2585	144	174	211	235	253	262
2586	130	158	197	214	238	241
2587	133	174	198	223	227	234
2588	131	155	190	224	230	233
2589	124	165	202	232	246	261
2590	126	166	208	227	258	261
MEAN	129	164	199	224	240	249
S.D.	8.3	7.7	10.4	9.8	14.2	13.0
N	10	10	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE G

G MTBE VC: 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 mg/m3

	WEEK OF STUDY					
ANIMAL#	-1	0	1	2	3	4
3581	143	175	213	244	269	271
3582	118	156	181	196	219	226
3583	122	151	180	198	214	213
3584	140	171	206	226	230	235
3585	128	154	188	208	222	216
3586	116	145	173	189	207	214
3587	130	173	210	235	246	264
3588	138	175	210	234	244	255
3589	125	159	195	218	231	240
3590	126	160	179	209	226	234
MEAN	129	162	193	216	231	237
S.D.	9.3	10.7	15.3	18.8	17.9	20.7
N	10	10	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE G

G MTBE VC: 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
4581	124	161	184	219	236	239
4582	119	142	173	194	204	206
4583	132	143	209	240	252	263
4584	142	174	211	234	247	257
4585	127	171	207	239	256	260
4586	130	178	220	253	267	278
4587	129	157	185	203	206	221
4588	115	156	188	220	239	248
4589	123	166	199	227	243	258
4590	141	179	211	224	252	255
MEAN	128	163	199	225	240	248
S.D.	8.8	13.4	15.3	17.7	20.6	21.4
N	10	10	10	10	10	10

TABLE G

G MTBE VC: 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 V POSITIVE CONTROL

	WEEK OF STUDY					
ANIMAL#	-1	0	1	2	3	4
5581	117	145	171	188	199	200
5582	118	145	180	202	215	210
5583	127	165	203	227	251	242
5584	135	154	177	200	210	203
5585	143	172	199	221	246	232
5586	125	152	188	209	220	212
5587	121	161	194	220	245	241
5588	131	159	186	207	213	208
5589	128	175	215	251	273	261
5590	142	191	243	256	296	287
MEAN	128	162	196	218	237	230
S.D.	9.1	14.4	21.1	21.9	31.0	28.4
N	10	10	10	10	10	10

TABLE H

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES GROUP I 0 mg/m3

	WEEK OF STUDY			
ANIMAL#	0-1	0-2	0-3	0-4
1581	21	43	58	67
1582	31	46	58	56
1583	41	65	99	97
1584	27	54	69	71
1585	32	68	77	92
1586	36	64	69	74
1587	36	64	90	99
1588	30	50	59	62
1589	36	67	76	81
1590	28	44	59	62
MEAN	32	56	72	76
S.D.	5.8	10.2	14.3	15.5
N	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE H

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES GROUP II 2,000 mg/m3

	WEEK OF STUDY			
ANIMAL#	0-1	0-2	0-3	0-4
2581	25	54	58	79
2582	37	62	71	85
2583	37	56	90	100
2584	39	65	80	89
2585	38	62	79	88
2586	38	55	79	82
2587	24	49	53	60
2588	35	69	74	78
2589	37	67	82	96
2590	42	62	92	95
MEAN	35	60	76	85
S.D.	5.9	6.2	12.4	11.6
N	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE H

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES GROUP III 10,000 mg/m3

	WEEK OF STUDY			
ANIMAL#	0-1	0-2	0-3	0-4
3581	39	70	94	96
3582	25	40	63	71
3583	28	46	63	62
3584	35	55	59	64
3585	33	54	67	62
3586	29	44	62	69
3587	37	62	73	91
3588	36	60	69	80
3589	36	59	72	82
3590	19	48	66	74
MEAN	32	54	69	75
S.D.	6.2	9.2	9.8	12.0
N	10	10	10	10

Huntingdon Life Sciences 00-6126R
Immunotoxicity Sub-Group

TABLE H

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES GROUP IV 20,000 mg/m3

	WEEK OF STUDY			
ANIMAL#	0-1	0-2	0-3	0-4
4581	23	57	75	77
4582	31	52	62	64
4583	67	97	109	120
4584	37	60	74	83
4585	36	68	84	88
4586	42	75	89	100
4587	28	46	49	64
4588	32	64	83	92
4589	34	62	78	92
4590	33	45	73	77
MEAN	36	63	78	86
S.D.	11.8	15.2	15.8	16.9
N	10	10	10	10

TABLE H

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES GROUP V POSITIVE CONTROL

	WEEK OF STUDY			
ANIMAL#	0-1	0-2	0-3	0-4
5581	26	43	54	55
5582	35	57	71	65
5583	38	62	85	77
5584	23	45	56	49
5585	28	49	74	60
5586	36	57	68	60
5587	34	59	85	80
5588	27	48	53	49
5589	40	77	98	86
5590	52	65	105	96
MEAN	34	56	75	68
S.D.	8.5	10.2	18.3	16.1
N	10	10	10	10

TABLE I

G MTBE VC: 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 I 0 mg/m3

	WEEK OF STUDY				
ANIMAL#	0	1	2	3	4
1581	137	88	77	77	81
1582	122	93	85	81	82
1583	139	100	83	85	77
1584	125	92	86	78	88
1585	141	101	86	79	88
1586	132	102	89	86	86
1587	128	94	87	87	87
1588	SF	107	90	SF	92
1589	140	96	87	80	84
1590	129	94	87	86	82
MEAN	133	97	86	82	85
S.D.	7.0	5.7	3.6	3.7	4.2
N	9	10	10	9	10

SF=Spilled Feeder

TABLE I

G MTBE VC: 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 II 2,000 mg/m3

	WEEK OF STUDY				
ANIMAL#	0	1	2	3	4
2581	134	103	98	88	97
2582	118	83	74	72	74
2583	138	97	83	86	83
2584	139	103	90	SF	90
2585	123	92	87	81	79
2586	137	107	98	97	93
2587	133	92	84	80	80
2588	127	101	96	SF	89
2589	142	100	90	85	88
2590	142	100	86	86	80
MEAN	133	98	89	84	85
S.D.	8.0	7.1	7.7	7.2	7.2
N	10	10	10	8	10

SF=Spilled Feeder

TABLE I

G MTBE VC: 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

	WEEK OF STUDY				
ANIMAL#	0	1	2	3	4
3581	128	99	88	86	86
3582	134	94	84	83	80
3583	128	93	80	75	80
3584	128	98	86	SF	84
3585	124	89	76	72	70
3586	131	93	90	86	84
3587	144	106	92	94	95
3588	134	96	84	82	84
3589	130	97	88	82	82
3590	138	91	92	86	87
MEAN	132	96	86	83	83
S.D.	5.8	4.9	5.2	6.4	6.4
N	10	10	10	9	10

SF=Spilled Feeder

TABLE I

G MTBE VC: 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/m3

	WEEK OF STUDY				
ANIMAL#	0	1	2	3	4
4581	128	89	89	84	88
4582	133	96	88	82	83
4583	131	117	91	84	87
4584	141	101	89	83	87
4585	144	105	98	85	83
4586	139	100	83	83	83
4587	124	93	85	84	87
4588	141	101	89	85	85
4589	CF	97	90	84	85
4590	135	94	85	88	85
MEAN	135	99	89	84	85
S.D.	6.7	7.8	4.3	1.8	1.9
N	9	10	10	10	10

CF=Contaminated Feeder

TABLE I

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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 POSITIVE CONTROL

	WEEK OF STUDY				
ANIMAL#	0	1	2	3	4
5581	134	101	91	85	87
5582	132	103	93	85	75
5583	139	106	91	86	72
5584	SF	99	95	91	SF
5585	127	92	87	87	78
5586	139	113	95	91	81
5587	138	102	91	87	77
5588	120	96	84	80	70
5589	142	109	100	90	77
5590	129	106	80	84	72
MEAN	133	103	91	86	77
S.D.	7.2	6.2	5.9	3.5	5.2
N	9	10	10	10	9

SF=Spilled Feeder

TABLE J

G MTBE VC: A 13-WEEK WHOLE-BODY INHALATION TOXICITY
STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

ANIMAL TERMINATION HISTORY

FEMALES GROUP I 0 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1581	TERMINAL SACRIFICE	29-AUG-01	3	27
1582	TERMINAL SACRIFICE	29-AUG-01	3	27
1583	TERMINAL SACRIFICE	29-AUG-01	3	27
1584	TERMINAL SACRIFICE	29-AUG-01	3	27
1585	TERMINAL SACRIFICE	29-AUG-01	3	27
1586	TERMINAL SACRIFICE	29-AUG-01	3	27
1587	TERMINAL SACRIFICE	29-AUG-01	3	27
1588	TERMINAL SACRIFICE	29-AUG-01	3	27
1589	TERMINAL SACRIFICE	29-AUG-01	3	27
1590	TERMINAL SACRIFICE	29-AUG-01	3	27

TABLE J

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STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

ANIMAL TERMINATION HISTORY

FEMALES GROUP II 2,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2581	TERMINAL SACRIFICE	29-AUG-01	3	27
2582	TERMINAL SACRIFICE	29-AUG-01	3	27
2583	TERMINAL SACRIFICE	29-AUG-01	3	27
2584	TERMINAL SACRIFICE	29-AUG-01	3	27
2585	TERMINAL SACRIFICE	29-AUG-01	3	27
2586	TERMINAL SACRIFICE	29-AUG-01	3	27
2587	TERMINAL SACRIFICE	29-AUG-01	3	27
2588	TERMINAL SACRIFICE	29-AUG-01	3	27
2589	TERMINAL SACRIFICE	29-AUG-01	3	27
2590	TERMINAL SACRIFICE	29-AUG-01	3	27

TABLE J

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IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

ANIMAL TERMINATION HISTORY

FEMALES GROUP III 10,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3581	TERMINAL SACRIFICE	29-AUG-01	3	27
3582	TERMINAL SACRIFICE	29-AUG-01	3	27
3583	TERMINAL SACRIFICE	29-AUG-01	3	27
3584	TERMINAL SACRIFICE	29-AUG-01	3	27
3585	TERMINAL SACRIFICE	29-AUG-01	3	27
3586	TERMINAL SACRIFICE	29-AUG-01	3	27
3587	TERMINAL SACRIFICE	29-AUG-01	3	27
3588	TERMINAL SACRIFICE	29-AUG-01	3	27
3589	TERMINAL SACRIFICE	29-AUG-01	3	27
3590	TERMINAL SACRIFICE	29-AUG-01	3	27

TABLE J

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STUDY IN RATS WITH NEUROTOXICITY ASSESSMENTS AND 4-WEEK
IN VIVO GENOTOXICITY AND IMMUNOTOXICITY ASSESSMENTS

ANIMAL TERMINATION HISTORY

FEMALES GROUP IV 20,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4581	TERMINAL SACRIFICE	29-AUG-01	3	27
4582	TERMINAL SACRIFICE	29-AUG-01	3	27
4583	TERMINAL SACRIFICE	29-AUG-01	3	27
4584	TERMINAL SACRIFICE	29-AUG-01	3	27
4585	TERMINAL SACRIFICE	29-AUG-01	3	27
4586	TERMINAL SACRIFICE	29-AUG-01	3	27
4587	TERMINAL SACRIFICE	29-AUG-01	3	27
4588	TERMINAL SACRIFICE	29-AUG-01	3	27
4589	TERMINAL SACRIFICE	29-AUG-01	3	27
4590	TERMINAL SACRIFICE	29-AUG-01	3	27

TABLE J

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ANIMAL TERMINATION HISTORY

FEMALES GROUP V POSITIVE CONTROL

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
5581	TERMINAL SACRIFICE	29-AUG-01	3	27
5582	TERMINAL SACRIFICE	29-AUG-01	3	27
5583	TERMINAL SACRIFICE	29-AUG-01	3	27
5584	TERMINAL SACRIFICE	29-AUG-01	3	27
5585	TERMINAL SACRIFICE	29-AUG-01	3	27
5586	TERMINAL SACRIFICE	29-AUG-01	3	27
5587	TERMINAL SACRIFICE	29-AUG-01	3	27
5588	TERMINAL SACRIFICE	29-AUG-01	3	27
5589	TERMINAL SACRIFICE	29-AUG-01	3	27
5590	TERMINAL SACRIFICE	29-AUG-01	3	27