Huntingdon Life Sciences (ERC) Report No: APT 004/012980

Study Title

SATELLITE PROCEDURE
BASELINE GASOLINE VAPOR CONDENSATE
RAT MICRONUCLEUS TEST

TEST 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.

AUTHOR: Christine E. Mason, B.Sc.(Hons.)

STUDY COMPLETED ON: 18 March 2005

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

HUNTINGDON LIFE SCIENCES LTD (PRC) STUDY NO.: 00-6125

HUNTINGDON LIFE SCIENCES LTD (ERC) STUDY NO.: APT/004

SUBCONTRACTOR'S SPONSOR: Huntingdon Life Sciences
Princeton Research Centre (PRC)
Mettlers Road
East Millstone, NJ 08875-2360
USA

CONTENTS

TABLES

APPENDICES

Huntingdon Life Sciences (ERC) Report No: APT 004/012980

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 1999 (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 1999/11/EC of 8 March 1999 (Official Journal No. L 77/8), as amended by 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.

C.E. Mason — 13th April 2005

Christine E. Mason, B.Sc. (Hons.), Date
Principal Investigator,
Huntingdon Life Sciences Ltd., ERC

.....

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 mixture has not been determined by the Testing Facility.

I Taylor

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

Huntingdon Life Sciences (ERC) Report No: APT 004/012980

ERC - QUALITY ASSURANCE STATEMENT

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

Study Phase	Date of Inspection	Date of Reporting to Principal Investigator and Test Site Management	Date of Reporting to Study Director, Test Facility Management and Lead QA
Process Based Inspection			
Slide scoring	14 March 2001	14 March 2001	-
Report Audit	18 July 2001 17 April 2003	18 July 2001 17 April 2003	19 December 2001 17 April 2003

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 test site Quality Assurance Department. These audits were conducted and reported to the Principal Investigator, test site Management, Study Director, test facility Management and lead Quality Assurance Department 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.

N Jolly

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

11 April 2005
Date

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	13-14 Nov 00	14 Nov 00
Dose Genotoxicity Positive Control	05 Feb 01	06 Feb 01
Genotoxicity Necropsy & Training Records	06 Feb 01	07 Feb 01
Subcontractor Final Reports	10, 11 & 13 Jul 01	13 Jul 01
Final In-Life, Pathology Reports & Study Data	31 Jul, 1-3, 6-11 & 13-18 Aug 01	20 Aug 01
Subcontractor In-life Reports & Micronucleus Report	15-17, 27 & 28 Aug 01	28 Aug 01
Sponsor Comments	21-25 Jul & 15 & 22 Aug & 2 Dec 03	2 Dec 03

Fran Jannone

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

26 May 05
Date

RESPONSIBLE PERSONNEL AND SCIENTIFIC APPROVAL

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

1 July 05
Date

C. E. Mason
Christine E. Mason, B.Sc.(Hons.),
Principal Investigator
Department of Genetic Toxicology, ERC

13th April 2005
Date

Lincoln Pritchard, B.Sc.,
Scientific Officer
Department of Genetic Toxicology, ERC

13 April 2005.
Date

Graham F. Healey, B.Sc., M.Sc., A.R.C.S.
Head of Department
Department of Statistics, HRC

6 Apr 2005
Date

SUMMARY

This satellite micronucleus study was designed to assess the potential induction of micronuclei by Baseline Gasoline 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^3.

The test substance and negative control were administered by inhalation. The negative control group received clean air. A positive control group was dosed 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^{th} 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 Baseline Gasoline Vapor Condensate compared to negative control values ($P>0.01$ in each case).

The positive control compound, Cyclophosphamide, produced large, 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 Baseline Gasoline Vapor Condensate did not show any evidence, as indicated by micronuclei evaluation, 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 Baseline Gasoline 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, the wealth of background data on this species, and 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 27 February 2001 and10 April 2001 respectively.

EXPERIMENTAL PROCEDURE

In-life phase

The in-life phase of the study was carried out at the Princeton Research Centre starting on 9 January 2001 and was completed on 6 February 2001.

All animals in the negative control and test substance groups were exposed for four weeks (5 days per week) by inhalation. The positive control group was dosed with Cyclophosphamide administered by intraperitoneal injection at a volume dosage of 10 ml/kg bodyweight. Cyclophosphamide (CP, CAS # 6055-19-2, lot number 108H0568, expiration 6 October 2003, white solid, 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 micronucleus study.

The experimental design is shown below:

Group	Treatment	Exposure Level (mg/m^3)	Animal Numbers	
			Male	Female
1	Air control	-	1031 - 1035	1541 – 1545
2	Test Material	2000	2021 - 2025	2531 – 2535
3	Test Material	10000	3021 - 3025	3531 – 3535
4	Test Material	20000	4031 – 4035	4541 – 4545
6	Cyclophosphamide	40 (mg/kg)	6031 – 6035	6541 - 6545

Five males and five females from the negative control, each of the test substance groups and the positive control group were killed, 24 hours after the final exposure period, by CO_2 asphyxiation. Both femurs 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 x 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 about 3 minutes in methanol, and aged overnight or longer prior to staining. Slides were labelled with experiment and animal number using a lead pencil.

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.

Side 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 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, *ie* 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).

Deviation from Protocol

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 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, Massachussetts). Comparison of several dose levels is made with the 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 inter-group comparisons

(*ie* the positive control group only) 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, *ie* 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 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 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 of 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 polychromatic erythrocyte counts.

Micronucleated immature erythrocyte counts (mie)

The test substance did not cause any statistically significant increases in the number of micronucleated immature erythrocytes [P>0.01].

Cyclophosphamide caused large, 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 [P>0.01].

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 Baseline Gasoline Vapor Condensate compared to negative control values (P>0.01 in each case).

It is concluded that Baseline Gasoline Condensate Vapour did not show any evidence, as indicated by micronuclei evaluation, of causing chromosome damage or bone marrow cell toxicity when administered by inhalation in this *in vivo* test procedure.

REFERENCES

AGRESTI, A., MEHTA, C.R. and PATEL, N.R. (1990) Exact inference for contingency tables with ordered categories. *Journal of the American Statistical Association,* **85**, 453.

BOLLER, K. and SCHMID, W. (1970) Chemical mutagenesis in mammals. The bone marrow of the Chinese hamster as an *in vivo* test system. Haematological findings after treatment with Trenimon (translation). *Humangenetik*, **11**, 34.

CYTEL (1995) *StatXact 3 for Windows: Statistical Software for Exact Nonparametric Inference.* Cytel Software Corporation, NC, USA.

GIBBONS, J.D. (1985) Nonparametric Statistical Inference, 2nd edition, Marcel Dekker, New York.

JONCKHEERE, A.R. (1954) A distribution-free k-sample test against ordered alternatives. *Biometrics,* **41**, 133-145.

KRUSKAL, W.H. and WALLIS, W.A. (1952) Use of Ranks in One-Criterion Variance Analysis. *Journal of the American Statistical Association,* **47**, 583-621.

KRUSKAL, W.H. and WALLIS, W.A. (1953) Errata for Kruskal-Wallis (1952). *Journal of the American Statistical Association,* **47**, 583-621.

MacGREGOR, J.T., HEDDLE, J.A., HITE, M., MARGOLIN, B.H., RAMEL, C., SALAMONE, M.F., TICE, R.R. and WILD, D. (1987) Guidelines for the conduct of micronucleus assays in mammalian bone marrow erythrocytes. *Mutation Research*, **189**, 103.

MATTER, B. and SCHMID, W. (1971) Trenimon-induced chromosomal damage in bone marrow cells of six mammalian species, evaluated by the micronucleus test. *Mutation Research*, **12**, 417.

MAVOURNIN, K.H., BLAKEY, D.H., CIMINO, M.C., SALAMONE, M.F. and HEDDLE, J.A. (1990) The *in vivo* micronucleus assay in mammalian bone marrow and peripheral blood. A report of the US Environmental Protection Agency Gene-Tox Program. *Mutation Research*, **239**, 29.

MORRISON, V. and ASHBY, J. (1995) High resolution rodent bone marrow micronucleus assays of 1,2-dimethylhydrazine : implication of systemic toxicity and individual responders. *Mutagenesis*, **10**, 129.

SAS INSTITUTE (1989) *SAS/STAT User's Guide, Version 6, Fourth Edition, Vol.2.* SAS Institute Inc., Cary, NC, USA.

SAS INSTITUTE (1996) *SAS/STAT Software: Changes and Enhancements through Release* 6.11. SAS Institute, Cary, NC, USA.

SAS INSTITUTE (1996) *SAS/STAT Software:* Changes and Enhancements for Release 6.12. SAS Institute, Cary, NC, USA.

SCHMID, W. (1976) The micronucleus test for cytogenetic analysis. In: HOLLANDER, A. (ed.) *Chemical Mutagens, Principles and Methods for their Detection*, **4**, 31. Published by Plenum Press, New York.

von LEDEBUR, M. and SCHMID, W. (1973) The micronucleus test. Methodological aspects. *Mutation Research*, **19**, 109.

WILCOXON, F. (1945). Individual comparisons by ranking methods. *Biometrics Bulletin,* **1**, 80-83.

TABLE 1

Summary of results and statistical analysis

Sampling time	Treatment	Exposure level (mg/m^3)	Proportion of ie† (Mean ± SD)	Incidence mie (Mean ± SD)	Incidence mme [a] (Mean ± SD)
24 Hours	Negative control	-	51 ± 7.7	0.6 ± 0.7	0.0 ± 0.0
	TS	2000	43 ± 9.8	0.7 ± 0.7	0.0 ± 0.0
	TS	10000	45 ± 5.6	0.8 ± 0.6	0.7 ± 0.4
	TS	20000	44 ± 8.0	0.6 ± 0.8	0.7 ± 0.4
	Cyclophosphamide	40 (mg/kg)	27 ± 6.2***	14.0 ± 5.5***	0.8 ±0.7

TS Baseline Gasoline Vapor Condensate
ie Immature erythrocyte
mie Number of micronucleated cells observed per 2000 immature erythrocytes examined
me Mature erythrocytes
mme Number of micronucleated cells 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)

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

[a] Formula for calculation of incidence mme (group mean):

$$\frac{\text{Sum of group incidence } \mathbf{mme} \text{ scored} \times 2000}{\text{Sum of group } \mathbf{me} \text{ scored}}$$

TABLE 2

Results for individual animals - 24 hour sampling time

Treatment	Exposure level (mg/m^3)	Animal number	ie	me	Proportion of ie	Incidence mie	Incidence mme
Air control	-	M 1031	507	500	50	0	0
		M 1032	464	571	45	0	0
		M 1033	468	557	46	1	0
		M 1034	535	489	52	0	0
		M 1035	421	608	41	1	0
		F 1541	561	443	56	1	0
		F 1542	489	514	49	0	0
		F 1543	551	458	55	1	0
		F 1544	494	511	49	0	0
		F 1545	724	321	69	2	0
TS	2000	M 2021	329	674	33	0	0
		M 2022	325	689	32	1	0
		M 2023	563	453	55	0	0
		M 2024	264	769	26	1	0
		M 2025	391	612	39	1	0
		F 2531	480	523	48	1	0
		F 2532	424	584	42	0	0
		F 2533	502	520	49	0	0
		F 2534	540	500	52	2	0
		F 2535	514	507	50	1	0
TS	10000	M 3021	408	611	40	2	0
		M 3022	399	649	38	1	0
		M 3023	480	534	47	1	0
		M 3024	350	661	35	0	0
		M 3025	487	523	48	1	0
		F 3531	469	551	46	0	1
		F 3532	437	574	43	0	0
		F 3533	504	498	50	1	0
		F 3534	519	490	51	1	0
		F 3535	500	500	50	1	1
TS	20000	M 4031	461	544	46	0	0
		M 4032	489	525	48	2	0
		M 4033	394	612	39	1	0
		M 4034	478	542	47	0	0
		M 4035	318	688	32	0	0
		F 4541	460	541	46	0	1
		F 4542	448	555	45	1	0
		F 4543	589	416	59	0	0
		F 4544	466	546	46	2	0
		F 4545	317	685	32	0	1

TS	Baseline Gasoline Vapor Condensate
ie	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

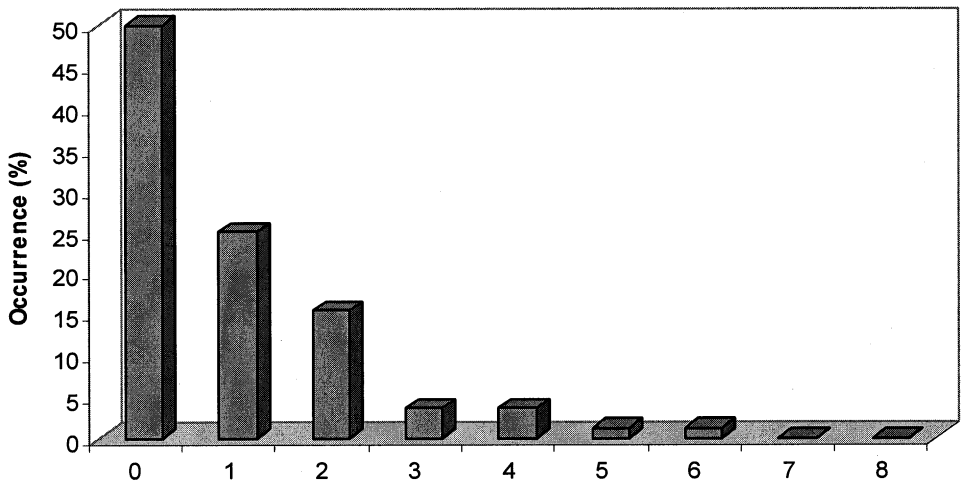
Results for individual animals - 24 hour sampling time

Treatment	Dosage (mg/kg)	Animal number	ie	me	Proportion of ie	Incidence mie	Incidence mme
Cyclophosphamide	40	M 6031	342	666	34	15	0
		M 6032	329	680	33	17	0
		M 6033	297	761	28	20	2
		M 6034	361	657	35	17	0
		M 6035	223	837	21	22	0
		F 6541	271	753	26	8	0
		F 6542	201	807	20	4	1
		F 6543	167	833	17	13	0
		F 6544	250	797	24	14	0
		F 6545	293	720	29	10	0

ie	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

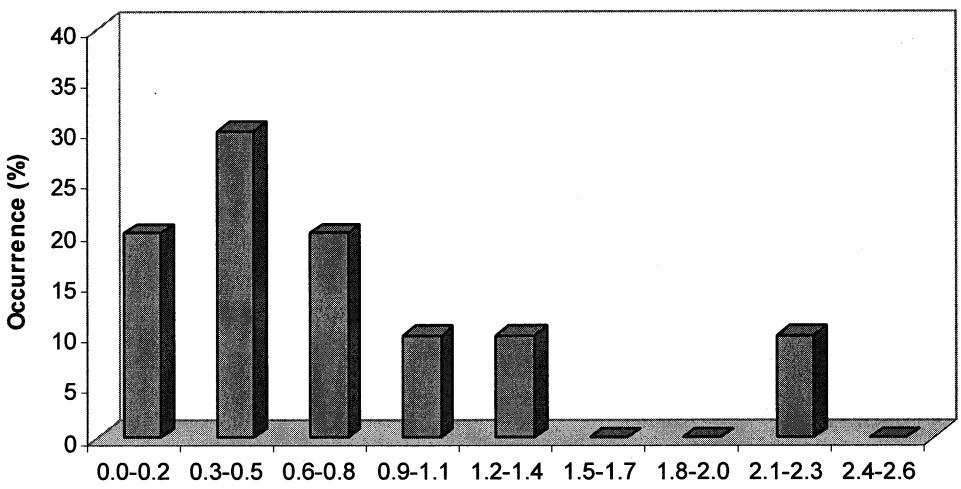
APPENDIX 1

Historical negative control values (1 February 1999 - 31 January 2001)
Frequency of micronucleated immature erythrocytes (individual animals)



Individual mean 0.94

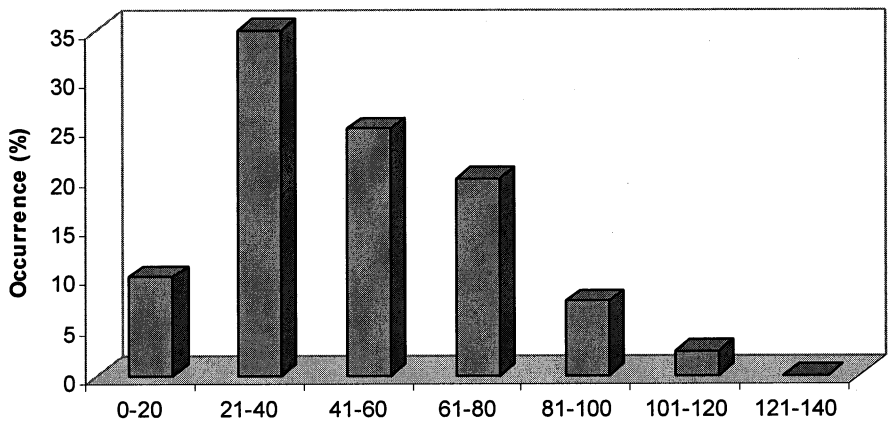
Historical negative control values (1 February 1999 - 31 January 2001)
Frequency of micronucleated immature erythrocytes (Group mean values)



Group mean 0.71

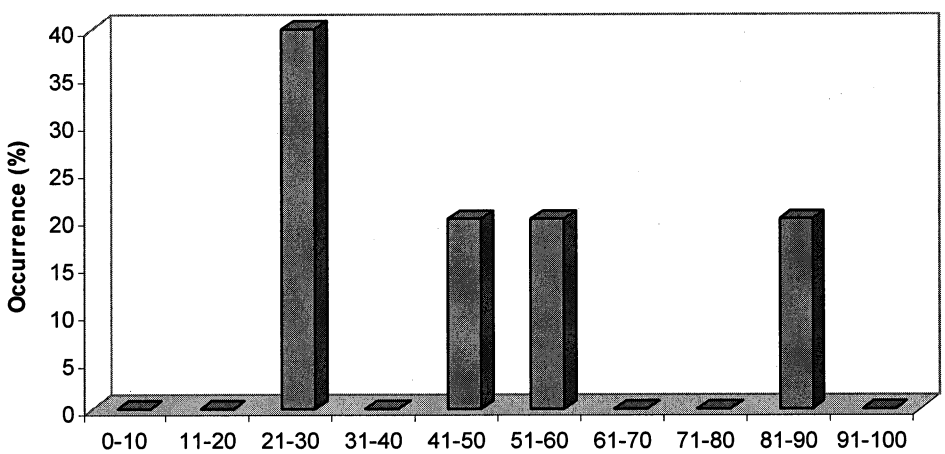
APPENDIX 1 – continued

Historical positive control values (1 February 1999 - 31 January 2001)
Frequency of micronucleated immature erythrocytes (Individual animals)
Cyclophosphamide



Number of micronucleated immature erythrocytes (MIE per 2000 cells)
Individual mean 48.03

Historical positive control values (1 February 1999 - 31 January 2001)
Frequency of micronucleated immature erythrocytes (Group mean values)
Cyclophosphamide



Number of micronucleated immature erythrocytes (MIE per 2000)
Group mean 49.2

APPENDIX 2

ANIMAL EXPOSURE AND OBSERVATIONS DATA

	Animal Exposure and Animal Data Preface	Appendix 2

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: Experimental Initiation Date: 9 January 2001 (in-life)

Experimental Completion Date: 6 February 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.

TABLE OF CONTENTS

TABLES

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

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)	(%)
0	9-Jan-01	1	0	0	0	0	0	0					24	49
1	10-Jan-01	2	0	0	0	0	0	0					24	51
2	11-Jan-01	3	0	0	0	0	0	0		1.309	1.957	3.30E-03	25	49
6	15-Jan-01	4	0	0	0	0	0	0					24	48
7	16-Jan-01	5	0	0	0	0	0	0					25	48
8	17-Jan-01	6	0	0	0	0	0	0					24	49
9	18-Jan-01	7	0	0	0	0	0	0					23	35
10	19-Jan-01	8	0	0	0	0	0	0		6.277	2.720	9.30E-03	24	48
13	22-Jan-01	9	0	0	0	0	0	0					24	48
14	23-Jan-01	0	0	0	0	0	0	0					24	51
15	24-Jan-01	11	0	0	0	0	0	0					24	51
16	25-Jan-01	12	0	0	0	0	0	0		0.7713	1.921	9.48E-03	25	49
17	26-Jan-01	13	0	0	0	0	0	0					24	50
20	29-Jan-01	14	0	0	0	0	0	0					25	49
21	30-Jan-01	15	0	0	0	0	0	0					25	47
22	31-Jan-01	16	0	0	0	0	0	0					24	47
23	1-Feb-01	17	0	0	0	0	0	0		1.863	2.328	4.91E-03	26	39
24	2-Feb-01	18	0	0	0	0	0	0					24	47
26	4-Feb-01	19	0	0	0	0	0	0					24	50
27	5-Feb-01	20	0	0	0	0	0	0					24	49
		Mean	**0**		**0**					**2.555**	**2.232**	**6.75E-03**	**24.3**	**47.7**
		S.D.	**0**		**0**					**2.521**	**0.374**	**3.12E-03**	**0.7**	**3.9**

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

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment Mean	
				Mean	Individual								Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)					MMAD (μm)	GSD	TMC (mg/m^3)	(°C)	(%)
0	9-Jan-01	1	0	0	0	0	0	0					24	46
1	10-Jan-01	2	0	0	0	0	0	0					24	48
2	11-Jan-01	3	0	0	0	0	0	0		5.045	2.663	6.71E-03	24	47
6	15-Jan-01	4	0	0	0	0	0	0					24	45
7	16-Jan-01	5	0	0	0	0	0	0					24	45
8	17-Jan-01	6	0	0	0	0	0	0					25	46
9	18-Jan-01	7	0	0	0	0	0	0					24	33
10	19-Jan-01	8	0	0	0	0	0	0		2.892	2.618	6.53E-03	25	44
13	22-Jan-01	9	0	0	0	0	0	0					25	45
14	23-Jan-01	0	0	0	0	0	0	0					25	46
15	24-Jan-01	11	0	0	0	0	0	0					24	47
16	25-Jan-01	12	0	0	0	0	0	0		0.8231	2.262	9.12E-03	24	46
17	26-Jan-01	13	0	0	0	0	0	0					24	46
20	29-Jan-01	14	0	0	0	0	0	0					24	47
21	30-Jan-01	15	0	0	0	0	0	0					24	45
22	31-Jan-01	16	0	0	0	0	0	0					25	44
23	1-Feb-01	17	0	0	0	0	0	0		4.006	2.464	7.15E-03	26	36
24	2-Feb-01	18	0	0	0	0	0	0					24	44
26	4-Feb-01	19	0	0	0	0	0	0					24	47
27	5-Feb-01	20	0	0	0	0	0	0					24	46
		Mean	**0**		**0**					**3.192**	**2.502**	**7.38E-03**	**24.4**	**44.7**
		S.D.	**0**		**0**					**1.807**	**0.181**	**1.19E-03**	**0.6**	**3.7**

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

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
				Mean	Individual								Mean Temperature	Humidity
			(mg/m^3)	(mg/m^3)	(mg/m^3)					MMAD (μm)	GSD	TMC (mg/m^3)	(°C)	(%)
0	9-Jan-01	1	2930	1993	2040	1820	2400	1710					23	50
1	10-Jan-01	2	2480	2018	2080	1910	1940	2140					23	51
2	11-Jan-01	3	2730	2148	2190	2070	2060	2270		5.233	2.265	8.38E-03	23	50
6	15-Jan-01	4	2730	1983	2050	1830	2090	1960					23	47
7	16-Jan-01	5	2750	1923	1980	1960	1880	1870					23	46
8	17-Jan-01	6	2760	2105	2230	2150	2100	1940					23	48
9	18-Jan-01	7	2660	2103	2080	2120	2100	2110					22	32
10	19-Jan-01	8	2560	2043	1900	2150	2060	2060		2.506	2.614	4.94E-03	23	47
13	22-Jan-01	9	2760	2083	2260	2060	2020	1990					23	49
14	23-Jan-01	0	2860	2053	2280	2120	1930	1880					23	49
15	24-Jan-01	11	2540	2158	2400	2190	2090	1950					23	49
16	25-Jan-01	12	2520	2093	2170	2070	2070	2060		0.7171	1.933	8.38E-03	24	48
17	26-Jan-01	13	2460	2088	2100	2050	2080	2120					23	49
20	29-Jan-01	14	2540	2168	2220	2140	2030	2280					24	48
21	30-Jan-01	15	2520	2108	2240	2070	2120	2000					24	45
22	31-Jan-01	16	2400	2085	2140	2090	2080	2030					23	46
23	1-Feb-01	17	2590	2128	2110	2040	2130	2230		1.952	2.258	4.86E-03	25	36
24	2-Feb-01	18	2490	2125	2130	2140	2040	2190					23	46
26	4-Feb-01	19	2540	2013	2080	1850	2060	2060					23	49
27	5-Feb-01	20	2600	2070	2080	2070	2070	2060					23	48
		Mean	**2621**		**2074**					**2.602**	**2.268**	**6.64E-03**	**23.2**	**46.7**
		S.D.	**143**		**122**					**1.907**	**0.278**	**2.01E-03**	**0.6**	**4.6**

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

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
				Mean	Individual								Mean	
			(mg/m^3)	(mg/m^3)	(mg/m^3)					MMAD (μm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	9-Jan-01	1	2930	2053	2240	2010	2360	1600					23	49
1	10-Jan-01	2	2480	2028	2070	1860	2000	2180					23	50
2	11-Jan-01	3	2730	2020	1990	2060	1980	2050		1.652	2.005	4.44E-03	24	48
6	15-Jan-01	4	2730	2070	2300	2080	1940	1960					23	47
7	16-Jan-01	5	2750	1885	1880	1830	1960	1870					23	47
8	17-Jan-01	6	2760	2183	2250	2230	2160	2090					24	48
9	18-Jan-01	7	2660	2065	2120	2070	2030	2040					23	33
10	19-Jan-01	8	2560	1928	2120	1830	1900	1860		0.8107	2.137	3.15E-03	24	47
13	22-Jan-01	9	2760	2028	2230	1990	1930	1960					24	47
14	23-Jan-01	0	2860	2035	2170	1900	2050	2020					24	48
15	24-Jan-01	11	2540	2133	2170	2180	2140	2040					23	48
16	25-Jan-01	12	2520	2103	2160	2060	2100	2090		0.7447	2.184	8.09E-03	23	47
17	26-Jan-01	13	2460	2068	2070	2070	2030	2100					23	48
20	29-Jan-01	14	2540	2125	2120	2160	2160	2060					23	47
21	30-Jan-01	15	2520	2055	2080	2080	2140	1920					24	45
22	31-Jan-01	16	2400	2043	2140	2080	2030	1920					24	45
23	1-Feb-01	17	2590	2080	2090	2000	2110	2120		1.172	2.118	3.99E-03	26	35
24	2-Feb-01	18	2490	2060	2170	2040	2030	2000					24	45
26	4-Feb-01	19	2540	1938	1870	2100	1910	1870					24	47
27	5-Feb-01	20	2600	2048	2050	2060	2020	2060					24	46
		Mean	**2621**		**2047**					**1.095**	**2.111**	**4.92E-03**	**23.7**	**45.9**
		S.D.	**143**		**121**					**0.416**	**0.076**	**2.18E-03**	**0.7**	**4.3**

Chamber Monitoring Results
Cumulative Exposure Record
Group IIIA - 10000 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)	(%)
0	9-Jan-01	1	10600	10340	9250	9710	11400	11000					23	49
1	10-Jan-01	2	10200	10180	10000	11100	9890	9710					24	50
2	11-Jan-01	3	10400	9898	8490	10000	10500	10600		2.031	2.222	3.90E-03	24	49
6	15-Jan-01	4	10200	8713	9040	6890	9340	9580					24	46
7	16-Jan-01	5	10700	9683	8610	10200	10000	9920					24	45
8	17-Jan-01	6	10200	10100	10300	9280	10600	10200					23	48
9	18-Jan-01	7	10800	10850	11300	10700	10500	10900					23	34
10	19-Jan-01	8	10500	10700	10800	10400	11100	10500		1.143	2.695	3.68E-03	23	46
13	22-Jan-01	9	10800	10570	11300	11200	9950	9830					23	49
14	23-Jan-01	0	10500	10030	10200	10100	9980	9830					23	50
15	24-Jan-01	11	10500	10120	9890	10200	10300	10100					24	48
16	25-Jan-01	12	9860	10000	10000	9920	9580	10500		0.8088	1.728	6.10E-03	24	48
17	26-Jan-01	13	10300	10250	10200	10100	10400	10300					24	48
20	29-Jan-01	14	10400	10540	10600	9640	10900	11000					24	45
21	30-Jan-01	15	9770	9825	10600	9980	9680	9040					24	44
22	31-Jan-01	16	10100	9805	10700	9740	9070	9710					24	46
23	1-Feb-01	17	10400	10110	9640	10300	10100	10400		1.221	2.081	3.59E-03	26	34
24	2-Feb-01	18	10100	9980	9520	10100	10000	10300					24	46
26	4-Feb-01	19	9970	9765	9310	9980	10000	9770					24	49
27	5-Feb-01	20	10100	10200	9980	10700	10000	10100					23	46
		Mean	**10320**		**10080**					**1.301**	**2.182**	**4.32E-03**	**23.8**	**46.0**
		S.D.	**292**		**694**					**0.518**	**0.400**	**1.20E-03**	**0.7**	**4.5**

Chamber Monitoring Results
Cumulative Exposure Record
Group IIIB - 10000 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)	(%)
0	9-Jan-01	1	10600	10020	9010	9770	11200	10100					23	50
1	10-Jan-01	2	10200	9855	9460	9460	10500	10000					23	51
2	11-Jan-01	3	10400	10580	10800	10600	11000	9920		3.730	2.850	6.44E-03	23	49
6	15-Jan-01	4	10200	9828	10100	8010	10100	11100					23	46
7	16-Jan-01	5	10700	9968	11000	9520	9710	9640					23	46
8	17-Jan-01	6	10200	10180	9740	9370	10800	10800					23	48
9	18-Jan-01	7	10800	10670	10900	9860	10500	11400					23	34
10	19-Jan-01	8	10500	9978	10000	9310	10300	10300		1.374	2.913	4.30E-03	23	47
13	22-Jan-01	9	10800	10280	10600	9610	10500	10400					24	50
14	23-Jan-01	0	10500	10850	11100	10700	10900	10700					23	50
15	24-Jan-01	11	10500	10530	10200	10600	10700	10600					23	49
16	25-Jan-01	12	9860	10190	11300	9830	9340	10300		1.604	2.747	9.74E-03	23	48
17	26-Jan-01	13	10300	10400	10300	10500	10300	10500					23	49
20	29-Jan-01	14	10400	10260	10300	9430	10900	10400					23	46
21	30-Jan-01	15	9770	9845	10600	9980	9520	9280					23	45
22	31-Jan-01	16	10100	10180	10400	10200	9520	10600					24	45
23	1-Feb-01	17	10400	9833	8250	10400	9980	10700		1.268	2.288	3.40E-03	25	35
24	2-Feb-01	18	10100	10250	9550	9860	10300	11300					24	46
26	4-Feb-01	19	9970	10040	10200	9980	10000	9980					24	49
27	5-Feb-01	20	10100	10060	9770	9770	10700	10000					23	46
		Mean	**10320**		**10190**					**1.994**	**2.700**	**5.97E-03**	**23.3**	**46.5**
		S.D.	**292**		**639**					**1.166**	**0.283**	**2.82E-03**	**0.6**	**4.5**

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

Day	Date	Exposure Number	Nominal	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
				Mean	Individual								Mean	
			(mg/m^3)	(mg/m^3)	(mg/m^3)					MMAD (μm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	9-Jan-01	1	20900	20630	20500	21000	19900	21100					24	50
1	10-Jan-01	2	20400	21830	23300	21800	21300	20900					24	52
2	11-Jan-01	3	21200	20700	20500	20100	20200	22000		1.020	2.154	4.67E-03	24	51
6	15-Jan-01	4	20700	20750	20400	22100	20300	20200					25	45
7	16-Jan-01	5	21200	19000	18000	18100	19800	20100					24	46
8	17-Jan-01	6	21600	21330	21900	22100	20600	20700					24	48
9	18-Jan-01	7	20200	20530	20200	20500	19800	21600					24	35
10	19-Jan-01	8	20200	20530	21300	19800	20800	20200		0.8457	2.105	4.18E-03	24	48
13	22-Jan-01	9	19600	19700	20400	19400	19400	19600					24	50
14	23-Jan-01	0	20300	20730	20800	21300	20800	20000					24	50
15	24-Jan-01	11	19900	20530	21100	20600	20300	20100					24	51
16	25-Jan-01	12	19700	20850	21900	20000	20400	21100		0.8621	2.170	8.35E-03	24	51
17	26-Jan-01	13	20300	20800	20900	21900	20200	20200					24	51
20	29-Jan-01	14	20200	21250	21000	20300	23000	20700					24	46
21	30-Jan-01	15	19800	20380	21200	19600	20800	19900					24	48
22	31-Jan-01	16	20400	20500	19900	20800	20800	20500					24	47
23	1-Feb-01	17	20100	20030	20000	19100	20600	20400		2.722	2.980	7.48E-03	26	37
24	2-Feb-01	18	20800	20400	19300	20100	18700	23500					24	47
26	4-Feb-01	19	19500	20050	21600	19200	18800	20600					24	50
27	5-Feb-01	20	19800	20200	19500	20300	20400	20600					24	48
		Mean	**20340**		**20530**					**1.362**	**2.352**	**6.17E-03**	**24.2**	**47.6**
		S.D.	**575**		**996**					**0.910**	**0.419**	**2.06E-03**	**0.5**	**4.4**

Chamber Monitoring Results
Cumulative Exposure Record
Group IVB - 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)	(%)
0	9-Jan-01	1	20900	19200	18700	18800	18700	20600					24	55
1	10-Jan-01	2	20400	18750	18000	19500	18100	19400					24	54
2	11-Jan-01	3	21200	20530	20300	19600	19600	22600		1.669	2.266	5.18E-03	24	55
6	15-Jan-01	4	20700	18450	19200	18000	18100	18500					24	49
7	16-Jan-01	5	21200	20180	21000	18700	20300	20700					24	50
8	17-Jan-01	6	21600	21650	22800	22800	20800	20200					25	50
9	18-Jan-01	7	20200	21700	23500	20600	20400	22300					25	36
10	19-Jan-01	8	20200	21180	22800	21000	20700	20200		0.7292	1.765	3.85E-03	25	50
13	22-Jan-01	9	19600	20050	21100	19600	19700	19800					25	51
14	23-Jan-01	0	20300	21080	20900	21500	21400	20500					25	52
15	24-Jan-01	11	19900	21480	21500	21400	22000	21000					24	53
16	25-Jan-01	12	19700	20350	19800	20200	20500	20900		2.122	3.118	1.19E-03	24	53
17	26-Jan-01	13	20300	21030	22500	18800	21200	21600					24	54
20	29-Jan-01	14	20200	21380	24000	22500	18600	20400					24	50
21	30-Jan-01	15	19800	20300	19900	19800	21400	20100					24	50
22	31-Jan-01	16	20400	20180	19300	20900	20500	20000					25	51
23	1-Feb-01	17	20100	20400	20100	19900	20900	20700		1.175	1.818	4.30E-03	26	36
24	2-Feb-01	18	20800	20500	19500	20000	22200	20300					25	50
26	4-Feb-01	19	19500	19500	18700	19700	19800	19800					25	51
27	5-Feb-01	20	19800	20450	21400	20300	20500	19600					25	50
		Mean	**20340**		**20420**					**1.424**	**2.242**	**3.63E-03**	**24.6**	**50.0**
		S.D.	**575**		**1292**					**0.603**	**0.626**	**1.72E-03**	**0.6**	**5.1**

TABLE B

BGVC: 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 WEEKLY CLINICAL OBSERVATIONS

	GROUP#	WEEK 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

TABLE B

BGVC: 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 WEEKLY CLINICAL OBSERVATIONS

	GROUP#	WEEK 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

TABLE C

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

MALES

MEAN BODY WEIGHTS (GRAMS)

DOSE GROUP:		I	II	III	IV	V	VI
DOSE LEVEL (mg/m3):		0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK -1	MEAN	199	197	199	199	199	194
	S.D.	5.7	6.7	7.6	9.3	9.5	20.6
	N	5	5	5	5	5	5
WEEK 0	MEAN	254	258	258	248	257	248
	S.D.	3.6	6.3	11.2	6.0	13.0	22.7
	N	5	5	5	5	5	5
WEEK 1	MEAN	297	304	305	291	305	303
	S.D.	9.0	15.1	8.7	3.6	20.4	24.7
	N	5	5	5	5	5	5
WEEK 2	MEAN	333	337	336	325	346	342
	S.D.	14.8	25.1	9.7	8.3	23.0	37.0
	N	5	5	5	5	5	5
WEEK 3	MEAN	355	365	362	353	378	374
	S.D.	18.8	28.4	8.2	14.2	25.7	42.2
	N	5	5	5	5	5	5

No statistically significant differences

TABLE C

BGVC: 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	VI
	DOSE LEVEL (mg/m3):	0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK -1	MEAN	158	158	159	159	158	157
	S.D.	7.6	7.7	6.9	7.1	7.9	16.1
	N	5	5	5	5	5	5
WEEK 0	MEAN	183	187	190	187	190	179
	S.D.	11.2	9.8	2.4	15.6	7.5	10.2
	N	5	5	5	5	5	5
WEEK 1	MEAN	196	207	209	208	222	207
	S.D.	19.6	11.2	4.1	12.1	8.6	12.3
	N	5	5	5	5	5	5
WEEK 2	MEAN	214	226	229	225	234	218
	S.D.	29.0	15.5	9.8	18.0	12.8	9.5
	N	5	5	5	5	5	5
WEEK 3	MEAN	229	241	248	245	245	240
	S.D.	27.4	19.0	11.7	20.5	15.3	9.4
	N	5	5	5	5	5	5

No statistically significant differences

Huntingdon Life Sciences 00-6125O
Genotoxicity Sub-Group

TABLE D

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

MALES

MEAN BODY WEIGHT CHANGE (GRAMS)

DOSE GROUP:		I	II	III	IV	V	VI
DOSE LEVEL (mg/m3):		0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK 0 TO 1	MEAN	43	46	47	42	48	55
	S.D.	6.4	10.7	6.4	4.2	7.9	2.5
	N	5	5	5	5	5	5
WEEK 0 TO 2	MEAN	79	78	79	77	89	94
	S.D.	11.7	20.4	12.6	13.3	11.9	17.2
	N	5	5	5	5	5	5
WEEK 0 TO 3	MEAN	102	107	105	104	121	126
	S.D.	16.2	23.1	12.4	19.2	15.7	22.8
	N	5	5	5	5	5	5

No statistically significant differences

TABLE D

BGVC: 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	VI
DOSE LEVEL (mg/m3):			0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK 0 TO 1	MEAN		13	20	20	21	32*	27
	S.D.		18.9	2.1	5.5	6.3	2.9	3.4
	N		5	5	5	5	5	5
WEEK 0 TO 2	MEAN		30	40	39	38	44	39
	S.D.		29.2	7.8	11.3	4.9	9.8	6.6
	N		5	5	5	5	5	5
WEEK 0 TO 3	MEAN		46	55	59	58	55	61
	S.D.		26.5	12.4	12.6	8.7	11.8	6.8
	N		5	5	5	5	5	5

Statistical key: * = p<0.05

TABLE E

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

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

	DOSE GROUP:	I	II	III	IV	V	VI
	DOSE LEVEL (mg/m3):	0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK 0	MEAN	103	106	107	102	106	106
	S.D.	7.4	3.7	5.9	2.9	4.7	3.4
	N	5	5	5	5	5	5
WEEK 1	MEAN	82	87	88	84	87	89
	S.D.	2.5	6.2	4.9	3.2	1.3	3.7
	N	5	5	5	5	5	5
WEEK 2	MEAN	72	76	77	74	79	77
	S.D.	8.7	4.0	5.3	3.5	2.2	4.4
	N	5	5	5	5	5	5
WEEK 3	MEAN	68	70	68	67	71	69
	S.D.	3.7	1.9	3.3	3.1	3.2	4.1
	N	5	5	5	5	5	5

No statistically significant differences

TABLE E

BGVC: 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	VI
	DOSE LEVEL (mg/m3):	0	2,000	10,000	20,000	SCE +CONTROL	MICRO +CONTROL
WEEK 0	MEAN	104	105	106	107	111	105
	S.D.	5.2	9.8	5.0	5.4	4.8	10.1
	N	5	5	5	5	5	5
WEEK 1	MEAN	86	89	90	92	99	94
	S.D.	8.9	7.1	4.9	0.8	7.3	7.6
	N	5	5	5	5	5	5
WEEK 2	MEAN	77	83	86	87	84	88
	S.D.	10.9	8.6	3.3	5.7	6.6	6.7
	N	5	5	4	5	4	5
WEEK 3	MEAN	80	81	84	83	78	82
	S.D.	3.4	8.6	6.3	2.3	6.7	4.9
	N	4	5	5	5	4	5

No statistically significant differences

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP I 0 mg/m3

ANIMAL#	OBSERVATIONS	WEEK 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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP II 2,000 mg/m3

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP III 10,000 mg/m3

ANIMAL#	OBSERVATIONS	WEEK 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

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP IV 20,000 mg/m3

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
4031	WITHIN NORMAL LIMITS		P
4032	WITHIN NORMAL LIMITS		P
4033	WITHIN NORMAL LIMITS		P
4034	WITHIN NORMAL LIMITS		P
4035	WITHIN NORMAL LIMITS		P

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP V SCE +CONTROL

ANIMAL#	OBSERVATIONS	WEEK OF STUDY - 1
5031	WITHIN NORMAL LIMITS	P
5032	WITHIN NORMAL LIMITS	P
5033	WITHIN NORMAL LIMITS	P
5034	WITHIN NORMAL LIMITS	P
5035	WITHIN NORMAL LIMITS	P

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

MALES GROUP VI MICRO +CONTROL

ANIMAL#	OBSERVATIONS	WEEK 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

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP I 0 mg/m3

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
1541	WITHIN NORMAL LIMITS		P
1542	WITHIN NORMAL LIMITS		P
1543	WITHIN NORMAL LIMITS		P
1544	WITHIN NORMAL LIMITS		P
1545	WITHIN NORMAL LIMITS		P

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP II 2,000 mg/m3

ANIMAL#	OBSERVATIONS	WEEK 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

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP III 10,000 mg/m3

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

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP IV 20,000 mg/m3

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
4541	WITHIN NORMAL LIMITS		P
4542	WITHIN NORMAL LIMITS		P
4543	WITHIN NORMAL LIMITS		P
4544	WITHIN NORMAL LIMITS		P
4545	WITHIN NORMAL LIMITS		P

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

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP V SCE +CONTROL

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
5541	WITHIN NORMAL LIMITS		P
5542	WITHIN NORMAL LIMITS		P
5543	WITHIN NORMAL LIMITS		P
5544	WITHIN NORMAL LIMITS		P
5545	WITHIN NORMAL LIMITS		P

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

Huntingdon Life Sciences 00-61250
Genotoxicity Sub-Group

TABLE F

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

INDIVIDUAL WEEKLY CLINICAL OBSERVATIONS

FEMALES GROUP VI MICRO +CONTROL

ANIMAL#	OBSERVATIONS	WEEK OF STUDY	- 1
6541	WITHIN NORMAL LIMITS		P
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

TABLE G

BGVC: 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)

MALES GROUP I 0 mg/m3

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
1031	201	255	305	349	380
1032	201	250	295	319	330
1033	208	257	305	345	360
1034	195	256	297	335	362
1035	193	250	283	317	344
MEAN	199	254	297	333	355
S.D.	5.7	3.6	9.0	14.8	18.8
N	5	5	5	5	5

TABLE G

BGVC: 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)

MALES GROUP II 2,000 mg/m3

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
2021	194	256	301	336	367
2022	188	250	292	315	333
2023	199	267	330	379	411
2024	206	259	298	328	359
2025	201	261	297	324	356
MEAN	197	258	304	337	365
S.D.	6.7	6.3	15.1	25.1	28.4
N	5	5	5	5	5

TABLE G

BGVC: 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)

MALES GROUP III 10,000 mg/m3

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
3021	198	254	301	325	353
3022	189	244	292	331	360
3023	195	256	312	351	375
3024	209	274	312	337	365
3025	202	260	308	339	359
MEAN	199	258	305	336	362
S.D.	7.6	11.2	8.7	9.7	8.2
N	5	5	5	5	5

TABLE G

BGVC: 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)

MALES GROUP IV 20,000 mg/m3

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
4031	197	249	292	332	365
4032	210	254	289	315	338
4033	185	238	285	334	369
4034	198	251	294	327	340
4035	204	251	293	319	352
MEAN	199	248	291	325	353
S.D.	9.3	6.0	3.6	8.3	14.2
N	5	5	5	5	5

TABLE G

BGVC: 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)

MALES GROUP V SCE +CONTROL

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
5031	200	263	314	353	386
5032	184	235	271	308	337
5033	210	265	314	348	374
5034	203	265	324	370	406
5035	197	256	303	351	386
MEAN	199	257	305	346	378
S.D.	9.5	13.0	20.4	23.0	25.7
N	5	5	5	5	5

TABLE G

BGVC: 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)

MALES GROUP VI MICRO +CONTROL

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
6031	177	226	276	300	326
6032	179	230	284	308	332
6033	182	241	296	351	388
6034	215	274	330	383	419
6035	219	271	328	369	404
MEAN	194	248	303	342	374
S.D.	20.6	22.7	24.7	37.0	42.2
N	5	5	5	5	5

TABLE G

BGVC: 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
1541	150	170	187	204	215
1542	153	173	204	230	244
1543	163	195	217	234	252
1544	168	191	207	233	248
1545	159	186	167	167	188
MEAN	158	183	196	214	229
S.D.	7.6	11.2	19.6	29.0	27.4
N	5	5	5	5	5

TABLE G

BGVC: 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
2531	159	177	198	208	218
2532	162	188	207	235	256
2533	152	186	206	233	251
2534	148	181	200	212	224
2535	167	202	226	244	258
MEAN	158	187	207	226	241
S.D.	7.7	9.8	11.2	15.5	19.0
N	5	5	5	5	5

TABLE G

BGVC: 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
3531	152	188	208	230	243
3532	158	193	211	230	254
3533	169	187	216	242	264
3534	161	190	205	228	247
3535	154	191	207	215	233
MEAN	159	190	209	229	248
S.D.	6.9	2.4	4.1	9.8	11.7
N	5	5	5	5	5

Huntingdon Life Sciences 00-6125O
Genotoxicity Sub-Group

TABLE G

BGVC: 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
4541	169	196	210	232	255
4542	153	167	192	199	211
4543	163	205	225	242	260
4544	160	192	208	238	259
4545	152	176	205	214	240
MEAN	159	187	208	225	245
S.D.	7.1	15.6	12.1	18.0	20.5
N	5	5	5	5	5

TABLE G

BGVC: 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 SCE +CONTROL

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
5541	155	182	216	235	249
5542	156	195	230	226	243
5543	165	185	218	225	235
5544	148	187	215	228	229
5545	167	201	233	256	268
MEAN	158	190	222	234	245
S.D.	7.9	7.5	8.6	12.8	15.3
N	5	5	5	5	5

TABLE G

BGVC: 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 VI MICRO +CONTROL

	WEEK OF STUDY				
ANIMAL#	-1	0	1	2	3
6541	142	170	200	217	239
6542	146	174	199	218	241
6543	147	171	194	207	225
6544	171	192	223	233	250
6545	177	188	216	218	244
MEAN	157	179	207	218	240
S.D.	16.1	10.2	12.3	9.5	9.4
N	5	5	5	5	5

TABLE H

BGVC: 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 0 mg/m3

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
1031	50	94	124
1032	44	68	80
1033	48	88	104
1034	40	79	106
1035	34	67	95
MEAN	43	79	102
S.D.	6.4	11.7	16.2
N	5	5	5

TABLE H

BGVC: 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 STUDY		
ANIMAL#	0-1	0-2	0-3
2021	46	81	111
2022	42	65	84
2023	64	113	144
2024	40	69	101
2025	37	63	95
MEAN	46	78	107
S.D.	10.7	20.4	23.1
N	5	5	5

Huntingdon Life Sciences 00-6125O
Genotoxicity Sub-Group

TABLE H

BGVC: 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 III 10,000 mg/m3

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
3021	47	71	99
3022	48	87	116
3023	56	95	119
3024	38	63	90
3025	48	78	99
MEAN	47	79	105
S.D.	6.4	12.6	12.4
N	5	5	5

TABLE H

BGVC: 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 20,000 mg/m3

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
4031	43	83	116
4032	35	61	84
4033	47	96	131
4034	43	76	89
4035	43	69	102
MEAN	42	77	104
S.D.	4.2	13.3	19.2
N	5	5	5

TABLE H

BGVC: 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 V SCE +CONTROL

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
5031	51	89	123
5032	37	74	102
5033	49	83	109
5034	58	105	141
5035	47	95	130
MEAN	48	89	121
S.D.	7.9	11.9	15.7
N	5	5	5

TABLE H

BGVC: 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 VI MICRO +CONTROL

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
6031	51	74	101
6032	54	78	102
6033	56	110	148
6034	56	110	145
6035	57	98	133
MEAN	55	94	126
S.D.	2.5	17.2	22.8
N	5	5	5

TABLE H

BGVC: 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
1541	17	34	45
1542	31	57	71
1543	22	39	57
1544	16	42	56
1545	-19	-19	2
MEAN	13	30	46
S.D.	18.9	29.2	26.5
N	5	5	5

TABLE H

BGVC: 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
2531	21	31	41
2532	19	47	68
2533	20	47	65
2534	19	32	43
2535	24	41	55
MEAN	20	40	55
S.D.	2.1	7.8	12.4
N	5	5	5

TABLE H

BGVC: 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
3531	21	42	56
3532	18	37	61
3533	29	56	77
3534	15	38	57
3535	17	24	42
MEAN	20	39	59
S.D.	5.5	11.3	12.6
N	5	5	5

TABLE H

BGVC: 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
4541	14	36	59
4542	25	32	45
4543	20	37	55
4544	16	46	67
4545	30	38	64
MEAN	21	38	58
S.D.	6.3	4.9	8.7
N	5	5	5

TABLE H

BGVC: 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 SCE +CONTROL

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
5541	33	53	67
5542	35	32	48
5543	33	40	49
5544	27	41	42
5545	32	55	68
MEAN	32	44	55
S.D.	2.9	9.8	11.8
N	5	5	5

TABLE H

BGVC: 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 VI MICRO +CONTROL

	WEEK OF STUDY		
ANIMAL#	0-1	0-2	0-3
6541	30	47	69
6542	25	44	67
6543	23	36	54
6544	31	41	58
6545	28	30	56
MEAN	27	39	61
S.D.	3.4	6.6	6.8
N	5	5	5

TABLE I

BGVC: 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 mg/m3

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
1031	98	78	73	66
1032	100	82	73	67
1033	97	82	57	65
1034	115	85	79	74
1035	103	83	78	70
MEAN	103	82	72	68
S.D.	7.4	2.5	8.7	3.7
N	5	5	5	5

TABLE I

BGVC: 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 II 2,000 mg/m3

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
2021	106	88	78	72
2022	103	89	76	69
2023	109	94	82	72
2024	101	77	72	67
2025	110	86	74	70
MEAN	106	87	76	70
S.D.	3.7	6.2	4.0	1.9
N	5	5	5	5

TABLE I

BGVC: 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 III 10,000 mg/m3

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
3021	106	88	74	67
3022	108	85	78	70
3023	115	96	85	73
3024	105	84	71	64
3025	99	89	75	68
MEAN	107	88	77	68
S.D.	5.9	4.9	5.3	3.3
N	5	5	5	5

TABLE I

BGVC: 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/m3

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
4031	104	87	72	67
4032	98	79	69	62
4033	104	86	78	69
4034	101	85	76	68
4035	105	85	75	70
MEAN	102	84	74	67
S.D.	2.9	3.2	3.5	3.1
N	5	5	5	5

TABLE I

BGVC: 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 V SCE +CONTROL

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
5031	106	86	78	72
5032	109	87	80	71
5033	98	85	76	67
5034	106	88	78	70
5035	110	89	82	76
MEAN	106	87	79	71
S.D.	4.7	1.3	2.2	3.2
N	5	5	5	5

TABLE I

BGVC: 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 VI MICRO +CONTROL

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
6031	111	93	79	73
6032	106	87	72	63
6033	107	92	82	73
6034	107	88	78	68
6035	101	84	73	68
MEAN	106	89	77	69
S.D.	3.4	3.7	4.4	4.1
N	5	5	5	5

TABLE I

BGVC: 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
1541	101	88	78	78
1542	104	98	84	78
1543	111	87	81	81
1544	97	84	82	SF
1545	106	74	58	85
MEAN	104	86	77	80
S.D.	5.2	8.9	10.9	3.4
N	5	5	5	4

SF=Spilled Feeder

TABLE I

BGVC: 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
2531	97	86	74	75
2532	103	89	87	81
2533	121	100	96	96
2534	106	87	80	80
2535	96	81	80	75
MEAN	105	89	83	81
S.D.	9.8	7.1	8.6	8.6
N	5	5	5	5

TABLE I

BGVC: 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
3531	109	87	85	80
3532	110	91	91	92
3533	106	97	SF	84
3534	98	84	83	77
3535	109	90	86	89
MEAN	106	90	86	84
S.D.	5.0	4.9	3.3	6.3
N	5	5	4	5

SF=Spilled Feeder

TABLE I

BGVC: 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
4541	110	91	91	84
4542	99	91	78	79
4543	114	91	89	81
4544	107	92	92	85
4545	106	93	84	84
MEAN	107	92	87	83
S.D.	5.4	0.8	5.7	2.3
N	5	5	5	5

Huntingdon Life Sciences 00-61250
Genotoxicity Sub-Group

TABLE I

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

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP V SCE +CONTROL

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
5541	107	94	87	82
5542	105	96	75	69
5543	112	112	SF	SF
5544	117	96	83	78
5545	112	97	90	84
MEAN	111	99	84	78
S.D.	4.8	7.3	6.6	6.7
N	5	5	4	4

SF=Spilled Feeder

TABLE I

BGVC: 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 VI MICRO +CONTROL

	WEEK OF STUDY			
ANIMAL#	0	1	2	3
6541	120	106	98	90
6542	104	88	82	80
6543	107	94	91	84
6544	104	94	84	78
6545	91	86	83	78
MEAN	105	94	88	82
S.D.	10.1	7.6	6.7	4.9
N	5	5	5	5

TABLE J

BGVC: 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

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1031	TERMINAL SACRIFICE	6-FEB-01	4	28
1032	TERMINAL SACRIFICE	6-FEB-01	4	28
1033	TERMINAL SACRIFICE	6-FEB-01	4	28
1034	TERMINAL SACRIFICE	6-FEB-01	4	28
1035	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 II 2,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2021	TERMINAL SACRIFICE	6-FEB-01	4	28
2022	TERMINAL SACRIFICE	6-FEB-01	4	28
2023	TERMINAL SACRIFICE	6-FEB-01	4	28
2024	TERMINAL SACRIFICE	6-FEB-01	4	28
2025	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 III 10,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3021	TERMINAL SACRIFICE	6-FEB-01	4	28
3022	TERMINAL SACRIFICE	6-FEB-01	4	28
3023	TERMINAL SACRIFICE	6-FEB-01	4	28
3024	TERMINAL SACRIFICE	6-FEB-01	4	28
3025	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 IV 20,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4031	TERMINAL SACRIFICE	6-FEB-01	4	28
4032	TERMINAL SACRIFICE	6-FEB-01	4	28
4033	TERMINAL SACRIFICE	6-FEB-01	4	28
4034	TERMINAL SACRIFICE	6-FEB-01	4	28
4035	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 V SCE +CONTROL

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
5031	TERMINAL SACRIFICE	6-FEB-01	4	28
5032	TERMINAL SACRIFICE	6-FEB-01	4	28
5033	TERMINAL SACRIFICE	6-FEB-01	4	28
5034	TERMINAL SACRIFICE	6-FEB-01	4	28
5035	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 VI MICRO +CONTROL

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
6031	TERMINAL SACRIFICE	6-FEB-01	4	28
6032	TERMINAL SACRIFICE	6-FEB-01	4	28
6033	TERMINAL SACRIFICE	6-FEB-01	4	28
6034	TERMINAL SACRIFICE	6-FEB-01	4	28
6035	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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
1541	TERMINAL SACRIFICE	6-FEB-01	4	28
1542	TERMINAL SACRIFICE	6-FEB-01	4	28
1543	TERMINAL SACRIFICE	6-FEB-01	4	28
1544	TERMINAL SACRIFICE	6-FEB-01	4	28
1545	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 II 2,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2531	TERMINAL SACRIFICE	6-FEB-01	4	28
2532	TERMINAL SACRIFICE	6-FEB-01	4	28
2533	TERMINAL SACRIFICE	6-FEB-01	4	28
2534	TERMINAL SACRIFICE	6-FEB-01	4	28
2535	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 III 10,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3531	TERMINAL SACRIFICE	6-FEB-01	4	28
3532	TERMINAL SACRIFICE	6-FEB-01	4	28
3533	TERMINAL SACRIFICE	6-FEB-01	4	28
3534	TERMINAL SACRIFICE	6-FEB-01	4	28
3535	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 IV 20,000 mg/m3

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4541	TERMINAL SACRIFICE	6-FEB-01	4	28
4542	TERMINAL SACRIFICE	6-FEB-01	4	28
4543	TERMINAL SACRIFICE	6-FEB-01	4	28
4544	TERMINAL SACRIFICE	6-FEB-01	4	28
4545	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 V SCE +CONTROL

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
5541	TERMINAL SACRIFICE	6-FEB-01	4	28
5542	TERMINAL SACRIFICE	6-FEB-01	4	28
5543	TERMINAL SACRIFICE	6-FEB-01	4	28
5544	TERMINAL SACRIFICE	6-FEB-01	4	28
5545	TERMINAL SACRIFICE	6-FEB-01	4	28

TABLE J

BGVC: 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 VI MICRO +CONTROL

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
6541	TERMINAL SACRIFICE	6-FEB-01	4	28
6542	TERMINAL SACRIFICE	6-FEB-01	4	28
6543	TERMINAL SACRIFICE	6-FEB-01	4	28
6544	TERMINAL SACRIFICE	6-FEB-01	4	28
6545	TERMINAL SACRIFICE	6-FEB-01	4	28