Appendix W

Huntingdon Life Sciences (ERC) Internal Reference No. APT 006/014352

## Study Title

# SATELLITE PROCEDURE GASOLINE TAME VAPOR CONDENSATE RAT MICRONUCLEUS TEST

**TEST GUIDELINES:**US EPA Micronucleus Assay 79.64, CFR Vol. 59, No.<br/>122, 27 June 1994.US EPA (1998) Health Effects Test Guidelines; OPPTS<br/>870.5395 Mammalian Erythrocyte Micronucleus Test.

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STUDY COMPLETED ON: 15 February 2011

SUBCONTRACTOR: Huntingdon Life Sciences Ltd., Eye Research Centre (ERC) Eye, Suffolk IP23 7PX ENGLAND.

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## **COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS**

The slide evaluation phase of the study described in this report was conducted in compliance with the following Good Laboratory Practice standards and I consider the data generated to be valid.

The UK Good Laboratory Practice Regulations (Statutory Instrument 1999 No. 3106, as amended by Statutory Instrument 2004 No. 994).

OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM(98)17.

EC Commission Directive 2004/10/EC of 11 February 2004 (Official Journal No L 50/44).

US EPA 79.60, CFR Vol. 59, No. 122, 27 June 1994.

No compliance is claimed for work presented in the Experimental Procedure – In-life phase or Appendix 2 of this report.

Lincoln Pritchard, B.Sc. (Hons.), Principal Investigator, Huntingdon Life Sciences Ltd.

15 February Lon

I am claiming compliance for the whole study with the following exceptions:

The identity, strength, purity and composition or other characteristics to define the positive control article has 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 mixture were not performed by the Testing Facility. The stability of the positive control article has not been determined by the Testing Facility. The stability 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.

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

600t11 Date

#### **ERC - QUALITY ASSURANCE STATEMENT**

The following inspection and audits have been carried out in relation to the slide evaluation phase of this study:

Study Phase	Date of Inspection	Date of Reporting
<b>Process Based Inspection</b> Slide scoring	8 November 2001	8 November 2001
Report Audit	17 December 2001 12-13 November 2006	17 December 2001 13 November 2006

**Process Based Inspection:** At or about the time this phase of the study was in progress, inspections of routine and repetitive procedures employed on this type of study were carried out. The slide scoring inspection was conducted and reported to appropriate Company Management as indicated above.

Report Audit: This appendix has been audited by the Quality Assurance Department. This audit was conducted and reported to the Principal Investigator and Company Management as indicated above.

Study based inspections were not performed on this phase of the study.

The methods, procedures and observations were found to be accurately described and the reported results of this appendix to reflect the raw data.

Helen Comb, B.Sc., M.R.Q.A., Group Manager, Department of Quality Assurance, Huntingdon Life Sciences Ltd.

bruary2011 Date

Huntingdon Life Sciences (ERC) Report No: APT 006/014352

# **PRC - 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	20,24 Apr 01	24 Apr 01
Exposure and Monitoring	2 Aug 01	2 Aug 01
Positive Control Genotoxicity Dose Administration	29 Aug 01	29 Aug 01
Genotoxicity Necropsy and Training Records	30 Aug 01	31 Aug 01
Subcontractor Final Report	22-25 Feb 02	26 Feb 02
Final Report Review and Protocol Amendments 1-5 Protocol Amendment 6	5-7 Jan 09 11 Aug 11	9 Jan 09 11 Aug 11
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8 Date

Fran Jannone, BA. RQAP-GLP Quality Assurance Group Leader

## **RESPONSIBLE PERSONNEL AND SCIENTIFIC APPROVAL**

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6 octa Date

Gary M. Hoffman, B.A., D.A.B.T., Study Director Department of Safety Assessment, PRC.

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Lincoln Pritchard, B.Sc. (Hons.), Principal Investigator Department of Genetic Toxicology, ERC

12 man Date

#### SUMMARY

This satellite micronucleus study was designed to assess the potential induction of micronuclei by Gasoline Tame Vapor Condensate in bone marrow cells of the rat. Animals were exposed for four weeks (5 days per week) by inhalation administration of the test substance at exposure levels of 2000, 10000 and 20000 mg/m<sup>3</sup>.

The test substance and negative control were administered by inhalation. The negative control group received clean air. A positive control group was dosed on one occasion by intraperitoneal injection, with cyclophosphamide at 40 mg/kg bodyweight.

Bone marrow smears were obtained from five male and five female animals in the negative control and each of the test substance groups 24 hours after the 20<sup>th</sup> exposure and from the positive control group 24 hours after dosing. One smear from each animal was examined for the presence of micronuclei in 2000 immature erythrocytes. The proportion of immature erythrocytes was assessed by examination of at least 1000 erythrocytes from each animal. A record of the incidence of micronucleated mature erythrocytes was also kept.

No statistically significant increases in the frequency of micronucleated immature erythrocytes and no substantial decrease in the proportion of immature erythrocytes were observed in rats treated with Gasoline Tame Vapor Condensate compared to negative control values.

The positive control compound, Cyclophosphamide, produced significant increases in the frequency of micronucleated immature erythrocytes and a decrease in the proportion of immature erythrocytes (P<0.001).

It is concluded that Gasoline Tame Vapor Condensate did not show any evidence of causing chromosome damage or bone marrow cell toxicity when administered by inhalation exposure in this *in vivo* test procedure.

#### INTRODUCTION

The purpose of this satellite micronucleus study was to assess the potential of Gasoline Tame Vapor Condensate to induce mutagenic effects in rats following inhalation administration using an *in vivo* cytogenetic system (Boller and Schmid 1970, MacGregor *et al* 1987, Mavournin *et al* 1990). The inhalation route was selected for use in this test as the most likely route of human exposure.

The procedures used were based on the recommendations of the following guidelines:

- US EPA Micronucleus Assay 79.64, CFR Vol. 59, No. 122, 27 June 1994.
- US EPA (1998) Health Effects Test Guidelines; OPPTS 870.5395 Mammalian Erythrocyte Micronucleus Test.

The bone marrow micronucleus test, originally developed by Matter and Schmid (1971), is a widely employed and internationally accepted short-term assay for identification of genotoxic effects (chromosome damage and aneuploidy) associated with mutagens and carcinogens (Mavournin *et al* 1990). This *in vivo* system allows consideration of various factors including pharmacokinetics, metabolism and DNA repair which cannot be accurately modelled in an *in vitro* system. Young adult rats are chosen for use because of the high rate of cell division in the bone marrow, because of the wealth of background data on this species, and because of their general suitability for toxicological investigations.

In mitotic cells in which chromosomal breakage has been caused by the test substance or its metabolites, acentric fragments of the chromosomes do not separate at the anaphase stage of cell division. After telophase these fragments may not be included in the nuclei of the daughter cells and hence will form single or multiple micronuclei (Howell-Jolly bodies) in the cytoplasm of these cells. Micronuclei are seen in a wide variety of cells, but erythrocytes are chosen for examination since micronuclei are not obscured by the main nucleus and are therefore easily detected in this cell type (Boller and Schmid 1970).

Micronucleated immature erythrocytes appear in the bone marrow approximately 24 hours after induction of chromosome damage. These immature erythrocytes can be differentiated by a variety of staining techniques which rely on their relatively high content of residual RNA. Using the Feulgen method, they stain blue while mature erythrocytes (which contain little RNA) are counterstained orange. An increased incidence of micronucleated immature erythrocytes is indicative of recent exposure to a chromosome-damaging agent. A simultaneous marked increase in the incidence of micronucleated mature erythrocytes is not expected and may be indicative of micronucleus-like artifacts (Schmid 1976).

Substances which interfere with the mitotic spindle apparatus will cause non-disjunction (unequal separation of the chromosomes at anaphase resulting in aneuploidy) or lagging chromosomes at anaphase which may not be incorporated into the daughter nuclei. These lagging chromosomes are not excluded from the erythroblast with the main nucleus and hence also give rise to micronuclei.

Any toxic effects of the test substance on the nucleated cells may lead either to a reduction in cell division or to cell death. These effects in turn lead to a reduction in the number of nucleated cells and immature erythrocytes; to compensate for this, peripheral blood is shunted into the bone marrow (von Ledebur and Schmid 1973). If the proportion of immature erythrocytes is found to be

significantly less than the control value, this is taken as being indicative of toxicity. A very large decrease in the proportion would be indicative of a cytostatic or cytotoxic effect.

The slide evaluation phase of the satellite micronucleus study was performed at the Department of Genetic Toxicology, Huntingdon Life Sciences (ERC), Eye, Suffolk, IP23 7PX, England. Subsequently statistical analysis was performed by the Department of Statistics, Huntingdon Life Sciences (HRC), Huntingdon, Cambridgeshire, PE28 4HS, England.

The experimental start and completion dates of the slide evaluation phase of the study were 11 September 2001 and 14 November 2001 respectively.

#### EXPERIMENTAL PROCEDURE

#### In-life phase

The in-life phase of the study was carried out at the Princeton Research Center starting on 2 August 2001 and was completed on 30 August 2001.

All animals in the negative control and test substance groups were exposed for four weeks (5 days per week) by inhalation. The non-exposed positive control group was dosed with Cyclophosphamide administered on one occasion by intraperitoneal injection at a volume dosage of 10 ml/kg bodyweight. Cyclophosphamide (CP, CAS # 6055-19-2, lot number 108H0568, received 28 August 2001, expiration 30 June 2002, white powder, storage 2-8°C, purity 99.2%), was obtained from the Sigma Chemical Company (responsible for its characterization), and was dissolved and diluted in sterile distilled water at Huntingdon Life Sciences to stock concentrations of 4.0 mg/mL for use as the positive control for the micronucleus study.

The experimental design is shown below:

Group	Group Treatment Exposu		ure Level Animal Numbers			
		(mg/m <sup>3</sup> )	Male	Female		
I	Air control	-	1031 - 1035	1541 - 1545		
п	Test Substance	2000	2021 - 2025	2531 - 2535		
III	Test Substance	10000	3021 - 3025	3531 - 3535		
IV	Test Substance	20000	4031 - 4035	4541 – 4545		
VI	Cyclophosphamide	40 (mg/kg)	6031-6035	6541 - 6545		

Five males and five females from the negative control and each of the test substance groups were sacrificed 24 hours after the final exposure period by isoflurane inhalation/exsanguination. Five males and five females from the positive control group were sacrificed 24 hours after CP dosing by  $CO_2$  inhalation/exsanguination. Both femures were exposed, cut just above the knee and the bone marrow was aspirated into a syringe containing a small volume (about 0.5 mL) of serum. The cells were then flushed into a centrifuge tube of cold serum. The tubes were identified by labels containing the study, group number, and animal number.

The bone marrow cells were pelleted by centrifugation at about  $150 \times g$  for about 5 min and the supernatant drawn off, leaving a small amount of serum with the cell pellet. The cells were resuspended by aspiration with a Pasteur pipette and a small drop of cells was spread onto a clean glass slide. Four slides were prepared from each animal. The slides were allowed to air dry, fixed by dipping for 3 to 10 minutes in absolute methanol, and aged overnight or longer prior to staining. Slides were labelled with experiment and animal number using either a lead pencil or a computer-generated printed label.

Two slides from each animal were despatched to Huntingdon Life Sciences (ERC), Eye, Suffolk, IP23 7PX, England for slide staining and analysis. The remaining 2 smears and the cell pellet (refrigerated) were held in reserve at PRC in case of technical problems with the first 2 smears.

#### Slide evaluation

Due to the presence of mast cell granules in rat bone smears, which appear identical to micronuclei when stained using the Romanowsky methods, a modified Feulgen staining method is employed for the rat micronucleus test in this laboratory. This method specifically stains DNA-containing bodies deep purple while leaving mast cell granules unstained. The method also allows reasonable differentiation of mature and immature erythrocytes and produces permanent preparations.

One slide from each animal was stained as follows, the remaining slide was held in reserve:

- 1. Hydrolysed in Bouin's fluid at room temperature for approximately 30 hours.
- 2. Washed three times in purified water (5 minutes per wash).
- 3. Stained in Schiff's reagent for one hour at room temperature.
- 4. Washed three times in purified water (5 minutes per wash).
- 5. Counter-stained for ten minutes in very dilute (approximately 0.06 g/l) aqueous Eosin yellowish.
- 6. Washed for five minutes in purified water.
- 7. Stained for 30 minutes in Mayer's Haemalum diluted 9 volumes: 1 volume with aqueous acridine orange solution in purified water (1 mg/ml).
- 8. Rinsed in purified water.
- 9. Rinsed in running tap water.
- 10. Washed for 5 minutes in purified water.
- 11. Air-dried.
- 12. Slides were mounted with coverslips using DPX mountant.
- 13. The mountant was allowed to harden at approximately 37°C.

NB All stains and Bouin's fluid were filtered immediately prior to use to remove particulate material.

The stained smears were examined (under code) by light microscopy to determine the incidence of micronucleated cells per 2000 polychromatic erythrocytes per animal. One smear per animal was examined. The remaining smears were held temporarily in reserve in case of technical problems with the first smear.

Micronuclei are identified by the following criteria:

- Large enough to discern morphological characteristics.
- Should possess a generally rounded shape with a clearly defined outline.
- Should be deeply stained and similar in colour to the nuclei of other cells not black.
- Should lie in the same focal plane as the cell.

- Lack internal structure, *i.e.* they are pyknotic.
- There should be no micronucleus-like debris in the area surrounding the cell.

The proportion of immature erythrocytes for each animal was assessed by examination of at least 1000 erythrocytes. A record of the number of micronucleated mature erythrocytes observed during assessment of this proportion was also kept as recommended by Schmid (1976).

#### **Deviations from Protocol**

This phase of the study was conducted in compliance with the following additional Good Laboratory Practice Standards: the UK Good Laboratory Practice Regulations (Statutory Instrument 1999 No. 3106, as amended by Statutory Instrument 2004 No. 994), the OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM(98)17 and the EC Commission Directive 2004/10/EC of 11 February 2004 (Official Journal No L 50/44).

The statistical analysis was performed at Huntingdon Life Sciences Ltd., Huntingdon Cambridgeshire, PE28 4HS, England.

## ASSESSMENT OF RESULTS

The results for each treatment group were compared with the results for the negative control group for the entire study using non-parametric statistics. Non-parametric statistical methods were chosen for analysis of results because:

- They are suited to analysis of data consisting of discrete/integer values with ties such as the incidence of micronucleated immature erythrocytes.
- The methods make few assumptions about the underlying distribution of data and therefore the values do not require transformation to fit a theoretical distribution (where data can be approximately fitted to a normal distribution, the results of non-parametric analysis and classical analysis of variance are very similar).
- 'Outliers' are frequently found in the proportion of immature erythrocytes for both control and treated animals; non-parametric analysis based on rank does not give these values an undue weighting.

Unless there is a substantial difference in response between sexes (which occurs only rarely) results for the two sexes are combined to facilitate interpretation and maximise the power of statistical analysis.

For incidences of micronucleated immature erythrocytes, exact one-sided p-values are calculated by permutation (StatXact, CYTEL Software Corporation, Cambridge, Massachusetts). Comparison of several dose levels is made with the concurrent control using the Linear by Linear Association test for trend, in a step-down fashion if significance is detected (Agresti *et al.* 1990); for individual intergroup comparisons (*ie* the positive control group) this procedure simplifies to a straightforward permutation test (Gibbons 1985). For assessment of effects on the proportion of immature

erythrocytes, equivalent permutation tests based on rank scores are used, *i.e.* exact versions of Wilcoxon's sum of ranks test and Jonckheere's test for trend.

A positive response is normally indicated by a statistically significant dose-related increase in the incidence of micronucleated immature erythrocytes for the treatment group compared with the concurrent control group (P<0.01); individual and/or group mean values should exceed the laboratory historical control range (Morrison and Ashby 1995).

A negative result is indicated where individual and group mean incidences of micronucleated immature erythrocytes for the group treated with the test substance are not significantly greater than incidences for the concurrent control group and where these values fall within the historical control range. An equivocal response is obtained when the results do not meet the criteria specified for a positive or negative response.

Bone marrow cell toxicity (or depression) is normally indicated by a substantial and statistically significant dose-related decrease in the proportion of immature erythrocytes (P<0.01).

## MAINTENANCE OF RECORDS

All raw data, samples and specimens arising from the performance of this phase of the study will remain the property of the Sponsor.

Types of sample and specimen that are unsuitable, by reason of instability, for long term retention and archiving may be disposed after the periods stated in Huntingdon Life Sciences, Standard Operating Procedures.

All other samples and specimens and all raw data will be retained by Huntingdon Life Sciences PRC in its archive for a period of one year from the date on which the Study Director signs the final report. After such time, the Sponsor will be contacted and their advice sought on the return, disposal or further retention of the materials. If requested, Huntingdon Life Sciences will continue to retain the materials subject to a reasonable fee being agreed with the Sponsor.

Huntingdon Life Sciences will retain the Quality Assurance records relevant to this study and a copy of the final report in its archive indefinitely.

#### RESULTS

## MICRONUCLEUS TEST

Table 1 gives a summary of the results of the micronucleus test and the results of statistical analysis. The results for individual animals are presented in Table 2. Appendix 1 summarises the historical control data for micronucleated immature erythrocyte counts.

## Micronucleated immature erythrocyte counts (mie)

The test substance did not cause any statistically significant increases in the number of micronucleated immature erythrocytes.

Cyclophosphamide caused significant increases in the frequency of micronucleated immature erythrocytes [P<0.001].

#### Micronucleated mature erythrocytes (mme)

The test substance did not cause any substantial increases in the incidence of micronucleated mature erythrocytes.

## Proportion of immature erythrocytes (% ie/[ie + me])

The test substance failed to cause any significant decreases in the proportion of immature erythrocytes.

Cyclophosphamide caused statistically significant decreases in the proportion [P<0.001].

#### CONCLUSION

No statistically significant increases in the frequency of micronucleated immature erythrocytes and no substantial decrease in the proportion of immature erythrocytes were observed in rats treated with Gasoline Tame Vapor Condensate compared to negative control values.

It is concluded that Gasoline Tame Vapor Condensate did not show any evidence of causing chromosome damage or bone marrow cell toxicity when administered by inhalation in this *in vivo* test procedure.

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## TABLE 1

## Summary of results and statistical analysis

Sampling time	Treatment	Exposure level (mg/m <sup>3</sup> )	Proportion of ie † (mean ± SD)	Incidence mie (mean ± SD)	Incidence mme (group mean $\pm$ SD) <sup>a</sup>
24 Hours	Negative control	-	49 ± 1.9	0.7 ± 1.3	0.4 ± 0.3
	TS	2000	$51 \pm 3.2$	$1.2 \pm 1.1$	$0.0 \pm 0.0$
	TS	10000	$50 \pm 1.7$	$0.4 \pm 0.5$	$0.0 \pm 0.0$
	TS	20000	$50 \pm 2.9$	$0.8 \pm 0.8$	$0.0 \pm 0.0$
	Cyclophosphamide	40 mg/kg	44 ± 3.1***	13.6 ± 9.5***	0.6 ± 0.6

TS	Gasoline Tame Vapor Condensate
ie	Immature erythrocytes
mie	Number of micronucleated cells observed per 2000 immature erythrocytes examined
me	Mature erythrocytes
mme	Number of micronucleated cells observed and calculated per 2000 mature erythrocytes
SD	Standard deviation

Results of statistical analysis using the appropriate nonparametric method of analysis based on permutation (one-sided probabilities):

***	P < 0.001	(significant)
otherwise	P > 0.01	(not significant)

<sup>†</sup> Occasional apparent errors of  $\pm$  1% may occur due to rounding of values for presentation in the table

<sup>a</sup> Formula for calculation of incidence mme (group mean):

Sum of group incidence mme scored x 2000 Sum of group me scored

## **TABLE 1 - continued**

Sampling time	Treatment	Exposure level (mg/m <sup>3</sup> )	Proportion of ie † (mean ± SD)	Incidence mie (mean ± SD)	Incidence mme (group mean ± SD) <sup>a</sup>
		MA	LES		
24 hours	Negative control	-	$49 \pm 2.1$	$1.0 \pm 1.7$	$0.0 \pm 0.0$
	TS	2000	$51 \pm 2.0$	$1.6\pm0.9$	$0.0 \pm 0.0$
	TS	10000	$49 \pm 0.9$	$0.4 \pm 0.5$	$0.0 \pm 0.0$
	TS	20000	$50 \pm 2.4$	$0.8 \pm 0.8$	$0.0 \pm 0.0$
	Cyclophosphamide	40 (mg/kg)	$44 \pm 3.5$	$13.2\pm9.7$	$0.0 \pm 0.0$
		FEM	ALES		
24 hours	Negative control	-	$49\pm2.0$	$0.4 \pm 0.9$	$0.7 \pm 0.4$
	TS	2000	$50 \pm 4.3$	$0.8 \pm 1.3$	$0.0 \pm 0.0$
	TS	10000	51 ± 1.7	$0.4 \pm 0.5$	$0.0 \pm 0.0$
	TS	20000	$50 \pm 3.7$	$0.8 \pm 0.8$	$0.0 \pm 0.0$
	Cyclophosphamide	40 (mg/kg)	$45 \pm 2.8$	$14.0 \pm 10.3$	$1.3 \pm 0.9$

#### Summary of results and statistical analysis – separate sexes

TSGasoline Tame Vapor CondensateieImmature erythrocytesmieNumber of micronucleated cells observed per 2000 immature erythrocytes examinedmeMature erythrocytesmmeNumber of micronucleated cells observed and calculated per 2000 mature erythrocytes

SD Standard deviation

<sup>†</sup> Occasional apparent errors of ± 1% may occur due to rounding of values for presentation in the table

<sup>a</sup> Formula for calculation of incidence mme (group mean):

Sum of group incidence mme scored x 2000 Sum of group me scored

Treatment	Exposure level	Animal	ie	me	Proportion	Incidence	Incidence
	$(mg/m^3)$	number			ofie	mie	mme
Negative control	-	M 1031	533	536	50	0	0
		M 1032	488	560	47	4	0
		M 1033	517	560	48	0	0
		M 1034	519	540	49	1	0
	۰.	M 1035	664	612	52	0	0
		F 1541	483	561	46	0	0
		F 1542	568	534	52	0	0
		F 1543	521	537	49	2 0	0
		F 1544	548	548	50	0	0
		F 1545	522	560	48	0	1
TS	2000	M 2021	524	533	50	2 3	0
		M 2022	517	527	50		0
		M 2023	525	500	51	1	0
		M 2024	592	505	54	1	0
		M 2025	560	502	53	1	0
		F 2531	501	534	48	0	0
		F 2532	565	483	54	1	0
		F 2533	575	677	46	0	0
		F 2534	535	592	47	0	0
		F 2535	583	461	56	3	0
TS	10000	M 3021	536	533	50	1	0
		M 3022	512	532	49	0	0
		M 3023	524	546	49	0	0
		M 3024	523	527	50	1	0
		M 3025	526	577	48	0	0
		F 3531	540	488	53	0	0
		F 3532	583	594	50	0	0
		F 3533	534	538	50	1	0
		F 3534	540	507	52	0	0
		F 3535	556	486	53	1	0
TS	20000	M 4031	518	561	48	1	0
		M 4032	537	481	53	1	0
		M 4033	553	511	52	0	0
		M 4034	529	581	48	0	0
		M 4035	515	544	49	2	0
		F 4541	505	606	45	ō	0
		F 4542	537	536	50	2	Ō
		F 4543	525	515	50	$\overline{1}$	Ő
		F 4544	532	524	50	ī	0
		F 4545	595	471	56	Ō	0

 TABLE 2

 Results for individual animals - 24 hour sampling time

TS ie

Gasoline Tame Vapor Condensate

Immature erythrocytes

mie Number of micronucleated cells observed per 2000 immature erythrocytes

me Total number of mature erythrocytes examined for micronuclei

mme Number of micronucleated mature erythrocytes observed

#### **TABLE 2 - continued**

Results for individual animals - 24 hour sampling time

#### Treatment Animal Incidence Dosage ie me Proportion Incidence (mg/kg) number of ie mie mme Cyclophosphamide 40 mg/kg M 6031 42 39 506 700 0 6 30 M 6032 404 625 0 M 6033 464 601 44 9 0 8 M 6034 521 616 46 0 M 6035 518 555 48 13 0 32 2 F 6541 564 604 48 9 0 F 6542 504 545 48 F 6543 478 632 43 7 0 9 F 6544 496 43 0 651 F 6545 487 654 43 13 0

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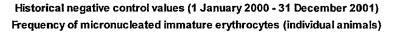
mme

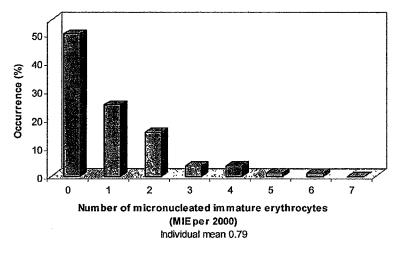
Immature erythrocytes

Number of micronucleated cells observed per 2000 immature erythrocytes Total number of mature erythrocytes examined for micronuclei Number of micronucleated mature erythrocytes observed

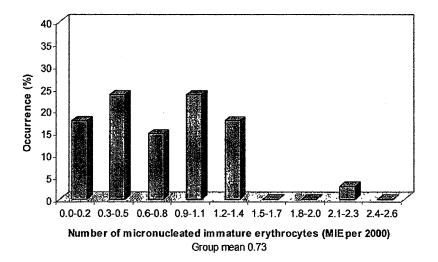
:21:

## **APPENDIX 1**

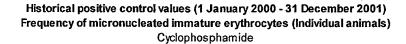


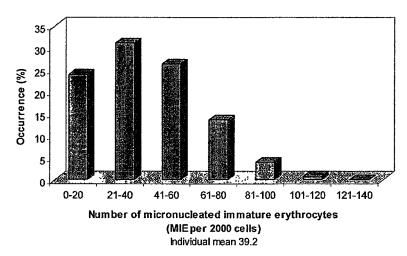


Historical negative control values (1 January 2000 - 31 December 2001) Frequency of micronucleated immature erythrocytes (Group mean values)

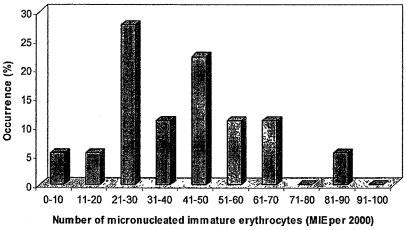


**APPENDIX 1 -- continued** 





Historical positive control values (1 January 2000 - 31 December 2001) Frequency of micronucleated immature erythrocytes (Group mean values) Cyclophosphamide





# **APPENDIX 2: GLP COMPLIANCE STATEMENTS**



## THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

## GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 88/320 EEC

LABORATORY

Huntingdon Life Sciences Eye Research Centre Eye Suffolk IP23 7PX TEST TYPE

Analytical Chemistry Clinical Chemistry Ecosystems Environmental Fate Environmental Toxicity Mutagenicity Phys/Chem Testing Toxicology

DATE OF INSPECTION

## 29<sup>th</sup> January 2001

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above laboratory as part of UK GLP Compliance Programme.

At the time of the inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

Lose J.

Dr. Roger G. Alexander Head, UK GLP Monitoring Authority



## THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

#### GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 88/320 EEC

LABORATORY

Huntingdon Life Sciences Huntingdon Research Centre Wooley Road Alconbury Huntingdon Cambs. PE28 4HS TEST TYPE

Analytical Chemistry Clinical Chemistry Ecosystems Environmental Fate Environmental Toxicity Phys/Chem Testing Toxicology

DATE OF INSPECTION 15<sup>th</sup> January 2001

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above laboratory as part of UK GLP Compliance Programme.

At the time of the inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

Kage J 3/4/01

Dr. Roger G. Alexander Head, UK GLP Monitoring Authority



# THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

#### **GOOD LABORATORY PRACTICE**

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 88/320 EEC

#### LABORATORY

Huntingdon Life Sciences Eye Research Centre Occold Eye Suffolk IP23 7PX TEST TYPE

Analytical Chemistry Ecosystems Environmental Fate Environmental Toxicity Mutagenicity Toxicology Phys/Chem Tests

DATE OF INSPECTION 22<sup>nd</sup> April 2003

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above laboratory as part of UK GLP Compliance Programme.

At the time of the inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

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Dr. Roger G. Alexander Head, UK GLP Monitoring Authority

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## THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

#### GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

#### LABORATORY

**Huntingdon Life Sciences** Eye Research Centre Occold Eye Suffolk **IP23 7PX** 

#### TEST TYPE

**Analytical Chemistry Clinical Chemistry** Ecosystems **Environmental Fate Environmental Toxicity** Mutagenicity Toxicology Phys/Chem Testing

DATE OF INSPECTION

12<sup>th</sup> April 2005

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above laboratory as part of the UK GLP Compliance Programme.

At the time of inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

Angen V. Winght 116/05

Mr. Bryan J. Wright Head, UK GLP Monitoring Authority



# THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

## GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY

Huntingdon Life Sciences Eye Research Centre Occold Eye Suffolk IP23 7PX TEST TYPE

Analytical Chemistry Ecosystems Environmental Fate Environmental Toxicity Mutagenicity Phys/Chem Testing Toxicology

DATE OF INSPECTION

2

28<sup>th</sup> January 2008

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK GLP Compliance Programme.

At the time of inspection no deviations were found of sufficient magnitude to affect, the validity of non-clinical studies performed at these facilities.

x/03/08

Dr. Andrew J. Gray Head, UK GLP Monitoring Authority





# THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

## **GOOD LABORATORY PRACTICE**

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY

Huntingdon Life Sciences Eye Research Centre Occold Eye Suffolk IP23 //PX TEST TYPE

Analytical/Clinical Chemistry Ecosystems Environmental Fate Environmental Toxicity Mutaganicity Phys/Chem Testing Toxicology

DATE OF INSPECTION

17-19 February 2009

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK GLP Compliance Programme.

At the time of inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

Dr. Andrew J. Gray Head, UK GLP Monitoring Authority





## THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

## GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY

TEST TYPE

Huntingdon Life Sciences Ltd. Huntingdon Research Centre Woolley Road Alconbury Cambridgeshire PE28 4HS Analytical Chemistry Clinical Chemistry Ecosystems Environmental Fate Environmental Toxicity Toxicology

DATE OF INSPECTION

2<sup>nd</sup> November 2009

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK GLP Compliance Programme.

At the time of inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

11/01/10

Dr. Andrew J. Gray Head, UK GLP Monitoring Authority





# THE DEPARTMENT OF HEALTH OF THE GOVERNMENT OF THE UNITED KINGDOM

## GOOD LABORATORY PRACTICE

#### STATEMENT OF COMPLIANCE IN ACCORDANCE WITH DIRECTIVE 2004/9/EC

TEST FACILITY

Huntingdon Life Sciences Eye Research Centre Occold Eye Suffolk IP23 7PX TEST TYPE

Analytical/Clinical Chemistry Ecosystems Environmental Fate Environmental Toxicity Mutagenicity Physico-chemical Testing Residue Studies Toxicology

#### DATE OF INSPECTION

26 January 2010

A general inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK GLP Compliance Programme.

At the time of inspection no deviations were found of sufficient magnitude to affect the validity of non-clinical studies performed at these facilities.

22/3/10 

Dr. Andrew J. Gray Head, UK GLP Monitoring Authority



# APPENDIX 3

# ANIMAL EXPOSURE AND OBSERVATIONS DATA

Huntingdon Life Sciences	00-6128	Page 1054
	211-TAME-S	Final Report

Animal Exposure and Animal Data	
Preface	Appendix 3

**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:	19 July 2001
	Experimental Initiation Date:	2 August 2001 (in-life)
	Experimental Completion Date:	30 August 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.

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I.	Individual Feed Consumption Values (grams/kg/day)	
J.	Animal Termination History	

Table A

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

00-6128

					Cum	mber Moni ulative E IA - 0 mg	xposure F	lecord					
												Chamber E	nvironment
									P	article #	Size	Me	an
Day	Date	Exposure	Nominal	Ana	lytical C	· · · · · · · · · · · · · · · · · · ·		on	De	terminat	ions	Temperature	Humidity
		Number		Mean Individual						GSD	TMC		
			(mg/m³)	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
37	2-Aug-01	1	0	0	0	0	0	0				24	47
38	3-Aug-01	2	0	0	0	0	0	0	1.281	1.730	2.50E-03	24	47
41	6-Aug-01	3	0	0.	0	0	0	0				24	49
42	7-Aug-01	4	0	0	0	0	0	0				25	48
43	8-Aug-01	5	0	0	0	0	0	0				26	50
44	9-Aug-01	6	0	0	0	0	0	0				26	49
45	10-Aug-01	7	0.	0	0	0	0	0	0.8679	1.733	6.82E-02	26	51
48	13-Aug-01	8	0	0	0	0	0	0				25	47
49	14-Aug-01	9	0	0	0	0	0	0				24	48
50	15-Aug-01	10	0	0	0	0	0	0				24	48
51	16-Aug-01	11	0	0	0	0	0	0	0.9270	1.631	3.16E-03	24	48
52	17-Aug-01	12	0	0	0	0	0	0				24	50
55	20-Aug-01	13	0	0	0	0	0	0				25	48
56	21-Aug-01	14	0	0	0	0	0	0				25	47
57	22-Aug-01	15	0	0	0	0	0	0			1	25	48
58	23-Aug-01	16	0	0	0	0	0	0				25	51
59	24-Aug-01	17	0	0	0	0	0	0	1.095	2.289	4.97E-03	25	48
62	27-Aug-01	18	0	0	0	0	0	0				26	46.
63	28-Aug-01	19	0	0	0	0	0	0				24	48
64	29-Aug-01	20	0	0	0	0	0	0				24	47
		Mean	0			0			1.043	1.846	1.97E-02	24.8	48.3
		S.D.	0			0			0.186	0.299	3.23E-02	0.8	1.4

Table A

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

00-6128

						Chamber Mor	nitoring	Results						
						Cumulative	Exposure	Record						
					Gro	up IB - 0 i	mg/m <sup>3</sup> (Ai	r Control	L)					
												Chamber En	vironment	
										Particle	Size	Mean		
Day	Date	Exposure	Nominal	Ana	lytical	Chamber Con	ncentrati	on	r	Determina	tions	Temperature	Humidity	
		Number		Mean		Indivi			MMAD	GSD	TMC			
			(mg/m³)	(mg/m <sup>3</sup> )		(mg/	m <sup>3</sup> )		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)	
37	2-Aug-01	1	0	0	0	0	0	0				25	50	
38	3-Aug-01	2	0	0	0	0	0	0	1.163	1.719	2.68E-03	25	49	
41	6-Aug-01	3	0	0	0	0	0	0				25	51	
42	7-Aug-01	4	0	0	0	0	0	0				24	53	
43	8-Aug-01	5	0	0	0	0	0	0				24	52	
44	9-Aug-01	6	0	0	0	0	0	0				24	51	
45	10-Aug-01	7	0	0	0	0	0	0	0.8617	1.638	6.21E-02	25	53	
48	13-Aug-01	8	0	0	0	0	0	0				24	49	
49	14-Aug-01	9	O	0	0	0	0	0				24	49	
50	15-Aug-01	10	0	0	0	0	0	0				25	51	
51	16-Aug-01	11	0	0	0	0	0	0	0.9082	1.518	3.36E-03	24	51	
52	17-Aug-01	12	0	0	0	0	0	0				24	51	
55	20-Aug-01	13	0	0	0	0	0	0	1			25	51	
56	21-Aug-01	14	0	0	0	0	0	0				24	49	
57	22-Aug-01	15	0	0	0	0	0	0				24	51	
58	23-Aug-01	16	O	0	0	0	0	0				24	51	
59	24-Aug-01	17	0	0	0	0	0	0	0.8564	1.629	3.35E-03	24	51	
62	27-Aug-01	18	0	0	0	0	0	0				24	49	
63	28-Aug-01	19	0	0	0	0	0	0				25	53	
64	29-Aug-01	20	0	0	0	0	0	0				25	50	
		Mean	D			0			0.947	1.626	1.79E-02	24.4	50.8	
		S.D.	0			0			0.146	0.083	2.95E-02	0.5	1.3	

Table A

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

00-6128

						Chamber Mo	nitoring	Results						
						Cumulative	Exposure	e Record						
						Group II	A - 2,000	mg/m³						
												Chamber 1	Chamber Environment	
								Particle Size				Mean		
Day	Date	Exposure	Nominal	Ana	lytical (	cal Chamber Concentration Determi				terminat	ions	Temperature	Humidity	
		Number		Mean		Indiv			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)	(%)	
37	2-Aug-01	1	2570	2145	2670	2140	1810	1960				23	46	
38	3-Aug-01	2	2330	1905	1940	1750	1970	1960	12.51	3.372	7.50E-03	23	46	
41	6-Aug-01	3	2570	1953	2270	2050	1710	1780				23	47	
42	7-Aug-01	4	2360	1933	2090	1990	1770	1880				24	45	
43	8-Aug-01	5	2310	1873	1780	1920	1770	2020				24	46	
44	9-Aug-01	6	2340	2060	2190	2020	2100	1930				24	46	
45	10-Aug-01	7	2380	1920	2030	1950	1770	1930	0.8634	1.724	5.97E-02	25	49	
48	13-Aug-01	8	2470	1993	1970	2150	1880	1970			1	24	45	
49	14-Aug-01	9	2410	2038	1880	1890	2140	2240				23	45	
50	15-Aug-01	10	2420	2045	2350	1890	1850	2090				23	45	
51	16-Aug-01	11	2430	1930	2120	1790	1950	1860	0.9240	2.335	5.21E-03	23	45	
52	17-Aug-01	12	2480	2070	2200	1960	2150	1970				23	46	
55	20-Aug-01	13	2460	1895	1630	1750	1980	2220				23	46	
56	21-Aug-01	14	2400	2105	2250	2220	1980	1970				24	44	
57	22-Aug-01	15	2440	2100	1850	2250	2150	2150				24	46	
58	23-Aug-01	16	2440	2023	2100	1930	2000	2060				24	45	
59	24-Aug-01	17	4480°	1995	1900	1990	2010	2080	0.9183	1.985	5.49E-03	24	46	
62	27-Aug-01	18	2380	1938	2180	1720	1990	1860				24	45	
63	28-Aug-01	19	2370	2045	1950	2100	2050	2080				23	46	
64	29-Aug-01	20	2540	2303	2320	2400	2250	2240				23	46	
		Mean	2529			2013			3.804	2.354	1.95E-02	23.6	45.8	
		S.D.	465			181			5.804	0.723	2.68E-02	0.6	1.0	

<sup>a</sup>Nominal high due to technical problem with the generation system.

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

00-6128

						Chamber Mo	nitoring	Results					
					1	Cumulative	Exposure	Record					
						Group III	3 - 2,000	mg/m <sup>3</sup>					
												Chamber 1	Environment
									Pa	article S	Size	М	ean
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	on	De	terminat	ions	Temperature	Humidity
		Number		Mean		Indiv:			MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/		····	(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
37	2-Aug-01	1	2570	2165	1980	2130	2150	2400				23	47
38	3-Aug-01	2	2330	1935	1770	1970	2000	2000	1.044	1.867	3.26E-03	23	47
41	6-Aug-01	3	2570	1970	2150	1910	1890	1930				23	49
42	7-Aug-01	4	2360	2015	1940	2060	2010	2050				23	49
43	8-Aug-01	5	2310	1978	1930	1970	1960	2050				23	49
44	9-Aug-01	6	2340	2148	2260	2150	2120	2060			1	23	48
45	10-Aug-01	7	2380	2065	1850	1870	2390	2150	0.8638	1.771	5.82E-02	23	51
48	13-Aug-01	8	2470	2030	1910	1640	2400	2170				23	48
49	14-Aug-01	9	2410	2060	2110	2340	1970	1820				23	48
50	15-Aug-01	10	2420	1915	1670	2060	2080	1850				23	49
51	16-Aug-01	11	2430	1938	1780	1980	2050	1940	0.9601	2.240	5.89E-03	23	48
52	17-Aug-01	12	2480	2218	2080	2350	2290	2150				23	49
55	20-Aug-01	13	2460	2085	2250	2090	2100	1900				23	48
56	21-Aug-01	14	2400	2035	2060	1820	2150	2110				23	46
57	22-Aug-01	15	2440	2138	2120	2190	2090	2150				23	47
58	23-Aug-01	16	2440	1945	1890	1790	2080	2020				23	48
59	24-Aug-01	17	4480 ª	1973	1970	1960	2000	1960	0.9272	1.840	5.41E-03	23	48
62	27-Aug-01	18	2380	1918	1860	1910	1820	2080				23	46
63	28-Aug-01	19	2370	2075	2300	2090	1970	1940				24	47
64	29-Aug-01	20	2540	2105	2150	2190	2030	2050		1	1 007 10	24	48
		Mean	2529			2035			0.949	1.930	1.82E-02	23.1	48.0
		S.D.	465			159			0.075	0.211	2.67E-02	0.3	1.2

<sup>a</sup>Nominal high due to technical problem with the generation system.

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

00-6128

					C	Chamber Mo	nitoring	Results					
					C	Cumulative	Exposure	Record					
						Group IIIA	A - 10,00	0 mg/m³					
		I										Chamber En	vironment
									P	article a	Size	Mea	n
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	on	De	eterminat	ions	Temperature	Humidit
		Number		Mean		Indivi	Idual		MMAD	GSD	TMC		
			(mg/m <sup>3</sup> )	(mg/m <sup>3</sup> )		(mg/	'm³)		(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
37	2-Aug-01	1	9750	10480	12000	10200	9630	10100				23	49
38	3-Aug-01	2	10000	10830	10000	11600	10900	10800	1.228	2.072	4.53E-03	23	48
41	6-Aug-01	3	9710	10500	10800	10300	10600	10300				23	51
42	7-Aug-01	4	9720	10110	10600	11000	10500	8330				24	50
43	8-Aug-01	5	10300	10380	8410	10700	12000	10400				24	51
44	9-Aug-01	6	9930	9495	7460	9130	11400	9990				24	49
45	10-Aug-01	7	10100	10380	10800	10200	10400	10100	0.8637	1.561	6.13E-02	25	52
48	13-Aug-01	8	10200	10350	11100	10100	10600	9590				24	49
49	14-Aug-01	9	9910	10730	10000	10200	12000	10700				23	48
50	15-Aug-01	10	9410	9935	11300	7530	9910	11000				23	48
51	16-Aug-01	11	9760	10110	10700	8620	10600	10500	1.456	2.932	8.24E-03	23	50
52	17-Aug-01	12	10400	11290	9040	11800	12800	11500				23	51
55	20-Aug-01	13	10200	10630	11700	11900	9450	9450				24	50
56	21-Aug-01	14	9130	9303	8990	10600	9140	8480				24	48
57	22-Aug-01	15	9370	10800	11500	11300	9590	10800				24	49
58	23-Aug-01	16	9630	10650	11000	9990	10900	10700				24	49
59	24-Aug-01	17	9960	11000	11300	10600	11400	10700	0.9396	2.104	4.77E-03	25	49
62	27-Aug-01	18	10200	10850	10300	11000	10900	11200				25	47
63	28-Aug-01	19	9710	9763	9000	11100	10000	8950				24	51
64	29-Aug-01	20	9330	9353	7300	8610	10700	10800				24	49
		Mean	9836			10350			1,122	2.167	1.97E-02	23.8	49,4
		s.D.	349			1090			0.273	0.567	2.78E-02	0.7	1.3

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

00-6128

						hamber Mor	5						
						Cumulative	-						
	r	n				Group IIIB	- 10,000	0 mg/m <sup>-</sup>	<u> </u>			I	
												Chamber E	nvironment
_									4	article &		Me	
Day	Date	Exposure	Nominal		lytical (	Chamber Con		on		terminat	·····	Temperature	Humidity
		Number	(	Mean		Indiv			MMAD	GSD	TMC		(
37	2-Aug-01		(mg/m <sup>3</sup> )	$(mg/m^3)$	11000	(mg/ 8850			(µm)		(mg/m <sup>3</sup> )	(°C)	(%)
37 38	2-Aug-01 3-Aug-01	1 2	9750 10000	10090 9630	11000 9550	8850 10200	9700 9630	10800 9140	0.9181	1.528	2 2 2 2 2 2 2	24	43
38 41	6-Aug-01	2	9710	9630 9265	9550 8930	9590	9520	9140	0.9181	1.528	3.26E-03	24 24	43
41 42	7-Aug-01	4	9710 9720	9265 9240	8930 8970	9590 9810	9520	9020 8630				24 24	45 46
43	8-Aug-01	5	10300	9240 9843	10700	9810 8940	8830	10900				24	46 46
44	9-Aug-01	6	9930	10800	12500	10500	10300	9910				24	46 45
45	10-Aug-01	7	10100	9865	9550	9450	10800	9660	0.8640	1.582	5.60E-02	24	45 49
48	13-Aug-01	8	10200	9798	9110	10100	10100	9880	0.0040	1.302	5.602-02	24	49
49	14-Aug-01	9	9910	9865	10200	10100	9480	9480				24	45
50	15-Aug-01	10	9410	9565	9370	9630	9630	9630				24	45
51	16-Aug-01	10	9760	10680	10600	10100	11100	10900	0.9497	2.008	5.76E-03	24	45
52	17-Aug-01	12	10400	11780	11700	11800	12200	11400	0.5157	2.000	5.702 05	24	48
55	20-Aug-01	13	10200	10120	9410	9080	10700	11300				25	45
56	21-Aug-01	14	9130	9758	. 11200	9630	9150	9050				24	45
57	22-Aug-01	15	9370	9945	11000	10600	9100	9080				24	45
58	23-Aug-01	16	9630	9913	10300	9410	9950	9990				24	47
59	24-Aug-01	17	9960	9838	8820	9730	10300	10500	0.8748	1.664	4.06E-03	24	46
62	27-Aug-01	18	10200	10580	9910	10300	11100	11000				24	44
63	28-Aug-01	19	9710	11400	12000	12000	10200	11400				25	46
64	29-Aug-01	20	9330	10500	11500	10900	10100	9480				24	45
	• • • • • • • • • • • • • • • • • • • •	Mean	9836			10120	<b>.</b>	A	0.902	1.696	1.73E-02	24.1	45.4
		S.D.	349			910			0.040	0.216	2.58E-02	0.3	1.4

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					C	hamber Mon umulative Group IVA	Exposure	Record					
						Group IVA	- 20,000	mg/ m				Chamber E	nvironment
									Pa	article S	Bize	Ме	an
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	on	De	terminat	ions	Temperature	Humidity
:		Number	(mg/m³)	Mean (mg/m³)		Indivi (mg/			MMAD (µm)	GSD	TMC (mg/m <sup>3</sup> )	(°C)	(%)
37	2-Aug-01	1	18200	20150	20000	21100	19700	19800	( )			25	48
38	3-Aug-01	2	19300	20630	19900	20600	21300	20700	4.537	2.957	8.77E-03	25	47
41	6-Aug-01	3	17900	19730	19400	20100	19700	19700				25	50
42	7-Aug-01	4	18500	20030	21000	18800	20900	19400				26	49
43	8-Aug-01	5	17900	18900	21100	16400	19000	19100				26	53
44	9-Aug-01	6	19400	20250	20600	21800	20200	18400				26	50
45	10-Aug-01	7	19200	20930	21300	19400	20200	22800	0.8520	1.431	5.01E-02	27	52
48	13-Aug-01	8	18500	19830	21400	18500	19800	19600				26	50
49	14-Aug-01	9	17700	19500	17900	21200	19300	19600				25	48
50	15-Aug-01	10	18000	18150	17200	18300	19500	17600				25	51
51	16-Aug-01	11	18000	19580	16100	19800	21200	21200	0.9696	2.431	5.60E-03	25	51
52	17-Aug-01	12	19100	20430	20100	20600	20700	20300				25	52
55	20-Aug-01	13	18800	20180	19700	20600	20300	20100				25	53
56	21-Aug-01	14	18500	18850	22400	18500	17400	17100				25	49
57	22-Aug-01	15	18500	18530	17100	17800	20100	19100				26	50
58	23-Aug-01	16	20000	20650	21700	19600	20900	20400				25	56
59	24-Aug-01	17	18500	19630	19700	20300	19400	19100	0.9608	2.041	5.93E-03	26	50
62	27-Aug-01	18	19200	19280	18200	19300	20500	19100				26	50
63	28-Aug-01	19	19300	20630	18700	21800	21100	20900				25	52
64	29-Aug-01	20	19600	19980	20900	17200	22000	19800			ļ	25	51
		Mean	18710			19790			1.830	2.215	1.76E-02	25.5	50.6
		s.D.	653			1382			1.806	0.643	2.17E-02	0.6	2.1

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

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						Chamber Mo	nitoring	Results					
						Cumulative	Exposure	Record					
						Group IVB	- 20,000	) mg/m³					
												Chamber H	Invironment
									Pa	article S	lize	Me	an
Day	Date	Exposure	Nominal	Ana	lytical (	Chamber Con	ncentrati	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> )		( <i>µ</i> m)		$(mg/m^3)$	(°C)	(%)
37	2-Aug-01	1	18200	19850	21200	19200	19600	19400				25	48
38	3-Aug-01	2	19300	20750	21200	21200	20600	20000	0.9733	1.736	3.11E-03	26	48
41	6-Aug-01	3	17900	20680	20600	20300	20900	20900				26	50
42	7-Aug-01	4	18500	19750	19900	19400	20400	19300				25	50
43	8-Aug-01	5	17900	19830	18300	21400	19700	19900				25	52
44	9-Aug-01	6	19400	20330	19500	20900	20900	20000				25	50
45	10-Aug-01	7	19200	20700	20200	21100	21600	19900	0.8423	1.453	4.13E-02	25	54
48	13-Aug-01	8	18500	19430	18300	20700	19100	19600				25	52
49	14-Aug-01	9	17700	19380	19400	18700	19900	19500				26	47
50	15-Aug-01	10	18000	20280	19800	19900	20300	21100				25	50
51	16-Aug-01	11	18000	19250	19800	18600	19800	18800	0.9267	1.785	4.15E-03	25	50
52	17-Aug-01	12	19100	19900	19500	20100	20100	19900				25	50
55	20-Aug-01	13	18800	20030	19700	19400	20500	20500				26	51
56	21-Aug-01	14	18500	21230	20400	21300	21900	21300				25	49
57	22-Aug-01	15	18500	20250	21600	19400	20700	19300				25	49
58	23-Aug-01	16	20000	20000	17600	21100	21400	19900				24	50
59	24-Aug-01	17	18500	20050	19400	20800	20200	19800	0.8972	1.956	5.41E-03	25	51
62	27-Aug-01	18	19200	19730	19800	20000	18400	20700				25	50
63	28-Aug-01	19	19300	19950	20200	20500	19600	19500				26	50
64	29-Aug-01	20	19600	20600	18100	22100	21600	20600				26	51
		Mean	18710			20100			0.910	1.733	1.35E-02	25.3	50.1
		S.D.	653			923			0.055	0.209	1.86E-02	0.6	1.6

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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

MALES			SUMMARY OF CLINICAL	OBSERVATIONS	
	group#	DAY OF STUDY -1 TOTAL			
# OF ANIMALS EXAMINED	1 2 3	5 5 5			
	4 6	5			

NORMAL

WITHIN NORMAL LIMITS	1 2 3 4	5 5 5 5	5 5 5 5	
	6	5	5	

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 OF CLINICAL OBSERVATIONS
	GROUP#	DAY OF STUDY ~1 TOTAL	
# OF ANIMALS EXAMINED	1	5	
	2	5	· · · · ·
	3	5	
	4	5	
	6	5	

NORMAL

WITHIN	NORMAL	LIMITS	1	5	5	
			· 2	5	5	
			3	5	5	
			4	5	5	
			6	5	5	

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# 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

LES			MEA	N BODY WEIGHTS (GI	(AMB)		
	DOSE (	GROUP :	I	II	III	IV	VI
	EXPOSURE LEVEL (mg	g/m3):	0	2,000	10,000	20,000	MICRO+CONTROL
WEEK	1	MEAN	156	162	158	157	164
WEEK	-1	S.D.	6.9	6.5	7.8	7.5	8.1
		8.D. N	5	5	5	,.5	5
			5	5		5	Ũ
WEEK	0	MEAN	224	224	221	220	225
		S,D.	6.9	7.0	10.4	. 12.7	9.7
		N	5	5	5	5	5
WEEK	1	MEAN	286	284	278	278	286
		S.D.	9.4	13.1	14.8	17.6	21.2
		N	5	5	5	5	5
WEEK	2	MEAN	334	333	318	318	329
		S.D.	15.4	22.5	22.1	20.4	26.2
		N	5	5	5	5	5
WEEK	3	MEAN	372	374	358	354	366
WELL'S IV	5	S.D.	17.2	27.3	28.0	19.9	.29.8
		N	5	5	5	5	5
WEEK	4	MEAN	408	411	390	383	400
- 1 4ad And 5 %	-	S.D.	25.2	33.9	31.7	20.3	26.5
		N	5	5	5	5	5

No statistically significant differences

#### 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

EMALES			MEA	N BODY WEIGHTS (GI	RAMS)		
		GROUP :	I	II	III	IV	VI
	EXPOSURE LEVEL (n	ng/m3):	0	2,000	10,000	. 20,000	MICRO+CONTROL
WEEK	-1	MEAN	141	145	143	143	144
(LDDI)		S.D.	4.5	6,2	6.6	6.2	7.5
		N	5	5	5	5	5
WEEK	0	MEAN	173	173	173	174	173
		S.D.	5.7	· 6.8	9.0	9.6	7.9
		N	5	5	5	5	5
WEEK	1	MEAN	198	203	197	204	. 206
		S.D.	5.4	10.4	6.3	10.6	12.1
		N	5	5	5	5.	5
WEEK	2	MEAN	218	225	218	221	224
		S.D.	9.2	5.1	15.8	12.1	15.2
		N	5	5	5	5	5
WEEK	3	MEAN	235	236	234	239	239
		S.D.	9.1	2.8	7.8	15.4	15.6
		N	5	. 5	5	5	5
WEEK	4	MEAN	253	252	244	252	250
		S.D.	11.6	5.6	9.4	10.3	15.6
		N	5	5	5	5	5

No statistically significant differences

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## 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

			E GROUP:	I	II	III	IV	VI
	EXPOSU	RE LEVEL	(mg/m3):	0	2,000	10,000	20,000	MICRO+CONTROL
WEEK	0 TO	1	MEAN	62	61	58	58	61
NGOL	0 10	т	S.D.	3.0	6.9	7.7	6.5	14.5
			N N	5	5	5	5	5
	0 50	2	MEAN	110	109	97	99	104
WEEK	0 ТО	4	S.D.	9.8	17.2	15.3	9.0	21.1
			N N	5	5	5	5	5
WEEK	0 TO	3	MEAN	148	150	137	134	141
	• • • •	-	S.D.	12.5	22.1	20.5	11.7	26.2
			N	5	5	5	5	5
WEEK	0 TO	4	MEAN	184	187	169	164	175
		-	S.D.	20.4	28.4	24.5	11.9	23.7
			N	5	5	5	5	5

No statistically significant differences

## 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

		DOSI	E GROUP:	I	II	III	IV	VI
	EXPOSU	RE LEVEL	(mg/m3):	0	2,000	10,000	20,000	MICRO+CONTROL
WEEK	0 TO	1	MEAN	25	29	24	30	34
W.D.D.K	0 10	-	S.D.	2.4	7.5	4.6	2.7	8.0
			N	5	5	5	5	5
WEEK	0 TO	2	MEAN	46	52	45	47	52
			S.D.	4.3	2.9	13.7	6.3	9.8
			N	5	5	5	5	5
WEEK	0 TO	3	MEAN	63	63	60	65	67
			S.D.	7.5	7.2	4.8	7.5	8.6
			N	5	5	5	5	5
WEEK	0 TO	4	MEAN	81	- 79	71	78	77
			S.D.	6.9	6.0	9.6	2.6	9.1
			N	5	5	5	5	5

No statistically significant differences

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

	DOGR	CROTTR	Ŧ	II	III	IV	VI	
	S.D. N MEAN S.D. N 2 MEAN S.D. N 3 3 MEAN S.D. N		I O	2,000	10,000	20,000	MICRO+CONTROL	
	EXPOSORE LEVEL (m	g/m3): 		2,000		20,000	MICKOFCOMIKOD	
WEEK	0	MEAN	130	131	126	129	125	
	•		6.2	2.6	4.4	6.5	4.0	
			5	5	5	5	5	
WEEK	1	MEAN	104	106	102	102	105	
		S.D.	4.1	2.5	2.4	5.2	4.4	
		N	5	5	5	5	5	
WEEK	2	MEAN	89	89	83	84	84	
		S.D.	4.2	2.6	3.3	5.1	6.1	
•		N	5	5	5	5	5	
WEEK	3	MEAN	78	80	77	77	75	
		S.D.	1.9	2.1	3.8	2.1	4.8	
		N	5.	5	5	5	5	
WEEK	4	MEAN	72	75	71	70	71	
		S.D.	4.5	4.7	2.8	2.7	2.5	
		N	5	. 5	5	5	5	

No statistically significant differences

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## 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

FEMALES			MEAN FEED CONS	SUMPTION VALUES (	(GRAMS/KG/DAY)			
	DOSE GROUP: EXPOSURE LEVEL (mg/m3):		r O	II 2,000	III 10,000	IV 20,000	VI MICRO+CONTROL	
WEEK	0	MEAN	110	111	115	117	111	
		S.D.	7.5	6.9	7.2	9.4	5.8	
		N	5	. 5	5	5	5	
WEEK	1	MEAN	91	100*	95	96	100*	
		S.D.	2.1	6.0	2.9	5.8	4.5	
		N	5	5	5	5	5	
WEEK	2	MEAN	87	93	88	86	91	
		S.D.	5.2	3.5	7.4	3.7	2.4	
		N	5	4	5	5	4	
WEEK	3	MEAN	83	90	88	84	84	
(ibbit	v	S.D.	4.9	4.8	10.5	3.6	1.9	
		N	5	5	5	5	5	
WEEK	4	MEAN	79	83	85	81	78	
	•	S.D.	1.6	2.3	12.5	3,7	3.3	
	•	N N	5	5	5	5	4	

Statistical key: \* = p<0.05

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## Huntingdon Life Sciences 00-6128G Genotoxicity Sub-Group

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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

MALES	ss GROUP I O mg/m3									
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1							
1031	WITHIN NORMAL LIMITS		P							
1032	WITHIN NORMAL LIMITS		P							
1033	WITHIN NORMAL LIMITS		P							
1034	WITHIN NORMAL LIMITS		P							
1035	WITHIN NORMAL LIMITS		P		. *					

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

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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

MALES (	3ROUP II 2,000 mg/m3				
animal#	OBSERVATIONS	DAY OF STUDY	ī		
					•
2021	WITHIN NORMAL LIMITS		P		
2022	WITHIN NORMAL LIMITS		P		
2023	WITHIN NORMAL LIMITS		P	• • • • • • • •	
2024	WITHIN NORMAL LIMITS		P		
2025	WITHIN NORMAL LIMITS		P		

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

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TABLE F

## GASOLINE TAME VAFOR 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

MALES								
animal#	OBSERVATIONS	DAY OF STUDY	- 1					
3021	WITHIN NORMAL LIMITS		P					
3022	WITHIN NORMAL LIMITS		P					
3023	WITHIN NORMAL LIMITS		P					
3024	WITHIN NORMAL LIMITS		P					
3025	WITHIN NORMAL LIMITS		P	i				

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

Huntingdon Life Sciences 00-6128G Genotoxicity Sub-Group

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

MALES	ALES GROUP IV 20,000 mg/m3									
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1							
4031	WITHIN NORMAL LIMITS		P							
4032	WITHIN NORMAL LIMITS		P							
4033	WITHIN NORMAL LIMITS		p							
4034	WITHIN NORMAL LIMITS		ę							
4035	WITHIN NORMAL LIMITS		Ρ							

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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

MALES	GROUP VI MICRO+CONTROL				
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1		
6031	WITHIN NORMAL LIMITS		P		
6032	WITHIN NORMAL LIMITS		P		
6033	WITHIN NORMAL LIMITS		P		
6034	WITHIN NORMAL LIMITS		P		
6035	WITHIN NORMAL LIMITS		P		
			••••••	 	

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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 I 0 mg/m3			
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1	
1541	WITHIN NORMAL LIMITS		P	
1542	WITHIN NORMAL LIMITS		P	
1543	WITHIN NORMAL LIMITS		P	3
1544	WITHIN NORMAL LIMITS		P	
1545	WITHIN NORMAL LIMITS		P	
			· · · · · · · · · · · · · · · · · · ·	

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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			
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1	
2531	WITHIN NORMAL LIMITS	· · · · · · · · · · · · · · · · · · ·	P	
2532	WITHIN NORMAL LIMITS		P	
2533	WITHIN NORMAL LIMITS		P	
2534	WITHIN NORMAL LIMITS		P	
2535	WITHIN NORMAL LIMITS		p	

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Huntingdon Life Sciences 00-6128G Genotoxicity Sub-Group

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			
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1	
3531	WITHIN NORMAL LIMITS		Ρ	
3532	WITHIN NORMAL LIMITS		P	
3533	WITHIN NORMAL LIMITS		₽	
3534	WITHIN NORMAL LIMITS		P	
3535	WITHIN NORMAL LIMITS		P	

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

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Genotoxici	ty Sub-Group				TABL	E 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										
FEMALES G	INDIVIDUAL CLINICAL OBSERVATIONS FEMALES GROUP IV 20,000 mg/m3									
ànimal#	OBSERVATIONS			DAY STUD		1				
4541	WITHIN NORMAL	LIMITS				P				
4542	WITHIN NORMAL	LIMITS				P				
4543	WITHIN NORMAL	LIMITS				Ę				
4544	WITHIN NORMAL	LIMITS				P				
4545	WITHIN NORMAL	LIMITS				P				

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

Huntingdon Life Sciences 00-6128G Genotoxicity Sub-Group

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 VI MICRO+CONTROL		
ANIMAL#	OBSERVATIONS	DAY OF STUDY	1
6541	WITHIN NORMAL LIMITS		Ρ .
6542	WITHIN NORMAL LIMITS		P
6543	WITHIN NORMAL LIMITS		P
6544	WITHIN NORMAL LIMITS		P
6545	WITHIN NORMAL LIMITS		P

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

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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)
MALES	GROUP I	0 π	ng/m3					
		WEEF	OF STU	DY				
ANIMAL#		-1	0	1	2	3	4	
1031		152	214	272	314	351	383	
1032		161	231	298	356	397	447	
1033		166	228	289	337	369	410	
1034		152	224	287	326	365	388	
1035		150	221	282	334	378	413	
MEAN		156	224	286	334	372	408	
S.D.		6.9	6.9	9.4	15.4	17.2	25.2	
N		5	5	5	5	5	5	

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)
MALES	GROUP II	2,000 m	g/m3				
	W	EEK OF S	TUDY				
ANIMAL#	-	1 0	1	2	3	4	
2021	15	3 215	267	311	350	375	
2022	15	9 223	290	350	395	439	
2023	16	2 219	274	306	340	375	· · · · · · · · · · · · · · · · · · ·
2024	16	9 233	297	352	400	445	
2025	16	7 229	294	346	383	419	
MEAN	16	2 224	284	333	374	411	
S.D.	6.	5 7.0	13.1	22.5	27.3	33.9	
N		5 5	5	5	5	5	

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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

MALES	GROUP III	:	10,000 r	ng/m3			INDIVID	JAL BODY WEIGHTS (GRAMS)
		WEEL	K OF STU	JDY				
ANIMAL#		-1	0	1	2	3	4	
3021		166	232	289	335	385	421	
3022		159	221	291	340	383	421	
3023	•	160	222	274	306	341	371	
3024	:	145	204	255	286	319	348	
3025	:	160	225	283	322	361	389	
MEAN	:	158	221	278	318	358	390	
s.D.		7.8	10.4	14.8	22,1	28.0	31.7	· · · · · · · · · · · · · · · · · · ·
N		5	5	. 5	5	5	5	

## Huntingdon Life Sciences 00-6128G Genotoxicity Sub-Group

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

MALES	GROUP IV	21	0,000 ma	- /m2		:	INDIVIDU	JAL BODY WEIGHTS (GRAMS)
MADES	GROOP IV							
		WEEL	K OF STU	JDY				
animal#		-1	0	1	2	3	4	
4031	]	160	218	267	305	331	361	
4032	]	159	226	291	329	367	400	
4033	1	164	233	297	342	372	404	
4034	1	144	199	254	291	333	363	
4035	1	157	223	280	326	364	389	
MEAN	1	157	220	278	318	354	383	
S.D.	5	7.5	12.7	17.6	20.4	19.9	20.3	
N		5	5	5	5	5	5	

TABLE G

## GASOLINE TAME VAFOR 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)
MALES	GROUP VI	MI	CRO+COI	NTROL				
		WEEH	COF STU	JDY				
ANIMAL#		-1	0	1	2	3	4	
6031		157	216	259	289	320	362	
6032		170	228	277	320	356	388	
6033		174	241	317	358	391	423	
6034		158	218	290	344	392	427	
6035		158	224	289	334	372	401	
MEAN		164	225	286	329	366	400	
S.D.		8.1	9.7	21.2	26.2	29.8	26.5	
N		5	5	5	5	5	5	

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	0 -	ncr/m3			:	INDIVIDU	AL BODY WEIGHTS (GRAMS)
F EFIALLES	GROOP 1							
		WEEF	OF STU	DY				
ANIMAL#		-1	0	1	2	3	4	
1541		143	164	191	203	220	234	
1542		134	172	200	222	241	257	
1543		142	172	193	219	241	253	
1544		142	180	205	228	233	260	
1545		146	175	199	218	241	263	
MEAN		141	173	198	218	235	253	
S.D.		4.5	5.7	5,4	9.2	9.1	11.6	
N		5	5	5	5	5	5	

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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 II	2,000 mg	/m3		C	INDIVIDU/	AL BODY WEIGHTS (GRAMS)
	WE	EK OF ST	UDY				
ANIMAL#	-1	0	1.	2	3	4	
2531	140	171	205	224	241	257	
2532	148	172	208	227	236	246	
2533	151	179	198	226	234	252	
2534	151	181	216	232	238	258	
2535	138	164	188	218	235	248	
MEAN	145	173	203	225	236	252	
S.D.	6.2	6.8	10.4	5.1	2.8	5.6	
N	5	5	5	5	5	5	

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## 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	: 1	.0,000 m	ıg/m3			
		WEEK	OF STU	DY			
ANIMAL#		-1	0	1	2	3	4
3531		140	162	190	210	221	230
3532		148	179	198	222	239	247
3533		152	185	205	226	238	243
3534		136	172	201	237	239	255
3535		139	169	191	196	230	247
MEAN		143	173	197	218	234	244
S.D.		6.6	9.0	6.3	15.8	7.8	9.4
N		5	5	5	5	5	5

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 IV	20	,000 mg	g/m3		:	INDIVIDU	JAL BODY WEIGHTS (GRAMS)
		 WEEK	OF STU	JDY				
ANIMAL#		-1	0	1	2	3	4	
4541	1	 44	169	196	215	230	247	
4542	1.	50	188	220	233	257	266	
4543	1:	35	163	193	204	218	238	
4544	1	48	179	206	225	245	254	
4545	1	39	173	206	230	247	254	
MEAN	1	43	174	204	221	239	252	
S.D.	6	.2	9.6	10.6	12.1	15.4	10.3	
N		5	5	5	5	5	5	

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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 WEIGH	ITS (GRAM	S)
-----------------------	-----------	----

FEMALES G	ROUP VI M	ICRO+CO	NTROL				
	WEE	K OF ST	UDY				
ANIMAL#	-1	0	1	2	3	4	
6541	149	175	207	223	243	256	
6542	135	165	186	202	217	226	
6543	141	173	209	224	243	254	
6544	142	166	210	227	233	246	
6545	155	184	219	244	260	268	
MEAN	144	173	206	224	239	250	
S.D.	7.5	7.9	12.1	15.2	15.6	15.6	
N	5	5	5	5	5	5	

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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

#### INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

MALES GR	OUP I	0 mg	g/m3			
	wi	EEK (	OF STUI	D¥		
animal#	0	-1	0-2	0~3	0 - 4	
1031		 59	101	137	169	
1032	(	67	125	166	215	
1033	(	60	108	141	181	
1034		63	102	141	164	
1035	(	61	113	157	192	
MEAN	(	62	110	148	184	
S.D.	3	.0	9.8	12.5	20.4	
N		5	5	5	5	

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TABLE H

## GASOLINE TAME VAFOR 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 WEIGHT CHANGE (GRAMS)

MALES GROUP II 2,000 mg/m3								
		WEEK	OF STUE	DY				
ANIMAL#		0-1	0-2	0-3	0 - 4			
2021		52	96	135	161			
2022		68	128	173	217			
2023		55	87	120	156			
2024		64	119	167	213			
2025		66	117	155	191			
MEAN		61	109	150	187			
S.D.		6.9	17.2	22.1	28.4			
N		5	5	5	5			

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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

#### INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

MALES	GROUP I	II 1	LO,000 T	ng/m3		
		WEEK	OF STU	DY		
animal#		0-1	0-2	0-3	0-4	
3021		57	103	153	189	
3022		70	120	162	200	
3023		51	84	119	149	
3024		51	83	115	144	
3025		58	97	136	164	
MEAN		58	97	137	169	
S.D.		7.7	15.3	20.5	24.5	
N		5	5	5	5	

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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

						INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)
MALES	GROUP IV	20	0,000 mg	g/m3		
		WEEK	OF STU	DY		
ANIMAL#		0-1	0-2	0 - 3	0-4	
4031		50	88	114	144	
4032		65	102	141	174	
4033		64	109	140	171	
4034		55	91	133	163	
4035		57	103	142	166	
MEAN		58	99	134	164	
S.D.		6.5	9.0	11.7	11.9	
N		5	5	5	5	

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TABLE H

INDIVIDUAL	RODY	WEIGHT	CHANGE	(GRAMS)	

MALES	GROUP VI	MI	CRO+CON	TROL		
		VEEK	OF STUI	DY		
ANIMAL#	(	0-1	0-2	0-3	0 - 4	
6031		42	73	104	146	
6032		49	93	128	161	
6033		76	117	151	182	
6034		71	126	173	209	
6035		65	110	148	177	
MEAN		61	104	141	175	
S.D.	14	4.5	21.1	26.2	23.7	
N		5	5	5	5	

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# 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 mg/m3										
	·	VEEK (	OF STUD	 Y						
ANIMAL#	c	)-1	0-2	0-3	0 - 4					
1541		27	39	56	70					
1542		27	50	69	84					
1543		22	47	70	82					
1544		25	49	53	80					
1545		24	43	66	88					
MEAN		25	46	63	81					
S.D.	2	2.4	4.3	7.5	6.9					
N		5	5	5	5					

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

INDIVIDUAL BODY WEIGHT CHANGE (GRAMS)

FEMALES	FEMALES GROUP II 2,000 mg/m3											
	w	VEEK	OF STUD	ч У								
ANIMAL#	C	)-1	0-2	0-3	0 - 4							
2531		34	54	70	87							
2532		36	55	64	74							
2533		19	48	55	74							
2534		34	51	56	77							
2535		24	54	70	84							
MEAN		29	52	63	79							
S.D.	7	7.5	2.9	7.2	6.0							
N		5	5	5	5							

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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 m	g/m3		
	W	EEK	OF STUD	 Y		
ANIMAL#	0	-1	0-2	0 - 3	0 - 4	
3531		28	49	60	68	
3532		19	43	60	68	
3533		20	41	54	59	
3534		29	65	67	83	
3535		22	27	62	78	
MEAN		24	45	60	71	
S.D.	4	.6	13.7	4.8	9.6	
N		5	5	5	5	

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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 IV 20,000 mg/m3										
		WEEK	OF STUD	Y						
ANIMAL#		0-1	0-2	0-3	0 - 4					
4541		27	46	61	78					
4542		32	45	69	78					
4543		30	41	56	75					
4544		27	46	66	75					
4545		33	58	75	81					
MEAN		30	47	65	78					
S.D.		2.7	б.З	7.5	2.6					
N		5	5	5	5					

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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	и мі	CRO+CON	TROL		
		WEEK	OF STUD	 Y		
ANIMAL#		0-1	0-2	0-3	0 - 4	
6541		32	48	68	81	
6542		22	37	52	61	
6543		36	51	71	81	
6544		44	61	67	79	
6545		34	60	75	84	
MEAN		34	52	67	77	· ·
S.D.	•	8.0	9.8	8.6	9.1	
N		5	5	5	. 5	

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)

MALES	GROUP I	0 π	ng/m3			•	
		WEEK	OF STU	DY			•••••
ANIMAL#		0	1	2	3	4	
1031		126	103	88	78	72	
1032	3	126	100	84	76	71	
1033	1	129	107	94	81	80	
1034	1	141	109	93	79	70	
1035	1	129	100	86	77	68	
MEAN	1	130	104	89	78	72	
s.D.	e	5.2	4.1	4.2	1.9	4.5	
N		5	5	5	5	5	

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TABLE I

	INDIVIDUAL	FEED	CONSUMPTION	VALUES	(GRAMS)	'KG/	DAY
--	------------	------	-------------	--------	---------	------	-----

MALES	GROUP II	2,	000 mg/	m3			
	~~~~~~	WEEK	OF STU	DY .			
animal#		0	1	2	3	4	
2021		129	102	87	79	73	
2022		130	108	92	82	79	
2023		130	108	90	80	78	
2024		133	106	91	83	79	
2025		135	105	86	78	68	
MEAN		131	106	89	80	75	
S.D.		2.6	2.5	2.6	2.1	4.7	
N		5	5	5	5	5	

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TABLE I

TNIDTUTUTUT	ธธธก	CONSUMPTION	VALUES	(GRAMS/KG/DAY)
TNDIVIDUAD	1 5 5 0	CONSOMETION	VALUES	(GRAMS/RG/DAI)

MALES	GROUP II	I 1	.0,000 m	ng/m3		
		WEEK	OF STU	IDY		
ANIMAL#		0	1	2	3	4
3021		130	103	86	81	76
3022		129	106	87	81	72
3023		119	99	82	74	69
3024		127	103	79	73	69
3025		124	102	82	76	70
MEAN		126	102	83	77	71
S.D.		4.4	2.4	3.3	3.8	2.8
N		5	5	5	5	5

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)	

MALES	GROUP IV	20	),000 mg	r/m3		
		WEEF	OF STU	DY		
ANIMAL#		0	1	2	3	4
4031		121	98	82	77	73
4032	5	127	96	77	73	67
4033		139	110	91	78	70
4034	:	129	103	84	78	68
4035	:	130	101	84	77	72
MEAN	:	129	102	84	77	70
S.D.	e	5.5	5.2	5.1	2,1	2.7
N		5	5	5	5	5

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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 FR	EED	CONSUMPTION	VALUES	(GRAMS/	′KG/	DAY)
---------------	-----	-------------	--------	---------	------	------

MALES	GROUP VI	MI	CRO+CON	TROL		V100mL 12	
		WEEK	OF STU	DY			
ANIMAL#		0	1	2	3	4	
6031		124	99	77	72	73	
6032		123	103	84	77	72	
6033		122	106	80	69	66	
6034		131	111	92	81	72	
6035		122	106	89	78	71	
MEAN		125	105	84	75	71	
S.D.		4.0	4.4	6.1	4.8	2.5	
N		5	5	5	5	5	

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### 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 I	0 m	ng/m3				
		WEEK	OF STU	DY			
ANIMAL#		0	1	2	3	4	
1541		98	89	80	83	77	
1542		118	92	88	80	78	
1543		111	94	92	88	77	
1544		113	90	83	77	81	
1545		108	92	91	87	80	
MEAN		110	91	87	83	79	
S.D.		7.5	2.1	5.2	4.9	1.6	
N		5	5	5	5	5	

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 GROU	PII 2,	000 mg/	′m3								
WEEK OF STUDY											
animal#	0	1	2	3	4						
2531	118	98	94	90	84						
2532	118	105	SF	95	83						
2533	110	103	92	83	79						
2534	103	91	88	88	85						
2535	106	104	96	93	83						
MEAN	111	100	93	90	83						
S.D.	6.9	6.0	3.5	4.8	2.3						
N	5	5	4	5	5						

SF=Spilled Feeder

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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 I	II 1	0,000 m	g/m3							
		WEEK	OF STU	DY			 	 	 	 	
ANIMAL#		0	1	2	3	4					
3531		108	95	80	101	103	 	 	 	 	
3532		111	99	90	85	79					
3533		112	91	82	75	71					
3534		125	97	99	83	79					
3535		121	94	91	96	91					
MEAN		115	95	88	88	85					
S.D.		7.2	2.9	7.4	10.5	12.5					
N		5	5	5	5	5					

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 GRO	OUP IV 20	,000 mg	/m3			
	WEEK	OF STU	DY		 	
ANIMAL#	0	1	2	3	4	
4541	103	88	84	81	79	 
4542	122	99	87	85	75	
4543	111	93	82	79	82	
4544	121	96	90	87	83	
4545	126	103	89	86	85	
MEAN	117	96	86	84	81	
S.D.	9.4	5.8	3.7	3.6	3.7	
N	5	5	5	5	5	

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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 FER	D CONSUMPTION	VALUES	(GRAMS/KG/DAY)
----------------	---------------	--------	----------------

FEMALES G	ROUP VI	MICRO+COI	NTROL			•		
	WE	EK OF STU	JDY					
ANIMAL#	0	1	2	3	4			
6541	105	96	SF	87	SF		 	
6542	117	100	91	83	75			
6543	116	102	89	84	81			
6544	113	107	90	82	82			
6545	105	97	94	83	76			
MEAN	111	100	91	84	78			
S.D.	5.8	4.5	2.4	1.9	3.3			
N	5	5	4	5	4			

SF=Spilled Feeder

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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

ANIMAL TERMINATION HISTORY								
MALES	GROUP I 0 mg/m3							
	TYPE OF	DATE OF	WEEK OF	STUDY				
ANIMAL#	DEATH	· DEATH	STUDY	DAY				
1031	TERMINAL SACRIFICE	30-AUG-01.	4	28				
1031	TERMINAL SACRIFICE	30-AUG-01	4	28				
1033	TERMINAL SACRIFICE	30-AUG-01	4	28				
1034	TERMINAL SACRIFICE	30-AUG-01	4	28				
1035	TERMINAL SACRIFICE	30-AUG-01	4	28				

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MALES GRO	OUP II 2,000 mg/m3			
ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2021	TERMINAL SACRIFICE	30-AUG-01	4	28
2022	TERMINAL SACRIFICE	30-AUG-01	4	28
2023	TERMINAL SACRIFICE	30-AUG-01	4	28
2024	TERMINAL SACRIFICE	30-AUG-01	4	28
2025	TERMINAL SACRIFICE	30-AUG-01	4	28

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ANIMAL	TERMINATION	HISTORY

DF I	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
SACRIFICE	30-AUG-01	4	28	
SACRIFICE	30-AUG-01	4	28	
SACRIFICE	30-AUG-01	4	28	
BACRIFICE	30-AUG-01	4	28	
SACRIFICE	30-AUG-01	4	28	
52	ACRIFICE ACRIFICE	ACRIFICE 30-AUG-01 ACRIFICE 30-AUG-01	ACRIFICE         30-AUG-01         4           ACRIFICE         30-AUG-01         4	ACRIFICE         30-AUG-01         4         28           ACRIFICE         30-AUG-01         4         28

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### 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

# ANIMAL TERMINATION HISTORY

	ТҮ	PE OF	DATE OF	WEEK OF	STUDY
NIMAL#	E	EATH	DEATH	STUDY	DAY
4031	TERMIN	AL SACRIFICE	30-AUG-01	4	28
4032	TERMIN	AL SACRIFICE	30-AUG-01	4	28
4033	TERMIN	AL SACRIFICE	30-AUG-01	4	28
4034	TERMIN	AL SACRIFICE	30-AUG-01	4	28
4035	TERMIN	AL SACRIFICE	30-AUG-01	4	28

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ANIMAL	TERMINATION	HISTORY

MALES	GROUP VI	MICRO+CONTROL				
		TYPE OF	DATE OF	WEEK OF	STUDY	
ANIMAL#		DEATH	DEATH	STUDY	DAY	
6031	 3	TERMINAL SACRIFICE	30-AUG-01	4	28	
6032	2	TERMINAL SACRIFICE	30-AUG-01	4	28	
6033	2	TERMINAL SACRIFICE	30-AUG-01	4	28	
6034	3	TERMINAL SACRIFICE	30-AUG-01	4	28	
6035	1	CERMINAL SACRIFICE	30-AUG-01	4	28	

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### 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 GR	OUP I 0 mg/m3				
animal#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
1541	TERMINAL SACRIFICE	30-AUG-01	4	28	
1542	TERMINAL SACRIFICE	30-AUG-01	4	28	
1543	TERMINAL SACRIFICE	30-AUG-01	4	28	
1544	TERMINAL SACRIFICE	30-AUG-01	4	28	
1545	TERMINAL SACRIFICE	30-AUG-01	4	28	

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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	DATE OF	WEEK OF	STUDY	
NIMAL#	DEATH	DEATH	STUDY	DAY	
2531	TERMINAL SACRIFICE	30-AUG-01	4	28	
2532	TERMINAL SACRIFICE	30-AUG-01	4	28	
2533	TERMINAL SACRIFICE	30-AUG-01	4	28	
2534	TERMINAL SACRIFICE	30-AUG-01	4	28	
2535	TERMINAL SACRIFICE	30-AUG-01	4	28	

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

FEMALES GR	2009 III 10,000 mg/m3				
ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
3531	TERMINAL SACRIFICE	30-AUG-01	4	28	
3532	TERMINAL SACRIFICE	30-AUG-01	4	28	
3533	TERMINAL SACRIFICE	30-AUG-01	4	28	
3534	TERMINAL SACRIFICE	30-AUG-01	4	28	
3535	TERMINAL SACRIFICE	30-AUG-01	4	28	

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### 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	 
4541	TERMINAL SACRIFICE	30-AUG-01	4	28	
4542	TERMINAL SACRIFICE	30-AUG-01	4	28	
4543	TERMINAL SACRIFICE	30-AUG-01	4	28	
4544	TERMINAL SACRIFICE	30-AUG-01	4	28	
4545	TERMINAL SACRIFICE	30-AUG-01	4	28	 

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ANIMAL	TERMINATION	HISTORY	

VI MICRO+CONTROL				
TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY	
TERMINAL SACRIFICE	30-AUG-01	4	28	
TERMINAL SACRIFICE	30-AUG-01	4	28	
TERMINAL SACRIFICE	30-AUG-01	4	28	
TERMINAL SACRIFICE	30-AUG-01	4	28	
TERMINAL SACRIFICE	30-AUG-01	4	28	
	TYPE OF DEATH TERMINAL SACRIFICE TERMINAL SACRIFICE TERMINAL SACRIFICE TERMINAL SACRIFICE	TYPE OF     DATE OF       DEATH     DEATH       TERMINAL SACRIFICE     30-AUG-01       TERMINAL SACRIFICE     30-AUG-01	TYPE OF     DATE OF     WEEK OF       DEATH     DEATH     STUDY       TERMINAL SACRIFICE     30-AUG-01     4       TERMINAL SACRIFICE     30-AUG-01     4       TERMINAL SACRIFICE     30-AUG-01     4       TERMINAL SACRIFICE     30-AUG-01     4       TERMINAL SACRIFICE     30-AUG-01     4	TYPE OF DEATHDATE OFWEEK OFSTUDYDEATHDEATHSTUDYDAYTERMINAL SACRIFICE30-AUG-01428TERMINAL SACRIFICE30-AUG-01428TERMINAL SACRIFICE30-AUG-01428TERMINAL SACRIFICE30-AUG-01428TERMINAL SACRIFICE30-AUG-01428TERMINAL SACRIFICE30-AUG-01428