Data Requirement

EPA OPPTS 870.3550 OECD 421

STUDY NO. 03-4246

PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Final Report

VOLUME II OF II

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1. INTRODUCTION

This appendix presents the methodology for exposure generation, monitoring and results.

2. MATERIALS AND METHODS

2.1. HUSBANDRY DURING EXPOSURE PERIODS

2.1.1. HOUSING

Animals were individually housed in polycarbonate tubes attached to a cast aluminum and alloy 40 Liter nose-only exposure chamber. The placement of the tubes in the nose-only chamber was rotated at each exposure to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.1.2. FEED

None was provided during exposure.

2.1.3. WATER

None was provided during exposure.

2.1.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were recorded every half-hour during exposure and maintained, to the maximum extent possible, within the ranges presented below. Excursions outside the specified range did not affect the integrity of the study.

Temperature

Desired:

20 to 24°C

Actual:

18 to 24°C

Relative Humidity

Desired:

40 to 60%

Actual:

10 to 68%

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2.2. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATIONS

2.2.1. ROUTE OF ADMINISTRATION

Inhalation, as a dust, via nose-only exposures.

2.2.2. TEST SUBSTANCE ADMINISTRATION

The test substance was administered as a dust in the breathing air of the animals by nose-only inhalation exposure. The test atmosphere was generated by an appropriate procedure (Wright Dust Feeder with a cyclone pre-collector) determined during pre-study trials. The trials were performed (at least two 6-hour periods) to select the optimal set of conditions to generate a stable and uniform atmosphere at the target exposure levels with a mass median aerodynamic diameter of 1.0 - 3.0 microns.

2.2.3. TARGET EXPOSURE LEVELS

Group 1 - 0 mg/m^3

Group 2 - 30 mg/m^3

Group $3 - 100 \text{ mg/m}^3$

Group 4 - 300 mg/m^3

2.2.4. DURATION AND FREQUENCY OF ADMINISTRATION

Male rats were exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of male rats continued during the mating and post-mating periods until euthanized on the day after a minimum exposure of 28 days. Female rats (12/group) were exposed once daily, seven days/week for at least two weeks prior to mating initiation. Female rats continued to be treated once daily during the mating period, but were separated from the males during actual exposure. Once mated, female rats were treated once daily during gestation (days 0-19). Female rats without evidence of mating continued to be treated for up to 19 days (6 hours/day) following completion of the mating period and then held for up to an additional 7 days. In the event that female rats without evidence of mating appeared pregnant (based on observations and body

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weights), exposure was terminated on the estimated Gestation Day 19.

2.2.5. CHAMBER OPERATIONS

The nose-only exposure chambers had a total volume of 40 Liters each and were operated dynamically under slight positive pressure at a flow rate of 25.0 Liters per minute (Lpm) for all groups.

The final airflow rate was calculated to provide one complete air change (calculated by dividing the chamber volume by the airflow rate) approximately every 1.6 minutes and a T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of approximately 8 minutes for all 4 groups.

This chamber size and airflow rate was considered adequate to maintain the oxygen level at 19% or higher. At the end of each exposure, all animals remained in the chamber for a minimum of 10 minutes. During this time, each chamber was operated at the same flow rate as used during the exposure. Recordings of chamber airflow rate and static pressure were made at the initiations of the exposures and every half-hour during the exposures.

The chamber was exhausted (via a 1" tubing) through the in-house filtering system, which consisted of a coarse filter, a HEPA filter and an activated charcoal bed. To prevent a static charge from building up, the chamber was grounded.

The nose-only chamber and generation system were enclosed in a 10 m³ glass and stainless steel chamber. Due to high temperatures, the 10 m³ chambers were equipped with a portable room air conditioner to maintain proper chamber environments.

Refer to Figures 1 and 2, and Table III for equipment details.

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2.2.6. EXPOSURE PROCEDURE

Group 1

House line air was delivered from a regulator and a backpressure gauge, via ¼" tubing to a "Y" tube, which split the airflow into the generation and dilution systems. The generation air (20.0 Lpm) was directed, via ¼" tubing, through a flowmeter, regulated by a metering valve, then into a backpressure gauge connected to the top of a cast aluminum and alloy exposure chamber equipped with polycarbonate nose-only tubes. The dilution air (5.0 Lpm) was directed, via ¼" tubing, to a flowmeter regulated by a metering valve into the dilution port at the top of the chamber.

Groups 2-4

After being sieved through a stainless steel sieve, the test substance was packed to 800 psi into dust feeder cups (small diameter) using a press. The cup was then mounted onto the dust feeder, which was controlled using a speed selector. The initial exposure started with the dust feeder at the speed settings listed below:

Group	Speed Setting (rpm)
2	0.100
3	0.290
4	0.950

House line air was delivered from a regulator and a backpressure gauge into the inlet of a gas drying unit, via 1/4" tubing to a "Y" tube, which split the airflow into the generation and dilution systems. The generation air (20.0 Lpm) was directed, via 1/4" tubing, through a flowmeter, regulated by a metering valve. then into a backpressure gauge connected to a Wright Dust feeder, via 1/4" tubing. The test substance was then directed into the inlet of a brass cyclone, via ½" tubing (for Groups 2 and 3 only). The test substance laden air was then directed into the top of a cast aluminum and alloy exposure chamber equipped polycarbonate nose-only tubes. The dilution air (5.0 Lpm) was

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directed, via ¼" tubing, to a flowmeter regulated by a metering valve into the dilution port at the top of the chamber.

Refer to Figures 1 and 2, and Table III for equipment details.

2.3. EXPOSURE CONCENTRATION DETERMINATION

2.3.1. NOMINAL CONCENTRATION

A nominal exposure concentration was calculated daily. The flow of air through the chambers was monitored using appropriate calibrated equipment. The nominal concentrations in mg/m³ were determined by weighing the generation apparatus containing the test substance before and after the exposure and dividing the difference in these weights by the total volume of air used during the exposure (flowrate multiplied by total exposure time).

Calculation

Conc (mg/m³) = $\frac{\text{amount consumed (g) x 1000 mg/g x 1000 L/m}^3}{\text{exposure duration (min) x airflow (Lpm)}}$

2.3.2. CHAMBER SAMPLING

Samples for determination of the exposure levels were withdrawn from the breathing zone in the exposure chambers through glass fiber filters mounted open-faced in a filter holder. Samples were withdrawn at least four times per exposure from the normal sampling portal. The filter papers were weighed before and after sample collection, and the gravimetric concentration in mg/m³ was calculated by dividing the weight difference by the volume of air sampled.

Calculation

Conc (mg/m³) = $\frac{\text{amount collected (mg) x 1000 (L/m}^3)}{\text{sample duration (min) x sample airflow (Lpm)}}$

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The sample flowrates, durations and volumes are summarized below:

Group	Sample Flowrate (Lpm)	Sample Duration (min)	Sample Volume (L)
1	10	30	300
2	10	30	300
3	10	10	100
4	10	3	30

See Table III (Inhalation Report) for equipment list.

2.3.3. PARTICLE SIZE DISTRIBUTION

Group 1

Particle size distribution measurements were performed once during each week of exposure using a TSI Aerodynamic Particle Sizer. The samples were drawn for 20 seconds at a rate of 5.0 Lpm. A computer was used to program the system to the appropriate settings prior to sampling. The particle size distributions were calculated by the computer and printed out. The mass median aerodynamic diameter, geometric standard deviation and total mass concentration were calculated. For comparison, room air samples were similarly collected at least once each week.

See Table III (Inhalation Report) for equipment list.

Groups 2, 3 and 4

Samples for particle size distribution assessment were drawn at least once per chamber during each week of exposure using a cascade impactor. The mass median aerodynamic diameter, the geometric standard deviation and the percent ≤1, 3 and 10 microns were calculated based on the amount of material collected on the six impactor stages (greased stainless steel slides) and a final filter

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stage using a graphical analysis of an assumed lognormal distribution.

The sample flowrates and durations are summarized below:

Group	Sample Flowrate (Lpm)	Sample Duration (min)	Sample Volume (L)			
2	12.6	30	378			
3	12.6	10	126			
4	12.6	3	37.8			

See Table III (Inhalation Report) for equipment list.

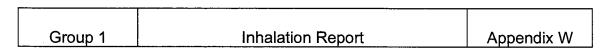
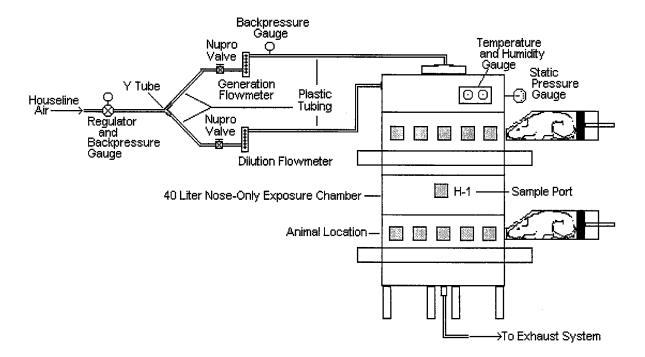


Figure 1
Diagram of 40 Liter Nose-Only Exposure
Chamber and Generation System^a



^aSystem enclosed in 10 m³ glass and stainless steel chamber.

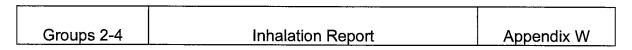
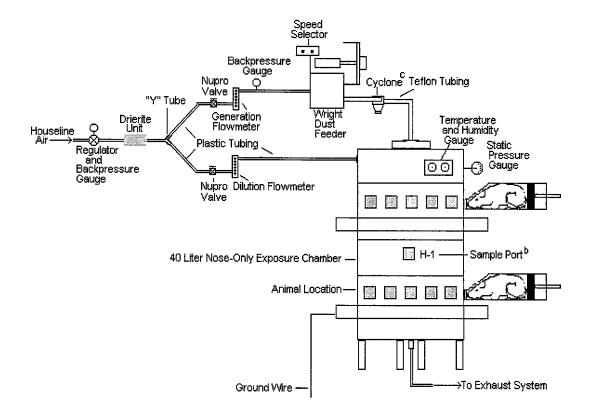


Figure 2
Diagram of 40 Liter Nose-Only Exposure
Chamber and Generation System^a



^cA cyclone was not used for Group 4.

^aSystem enclosed in 10 m³ glass and stainless steel chamber.

^b The distribution sample port H-2 was located on the side opposite the H-1 port. Distribution sample ports H-3 and H-4 were located in a similar configuration relative to the upper animal location.

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			Summ	ary of l	Tab n-Cha		Observa	ations						
Exposure Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13
Group 1 – 0 mg/m³														
Within Normal Limits	24	24	24	24	24	24	24	24	24	24	24	24	24	24
Group 2 – 30 mg/m³														
Within Normal Limits	24	24	24	24	24	24	24	24	24	24	24	24	24	24
Group 3 – 100 mg/m³														
Within Normal Limits Black/Test Material on Fur	24 0	24 0	24 0	24 0	24 0	24 0	24 0	24 0	24 0	24 0	21 3	21 3	21 3	20 4
Group 4 – 300 mg/m³														
Within Normal Limits	24	24	24	24	24	24	24	24	24	24	24	24	24	24

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		•			Table l		•						
		S	ummai	y of In-	Chamb	er Obs	ervatio	ns					
Exposure Day	14	15	16	17	18	19	20	21	22	23	24	25	26
Group 1 – 0 mg/m³													
Within Normal Limits	24	24	24	24	24	24	24	24	24	24	24	24	24
Group 2 – 30 mg/m³													
Within Normal Limits	24	24	24	24	24	24	24	24	24	24	24	24	24
Group 3 – 100 mg/m³													
Within Normal Limits Black/Test Material on Fur	20 4	21 3	21 3	21 3	21 3	21 3	21 3	24 0	21 3	21 3	21 3	20 4	21 3
Group 4 – 300 mg/m ³													
Within Normal Limits Black/Test Material on Fur	24 0	24 0	24 0	21 3	21 3	21 3	21 3	22 2	22 2	22 2	21 3	22 2	21 3

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			Summa	ary of I	Tab)hean/	atione						
			Summ	ary Or i	II-Cilai	ilibei C)DSGI V	3110113						
Exposure Day	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Group 1 – 0 mg/m³														
Within Normal Limits	24	24	24	24	12	12	12	12	11	8	5	1	1	1
Group 2 – 30 mg/m³														
Within Normal Limits	24	24	24	24	12	12	12	12	11	7	2			
Group 3 – 100 mg/m³														
Within Normal Limits Black/Test Material on Fur	22 2	22 2	22 2	21 3	11 1	10 2	10 2	10 2	9 1	7 1	4 1	0 1		
Group 4 – 300 mg/m³														
Within Normal Limits Black/Test Material on Fur	23 1	22 2	22 2	21 3	10 2	11 1	11 1	11 1	8 2	3 2	0 2	0 2	0 2	0 2

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Table I Summary of In-Chamber Observations

Exposure Day	41	42	43	44	45	46	47
Group 1 – 0 mg/m³							
Within Normal Limits	1	1	1	1	1	1	1
Group 4 – 300 mg/m³							
Within Normal Limits Black/Test Material on Fur	0	0	0	0	0	0	0

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Table II Chamber Monitoring Results Preface

Key to Abbreviations

Mass Median Aerodynamic Diameter Geometric Standard Deviation MMAD

GSD =

TMC **Total Mass Concentration**

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record

Group 1 - 0 mg/m³ (Air only) **Chamber Environment** Particle Size Mean Day Date **Gravimetric Chamber Concentration Exposure** Determinations Temperature Humidity Number Nominal Mean Individual MMAD GSD TMC (mg/m³) (mg/m³) (mg/m³)(mg/m³)(µm) (°C) (%) 25-May-04 1 0 0.00 0.00 0.00 0.00 0.00 20 42 26-May-04 2 0 0.00 0.00 0.00 0.00 0.00 4.215 2.148 2.76E-03 20 58 27-May-04 3 0 0.00825 0.033 0.00 0.00 0.00 19 64 3 28-May-04 4 0 0.00 0.00 0.00 0.00 0.00 21 54 29-May-04 5 0 0.00 0.00 0.00 0.00 0.00 19 48 30-May-04 6 0 0.0168 0.067 0.00 0.00 0.00 19 48 31-May-04 7 0 0.00 0.00 0.00 0.00 0.00 20 59 1-Jun-04 8 0 0.00825 0.00 0.00 0.033 0.00 20 42 8 2-Jun-04 9 0 0.00 0.00 0.00 0.00 0.00 1.759 1.511 7.54E-04 20 47 9 3-Jun-04 10 0 0.00 0.00 0.00 0.00 0.00 19 43 10 4-Jun-04 11 0 0.00 0.00 0.00 0.00 0.00 19 42 11 5-Jun-04 12 0 0.00 0.00 0.00 0.00 0.00 19 44 12 6-Jun-04 13 0 0.00 0.00 0.00 0.00 0.00 18 48 13 7-Jun-04 14 0 0.00 0.00 0.00 0.00 0.00 20 49 14 8-Jun-04 15 0 0.00 0.00 0.00 0.00 0.00 20 48 15 9-Jun-04 16 0 0.00 0.00 0.00 0.00 0.00 0.8269 2.332 2.55E-03 20 47 16 10-Jun-04 17 0 0.00 0.00 0.00 0.00 0.00 20 42 17 11-Jun-04 18 0 0.00 0.00 0.00 0.00 0.00 19 46 12-Jun-04 18 19 0 0.00 0.00 0.00 0.00 0.00 20 43 19 13-Jun-04 20 0 0.00 0.00 0.00 0.00 0.00 20 43 20 14-Jun-04 21 0 0.00 0.00 0.00 0.00 0.00 20 48 21 15-Jun-04 22 0 0.00 0.00 0.00 0.00 0.00 21 47 22 16-Jun-04 23 0 0.00 0.00 0.00 0.00 0.00 1.380 1.703 1.61E-03 20 47 23 17-Jun-04 24 0 0.00 0.00 0.00 0.00 0.00 20 43

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 mg/m³ (Air only)

Particle Size Mean
Particle Size Mean
Mumber Nominal Mean Individual MMAD GSD TMC

Chamber Environment
Mean
Temperature Humidity
Man Individual MMAD GSD TMC

							Chamber Environment						
_		l _							Particle Size			Me	an
Day	Date	Exposure	İ						Temperature	Humidity			
		Number	Nominal	Mean		Indiv			MMAD	GSD	TMC		
		ļ	(mg/m³)	(mg/m³)		(mg		,	(µm)		(mg/m³)	(°C)	(%)
24	18-Jun-04	25	0	0.00	0.00	0.00	0.00	0.00				19	50
25	19-Jun-04	26	0	0.00	0.00	0.00	0.00	0.00			•	20	54
26	20-Jun-04	27	0	0.00	0.00	0.00	0.00	0.00]	20	48
27	21 - Jun-04	28	0	0.00	0.00	0.00	0.00	0.00			l	19	45
28	22 - Jun-04	29	0	0.00	0.00	0.00	0.00	0.00]	20	55
29	23-Jun-04	30	0	0.00	0.00	0.00	0.00	0.00	1.485	1.817	1.03E-03	20	54
30	24-Jun-04	31	0	0.00	0.00	0.00	0.00	0.00				20	53
31	25 - Jun-04	32	0	0.00	0.00	0.00	0.00	0.00		:		21	40
32	26-Jun-04	33	0	0.00	0.00	0.00	0.00	0.00				20	56
33	27-Jun-04	34	0	0.00	0.00	0.00	0.00	0.00			ŀ	20	35
34	28-Jun-04	35	0	0.00	0.00	0.00	0,00	0.00				20	37
35	29-Jun-04	36	0	0.00	0.00	0.00	0.00	0.00			1	20	31
36	30-Jun-04	37	0	0.00	0.00	0.00	0.00	0.00	1.785	1.659	2.23E-03	21	34
37	1-Jul-04	38	0	0.00	0.00	0.00	0.00	0.00				20	31
38	2-Jul-04	39	0	0.00	0.00	0.00	0.00	0.00				20	34
39	3-Jul-04	40	0	0.00	0.00	0.00	0.00	0.00				19	25
40	4-Jul-04	41	0	0.00	0.00	0.00	0.00	0.00				20	46
41	5-Jul-04	42	0	0.00	0.00	0.00	0.00	0.00				20	31
42	6-Jul-04	43	0	0.00	0.00	0.00	0.00	0.00				20	19
43	7-Jul-04	44	0	0.00	0.00	0.00	0.00	0.00	1.612	1.698	1.24E-04	20	36
44	8-Jul-04	45	0	0.00	0.00	0.00	0.00	0.00				21	21
45	9-Jul-04	46	0	0.00	0.00	0.00	0.00	0.00				20	45
46	10-Jul-04	47	0	0.00	0.00	0.00	0.00	0.00				19	45
47	11-Jul-04	48	0	0.00	0.00	0.00	0.00	0.00				20	45
		Mean	0		0.001			1.866	1.838	1.58E-03	20	44	
		S.D.	0			0.01			1.1	0.3	0.0	0.6	9.4

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record

Group 2 - 30 mg/m³

	1	T	T				Group 2	- 30 mg/	m ⁻		·			· · · · · · · · · · · · · · · · · · ·	
	i									Particle Size				Chamber En	
Day	Date	Exposure		Gravin	netric Ch	amber C	oncentrat	ion		Determinations				Mea	
,		Number	Nominal	Mean			/idual	1011	MMAD	GSD		of Partic	los	Temperature	Humidity
			(mg/m³)	(mg/m³)			g/m³)		(µm)	405	< 1 µm		<u>≤</u> 10 μm	(°C)	(%)
0	25-May-04	1	54	22.3	16	21	25	27			 '			22	53
1	26-May-04	2	93	36.0	23	24	58	39	1.694	2.727	29.96	71.55	96.16	21	56
2	27-May-04	3	66	32.0	26	34	33	35						20	58
3	28-May-04	4	61	32.8	33	34	35	29						22	60
4	29-May-04	5	58	30.3	26	29	35	31				·		20	47
5	30-May-04	6	66	32.5	27	35	34	34		ļ				20	47
6	31-May-04	7	61	33.8	30	38	32	35		1				21	57
7	1-Jun-04	8	46	34.5	36	35	33	34						20	54
8	2-Jun-04	9	58	31.8	30	30	33	34	2.605	3.093	19.91	55.04	88.33	22	53
9	3-Jun-04	10	57	31.0	32	28	32	32						20	57
10	4-Jun-04	11	57	32.0	29	35	31	33						19	53
11	5-Jun-04	12	52	30.3	26	30	34	31						19	49
12	6-Jun-04	13	53	32.0	31	32	32	33						18	58
13	7-Jun-04	14	57	30.0	29	33	29	29						20	63
14	8-Jun-04	15	50	30.3	27	35	29	30						20	64
15	9-Jun-04	16	51	32.0	33	32	33	30	2.225	3.445	25.90	59.55	88.78	21	63
16	10-Jun-04	17	40	29.8	25	34	30	30			ļ		i l	21	59
17	11-Jun-04	18	62	29.5	27	28	32	31						20	58
18	12-Jun-04	19	52	31.0	26	35	32	31						20	53
19	13-Jun-04	20	59	29.5	26	28	32	32						21	51
20	14-Jun-04	21	59	32.5	34	32	32	32						2 2	52
21	15-Jun-04	22	40	31.8	26	36	34	31						23	53
22	16-Jun-04	23	54	30.8	35	32	28	28	1.843	3.101	29.46	66.66	93.25	22	50
23	17-Jun-04	24	56	32.0	27	38	36	27						22	50

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record Group 2 - 30 mg/m³

	Į	i												Chamber En	vironment
_		l _							j		Particle Siz	-		Mea	n
Day	Date	Exposure	l		netric Ch	etric Chamber Concentration					etermination			Temperature	Humidity
		Number	Nominal	Mean (mg/m³)			ridual		MMAD	GSD		of Partic			
			(mg/m³)				//m³)		(µm)		≤1 μm	≤3 µm	≤ 10 µm	(°C)	(%)
24	18-Jun-04	25	54	30.0	32	33	29	26			l			20	54
25	19-Jun-04	26	63	30.0	32	29	31	28			!			21	55
26	20-Jun-04	27	37	30.5	29	34	29	30	1					20	51
27	21-Jun-04	28	51	32.5	28	28	35	39						20	44
28	22-Jun-04	29	54	29.0	27	31	28	30			<u> </u>			21	49
29	23-Jun-04	30	53	31.0	31	33	29	31	1.890	2.610	25.35	68.50	95.88	21	49
30	24-Jun-04	31	53	29.3	28	29	29	31						20	49
31	25-Jun-04	32	57	32.5	30	38	32	30	i i			'		21	52
32	26-Jun-04	33	54	31.0	33	31	32	28						21	50
33	27-Jun-04	34	51	27.0	24	24	24	36						20	40
34	28-Jun-04	35	64	34.3	16	45	40	36						20	46
35	29-Jun-04	36	62	31.8	24	35	32	36				:		20	49
36	30-Jun-04	37	60	34.5	37	35	31	35	2.922	2.437	11.44	51.18	91.64	21	49
37	1-Jul-04	38	47	30.8	28	30	34	31			<u> </u>			21	45
		Mean	56		-	31.2			2.197	2.902	23.67	62.08	92.34	21	53
		S.D.	9			4.6			0.4	0.3	6.4	7.4	3.1	1.0	5.4

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record Group 3 - 100 mg/m³

														Chamber Env	/ironment
_	l <u>.</u> .	_					 				Particle Si			Mear	_
Day	Date	Exposure					Temperature	Humidity							
		Number	Nominal	Mean			idual		MMAD	GSD	·····	of Partic			
			(mg/m³)	(mg/m³)	-	(mg			(µm)		<u>≤</u> 1 μm	≤ 3 µm	<u><</u> 10 µm	(°C)	(%)
0	25-May-04	1	143	73.0	29	91	79	93						21	54
1	26-May-04	2	160	85.8	26	120	97	100						21	49
2	27-May-04	3	120	93.5	88	83	110	93	2.030	2.907	25.36	64.29	93.25	20	33
3	28-May-04	4	120	106	95	100	110	120					ł	21	33
4	29-May-04	5	120	95.3	71	100	100	110						19	33
5	30-May-04	6	130	107	87	120	120	100						20	33
6	31-May-04	7	120	99.0	81	110	110	95						20	35
7	1-Jun-04	8	130	101	85	110	100	110						20	31
8	2-Jun-04	9	130	101	98	120	100	85				i		22	30
9	3-Jun-04	10	130	92.0	85	95	94	94	1.785	3.170	30.78	67.37	93.24	20	35
10	4-Jun-04	11	130	100	80	110	110	100		ļ				19	32
11	5-Jun-04	12	130	91.0	81	92	98	93						19	32
12	6-Jun-04	13	120	103	93	120	98	100		[18	34
13	7-Jun-04	14	120	105	88	120	110	100						20	36
14	8-Jun-04	15	120	91.5	83	98	91	94						20	45
15	9-Jun-04	16	120	108	110	110	100	110						21	40
16	10-Jun-04	17	130	96.5	94	100	98	94	2.057	2.952	25.57	64.45	92.80	20	45
17	11-Jun-04	18	120	105	80	110	110	120						20	40
18	12-Jun-04	19	130	98.0	82	110	100	100						21	39
19	13-Jun-04	20	140	103	100	100	100	110						22	35
20	14-Jun-04	21	140	113	100	130	110	110						21	42
21	15-Jun-04	22	120	99.8	92	100	97	110						22	43
22	16-Jun-04	23	130	105	100	110	110	98						20	44
23	17-Jun-04	24	130	95.0	80	100	100	100	1.797	2.645	27.35	70.09	96.12	20	44

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record

Group 3 - 100 mg/m³ **Chamber Environment Particle Size** Mean Day Date **Exposure Gravimetric Chamber Concentration Determinations** Temperature | Humidity Number Nominal Mean Individual MMAD GSD % of Particles (mg/m³) (mg/m^3) (mg/m³) (µm) ≤ 1 µm | ≤ 3 µm | ≤ 10 µm (°C) (%) 18-Jun-04 19-Jun-04 20-Jun-04 92.8 21-Jun-04 98.8 22-Jun-04 94.3 23-Jun-04 92.0 24-Jun-04 91.8 2.275 2.996 22.69 59.95 91.14 25-Jun-04 26-Jun-04 27-Jun-04 98.5 28-Jun-04 94.8 29-Jun-04 30-Jun-04 1-Jul-04 2.259 1.934 10.84 66.63 98.79 2-Jul-04 97.8 Mean 99.4 2.034 2.767 23.77 65.46 94.22 S.D. 13.9 0.2 0.4 6.3 3.1 2.5 0.9 6.8

Table II
PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record Group 4 - 300 mg/m³

Chamber Environment **Particle Size** Mean Day Date **Exposure Gravimetric Chamber Concentration Determinations** Temperature Humidity Number Nominal Mean Individual MMAD GSD % of Particles (mg/m³) (mg/m³) (mg/m^3) (µm) $\leq 1 \, \mu \text{m} \, | \leq 3 \, \mu \text{m} \, | \leq 10 \, \mu \text{m}$ (°C) (%) 25-May-04 26-May-04 27-May-04 28-May-04 2.256 3.009 23.01 60.21 91.18 29-May-04 30-May-04 31-May-04 1-Jun-04 2-Jun-04 3-Jun-04 4-Jun-04 2.722 3.486 21.13 53.10 85.13 5-Jun-04 6-Jun-04 7-Jun-04 8-Jun-04 9-Jun-04 10-Jun-04 11-Jun-04 2.107 2.907 24.29 62.98 92.85 12-Jun-04 13-Jun-04 14-Jun-04 15-Jun-04 16-Jun-04 17-Jun-04 18-Jun-04 2.873 2.985 16.72 51.57 87.29

Table II PETROLEUM COKE: REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

Chamber Monitoring Results Cumulative Exposure Record

	,	r					Group	4 - 300 r	ng/m*						
											D	•		Chamber Env	
Day	Date	Exposure		Gravin	netric Ch	amber C	oncentra	tion	Particle Size Determinations					Mear Temperature	1 Humidity
•		Number	Nominal	Mean		Indiv			MMAD	GSD		of Partic	cles	remperature	пиници
			(mg/m³)	(mg/m³)		(mg			(µm)	5.52		≤ 3 µm	<u>≤</u> 10 μm	(°C)	(%)
25	19-Jun-04	26	750	305	320	300	310	290						21	48
26	20-Jun-04	27	750	325	300	300	330	370						21	43
27	21-Jun-04	28	830	310	310	290	330	310						20	37
28	22-Jun-04	29	790	308	320	310	300	300						20	40
29	23-Jun-04	30	780	318	310	340	320	300						21	39
30	24-Jun-04	31	790	290	280	290	320	270						20	40
31	25-Jun-04	32	650	335	380	340	310	310	2.775	2.857	16.96	53.32	88.87	20	34
32	26-Jun-04	33	640	308	310	350	310	260						20	38
33	27-Jun-04	34	700	288	270	290	290	300						20	33
34	28-Jun-04	35	670	308	330	320	300	280			•			20	38
35	29-Jun-04	36	640	303	270	300	330	310						21	34
36	30-Jun-04	37	690	325	310	350	320	320						21	31
37	1-Jul-04	38	660	290	240	330	280	310						20	26
38	2-Jul-04	39	640	310	300	290	330	320	2.939	1.923	4.96	51.25	96.94	20	23
39	3-Jul-04	40	680	348	340	370	350	330						19	20
40	4-Jui-04	41	580	315	350	320	300	290			<u> </u>			20	24
41	5-Jul-04	42	610	293	290	250	300	330						21	19
42	6-Jul-04	43	620	308	300	320	300	310						20	19
43	7-Jul-04	44	590	310	310	300	300	330	2.738	2.954	17.62	53.36	88.41	20	23
44	8-Jul-04	45	570	300	300	320	290	290						21	21
45	9-Jul-04	46	580	268	280	230	290	270						21	48
46	10-Jul-04	47	430	278	240	320	290	260						19	49
47	11-Jul-04	48	520	268	220	310	310	230						20	46
		Mean	798			300.7			2.630	2.874	17.81	55.11	90.10	20	42
		S.D.	218			34.7			0.3	0.5	6.4	4.6	3.9	0.8	11.0

<u> </u>	
Inhalation Report	Appendix W

Table III Equipment List

Exposure Chambers

40 Liter cast aluminum and alloy chamber with Polycarbonate nose-only tubes (ADG Limited, Inc.).

Compound Generator

Wright Dust Feeder, Model Mark II/WDF-II (small diameter cups) with a Wright Dust Feeder Speed Selector, Model E-352-BM (BGI, Inc.).

Flowmeters

Flowmeter, size 0 - 10, 0 - 20, 0 - 30, 0 - 40 Lpm (Dwyer®), calibrated with a Top TrakTM Mass Flowmeter, Model 822-13-OV1 PV1-V1 (Sierra Instruments).

Chamber Static Pressure Gauges

Dwyer[®] Magnehelic[®] gauge (Dwyer[®] Instruments Inc.); calibrated with a Dwyer[®] Mark II Manometer, Model 25 (Dwyer[®] Instruments Inc.).

Pressure Gauges

USG backpressure gauge, PN 12672-1. Norgreen backpressure gauge, PN 9892K23. Ashcroft backpressure gauge, PN 733-47. Marshall Town backpressure gauge.

Regulators

Union Carbide, P/N SG 3800 30. Norgreen, PN 9892K23

Valves

Metering Valve, Model SS-4L Series (Nupro® Co.).

Tubing

Plastic, size ¼", ½", 1" (Norton, Baxter). Teflon[®], size ½". Y-Tube, plastic. Stainless Steel, size ½".

Inhalation Report	Appendix W

Table III Equipment List

Filter

Glass fiber filter paper, Type A/E, Size 3.7 cm, Lot No. 32928 (Gelman Sciences Inc.).

Filter holder

Open-faced filter holder (Gelman Sciences Inc.).

Drying Unit

Drierite® Laboratory Gas Drying Unit (W. A. Hammond Drierite® Co.).

Particle Sizer/Analyzer

TSI Aerodynamic Particle Sizer, Model 331001 and a DELL computer, Model 486P/25, equipped with Epson Dot matrix printer, Model P630B.

Delron DCI-6 Cascade Impactor, Serial No. 695 with stainless steel slides, greased with lubricant (Dow-Corning) and a glass fiber filter paper, Type A/E, size 7.6 cm, Lot No. 00830 (Gelman Sciences, Inc.).

Vacuum Pump

Thomas Industries, Inc., Model 707CM50.

Timers

Gralab Universal Timer, Model 171.

Environmental Monitoring

Sunbeam and Springfield Temperature and Humidity Gauge, calibrated with Digital Hygrometer-Thermometer, Model/Part No. 61161-382 (VWR).

Balances

Sartorius LC6200S (Sartorius Corporation). AND ER-182A.

Miscellaneous

Brass Cyclone #1 (Intox). Carver Laboratory press model #C, serial # 32000-136. Stainless Steel Sieve, #60 opening, Fisher Scientific Co. Portable Room Air Conditioner, Model MPC-09ER (Pelonis).

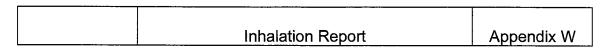


Table IV Chamber Distribution Records

Group (target)	Date	Port	Gravimetric Concentration (mg/m³)	Ratio to H-1
2 (30 mg/m³)	07 May 2004	H-1 H-2 H-1	26 25 27	1.00 0.96 1.00
		H-3	27	1.00
	19 May 2004	H-1	36	1.00
		H-2 H-1	35 26	0.97 1.00
		H-3	29	1.12
	20 May 2004	H-1	22	1.00
		H-4	24	1.09
	21 May 2004	H-1	33	1.00
		H-3 H-1	28 32	0.85 1.00
		H-4	32	1.00
3 (100 mg/m³)	07 May 2004	H-1	84	1.00
		H-2 H-1	110 84	1.31 1.00
		H-3	84	1.00
		H-1	75	1.00
		H-4	89	1.19
		H-1 H-2	79 77	1.00 0.97
	19 May 2004	H-1	97	1.00
	,	H-2	92	0.95
		H-1	110	1.00
		H-3	100	0.91
		H-1	91	1.00
		H-4	92	1.01
4 (300 mg/m³)	07 May 2004	H-1	190	1.00
		H-2	180	0.95
		H-3 H-1	220 210	1.16
		H-4	180	1.00 0.86
		• • •		5.55



Table IV
Chamber Distribution Records

Group			Gravimetric Concentration	
(target)	<u>Date</u>	Port	<u>(mg/m³)</u>	Ratio to H-1
4 (300 mg/m³)	19 May 2004			
,	•	H-1	270	1.00
		H-2	270	1.00
		H-1 ·	310	1.00
		H-3	240	0.77
	20 May 2004			
	•	H-1	300	1.00
		H-3	290	0.97
		H-1	260	1.00
		H-4	250	0.96
	21 May 2004			
		H-1	310	1.00
		H-2	330	1.06
		H-1	290	1.00
•		H-3	280	0.97
		H-1	290	1.00
		H-4	320	1.10

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STUDY NO. 03-6147

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

Final Report

Author:

Performed by: Huntingdon Life Sciences (HLS)

100 Mettlers Road

East Millstone, New Jersey 08875-2360

Submitted to: American Petroleum Institute (API)

1220 L Street, Northwest

Washington, D.C. 20005-4070

Attn:

Date: 3 April 2009

STATEMENT OF COMPLIANCE

This study was conducted in compliance with the United States Environmental Protection Agency's (EPA) Good Laboratory Practice Standards 40 CFR Part 792 (TSCA) and the Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM/(98)17, with the following exception:

The Supplier was responsible for the characterization and stability of the test substance and those tests were not performed at a GLP compliant laboratory nor were conducted under GLP regulations.



SIGNATURE PAGE

SCIENTIST

The following Scientists were responsible for the overall conduct of this study. Departmental supervisory personnel are listed on the personnel page of this report (Appendix M).



FLAPROG

Date

Date

SCIENTIFIC REVIEW

The following Scientist has reviewed and approved this report:



2 APRO9

¹ Wanda B. High was the Study Pathologist for this study and for submission of the draft report and is no longer employed at the Testing Facility. Dianne Creasy is assuming responsibility for finalization of the pathology evaluation of this report.

² Keith P. Hazelden was the original scientific reviewer of this report and is no longer employed at the Testing Facility. Robert M. Parker is assuming responsibility for final review of this report.

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	16 Feb 04	16 Feb 04	
Exposure, Monitoring & Equipment Records	3 Mar 04	9 Mar 04	
Body Weight Data Collection	9 Mar 04	9 Mar 04	
Detailed Physical Observations Data Collection & Protocol Amendment No. 1	10 Mar 04	15 Mar 04	
Terminal Necropsy & Training Records	16 Mar 04	19 Mar 04	
Final Report & Study Data	24 May – 2 Jun 04	2 Jun 04	
Final Report Review & Protocol Amendment No. 2	29 & 30 Oct 08	30 Oct 08	



3 apr 09

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

SUMMARY

This study was designed to provide a preliminary assessment of the toxicity of petroleum coke when administered, as a dust, via nose-only inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 421 reproductive/developmental toxicity screening study. Male and female Sprague-Dawley CD® rats (10/sex/group) were exposed for 6 hours/day, 7 days/week for 2 weeks to 0 (Air only), 25, 75 or 200 mg/m³ of petroleum coke. At the end of the treatment period, all animals were euthanized and necropsied. The following parameters were evaluated: viability, clinical observations, body weights, feed consumption, organ weights and macroscopic observations. Histopathological evaluation of the lungs was conducted on all animals. Exposure levels were determined using a gravimetric sampling procedure 4 times per chamber per day. Particle size distribution measurements were also made once per chamber per day.

The mean (± standard deviation) exposure concentrations of petroleum coke were determined to be 23.8 \pm 5.2, 68.6 \pm 14.5 and 199 \pm 35 mg/m³ for the three test substance exposed groups, respectively. The average mass median diameter was determined to be 2.064 µm with an average geometric standard deviation of 2.670 indicating that the particles for the test substance exposed groups were highly respirable to the test animals. All animals survived to termination and were unremarkable during the exposure periods and the non-exposure periods. There were no exposure-related differences in body weights or in feed consumption in the test substance exposed animals, compared to the air control animals. There were exposure-related increases in lung weights (absolute and relative to body weight or brain weight) in the test substance exposed male animals (all groups) and female animals (high exposure level), compared to the Air Control animals. Lungs from all test substance exposed animals were slightly to severely discolored black. In addition, there was an exposure level related incidence of discoloration and enlargement of the mediastinal lymph nodes. Microscopically, test substance related pulmonary changes were present in all exposure groups examined. The changes were characterized by the presence of histiocytes containing black pigment within the alveoli and hyperplasia/hypertrophy of the bronchiolo-alveolar epithelium.

In conclusion, two weeks of exposure of rats to petroleum coke at exposure levels of 25. 75 and 200 mg/m³ resulted in discolored lungs, increased lung weights, the presence of histiocytes containing black pigment within the alveoli and slight hyperplasia/hypertrophy of the bronchiolar epithelium. Based on increased lung weights, the portal of entry LOAEL for males was 25 mg/m³ and the NOAEL for females was 75 mg/m³. There were no systemic effects observed, consequently the systemic NOAEL for both males and females was 200 mg/m³. Consequently, higher exposure levels of 30, 100 and 300 mg/m³ were selected for the definitive OECD 421 screening study 04-4246 to maximize the likelihood of systemic effects at the highest exposure level.

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Final Report

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1. INTRODUCTION

The purpose of this study was designed to provide a preliminary assessment of the toxicity of petroleum coke when administered as a dust via nose-only inhalation to rats for 6 hours/day for 7 days per week for 2 weeks, in order to determine exposure levels for a subsequent OECD 421 reproductive/developmental toxicity screening study.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

American Petroleum Institute (API) 1220 L Street, Northwest Washington, DC 20005-4070

2.1.2. SPONSOR REPRESENTATIVE

2.1.3. TESTING FACILITY

Huntingdon Life Sciences (HLS) 100 Mettlers Road East Millstone, New Jersey 08875-2360

2.1.4. STUDY DIRECTOR

2.2. STUDY DATES

2.2.1. STUDY INITIATION

17 February 2004 (Date Study Director signed the Protocol)

2.2.2. DATE OF ANIMAL RECEIPT

17 February 2004 (Experimental Start Date, per OECD GLP's)

2.2.3. INITIATION OF EXPOSURES

2 March 2004 - Males (Experimental Start Date, per EPA GLP's)

3 March 2004 - Females

2.2.4. TERMINATION OF EXPOSURES

15 March 2004 - Males

16 March 2004 - Females

2.2.5. TERMINAL SACRIFICE

16 March 2004 - Males

17 March 2004 - Females

2.2.6. EXPERIMENTAL TERMINATION

2 April 2009 (Date of last data collection = Date final report is signed by the Pathologist)

2.2.7. STUDY COMPLETION

3 April 2009 (Date Study Director signed the Final Report)

2.3. EXPERIMENTAL OUTLINE

		Exposure		Number o	umber of Animals			
	Group	Levela	Ini	tial	Necr	opsy		
Group	Designation	mg/m³	M	F	M	F		
1	Air Control	0	10	10	10	10		
2	Low	25	10	10	10	10		
3	Mid	75	10	10	10	10		
4	High	200	10	10	10	10		

^aExposures were 6 hours per day for 7 consecutive days per week for 2 weeks for a total of 14 exposures. Exposure levels were expressed as mg/m³ of test substance. The exposures were conducted via nose-only exposure because this regimen minimized the dermal deposition and possible oral absorption of the test substance.

M = male; F = female

The first day of exposure was defined as Day 0 of the study.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures were considered the minimum necessary for determining the exposure levels for a subsequent OECD 421 study.

2.4.2. TEST ANIMAL SELECTION

The rat is a rodent animal model commonly utilized in toxicity studies, as recommended in OECD and EPA guidelines. In addition, a historical database is available for comparative evaluation.

2.4.3. NUMBER OF ANIMALS

The number of animals in the study was considered to be the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

2.4.4. EXPOSURE LEVEL SELECTION

The exposure levels were selected, based on prior results (HLS study 97-6119) of pulmonary toxicity after 5 days of exposure at exposure levels greater than 50 mg/m³, in order to determine exposure levels for a subsequent OECD 421 Study 03-4246. Based on a subsequent re-review, it was decided that the initial high exposure level of 50 mg/m³ was not high enough to sufficiently assess a maximum tolerated exposure level. Therefore, the high exposure level was increased to 200 mg/m³ (expected to result in marked pulmonary toxicity and body weight effects). This resulted in an essentially 12 times higher exposure than the prior 5 days study since the exposure level increased by a factor of 4 (from 50 to 200 mg/m³) and the duration of the exposures increased by a factor of 3 (from 5 to 14 days). The lower exposures levels were also proportionately adjusted.

2.5. TEST SUBSTANCE

Petroleum Coke

2.5.1. TEST SUBSTANCE CATEGORY

Residual product from petroleum refining.

2.5.2. SUPPLIER

EPL Archives, Inc. 45610 Terminal Drive Sterling, VA 20166

2.5.3. LOT NUMBER

M05369A

2.5.4. PURITY

See Appendix L (COA)

2.5.5. DESCRIPTION

Black powder

2.5.6. DATE RECEIVED

22 October 2003

2.5.7. EXPIRATION DATE

Not available, but stable as per COAs (see Appendix Y in 03-4246).

2.5.8. ANALYSIS

Documentation of the identity, strength, purity, composition, stability, and method of synthesis, fabrication, and/or derivation of the batch of the test substance and the maintenance of these records were the responsibility of the sponsor.

2.5.9. STORAGE

Room temperature (ambient)

2.5.10. ARCHIVAL SAMPLE

A sample from the lot of the test substance was taken and stored in the archives of the sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, Virginia 20166) on 21 June 2004. A common archival sample was taken for this range-finding study and the subsequent OECD 421 study (HLS Study No. 03-4246).

2.5.11. DISPOSITION

The unused portion of the test substance and any empty test substance containers will be returned to the archives of the sponsor following submission of the final report of the final study with this test substance.

2.6. TEST ANIMALS

2.6.1. SPECIES

Albino Rats (Outbred) VAF/Plus[®] Sprague-Dawley – derived (CD[®]) Crl:CD[®] (SD) IGS BR

2.6.2. SUPPLIER

Charles River Laboratories Kingston, New York 12484

2.6.3. NUMBER OF ANIMALS

Received:

88 total (44 males, 44 females)

Placed on test:

80 total (40 males, 40 females)

Females were nulliparous and non-pregnant.

2.6.4. AGE AT RECEIPT

Approximately 6 weeks

2.6.5. AGE AT INITIATION OF EXPOSURES

Approximately 8 weeks

2.6.6. WEIGHT AT INITIATION OF EXPOSURES (GRAMS)

	Mean	Range		
Male:	265	247 - 287		
Female:	209	183 - 225		

Individual weights of animals placed on test were within $\pm 20\%$ of the mean weight for each sex.

2.6.7. ACCLIMATION PERIOD

Animals were acclimated for approximately 2 weeks. All animals were examined during the acclimation period to confirm suitability for study.

2.7. ANIMAL ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered unsuitable for the study on the basis of pretest physical examinations or outlying body weight data were eliminated prior to random selection for group assignment. Animals considered suitable for study were distributed into 4 groups of 10 animals per sex by a computerized random sort program so that body weight means for each group were comparable. Disposition of all animals not utilized in the study is maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each rat was identified with a tail tattoo bearing its assigned animal number. The assigned animal number plus the study number comprised the unique animal number for each animal. In addition, each cage was provided with a cage card that was color-coded for exposure level identification and contained animal number information.

2.9. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

2.10. HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.10.2. HOUSING

Animals were individually housed in suspended, stainless steel, wire mesh cages during the study.

2.10.3. FEED

Certified Rodent Diet, No. 5002 (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly.

2.10.4. FEED ANALYSIS

Analysis of each feed lot used during this study was performed by the manufacturer. Results are maintained on file at the testing facility. There were no known contaminants in the feed which were expected to interfere with the results of this study.

2.10.5. WATER

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction via an automated watering system.

2.10.6. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). In addition, water samples are collected biannually from representative rooms in the testing facility; chemical and microbiological water analyses

are conducted on these samples by a subcontract laboratory. Results of all water analyses are maintained on file at the testing facility. There were no known contaminants in the water, which were expected to interfere with the results of this study.

2.10.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve hour light/dark cycle controlled via an automatic timer.

Temperature

Temperature was monitored in accordance with testing facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:

18 to 26°C

Actual Range:

21.0 to 24.6°C

Daily Average Range: 21.1 to 22.7°C

Relative Humidity

Relative humidity was monitored in accordance with testing facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:

30 to 70%

Actual Range:

38.99 to 65.46%

Daily Average Range: 45.58 to 59.96%

2.11. HUSBANDRY DURING EXPOSURE PERIODS

2.11.1. HOUSING

Animals were individually housed in polycarbonate tubes attached to a cast aluminum and alloy 40 Liter nose-only exposure chamber. The placement of the animal in the nose-only exposure cone was rotated at each exposure to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.11.2. FEED

None was provided during exposure.

2.11.3. WATER

None was provided during exposure.

2.11.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were recorded every half-hour during exposure and maintained, to the maximum extent possible, within the ranges presented below. Excursions outside the specified ranges were not considered to have affected the integrity of the study.

Temperature

Desired Range:

20 to 24°C

Actual Range:

19 to 23°C

Relative Humidity

Desired Range:

40 to 60%

Actual Range:

11 to 46%

2.12. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

2.12.1. ROUTE OF ADMINISTRATION

Inhalation, as a dust, via nose-only exposures.

2.12.2. EXPOSURE LEVELS

Group 1 - 0 mg/m³

Group 2 - 25 mg/m^3

Group $3 - 75 \text{ mg/m}^3$

Group $4 - 200 \text{ mg/m}^3$

2.12.3. FREQUENCY AND DURATION ADMINISTRATION

The test substance was administered for 6 hours per day for 7 consecutive days per week for 2 weeks. Test substance administration continued through the day prior to necropsy.

2.12.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance was administered as a dust in the breathing air of the animals.

2.12.5. PRE-STUDY TRIALS

Trials were performed (at least one 6-hour period) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the targeted exposure levels with a mass median aerodynamic diameter of 1.0-3.0 microns. Prior to initiation of animal exposures, additional samples were taken to determine the distribution of the test substance in the exposure chamber.

2.12.6. CHAMBER OPERATION

The nose-only exposure chambers had a total volume of 40 Liters each and were operated dynamically under slight positive pressure at a flow rate of 25.0 Liters per minute (Lpm) for all groups.

The final airflow rate was calculated to provide one complete air change (calculated by dividing the chamber volume by the airflow rate) approximately every 1.6 minutes and a T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of 7.4 minutes for all 4 groups.

This chamber size and airflow rate were considered adequate to maintain the oxygen level at 19% or higher. At the end of each exposure, all animals remained in the chamber for a minimum of 30 minutes. During this time, each chamber was operated at the same flow rate as used during the exposure. Recordings of chamber airflow rate and static pressure were made at the initiations of the exposures and every half-hour during the exposures.

The chamber was exhausted (via a 1" tubing) through the in-house filtering system, which consisted of a coarse filter, a HEPA filter and an activated charcoal bed.

Refer to Figure 1 and Appendix I for equipment details.

2.12.7. EXPOSURE PROCEDURE

Group 1

House line air was delivered from a regulator and a backpressure gauge, via ¼" tubing to a "Y" tube, which split the airflow into the generation and dilution systems. The generation air (20.0 Lpm) was directed, via ¼" tubing, through a flowmeter, regulated by a metering valve, then into a backpressure gauge to the top of a cast aluminum and alloy exposure chamber equipped with polycarbonate nose-only tubes. The dilution air (5.0 Lpm) was directed, via ¼" tubing, to a flowmeter regulated by a metering valve into the dilution port at the top of the chamber.

The exposure chamber and generation system were enclosed in a 10 m³ glass and stainless steel chamber.

Groups 2, 3 and 4

After being sieved through a stainless steel sieve, the test substance was packed to 700 psi into dust feeder cups (small diameter) using a press. The cup was then mounted onto the dust feeder, which was controlled using a speed selector. The exposure started with the dust feeder at the speed settings listed below:

Group	Speed Setting (rpm)
2	0.110
3	0.290
4	0.427

House-line air was delivered from a regulator and a backpressure gauge to the inlet of a gas drying unit via ¼" tubing. From the drying unit, the air was directed to a "Y" tube, which split the airflow into the generation and dilution systems. The generation

air flowed through ¼" tubing into the inlet of a flowmeter, regulated by a metering valve, then into a backpressure gauge. From the backpressure gauge, the air (20.0 Lpm) flowed through ¼" tubing to the inlet of the dust feeder. The test substance laden air was directed, via ½" tubing into the inlet of a brass cyclone (Groups 2 and 3 only, a cyclone was not used for Group 4) to remove the largest particles. The test substance laden air was then directed into the top of the 40 Liter cast aluminum and alloy exposure chamber equipped with polycarbonate nose-only tubes. The dilution air (5.0 Lpm) was directed via ¼" tubing to a flowmeter regulated by a metering valve into the dilution port at the top of the chamber.

The exposure chamber and generation system were enclosed in a 10 m³ glass and stainless steel chamber.

Refer to Figure 1 and Appendix I for equipment details.

2.13. EXPOSURE CHAMBER SAMPLING

2.13.1. CHAMBER SAMPLING

Samples for determination of the exposure levels were withdrawn from the breathing zone in the exposure chambers through glass fiber filters mounted open-faced in a filter holder. Samples were withdrawn at least four times per exposure from the normal sampling portal. The filter papers were weighed before and after sample collection, and the gravimetric concentration in mg/m³ was calculated by dividing the weight difference by the volume of air sampled.

Calculation

Conc (mg/m³) = $\frac{\text{amount collected (mg) x 1000 (L/m}^3)}{\text{sample duration (min) x sample airflow (Lpm)}}$

The sample flowrates, durations and volumes are summarized below:

Group	Sample Flowrate (Lpm)	Sample Duration (min)	Sample Volume (L)
1	10	30	300
2	10	30	300
3	10	10	100
4	10	3	30

Refer to Appendix I for equipment details.

2.13.2. PARTICLE SIZE DISTRIBUTION ANALYSIS

Group 1

Particle size distribution measurements were performed once during each exposure using a TSI Aerodynamic Particle Sizer. The samples were drawn for 20 seconds at a rate of 5.0 Lpm. A computer was used to program the system to the appropriate settings prior to sampling. The particle size distributions were calculated by the computer and printed out. The mass median aerodynamic diameter, geometric standard deviation and total mass concentration were calculated. For comparison, room air samples were similarly collected at least once each exposure day.

Refer to Appendix I for equipment details.

Groups 2, 3 and 4

Samples for particle size distribution assessment were drawn at least once per chamber during each exposure using a cascade impactor. The mass median aerodynamic diameter, the geometric standard deviation and the percent ≤ 1 , 3 and 10 microns were calculated based on the amount of material collected on the six impactor stages (greased stainless steel slides) and a final filter stage using a graphical analysis of an assumed lognormal distribution.

Final Report

The sample flowrates and durations are summarized below:

Group	Sample Flowrate (Lpm)	Sample Duration (min)	Sample Volume (L)
2	12.6	25	315
3	12.6	8	100.8
4	12.6	3	37.8

Refer to Appendix I for equipment details.

2.13.3. NOMINAL CONCENTRATION

The nominal concentrations in mg/m³ were determined by weighing the generation apparatus containing the test substance before and after the exposure and dividing the difference in these weights by the total volume of air used during the exposure (flowrate multiplied by total exposure time).

Calculation

Conc (mg/m³) = $\frac{\text{amount consumed (g) x 1000 mg/g x 1000 L/m}^3}{\text{exposure duration (min) x airflow (Lpm)}}$

2.14. EXPERIMENTAL EVALUATIONS

2.14.1. VIABILITY CHECKS

Animals were observed in their cages twice daily (once in the morning and once in the afternoon) for mortality and signs of severe toxic or pharmacologic effects.

2.14.2. PHYSICAL EXAMINATIONS

Exposure Observations

All animals were observed as a group once during each exposure. This was routinely done near the middle of each exposure.

Detailed Physical Examination

Animals were removed from their cages and examined twice pretest and weekly during the study period. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) were recorded.

2.14.3. BODY WEIGHT

Animals were removed from their cages and weighed twice pretest and once per week during the study period. Fasted weights were obtained prior to necropsy.

2.14.4. FEED CONSUMPTION

Feed was available without restriction 7 days/week. Animals were presented with weighed feeders (weight included feed, jar and lid). After 7 or 6 days, feeders were reweighed and the resulting weight was subtracted from the full feeder weight to obtain the grams consumed per animal over the 7 or 6-day period. Feed consumption was measured (weighed) during the week prior to treatment initiation and weekly during the study period.

Calculation

Feed Consumption (g/kg/day) = $\underline{\text{grams of feed consumed}} \div 7 \text{ or } 6 \text{ days}$ body weight (kg)^a

2.15. POSTMORTEM

2.15.1. NECROPSY INFORMATION

Necropsy was performed on all animals after they had been treated for 14 days. Animals were fasted overnight prior to necropsy. A

^aAverage of current and prior measurement

necropsy schedule was established to ensure that approximately equal numbers of males and females from each group were examined at similar times of day throughout the necropsy period.

Method of Euthanasia

Exsanguination following carbon dioxide inhalation.

2.15.2. MACROSCOPIC EXAMINATIONS

Complete macroscopic examinations were performed on all animals. The macroscopic examination included examination of the external surface and all orifices; the external surfaces of the brain and spinal cord; the organs and tissues of the cranial, thoracic, abdominal and pelvic cavities and neck; and the remainder of the carcass for the presence of macroscopic morphologic abnormalities. Special attention was paid to the organs of the reproductive system.

2.15.3. ORGAN WEIGHTS

Organs indicated in Table I (page 560) were weighed for all animals at the scheduled sacrifice interval. Prior to weighing, the organs were carefully dissected and properly trimmed to remove fat and other contiguous tissues in a uniform manner. Organs were weighed as soon as possible after dissection in order to avoid drying. Paired organs were weighed together.

2.15.4. TISSUES PRESERVED AND EXAMINED HISTOLOGICALLY

The tissues listed in Table I (page 560) were obtained at necropsy for all animals. Slides of the lungs were prepared and examined microscopically for all animals.

TABLE I

ORGAN NAME	WEIGHED	PRESERVED	EXAMINED MICROSCOPICALLY All Animals
Adrenal glands	X	X	
Aorta (thoracic)		X	
Bone (sternum/femur)		X	
Bone marrow (rib) ^a		X	
Brain (medulla/pons, cerebrum and cerebellum)	X	X	
Epididymides	X	X	
Esophagus		X	
Eye (with optic nerve)		X	
Heart	X	X	
Kidneys	X	X	
Lacrimal glands		X	
Large intestine (cecum, colon, rectum)		X	
Larynx		X	
Liver	X	X	
Lungs (with mainstem bronchi)	X	X	X
Lymph nodes (mesenteric and mediastinal)		X	
Mammary gland		X	
Muscle (biceps femoris)		X	
Nasopharyngeal tissue		X	
Nerve (sciatic)		X	
Ovaries	X	X	
Pancreas		X	
Pituitary gland	X	X	
Salivary glands with submandibular lymph nodes	_	X	
Seminal vesicles (with prostate gland)	X	Х	
Skin	}	X	

ORGAN NAME	WEIGHED	PRESERVED	EXAMINED MICROSCOPICALLY All Animals
Small intestine (duodenum, ileum, jejunum)		X	
Spinal cord (cervical, thoracic, lumbar)		X	
Spleen	X	X	
Stomach		X	
Testes	X	X	
Thymus	X	X	
Thyroid (with parathyroid)		X	
Trachea		X	
Urinary bladder		X	
Uterus (body/horns) with cervix	X	X	
Zymbal's gland		X	
Gross lesions and tissue masses		X	

^aBone marrow smears were prepared and archived without examination.

Preservatives

All tissues - 10% neutral buffered formalin.

Eyes and testes and epididymides were placed in Modified Davidson's solution initially and then retained in 10% formalin. Lungs (gravity method) and urinary bladder were infused with formalin prior to their immersion into a larger volume of the same fixative.

Smear preparations of the marrow from the rib were air dried and fixed in absolute methanol.

Processing

After fixation, the lungs from all animals were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy.

2.16. STATISTICAL ANALYSIS

The following parameters were analyzed statistically:

mean body weight values
mean feed consumption values
mean terminal organ weight, mean organ/body and mean organ/brain
weight ratios

2.16.1. METHOD OF ANALYSIS

Mean values of all exposure groups were compared to the mean value for the control group at each time interval.

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Snedecor & Cochran, 1967; Sokal and Rohlf, 1995) was performed to determine if groups had equal For all parameters except organ weights, if the variances. variances were equal, parametric procedures were used: if not, nonparametric procedures were used. Organ weight data was analyzed only by parametric methods. The parametric method was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Dunlap and Duffy, 1975). significant differences among the means were indicated, additional tests were used to determine which means were significantly different from the control: Dunnett's (Dunlap et al., 1981); Dunnett, 1955, 1964) or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) were used to determine which means differed from control. Bartlett's test for equality of variance was conducted at the 1% significance level; all other statistical tests were conducted at the 5% and 1% significance levels.

2.17. DATA STORAGE

All raw data, preserved archival specimens and retained samples, as well as the original study protocol and the original final report, are to be maintained in the Archives of the testing facility upon completion of the study. The sponsor will determine the final disposition of these materials.

2.18. REGULATORY REFERENCES

2.18.1. TEST GUIDELINES

This study was not designed to meet or exceed any regulatory requirements. It was designed to assess the toxicity of the test substance in order to determine exposure levels for a subsequent OECD 421 reproductive/developmental toxicity screening study.

2.18.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and OECD Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.

2.18.3. ANIMAL WELFARE ACT COMPLIANCE

This study complied with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163, effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505, effective March 18, 1991.

2.19. PROTOCOL DEVIATION

The following protocol deviation occurred during the study but was not considered to have compromised the validity or integrity of the study:

1. Groups 2 and 3 had only one 6-hour trial period (rather than at least two trial periods) for exposure levels of 25 and 75 mg/m³.

3. RESULTS AND DISCUSSION

3.1. CHAMBER MONITORING

(Appendices A and J)

Prestudy chamber distribution analyses showed the test substance was evenly distributed within each chamber.

The target and mean gravimetric and nominal concentrations are summarized as follows:

Group	Target Concentration (mg/m³)	Gravimetric Concentration (mg/m³)	Nominal Concentration (mg/m³)
1	0	0 ± 0	-
2	25	23.8 ± 5.2	24 ± 7
3	75	68.6 ± 14.5	136 ± 27
4	200	199 ± 35	563 ± 45

The achieved mean gravimetric exposure concentration for the test substance groups were acceptably close (within \pm 30 or 40%) in the opinion of the study director to the target concentrations. The differences between measured and nominal concentrations were typical for this type of dust exposure and considered to represent deposition of test substance on surfaces within the exposure chambers.

Chamber environmental conditions averaged 21°C temperature and 27% relative humidity.

Particle size distribution measurements for the test substance exposures are summarized as follows:

Group	Mass Median Aerodynamic Diameter	Geometric Standard Deviation	% of Particles		
	(μ m)		≤ 1.0 µm	≤ 3.0 µm	≤ 10 µm
2	1.586	2.706	33.09	74.81	96.40
3	2.174	2.650	21.95	64.27	93.87
4	2.432	2.654	18.61	58.91	92.59
Mean	2.064	2.670	24.55	66.00	94.29

These results indicated that the particles for the test substance exposed groups were highly respirable to the test animals.

3.2. MORTALITY

(Appendix B)

All animals survived to termination.

3.3. CLINICAL OBSERVATIONS

3.3.1. IN-CHAMBER OBSERVATIONS

(Table 1)

The test animals were unremarkable during the exposure periods.

3.3.2. DETAILED OBSERVATIONS

(Table 2, Appendix C)

The test animals were generally unremarkable during the non-exposure periods. Scattered observations such as chromodacryorrhea and red nasal discharge were noted but were not attributed to treatment. Black test substance on fur was also frequently noted in the test substance exposed groups but this was considered an artifact of the exposure regime.

3.4. BODY WEIGHTS

(Figures 2 and 3, Tables 3 and 4, Appendices D and E)

There were no exposure-related differences in absolute body weights or in body weight changes in the test substance exposed animals, compared to the Air Control animals.

3.5. FEED CONSUMPTION

(Figures 4 and 5, Table 5, Appendix F)

There were no exposure-related differences in feed consumption in the test substance exposed animals, compared to the Air Control animals.

3.6. ORGAN WEIGHTS

(Table 6, Appendix G)

There were exposure-related increases (up to 17%) in lung weights (absolute and relative to body weight or brain weight) in the test substance exposed male animals (all groups) compared to the Air Control animals. Similar increases (up to 15%) were seen in the exposed female animals only at the high exposure level. A number of statistically significant increases were noted in pituitary weights (absolute and/or relative to body weight or brain weight) in the test substance exposed male animals (all groups) and female animals (low exposure group) compared to the Air Control animals. However, in the absence of any corresponding macroscopic postmortem findings or meaningful relationship to exposure, these differences were not attributed to the exposures. A statistically significant decrease was noted in ovary weights (absolute) in the test substance exposed female animals (middle exposure group) compared to the Air Control animals. However, in the absence of an exposure level related pattern, this difference also was not attributed to the exposures.

3.7. PATHOLOGY

3.7.1. MACROSCOPIC OBSERVATIONS

(Table 7, Appendix H)

Lungs from all test substance exposed animals were slightly to severely discolored black. The severity of the finding showed an exposure level related trend. In addition, there was an exposure level related incidence of discoloration and enlargement of the mediastinal lymph nodes.

3.7.2. MICROSCOPIC OBSERVATIONS

(Table 8, Appendix H)

Slight to moderate brown-black pigment deposits were present in the lungs of animals from all test substance exposed groups. The severity showed an exposure related increase. The pigment was generally present in alveolar macrophages, which were located within the alveolar lumens but could often be found within the bronchial associated lymphoid tissue. This indicates that the lymphatics are a route for clearance of the pigment containing macrophages. An exposure related increase was also seen in the numbers of alveolar/intraalveolar macrophages in all test substance exposed groups. Slight hyperplasia/hypertrophy of the bronchiolar epithelium was present in 8/10 of the males and 4/10 of the females from the high exposure group. Slight to moderate hyperplasia/hypertrophy of the alveolar duct/alveolar epithelium was present in animals from all test substance exposed groups and the severity showed an exposure related trend. The findings were not equally distributed in all 5-6 lobes of the lung. In most cases, 1-2 lobes were more affected than the others. The findings recorded reflect the worst affected lobes.

Overall, test substance related pulmonary changes were present in all exposure groups examined. The changes were characterized by the presence of histiocytes containing black pigment within the alveoli and hyperplasia/hypertrophy of the bronchiolo-alveolar epithelium. The severity of these changes was exposure level related. On the basis that there was a general lack of inflammatory response to the inhaled particles and that only a proportion of the lobes of each lung were affected, pulmonary function was probably not significantly compromised.

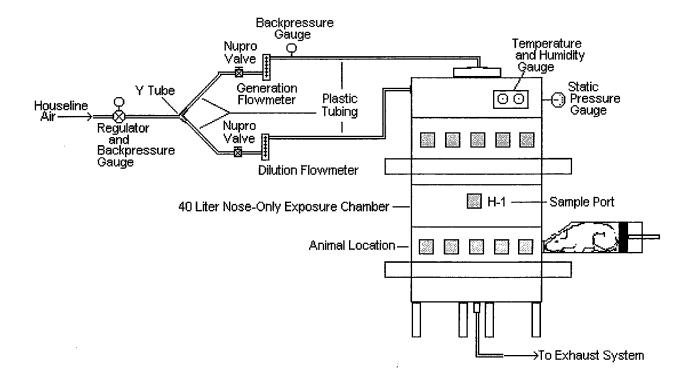
4. CONCLUSION

Two weeks of exposure of rats to petroleum coke at exposure levels of 25, 75 and 200 mg/m³ resulted in discolored lungs, increased lung weights, the presence of histiocytes containing black pigment within the alveoli and slight hyperplasia/hypertrophy of the bronchiolar epithelium. Based on increased lung weights, the portal of entry LOAEL for males was 25 mg/m³ and the NOAEL for females was 75 mg/m³. There were no systemic effects observed, consequently the systemic NOAEL for both males and females was 200 mg/m³. Consequently, higher exposure levels of 30, 100 and 300 mg/m³ were selected for the definitive OECD 421 screening study 04-4246 to maximize the likelihood of systemic effects at the highest exposure level.

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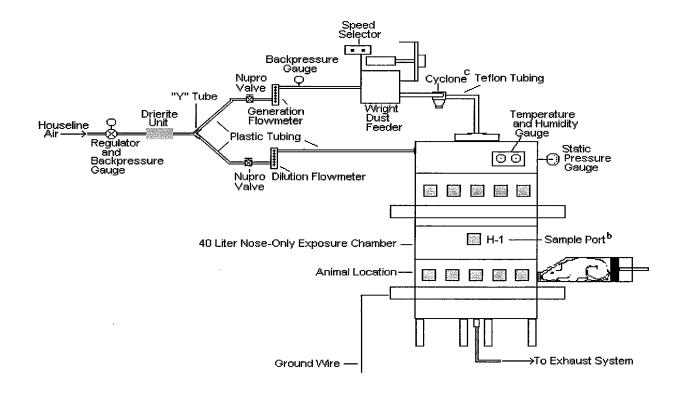
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	Diagram of 40 Liter Nose-Only Exposure	
Group 1	Chamber and Generation System ^a	Figure 1



^a System enclosed in 10 m³ glass and stainless steel chamber.

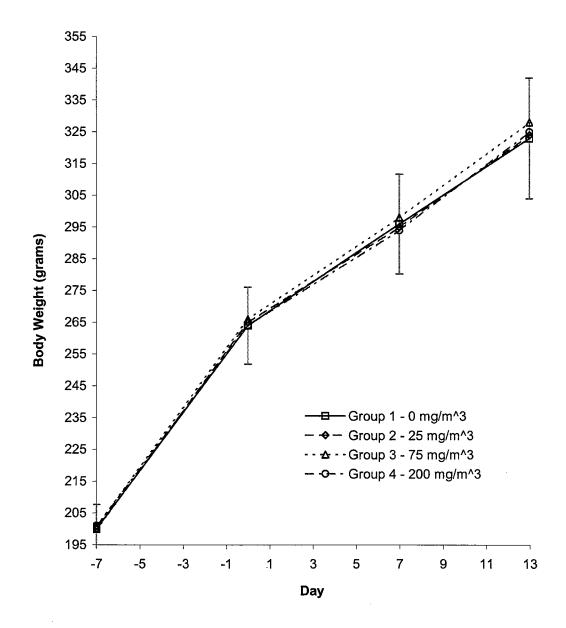
	Diagram of 40 Liter Nose-Only Exposure	
Groups 2 - 4	Chamber and Generation System ^a	Figure 1

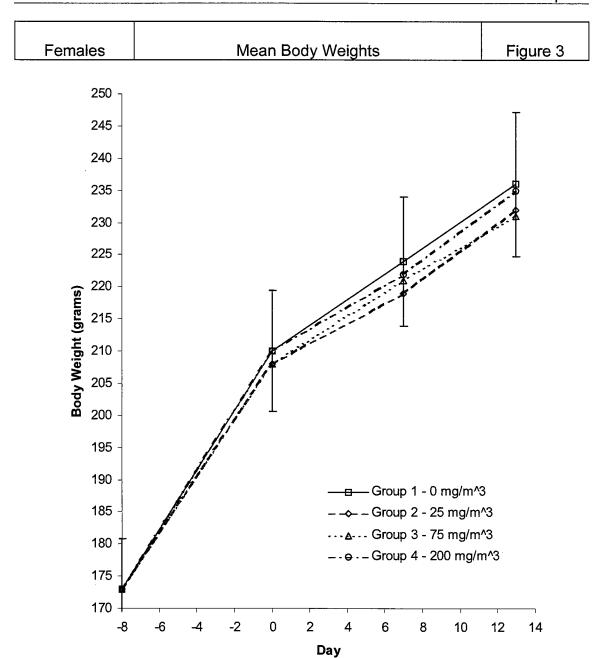


^c A cyclone was not used for Group 4.

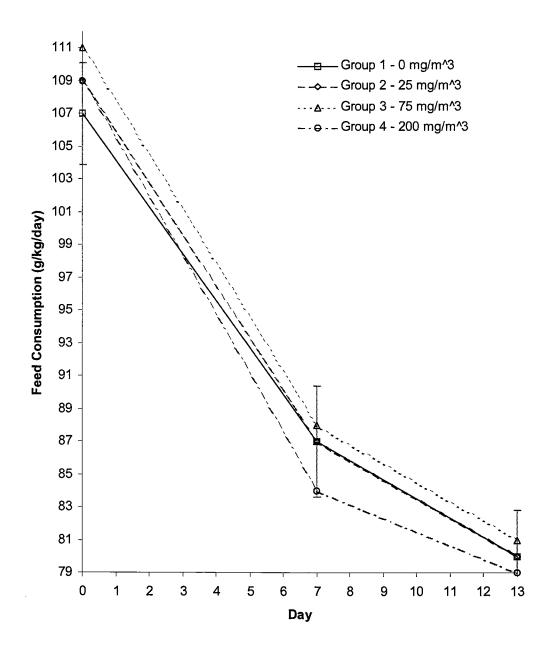
^a System enclosed in 10 m³ glass and stainless steel chamber. ^b The distribution sample port (H-2) was located on the side opposite the H-1 port.

Males	Mean Body Weights	Figure 2

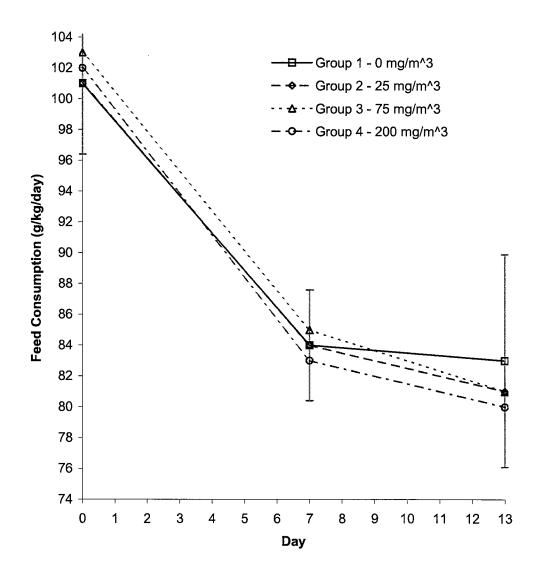




Males	Mean Feed Consumption	Figure 4



Females	Mean Feed Consumption	Figure 5



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General Preface	

General Notes

Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

M = Male; F = Female

			;	Summ	ary of I	n-Cha	mber (Observ	ations			Table 1			
Exposure Day	1ª 	2 1 ^b	3 2	4 3	5 4	6 5	7 6	8 7	9	10 9	11 10	12 11	13 12	14 13	14
Group 1 – 0 mg/m³															
Number Examined Within Normal Limits	10 10	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	10 10
Group 2 – 25 mg/m³															
Number Examined Within Normal Limits	10 10	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	10 10
Group 3 – 75 mg/m ³															
Number Examined Within Normal Limits	10 10	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	10 10
Group 4 – 200 mg/m ³						•									
Number Examined Within Normal Limits	10 10	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	20 20	10 10

^aDay 1 for the male animals. ^bDay 1 for the female animals.

Summary of Clinical Observations	
 Preface	Table 2

Number of animals examined represents the total number of animals observed for a given interval.

For summarization purposes, descriptive comments [i.e., location of scab(s) and/or sore(s), etc.] are not presented in this table. These data are contained in the study raw data if needed.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³

Group 2 - 25 mg/m³

Group 3 - 75 mg/m³

Group 4 - 200 mg/m³

TABLE 2

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES						SU	MMARY OF CLINICAL OBSERVATIONS
		D.F	Y C)F S1	YDDY		
	GROUP#	-7	0	7	13	14	
# OF ANIMALS EXAMINED	1	10	10	10	10	10	······································
	2	10	10	10	10	10	
	3	10	10	10	10	10	
	4	10	10	10	10	10	
NORMAL							
WITHIN NORMAL LIMITS	1	10	10	7	7	0	10
	2	10	10	0	0	0	10
	3	10	10	0	0	0	10
	4	10	10	0	0	0	10
DEAD							
Terminal Sacrifice	1	0	0	0		10	
	2	0	0	0	0	10	10
	3	0	0	0	0	10	10
	4	0	0	0	0	10	10
APPEARANCE							
TEST MATERIAL ON FUR	1	0	0	0	0	0	0
(BLACK)				10		ō	
	3		0		10	0	
	4	0	0	10	10		10
OCULAR							
Chromodacryorrhea -	1	0	0	2	1	0	2
Unilateral	2	0	ō			ō	
	3	0	ō			ō	
	4	0	Ō	0		0	0

TABLE 2

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY

MALES						S	SUMMARY OF CLINICAL OBSERVATIONS
		D?	AY C	F ST	YDU		
	GROUP#	-7	0	7	13	14	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	10)
	2	10	10	10	10	10	
	3	10	10	10	10	10	
	4	10	10	10	10	10	
Chromodacryorrhea -	1	0	0	0	0	0	0
Bilateral	2	0	0	0	0	0	0
	3	0	0	1	0	0	1
	4	0	0	1	0	0	1
ORAL/BUCCAL							
Nasal Discharge - Red	1	0	0	3	3	0	4
5	2	0		0		0	
	3	0	0	0	0	0	0
	4	0	0	0	0	0	

STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

TABLE 2

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

FEMALES						St	SUMMARY OF CLINICAL OBSERVATIONS
			Y C				
	GROUP#			7	13	14	4 TOTAL
# OF ANIMALS EXAMINED		10		10	10	10	0
	2	10	10	10	10	10	0
	3	10	10	10	10	10	3
	4	10	10	10	10	10	
NORMAL							
WITHIN NORMAL LIMITS	1	10	10	8	8	0	0 10
	2	10	10				0 10
	3	10	10	0	0	0	0 10
	4	10	10	0	0	0	0 10
DEAD							
Terminal Sacrifice	1	0	0	0	0	10	0 10
	2		0		0	10	0 10
	3	0	0	0		10	
	4	0	0	0	0	10	0 10
APPEARANCE							
TEST MATERIAL ON FUR	1	0	0	0	0	0	0 0
(BLACK)	2	0	0	10	10	0	0 10
	3		0	10	10	0	0 10
	4	0	0	10	10	0	0 10
OCULAR							
Chromodacryorrhea -	1	0	0		2	0	0 2
Unilateral	2	0	0		0		
	3	0	0		0		
	4	0	0	1	1	0	0 1

TABLE 2

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

FEMALES							SUMMARY OF CLINICAL OBSERVATIONS				
	GROUP#		0 XY C			14 :	TOTAL				
		-									
# OF ANIMALS EXAMINED	1	10	10	10	10	10					
	2	10	10	10	10	10					
	3	10	10	10	10	10					
	4	10	10	10	10	10					
Chromodacryorrhea -	1	0	0	0	0	0	0				
Bilateral	2	0	0	0	0	0	0				
	3	0	0	1	0	0	1				
			^	-	_	_	•				

TABLE 3

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

		DOSE GROUP:	1	2	3	4	
	DOSE LEV	EL (MG/M3):	0	25	75	200	
DAY	-7	MEAN	200	200	201	201	
		S.D.	7.7	7.3	7.9	8.6	
		N	10	10	10	10	
DAY	0	MEAN	264	265	266	264	
		S.D.	12.1	8.8	9.9	11.3	
		N	10	10	10	10	
DAY	7	MEAN	296	295	298	294	
		S.D.	15.7	16.6	15.9	13.5	
		N	10	10	10	10	
DAY	13	MEAN	323	324	328	325	
		S.D.	19.0	23.5	17.9	15.4	
		N	10	10	10	10	

TABLE 3

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES		MEAN BODY WEIGHTS (GRAMS)									
		DOSE GROUP: EL (MG/M3):	1 0	2 25	3 . 75	4 200					
DAY	-8	MEAN	173	173	173	173					
		S.D.	7.8	7.8	7.8	7.3					
		N	10	10	10	10					
DAY	0	MEAN	210	208	208	210					
		S.D.	9.4	10.5	13.9	9.2					
		N	10	10	10	10					
DAY	7	MEAN	224	219	221	222					
		S.D.	10.0	12.0	13.2	12.8					
		N	10	10	10	10					
DAY	13	MEAN	236	232	231	235					
		S.D.	11.2	11.6	17.1	13.1					
		N	10	10	10	10					

TABLE 4

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY

STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES			MEAN BODY WEIGHT CHANG	GE FROM INTERVAL TO IN	TERVAL (GRAMS)		
	DOSE I	DOSE GROUP: LEVEL (MG/M3):	1 0	2 25	3 75	4 200	
DAY	0 TO 7	MEAN S.D.	32 7.4	30 11.7	31 10.0	29 5.0	
		N	10	10	10	10	
DAY	7 TO 13	MEAN S.D.	26 5.3	29 7.9	30 6.4	32 3.9	
		N	10	10	10	10	
DAY	0 TO 13	MEAN S.D.	58 11.2	59 18.2	61 13.2	61 8.0	
		N	10	10	10	10	

TABLE 4

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY

STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES				MEAN BODY WEIGHT CHANG	E FROM INTERVAL TO IN	TERVAL (GRAMS)		
	DO	DOS SE LEVEL	E GROUP: (MG/M3):	1 0	2 25	3 75	4 200	
DAY	0 TO	7	MEAN	14	11	14	12	
			s.D.	10.5	6.9	5.5	9.3	
			N	10	10	10	10	
DAY	7 TO	13	MEAN	12	13	10	13	
			S.D.	7.6	6.9	7.2	6.4	
			N	10	10	10	10	
DAY	0 TO	13	MEAN	26	24	24	25	
			S.D.	9.7	5.2	6.1	7.5	
			N	10	10	10	10	

TABLE 5

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

		DOSE GROUP:	1	2	3	4	
DOSE LEVEL		EL (MG/M3):	0	25	75	200	
DAY	0	MEAN	107	109	111	109	
		S.D.	3.1	2.8	5.5	3.7	
		N	10	10	10	10	
DAY	7	MEAN	87	87	88	84	
		s.D.	3.4	3.6	6.0	6.5	
		N	10	10	10	10	
DAY 13	MEAN	80	80	81	79		
		S.D.	2.8	4.9	3.0	1.8	
		N	10	10	10	10	

TABLE 5

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	1	DOSE GROUP:	1	2	3	4	
	DOSE LEVEL (MG/M3):		0	25	75	200	
DAY	0	MEAN	101	101	103	102	
		S.D.	4.6	3.5	6.1	3.0	
		N	10	10	9	9	
DAY	7	MEAN	84	84	85	83	
		S.D.	3.6	2.8	3.4	5.5	
		N	10	10	10	10	
DAY	13	MEAN	83	81	81	80	
		S.D.	6.9	3.2	5.9	3.7	
		N	10	10	10	10	

Mean Organ Weights	
Preface	Table 6

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Absolute Organ Weights	590
% Organ to Body Weight Ratios	
% Organ to Brain Weight Ratios	

Key to Abbreviations:

g = Grams wt. = Weight observ. = Observed semis w/prostate = Seminal vesicles

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³ Huntingdon Life Sciences Princeton Research Center East Millstone, New Jersey

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Terminal Sacrifice

Group	Terminal		Brain		Heart		Liver	
	Body wt. (g)	Adrenal Glands	Epididymides			Kidneys		Lungs
			Male	Anim	als			
1								
Mean	: 289.1	0.0581	1.9281	0.8372	1.1704	2.7726	10.6530	1.6978
Standard deviation	: 18.2	0.0063	0.0638	0.0699	0.1005	0.1315	1.1241	0.2055
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean	: 290.1	0.0572	1.9555	0.7993	1.2038	2,7946	10.8094	1.8967
Standard deviation	: 20.3	0.0082	0.0991	0.0999	0.1163	0.2322	1.1355	0.1714
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean	: 292.4	0.0612	1.9479	0.7989	1.2032	2.8141	10.7649	1.9129
Standard deviation	: 16.3	0.0057	0.0717	0.0607	0.1101	0.3068	1.4373	0.2749
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean	290.0	0.0569	1.9547	0.7858	1,2259	2.9085	10.4551	1.9841+
Standard deviation:	: 14.9	0.0079	0.0790	0.1131	0.1003	0.2266	0.6942	0.1249
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$)} = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary statistics for absolute organ weights (g) Study number: 036147

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Group	Terminal	Semis w	/prostate		Testes		
	Body wt. (g)	Pituitary gland		Spleen		Thymus	
			Mal'e	Anim	als		
1							
Mean	: 289.1	0.0079	1.7562	0.6106	3.0666	0.5312	
Standard deviation	: 18.2	0.0022	0.2477	0.0861	0.2086	0.0819	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
2							
Mean	: 290.1	0.0098*	1.7836	0.6234	3.1733	0.5228	
Standard deviation:	: 20.3	0.0011	0.2351	0.0612	0.1766	0.1629	
Number of observ.	: (10)	(10)	(10)	(10)	. (10)	(10)	
3							
Mean	: 292.4	0.0100+	1.8564	0.6274	3.0272	0.5269	
Standard deviation	: 16.3	0.0011	0.1836	0.0702	0.3431	0.1138	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
4							
Mean	: 290.0	0.0102+	1.6842	0.6109	3.0587	0.4784	
Standard deviation	: 14.9	0.0012	0.2396	0.0674	0.3078	0.0885	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{*(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary statistics for absolute organ weights (g) Study number: 036147

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Group	Terminal		Brain		Kidneys		Lungs	
	Body wt. (g)	Adrenal Glands		Heart	-	Liver	-	Ovaries
			Fema	le An	imals			
1								
Mean	: 209.1	0.0694	1.8873	0.8816	1.9269	7.8776	1.5714	0.0954
Standard deviation	: 8.7	0.0087	0.0596	0.0656	0.1558	0.8528	0.1644	0.0188
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean	205.2	0.0728	1.8821	0.8669	1.9193	8.2483	1.4827	0.0882
tandard deviation:	: 10.8	0.0093	0.0691	0.0671	0.1382	0.7047	0.3014	0.0091
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean	: 203.5	0.0746	1.8632	0.8846	1.8737	7.8500	1.5393	0.0800
tandard deviation:	: 15.4	0.0109	0.0566	0.1203	0.2322	1.0285	0.2808	0.0108
number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean	: 207.2	0.0738	1.8412	0.8723	1.9442	7.9281	1.7683	0.0966
Standard deviation:	: 10.5	0.0067	0.0494	0.0706	0.1219	0.5456	0.1944	0.0126
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

^{*(+)} = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance %(\$) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal		Spleen		Uterus	
	Body wt. (g)	Pituitary gland	•	Thymus		
			Fema	le An	imals	
1						
Mean	: 209.1	0.0119	0.5171	0.5576	0.5998	
Standard deviation	: 8.7	0.0029	0.0527	0.1004	0.1589	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	
2						
Mean	: 205.2	0.0140	0.4885	0.5189	0.6050	
Standard deviation	: 10.8	0.0006	0.0686	0.0770	0.1945	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	
3						
Mean	: 203.5	0.0133	0.4902	0.5132	0.5913	
Standard deviation	: 15.4	0.0019	0.0722	0.0947	0.1537	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	
4						
Mean	: 207.2	0.0116	0.5249	0.4952	0.6783	
Standard deviation	: 10.5	0.0045	0.0996	0.0985	0.2118	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Body Weight Study number: 036147

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Group	Terminal		Brain		Heart	· · · · · · · · · · · · · · · · · · ·	Liver	
	Body wt. (g)	Adrenal Glands	Epid	ldymides		Kidneys		Lungs
			Male	Anim	als		••••	
1								
Mean	: 289.1	0.0202	0.6685	0.2903	0.4051	0.9608	3.6863	0.5868
Standard deviation:	: 18.2	0.0026	0.0331	0.0269	0.0292	0.0471	0.3353	0.0557
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean	: 290.1	0.0198	0.6767	0.2763	0.4150	0.9633	3.7377	0.6541*
Standard deviation:	: 20.3	0.0035	0.0537	0.0358	0.0288	0.0418	0.4347	0.0434
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	292.4	0.0210	0.6674	0.2734	0.4114	0.9611	3.6729	0.6543*
Standard deviation:	: 16.3	0.0019	0.0328	0.0185	0.0298	0.0804	0,3600	0.0891
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	290.0	0.0197	0.6755	0.2713	0.4232	1.0038	3.6116	0.6850+
Standard deviation:	: 14.9	0.0029	0.0379	0.0390	0.0329	0.0712	0.2677	0.0421
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Body Weight Study number: 036147

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Group	Terminal	Semis w/	prostate		Testes		
	Body wt. (g)	Pituitary gland	-	Spleen		Thymus	
			Male	Anim	a 1 s		
1							
Mean	: 289.1	0.0027	0.6075	0.2110	1.0644	0.1841	
Standard deviation	: 18.2	0.0008	0.0791	0.0237	0.0967	0.0285	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
2							
Mean	: 290.1	0.0034	0.6149	0.2149	1,0982	0.1798	
Standard deviation	: 20.3	0.0005	0.0701	0.0148	0.0929	0.0511	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
3							
Mean	: 292.4	0.0034	0.6366	0.2147	1.0390	0.1797	
Standard deviation	: 16.3	0.0004	0.0729	0.0225	0.1393	0.0350	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
4							
Mean	: 290.0	0.0035%	0.5816	0.2104	1.0561	0.1652	
Standard deviation	: 14.9	0.0004	0.0815	0.0171	0.1049	0.0308	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	

^{*(+)} = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$)} = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Body Weight Study number: 036147

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Group	Terminal		Brain		Kidneys		Lungs	
	Body wt. (g)	Adrenal Glands		Heart	_	Liver	-	Ovaries
			Fema	le An	imals			
1								
Mean	: 209.1	0.0331	0.9041	0.4214	0.9208	3.7621	0.7534	0.0455
standard deviation	: 8.7	0.0038	0.0494	0.0219	0.0514	0.3205	0.0912	0.0079
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean	: 205.2	0.0356	0.9198	0.4226	0.9360	4.0253	0.7278	0.0430
tandard deviation	: 10.8	0.0053	0.0666	0.0275	0.0586	0.3546	0.1755	0.0049
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean	: 203.5	0.0366	0.9213	0.4345	0.9193	3.8548	0.7552	0.0394
tandard deviation	: 15.4	0.0041	0.0897	0.0445	0.0721	0.3761	0.1173	0.0050
umber of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean	: 207.2	0.0357	0.8904	0.4209	0.9396	3.8338	0.8528	0.0467
tandard deviation	: 10.5	0.0033	0.0495	0.0256	0.0645	0.3178	0.0760	0.0060
Tumber of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

^{*(+)} = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{*(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences Princeton Research Center East Millstone, New Jersey

Summary Statistics for % Organ to Body Weight Study number: 036147

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Group	Terminal		Spleen		Uterus	
• •	Body wt. (g)	Pituitary gland		Thymus		
			Fema	le An	i m a l s	
1						
Mean:	209.1	0.0057	0.2476	0.2674	0.2861	
Standard deviation:	8.7	0.0013	0.0255	0.0502	0.0713	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	
2						
Mean:	205.2	0.0068%	0.2382	0.2529	0.2962	
Standard deviation:	: 10.8	0.0005	0.0333	0.0346	0.0996	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	
3						
Mean:	203.5	0.0066	0.2403	0.2519	0.2898	
Standard deviation:	: 15.4	0.0010	0.0251	0.0411	0.0668	
Tumber of observ.	: (10)	(10)	(10)	(10)	(10)	
4						
Mean:	207.2	0.0056	0.2525	0.2392	0.3271	
Standard deviation:	: 10.5	0.0022	0.0399	0.0489	0.0986	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

 $[\]frac{1}{2}$ (\$) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Group	Terminal		Brain		Heart		Liver	
	Body wt. (g)	Adrenal Glands	Epid	lidymides		Kidneys		Lungs
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	*		Male	Anim	a 1 c			
1								
Mean	: 289.1	3.0140	100.0000	43.4246	60.6473	143.8586	552.2018	87.9308
Standard deviation	: 18.2	0.3344	0.0000	3.3229	4.0306	6.5480	51.2122	8.9177
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2		,						
Mean	290.1	2.9265	100.0000	40.8788	61.6734	143.1869	553.1696	97.3402
Standard deviation	: 20.3	0.4067	0.0000	4.6716	6.3917	13.1060	54.7162	11.5398
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean	292.4	3.1449	100.0000	41.0586	61.7693	144.4490	551.7009	97.9754
Standard deviation:	: 16.3	0.3151	0.0000	3.3991	5.1712	14.9485	62,2661	11.6529
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean	290.0	2.9145	100.0000	40.2125	62.7396	148.8471	535.2709	101.5752*
Standard deviation	: 14.9	0.4074	0.0000	5.5929	4.8524	10.7335	35.8176	6.4333
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

^{*(+)} = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$)} = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Group	Terminal	Semis w	/prostate		Testes		
	Body wt. (g)	Pituitary gland	-	Spleen		Thymus	
			Male	Anim	a 1 e		
1					u 1 b		
Mean	: 289.1	0.4080	91.0915	31.6004	159.1062	27.5349	
Standard deviation	: 18.2	0.1147	12.5856	3.7230	10.4473	4.0340	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
2							
Mean	290.1	0.5012*	91.6498	31.9349	162.6879	26.5731	
Standard deviation	: 20.3	0.0698	14.6122	3.3657	12.7244	7.1039	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
3							
Mean	292.4	0.5110*	95.5580	32.2136	155.5860	27.0076	
Standard deviation	: 16.3	0.0583	11.3027	3.5249	18.2033	5.5834	
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	
4							
Mean	290.0	0.5238+	86.0387	31.2429	156.3267	24.5106	
Standard deviation:	: 14.9	0.0572	10.2473	3.1972	12.3801	4.5774	
Number of observ.	(10)	(10)	(10)	(10)	(10)	(10)	

^{*(+) =} mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Group	Terminal		Brain		Kidneys		Lungs	
-	Body wt. (g)	Adrenal Glands		Heart	_	Liver		Ovaries
			Fema	le An	imals		· · · · · · · · · · · · · · · · · · ·	
1								
Mean	: 209.1	3.6783	100.0000	46.7684	102.2327	417.6746	83.1995	5.0517
Standard deviation	: 8.7	0.4730	0.0000	4.0273	9.4727	45.8749	7.5905	0.9632
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean	: 205.2	3.8754	100.0000	46.0741	102.1057	438.7241	78.6538	4.6947
Standard deviation	: 10.8	0.5644	0.0000	3.3556	8.2196	39.5412	14.7376	0.5654
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean	: 203.5	4.0155	100.0000	47.6261	100.8253	421.3821	82.5821	4.2956
Standard deviation	: 15.4	0.6668	0.0000	7.6307	14.4688	53.3788	14.6658	0.5745
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean	: 207.2	4.0128	100.0000	47.4499	105.5877	430.7166	96.0870	5.2445
Standard deviation	: 10.5	0.3917	0.0000	4.5366	5.8509	29.4381	10.6748	0.6444
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

 $[\]star$ (+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$) =} mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Group	Terminal		Spleen		Uterus	
-	Body wt. (g)	Pituitary gland	•	Thymus		
,			Fema	ale An	imals	
1						
Mean:	209.1	0.6283	27.4015	29.4569	31.6963	
Standard deviation:	8.7	0.1507	2.7680	4.6726	7.9027	
Number of observ.	(10)	(10)	(10)	(10)	(10)	
2						
Mean:	205.2	0.7460%	25.9579	27.5918	32.0962	
Standard deviation:	10.8	0.0457	3.5360	4.1516	10.0479	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	
3						
Mean:	203.5	0.7153	26.4065	27.6714	31.7636	
Standard deviation:	15.4	0.1008	4.4950	5.8310	8.3577	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	
4						
Mean:	207.2	0.6281	28.5062	26.8502	36.9098	
Standard deviation:	10.5	0.2415	5.3351	5.0850	11.7942	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	

^{*(+)} = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance

^{%(\$)} = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Page 602 Final Report

Incidence Summary Report	
for Gross Necropsy Observations	
Preface	Table 7

Key to Abbreviation:

LN

Lymph Node

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³

Incidence Summary Report for Gross Necropsy Observations Study number: 036147

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	-	- Male	s			- Femal	les	
Group:	1.	2	3	4	1	2	3	4
Number in group:	10	10	10	10	10	10	10	10
Within normal limits	10	0	0	0	10	0	0	0
Epididymides Small	0	0	1	0	i 0	0	0	0
Lungs Discolored	0	10	10	10	0	10	10	10
Mediastinal LN					1			
Discolored	0	0	3	10 7	0	1	6	10
Enlarged	0	4	5	7	0	2	4	10 7
Prostate					1			
Small	0	0	1	0	į o	0	0	0
Testes					1			
Enlarged	0	0	1	0	j o	0	0	0
Small	0	0	1	0	i o	0	0	0

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Page 604 Final Report

Incidence Summary of Microscopic Findings with Severity Levels	
 Preface	Table 8

Key to Abbreviations

Ctls

= Controls

NAD

= No abnormal diagnoses

No.

= Number

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Incidence Summary of Microscopic Findings with Severity Levels Terminal Sacrifice

		-							- -	
			An.	i m a :	ls	Affec	te	d		
Controls from group(s): 1 Animal sex:		Ма	l e s		i	F	e m	ale	g	
Dosage group:	Ctls	2	3	4	1	Ctls	2	3	4	
Tissues With Diagnoses No. in group:	10	10	10	10		10	10	10	10	
LungsNumber examined: BROWN-BLACK PIGMENT DEPOSITS	10	10	10	10		10	10	10	10	
Nad>	10	1	0	0	ì	10	0	0	0	
Slight>	0	7	1	0	1	0	8	2	0	
Moderate>	0	2	9	10	Ì	0	2	8	10	
	0	9	10	10	ĺ	0	10	10	10	
BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY										
Nad>	10	10	8	2	ļ	10	10	9	6	
Slight>	0	0	2	8	- 1	0	0	1	4	
	0	0	2	8	1	0	0	1	4	
ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY										
Nad>	10	4	2	0	ļ	8	4	0	0	
Slight>	0	4	6	2]	2	5	5	2	
Moderate>	0	2	2	8	}		ı	5	8	
	0	6	8	10	I	2	6	10	10	
ALVEOLAR/INTRAALVEOLAR MACROPHAGES										
Minimal>	10	0	0	0	Ţ	7	0	0	0	
Slight>	0	6	3	0	\ \	3	9	3	0	
Moderate>	0	4	7	10	ļ	0	1	7	10	
	10	10	10	10	I	10	10	10	10	
BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT -DEPOSITS										
Nad>	. 10	5	3	6	1	10	6	5	3	
Minimal>	0	1	3	0	j	0	3	2	1	
Slight>	D	0	3	1	į	0	0	0	2	
Moderate>	0	4	1	3	į	0	1	3	4	
	0	5	7	4	Ì	0	4	5	7	

All Diagnoses; Phases: P2; Death types: All unscheduled plus FS; Date of death range: 16-Mar-04 To 17-Mar-04

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Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Incidence Summary of Microscopic Findings with Severity Levels Terminal Sacrifice

				A n	i mai	ls	Affec	teo	d	
Controls from group(s): 1	Animal sex:		ма:	les		1	F	e m a	ale	s
	Dosage group:	Ctls	2	3	4	j	Ctls	2	3	4
<u> Pissues With Diagnoses</u>	No. in group:	10	10	10	10	İ	10	10	10	10
OSSEOUS METAPLASIA	.Number examined:	10	10	10	10		10	10	10	10
	Nad>	10	10	9	10	1	10	10	9	10
	Slight>	0	0	1	0	İ	0	0	1	0
Total Incidence of I	Finding Observed:	0	0	1	0	İ	0	0	1	0

All Diagnoses; Phases: P2; Death types: All unscheduled plus FS; Date of death range: 16-Mar-04 To 17-Mar-04

Chamber Monitoring Results Cumulative Exposure Record Group 1 - 0 mg/m³ (Air only) **Chamber Environment** Particle Size Mean Day Date Exposure **Gravimetric Chamber Concentration Determinations**^a Temperature Humidity Mean Number Nominal Individual MMAD GSD TMC (mg/m³)М F (mg/m³) (mg/m³) (µm) (mg/m³)(°C) (%) 0 2-Mar-04 0.00 0.00 0.00 0.00 0.00 2.753 1.693 5.50E-05 21 26 3-Mar-04 1 0.00 0 0.00 0.00 0.00 0.00 1.059 1.500 3.13E-05 22 28 2 4-Mar-04 2 0 0.00 0.00 0.00 0.00 0.00 1.244 1.726 3.60E-05 21 28 3 5-Mar-04 3 0 0.00 0.00 0.00 0.00 0.00 2.696 1.624 6.96E-05 20 29 5 6-Mar-04 4 0 0.00 0.00 0.00 0.00 0.00 4.084 1.834 3.46E-04 21 33 5 7-Mar-04 5 6 0 0.00 0.00 0.00 0.00 0.00 2.588 1.840 3.80E-04 21 29 6 8-Mar-04 7 6 0 0.00 0.00 0.00 0.00 0.00 2.339 1.865 3.53E-04 20 28 7 9-Mar-04 7 8 0 0.00 0.00 0.00 0.00 4.971 0.00 2.267 2.41E-04 19 29 8 10-Mar-04 9 8 0 0.00 0.00 0.00 2.583 0.00 0.00 1.520 3.00E-04 19 30 9 11-Mar-04 10 9 0 0.00 0.00 0.00 0.00 0.00 0.8248 1.241 1.08E-05 19 19 12-Mar-04 10 11 10 0 0.00 0.00 0.00 5.021 1.794 1.96E-04 20 0.00 0.00 18 11 13-Mar-04 12 11 0 0.00 0.00 0.00 0.00 0.00 0.8984 1.318 2.60E-05 19 17 12 12 14-Mar-04 13 0 0.00 0.00 0.00 0.00 0.00 1.465 1.409 2.24E-05 19 18 13 15-Mar-04 14 13 0 0.00 0.00 0.00 0.00 0.00 2.844 1.816 2.70E-04 20 17 14 16-Mar-04 14 0 0.00 0.00 0.00 0.00 0.00 0.6487 1.172 4.41E-06 19 11 Mean 0 0.00 1.675 1.67E-04 20 24 2.526 0 S.D. 0.00 1.396 0.266 1.42E-04 1 7

M = Male; F = Female

^aAverage daily room air samples were : MMAD = 2.674 ; GSD = 1.857; TMC = 3.80E-02

Chamber Monitoring Results Cumulative Exposure Record Group 2 - 25 mg/m3 Chamber Environment Particle Size Mean Day Date **Exposure Gravimetric Chamber Concentration Determinations** Temperature Humidity Number Nominal Mean Individual **MMAD** GSD % of Particles (mg/m³) (mg/m³) (mg/m³) $\leq 1 \, \mu \text{m} \, | \, < 3 \, \mu \text{m} \, | \, < 10 \, \mu \text{m}$ (μm) (°C) (%) 0 2-Mar-04 1 12 19.3 8.3 23 22 24 1.185 2.371 42.21 85.91 99.33 21 23 1 3-Mar-04 2 1 29 23.8 23 22 24 26 2.076 3.466 27.84 61.65 89.70 22 26 2 4-Mar-04 3 2 22 22.5 23 21 22 24 2.069 2.695 23.16 64.61 94.40 21 31 3 5-Mar-04 4 3 30 21.5 15 21 27 23 1.685 2.731 30.18 71.71 96.19 21 29 5 4 6-Mar-04 4 28 25.8 27 28 27 21 2.578 1.730 28.15 71.95 96.80 21 33 5 6 7-Mar-04 5 19 21.5 16 23 26 21 1.528 3.101 72.45 35.41 95.16 21 31 6 8-Mar-04 7 6 17 22.3 16 22 27 24 1.233 2.059 38.61 89.09 99.81 21 30 7 9-Mar-04 8 7 23 26.3 20 28 30 27 1.355 2.960 38.98 76.81 96.72 19 30 8 10-Mar-04 9 8 16 24.0 22 21 26 27 1.629 3.057 33.12 70.77 94.78 20 31 9 11-Mar-04 10 9 24 21.3 15 19 24 27 1.185 2.268 41.78 87.16 99.54 20 21 10 12-Mar-04 11 10 29 26.8 22 28 32 25 1.289 2.708 39.94 80.18 98.01 20 20 11 13-Mar-04 12 11 34 28.3 20 26 43 24 1.624 2.935 32.62 71.56 95.43 20 18 12 14-Mar-04 13 12 18 24.0 15 19 25 37 1.808 2.212 22.80 73.83 98.44 19 20 13 15-Mar-04 14 13 32 24.5 25 27 23 23 1.955 2.971 26.91 65.30 93.31 21 20 14 16-Mar-04 14 29 24.8 19 25 27 28 1.432 2.485 34.66 79.17 98.36 20 17

1.586

0.306

2.706

0.385

33.09

6.45

74.81

8.24

96.40

2.73

21

1

26

5

23.8

5.2

M = Male; F = Female

Mean

S.D.

24

7

								nulative		Results e Record g/m³						
Day	Date	Expo	sure		Gravin	netric Ch	amber Co	oncentra	tion			Particle Si			Chamber Env Mear Temperature	
•			nber	Nominal	Mean	Ī		idual		MMAD	GSD		of Partic	eles	Tomportune	Traitingity
		М	F	(mg/m³)	(mg/m³)		(mg	/m³)		(µm)		$\leq 1 \mu \text{m} \leq 3 \mu \text{m} \leq 10 \mu \text{m}$			(°C)	(%)
0	2-Mar-04	1	l	78	44.3	36	48	44	51	1.493	3.344	36.99	71.83	94.24	21	33
1	3-Mar-04	2	1	73	53.5	55	45	54	60	2.808	3.377	19.81	52.17	85.17	23	32
2	4-Mar-04	3	2	170	84.8	76	91	80	92	2.632	2.792	17.30	55.07	90.32	22	37
3	5-Mar-04	4.	3	160	82.0	56	93	100	79	1.846	2.266	22.68	72.35	98.05	21	37
4	6-Mar-04	5	4	140	83.5	73	87	91	83	2.552	2.869	18.70	56.10	90.25	22	46
5	7-Mar-04	6	5	140	66.0	48	71	72	73	1.631	2.538	29.97	74.35	97.42	21	30
6	8-Mar-04	7	6	130	62.8	56	68	68	59	1.659	2.200	26.05	77.38	98.87	21	32
7	9-Mar-04	8	7	150	67.8	58	72	68	73	2.065	2.820	24.21	64.07	93.59	20	32
8	10-Mar-04	9	8	150	72.8	82	70	73	66	2.088	2.710	23.02	64.19	94.19	20	33
9	11-Mar-04	10	9	150	57.8	31	38	81	81	1.667	2.152	25.23	77.83	99.03	20	22
10	12-Mar-04	11	10	150	64.8	56	62	70	71	2.280	2.924	22.12	60.09	91.58	20	20
11	13-Mar-04	12	11	150	72.3	61	74	82	72	2.090	2.332	19.19	66.53	96.78	20	17
12	14-Mar-04	13	12	140	69.5	61	70	74	73	2.186	2.157	15.45	65.98	97.61	19	16
13	15-Mar-04	14	13	130	72.3	66	74	74	75	2.989	2.880	15.04	50.14	87.32	21	21
14	16-Mar-04		14	130	74.3	61	73	86	77	2.628	2.396	13.44	56.02	93.69	20	20
		Ме	an	136			68.6			2.174	2.650	21.95	64.27	93.87	21	29
		S.	D.	27			14.5			0.467	0.402	6.16	9.15	4.26	1	9

M = Male; F = Female

Chamber Monitoring Results Cumulative Exposure Record Group 4 - 200 mg/m³ **Chamber Environment** Particle Size Mean Dav Date **Exposure Gravimetric Chamber Concentration Determinations** Temperature Humidity Number Nominal Mean Individual MMAD GSD % of Particles F (mg/m³)(mg/m³) (mg/m³) (µm) ≤ 1 μm < 3 µm < 10 µm (°C) (%) 0 2-Mar-04 490 1 183 140 160 220 210 2.075 2.644 22.64 64.77 94.71 21 25 3-Mar-04 2 1 500 165 130 140 170 220 3.061 3.002 15.44 49.26 85.92 22 29 2 4-Mar-04 3 2 530 173 140 210 170 170 2.414 2.855 20.05 58.21 91.23 21 34 3 5-Mar-04 4 3 520 193 240 180 150 200 2.061 2.430 20.77 66.38 96.24 21 34 6-Mar-04 5 4 530 195 170 220 190 200 2.748 2.417 12.60 53.96 92.83 21 38 6 5 5 7-Mar-04 590 188 170 190 200 190 2.591 2.603 15.75 55.92 92.12 21 32 6 7 6 8-Mar-04 540 223 260 200 220 210 1.694 2.684 29.66 71.85 96.39 20 32 7 8 7 9-Mar-04 550 198 150 230 180 230 2.016 2.922 25.67 64.47 93.24 19 32 8 10-Mar-04 9 590 195 190 210 170 210 2.589 2.768 17.51 55.76 90.78 33 19 9 9 11-Mar-04 10 620 198 140 200 210 240 2.213 2.449 18.76 63.29 95.39 19 22 10 12-Mar-04 11 10 610 215 170 220 260 210 2.502 2.757 18.29 57.11 91.41 20 21 11 13-Mar-04 12 11 630 205 160 240 220 200 2.535 2.506 15.56 57.27 93.24 20 20 12 14-Mar-04 13 12 620 223 150 280 210 250 2.749 2.616 17.08 55.39 90.76 19 18 14 13 15-Mar-04 13 570 218 170 250 230 220 3.004 2.464 11.13 49.94 90.89 20 21

M = Male; F = Female

16-Mar-04

14

Mean

S.D.

560

563

45

213

190

190

199

35

220

250

2.355

2.432

0.374

2.578

2.654

0.186

18.29

18.61

4.77

60.09

58.91

6.24

93.66

92.59

2.67

19

20

1

19

27

7

14

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

ANIMAL TERMINATION HISTORY

NIMAL#	TYPE OF # DEATH		DATE OF DEATH	WEEK OF	STUDY
			DEATH	STUDY	DAY
1001	Terminal	Sacrifice	16-MAR-04	3	14
1002	Terminal	Sacrifice	16-MAR-04	3	14
1003	Terminal	Sacrifice	16-MAR-04	3	14
1004	Terminal	Sacrifice	16-MAR-04	3	14
1005	Terminal	Sacrifice	16-MAR-04	3	14
1006	Terminal	Sacrifice	16-MAR-04	3	14
1007	Terminal	Sacrifice	16-MAR-04	3	14
1008	Terminal	Sacrifice	16-MAR-04	3	14
1009	Terminal	Sacrifice	16-MAR-04	3	14
1010	Terminal	Sacrifice	16-MAR-04	3	14

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

ANIMAL TERMINATION HISTORY

	TYPE (OF	DATE OF	WEEK OF	STUDY
NIMAL#	DEAT	Н	DEATH	STUDY	DAY
2001	Terminal :	Sacrifice	16-MAR-04	3	14
2002	Terminal :	Sacrifice	16-MAR-04	3	14
2003	Terminal :	Sacrifice	16-MAR-04	3	14
2004	Terminal S	Sacrifice	16-MAR-04	3	14
2005	Terminal S	Sacrifice	16-MAR-04	3	14
2006	Terminal S	Sacrifice	16-MAR-04	3	14
2007	Terminal S	Sacrifice	16-MAR-04	3	14
2008	Terminal 8	Sacrifice	16-MAR-04	3	14
2009	Terminal S	Sacrifice	16-MAR-04	3	14
2010	Terminal S	Sacrifice	16-MAR-04	3	14

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

ANIMAL TERMINATION HISTORY

NIMAL#	TYPE DEAT		DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3001	Terminal	Sacrifice	16-MAR-04	3	14
3002	Terminal	Sacrifice	16-MAR-04	3	14
3003	Terminal	Sacrifice	16-MAR-04	3	14
3004	Terminal	Sacrifice	16-MAR-04	3	14
3005	Terminal	Sacrifice	16-MAR-04	3	14
3006	Terminal	Sacrifice	16-MAR-04	3	14
3007	Terminal	Sacrifice	16-MAR-04	3	14
3008	Terminal	Sacrifice	16-MAR-04	3	14
3009	Terminal	Sacrifice	16-MAR-04	3	14
3010	Terminal	Sacrifice	16-MAR-04	3	14

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

vimal#	TYPE DEAT		DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4001	Terminal	Sacrifice	16-MAR-04	3	14
4002	Terminal	Sacrifice	16-MAR-04	3	14
4003	Terminal	Sacrifice	16-MAR-04	3	14
4004	Terminal	Sacrifice	16-MAR-04	3	14
4005	Terminal	Sacrifice	16-MAR-04	3	14
4006	Terminal	Sacrifice	16-MAR-04	3	14
4007	Terminal	Sacrifice	16-MAR-04	3	14
4008	Terminal	Sacrifice	16-MAR-04	3	14
4009	Terminal	Sacrifice	16-MAR-04	3	14
4010	Terminal	Sacrifice	16-MAR-04	3	14

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

TYPE OF		DATE OF	WEEK OF	STUDY	
NIMAL#	DEATH	DEATH	STUDY	DAY	
1501	Terminal Sacrifice	17-MAR-04	3	14	
1502	Terminal Sacrifice	17-MAR-04	3	14	
1503	Terminal Sacrifice	17-MAR-04	3	14	
1504	Terminal Sacrifice	17-MAR-04	3	14	
1505	Terminal Sacrifice	17-MAR-04	3	14	
1506	Terminal Sacrifice	17-MAR-04	3	14	
1507	Terminal Sacrifice	17-MAR-04	3	14	
1508	Terminal Sacrifice	17-MAR-04	3	14	
1509	Terminal Sacrifice	17-MAR-04	3	14	
1510	Terminal Sacrifice	17-MAR-04	3	14	

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	TYPE OF	DATE OF	WEEK OF	STUDY	
NIMAL#	DEATH	DEATH	STUDY	DAY	
2501	Terminal Sacrifice	17-MAR-04	3	14	
2502	Terminal Sacrifice	17-MAR-04	3	14	
2503	Terminal Sacrifice	17-MAR-04	3	14	
2504	Terminal Sacrifice	17-MAR-04	3	14	
2505	Terminal Sacrifice	17-MAR-04	3	14	
2506	Terminal Sacrifice	17-MAR-04	3	14	
2507	Terminal Sacrifice	17-MAR-04	3	14	
2508	Terminal Sacrifice	17-MAR-04	3	14	
2509	Terminal Sacrifice	17-MAR-04	3	14	
2510	Terminal Sacrifice	17-MAR-04	3	14	

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

TYPE OF		DATE OF	WEEK OF	STUDY	
NIMAL#	DEATH	DEATH	STUDY	DAY	
3501	Terminal Sacrifice	17-MAR-04	3	14	
3502	Terminal Sacrifice	17-MAR-04	3	14	
3503	Terminal Sacrifice	17-MAR-04	3	14	
3504	Terminal Sacrifice	17-MAR-04	3	14	
3505	Terminal Sacrifice	17-MAR-04	3	14	
3506	Terminal Sacrifice	17-MAR-04	3	14	
3507	Terminal Sacrifice	17-MAR-04	3	14	
3508	Terminal Sacrifice	17-MAR-04	3	14	
3509	Terminal Sacrifice	17-MAR-04	3	14	
3510	Terminal Sacrifice	17-MAR-04	3	14	

APPENDIX B

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	TYPE OF	DATE OF	WEEK OF	STUDY	
ANIMAL#	DEATH	DEATH	STUDY	DAY	
4501	Terminal Sacrifice	17-MAR-04	3	14	
4502	Terminal Sacrifice	17-MAR-04	3	14	
4503	Terminal Sacrifice	17-MAR-04	3	14	
4504	Terminal Sacrifice	17-MAR-04	3	14	
4505	Terminal Sacrifice	17-MAR-04	3	14	
4506	Terminal Sacrifice	17-MAR-04	3	14	
4507	Terminal Sacrifice	17-MAR-04	3	14	
4508	Terminal Sacrifice	17-MAR-04	3	14	
4509	Terminal Sacrifice	17-MAR-04	3	14	
4510	Terminal Sacrifice	17-MAR-04	3	14	

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Individual Clinical Observations	
individual Climical Coccivations	
Preface	Appendix C
1 161806	Appendix C

For summarization purposes, descriptive comments [i.e., location of scab(s) and sore(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

LES (GROUP 1 0 MG/M3		
		DAY OF	- 11
			7 0 7 3 4
1001	WITHIN NORMAL LIMITS		ррр
	Terminal Sacrifice		p .
	ORAL/BUCCAL: Nasal Discharge - Red		P
1002	WITHIN NORMAL LIMITS		PPP
	Terminal Sacrifice		P
1003	WITHIN NORMAL LIMITS		PPPP
	Terminal Sacrifice		P
1004	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		P
	OCULAR: Chromodacryorrhea - Unilateral		р р
	ORAL/BUCCAL: Nasal Discharge - Red		р р
1005	WITHIN NORMAL LIMITS		рррр
	Terminal Sacrifice		P
1006	WITHIN NORMAL LIMITS		PPPP
	Terminal Sacrifice		P
1007	WITHIN NORMAL LIMITS		PPPP
	Terminal Sacrifice		P
1008	WITHIN NORMAL LIMITS		рррр
	Terminal Sacrifice		p
1009	WITHIN NORMAL LIMITS		рр р
	Terminal Sacrifice		P
	OCULAR: Chromodacryorrhea - Unilateral		P
	ORAL/BUCCAL: Nasal Discharge - Red		P

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 MG/M3

DAY OF - 1 1 1 ANIMAL# OBSERVATIONS STUDY 7 0 7 3 4

1010 WITHIN NORMAL LIMITS P P

Terminal Sacrifice P
ORAL/BUCCAL: Nasal Discharge - Red P P

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

		DF - 11
NIMAL# 		7 0 7 3 4
2001	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2002	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2003	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2004	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2005	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2006	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2007	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
2008	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES (GROUP 2 25 MG/M3		·	
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 11 70734	
2009	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	P P P 1 1	
2010	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	P P P 1 1	

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MLAMINAL#	DAY OBSERVATIONS STU	
3001	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
	OCULAR: Chromodacryorrhea - Bilateral	P
3002	WITHIN NORMAL LIMITS	р р
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3003	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
3004	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 1
3005	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
3006	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
	OCULAR: Chromodacryorrhea - Unilateral	Р
3007	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3008	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

		DAY OF	- 11	
ANIMAL#	OBSERVATIONS	STUDY	7 0 7 3 4	
3009	WITHIN NORMAL LIMITS		рр	
	Terminal Sacrifice		P	
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	2 1	
3010	WITHIN NORMAL LIMITS		P P	
	Terminal Sacrifice		P	
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	2 2	

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APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

ALES (GROUP 4 200 MG/M3	L CLINICAL OBSERVATIONS
	DAY OF	- 11
ANIMAL#		7 0 7 3 4
4001	WITHIN NORMAL LIMITS	р р
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
4002	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
	OCULAR: Chromodacryorrhea - Bilateral	Р
4003	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	Р
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 3
4004	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
4005	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 2
4006	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
4007	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
4008	WITHIN NORMAL LIMITS	p p
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES (GROUP 4 200 MG/M3		······
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 11 70734
4009	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	P P P 3 3
4010	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	P P

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES (GROUP 1 0 MG/M3	INDIVIDUAL CLINICAL OBSERVATIONS
		DAY OF - 11 STUDY 80734
1501	WITHIN NORMAL LIMITS Terminal Sacrifice OCULAR: Chromodacryorrhea - Unilateral	рр Р рр
1502	WITHIN NORMAL LIMITS Terminal Sacrifice	PPPP
1503	WITHIN NORMAL LIMITS Terminal Sacrifice	рррр Р
1504	WITHIN NORMAL LIMITS Terminal Sacrifice OCULAR: Chromodacryorrhea - Unilateral	ъъ ъ ъ
1505	WITHIN NORMAL LIMITS Terminal Sacrifice	р р р р Р
1506	WITHIN NORMAL LIMITS Terminal Sacrifice	р Р Р Р Р
1507	WITHIN NORMAL LIMITS Terminal Sacrifice	рррр Р
1508	WITHIN NORMAL LIMITS Terminal Sacrifice	PPPP
1509	WITHIN NORMAL LIMITS Terminal Sacrifice	P P P P
1510	WITHIN NORMAL LIMITS Terminal Sacrifice	PPPP

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APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

	GROUP 2 25 MG/M3		
#LAMIK	OBSERVATIONS	DAY OF STUDY	8 0 7 3 4
2501	WITHIN NORMAL LIMITS		рр
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2502	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2503	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2504	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2505	WITHIN NORMAL LIMITS		р р
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2506	WITHIN NORMAL LIMITS		РР
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2507	WITHIN NORMAL LIMITS		рр
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1
2508	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

EMALES (GROUP 2 25 MG/M3			
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1 1 8 0 7 3 4	
2509	WITHIN NORMAL LIMITS		P P	
	Terminal Sacrifice		. p	
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1	
2510	WITHIN NORMAL LIMITS		P P	
	Terminal Sacrifice		P	
	APPEARANCE: TEST MATERIAL ON FUR	(BLACK)	1 1	

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

NIMAL#		- 11 80734
	01051	0 0 7 3 4
3501	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3502	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
3503	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 1
3504	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3,505	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3506	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 2
3507	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	1 1
3508	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES (GROUP 3 75 MG/M3		OBSERVATIONS	
ANIMAL#	OBSERVATIONS	DAY OF STUDY	- 1 1 8 0 7 3 4	
3509	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON OCULAR: Chromodacryorrhea - B		P P	
3510	WITHIN NORMAL LIMITS Terminal Sacrifice APPEARANCE: TEST MATERIAL ON	FUR (BLACK)	P P P	

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APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

EMALES (GROUP 4 200 MG/M3	
ANIMAL#	OBSERVATIONS STUDY	- 1 1 8 0 7 3 4
4501	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
4502	··	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
4503	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
4504	WITHIN NORMAL LIMITS	P P
	Terminal Sacrifice	P .
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 3
4505	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	р
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	
	OCULAR: Chromodacryorrhea - Bilateral	P
4506	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	3 3
4507	WITHIN NORMAL LIMITS	рр
	Terminal Sacrifice	P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
4508	WITHIN NORMAL LIMITS	РР
	Terminal Sacrifice	p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2

APPENDIX C

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

EMALES (
ANIMAL#		AY OF STUDY	- 1 1 8 0 7 3 4
4509	WITHIN NORMAL LIMITS		-
4509			РР
	Terminal Sacrifice		P
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2
	OCULAR: Chromodacryorrhea - Unilateral		P P
4510	WITHIN NORMAL LIMITS		P P
	Terminal Sacrifice		p
	APPEARANCE: TEST MATERIAL ON FUR (BLACK)	2 2

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

Males Gi	ROUP 1 0 1	MG/M3			
	DAY	OF ST	UDY		***************************************
ANIMAL#	-7	0	7	13	
1001	212	282	326	353	
1002	189	255	294	325	
1003	208	272	301	319	
1004	201	260	300	328	
1005	199	256	282	304	
1006	194	260	280	299	
1007	204	283	318	350	
1008	209	274	300	332	
1009	196	250	284	310	
1010	192	254	281	305	
MEAN	200	264	296	323	
3.D.	7.7	12.1	15.7	19.0	
N	10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 2	25	MG/M3			INDIVIDUAL BODY WEIGHTS (GRAMS)
		DAY	OF ST	UDY		
ANIMAL#		-7	0	7	13	
2001		211	272	310	344	
2002		202	269	306	334	
2003		209	281	310	345	
2004		190	254	272	301	
2005		200	266	308	340	
2006		198	256	282	301	·
2007		193	257	291	318	
2008		192	258	287	310	
2009		204	266	271	288	
2010		207	271	316	359	
MEAN		200	265	295	324	
S.D.		7.3	8.8	16.6	23.5	
N		10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES (GROUP 3	75	MG/M3		
		DAY	OF ST	JDY	
ANIMAL#		-7	0	7	13
2001					
3001		202	266	299	323
3002		206	257	297	333
3003		215	287	330	357
3004		189	252	280	303
3005		209	273	294	317
3006		194	259	273	302
3007		193	265	303	330
3008		197	262	292	332
3009		199	270	314	351
3010		203	273	295	331
MEAN		201	266	298	328
S.D.		7.9	9.9	15.9	17.9
N		10	10	10	10

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF ST	UDY		
ANIMAL#	-7	0	7	13	
4001	206	269	304	336	
4002	204	263	286	320	
4003	187	247	279	313	
4004	216	285	321	359	
4005	196	252	282	315	
4006	202	269	290	316	
4007	196	268	298	326	
4008	210	275	305	336	
4009	198	262	292	327	
4010	192	255	279	306	
IEAN	201	264	294	325	
.D.	8.6	11.3	13.5	15.4	
N	10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF ST	UDY		
ANIMAL#	-8	0	7	13	
1501	186	216	231	252	
1502	172	209	206	215	
1503	160	191	209	227	
1504	177	213	232	242	
1505	179	211	228	233	
1506	164	198	220	226	
1507	169	203	235	241	
1508	170	214	231	234	
1509	175	221	219	241	
1510	181	218	227	249	
MEAN	173	210	224	236	
3.D.	7.8	9.4	10.0	11.2	
N	10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

FEMALES	GROUP 2 25	MG/M3			
	DAY	OF ST	UDY		
ANIMAL#	-8	0	7	13	
2501	178	215	225	232	
2502	173	210	215	233	
2503	174	188	208	217	
2504	179	215	231	246	
2505	161	193	203	218	
2506	179	219	229	243	
2507	167	206	228	225	
2508	163	205	207	229	
2509	186	220	238	252	
2510	170	208	212	226	
MEAN	173	208	219	232	
S.D.	7.8	10.5	12.0	11.6	
N	10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF ST	UDY		
ANIMAL#	-8	0	7	13	
3501	182	220	232	244	
3502	165	183	208	205	
3503	170	202	215	230	
3504	173	211	218	238	
3505	161	191	200	207	
3506	166	201	213	221	
3507	171	206	221	219	
3508	176	218	239	251	
3509	185	225	235	246	
3510	178	221	235	249	
EAN	173	208	221	231	
.D.	7.8	13.9	13.2	17.1	
N	10	10	10	10	

APPENDIX D

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF ST	UDY	
ANIMAL#	-8	0	7	13
4501	170	209	213	230
4502	185	215	239	244
4503	172	204	206	223
4504	183	225	240	252
4505	169	199	223	233
4506	176	220	229	242
4507	166	205	203	218
4508	162	197	215	216
4509	178	217	226	250
4510	174	209	227	242
MEAN	173	210	222	235
S.D.	7.3	9.2	12.8	13.1
N	10	10	10	10

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	GROUP 1		MG/M3	INDIVIDUAL BODI WEIGHT CHANGE FROM BASELINE (GRAMS)
			OF STUDY	
ANIMAL#		0-7	0-13	
1001		44	72	
1002		39	70	
1003		29	48	
1004		40	68	
1005		26	48	
1006		21	39	
1007		35	68	
1008		26	58	
1009		34	60	
1010		27	52	
IEAN		32	58	
3.D.		7.4	11.2	
N		10	10	

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 2	25	MG/M3	INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)
ANIMAL#		DAY 0-7	OF STUDY 0-13	
2001		37	72	
2002		37	65	
2003		29	64	
2004		18	48	
2005		42	73	
2006		26	45	·
2007		34	61	
2008		29	52	
2009		6	22	
2010		45	88	
MEAN		30	59	
S.D.		11.7	18.2	
N		10	10	

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 3	75	MG/M3	INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)
			OF STUDY	
ANIMAL#		0-7	0-13	
3001		33	57	
3002		39	76	
3003		43	70	
3004		27	51	
3005		21	44	
3006		14	43	
3007		38	64	
3008		31	71	
3009		44	82	
3010		22	58	
MEAN		31	61	
S.D.		10.0	13.2	
N		10	10	

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	GROUP 4	20	0 MG/M3
		DAY	OF STUDY
ANIMAL#		0-7	0-13
			
4001		35	67
4002		23	57
4003		32	66
4004		36	74
4005		30	63
4006		21	47
4007		30	59
4008		30	61
4009		30	66
4010		24	50
MEAN		20	63
MEAN		29	61
S.D.		5.0	8.0
N		10	10

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF STUDY
ANIMAL#	0 - 7	0-13
1501	15	35
1502	-3	6
1503	18	36
1504	19	29
1505	17	22
1506	21	27
1507	32	38
1508	17	20
1509	-2	20
1510	9	31
MEAN	14	26
s.D.	10.5	9.7
N	10	10

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF STUDY
ANIMAL#	0-7	0~13
2501	10	17
2502	6	24
2503	19	29
2504	16	31
2505	10	25
2506	9	24
2507	22	19
2508	2	24
2509	18	32
2510	3	18
MEAN	11	24
S.D.	6.9	5.2
N	10	10

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF STUDY
ANIMAL#	0-7	0-13
3501	13	25
3502	25	23
3503	13	29
3504	7	27
3505	9	17
3506	12	21
3507	15	13
3508	21	33
3509	10	21
3510	14	28
MEAN	14	24
S.D.	5.5	6.1
N	10	10

APPENDIX E

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES	GROUP 4 20	00 MG/M3	INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)
ANIMAL#	0-7	OF STUDY 0-13	
4501	3	21	
4502	23	29	
4503	2	19	
4504	15	27	
4505	25	35	
4506	9	22	
4507	- 3	12	
4508	18	19	
4509	9	33	
4510	18	33	
MEAN	12	25	
S.D.	9.3	7.5	
N	10	10	

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 1 C	MG/M3		
	DA	Y OF S	TUDY	
ANIMAL#				
1001				
1002		92	83	
1003	103	87	79	
1004	104	91	. 83	
1005	108	85	82	
1006	112	86	77	
1007	110	89	81	
1008	104	80		
1009	106			
1010	106	89		
MEAN	107	87	80	
S.D.	3.1	3.4	2.8	
N	10			

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 2	25	MG/M3		INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/RG/DAY)
		DAY	OF ST	JDY	
ANIMAL#		0	7	13	
2001		111	88	80	
2002		107	85	78	
2003		109	89	85	
2004		110	90	85	
2005		114	92	86	
2006		106	81	74	
2007		105	83	78	
2008		106	83	75	
2009		108	86	75	
2010		110	89	86	
MEAN		109	87	80	
S.D.		2.8	3.6	4.9	
N		10	10	10	

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

	DAY	OF STU	JDY
ANIMAL#	0	7	13
3001	105		70
	105	91	79
3002	101	84	80
3003	114	90	81
3004	112	75	77
3005	112	93	81
3006	108	87	79
3007	115	95	82
3008	108	85	83
3009	118	95	88
3010	117	89	83
MEAN	111	88	81
S.D.	5.5	6.0	3.0
N	10	10	10

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

MALES	GROUP 4	200	MG/M3	
		DAY	OF STU	my
ANIMAL#		0	7	13
4001		107	69	77
4002		105	87	78
4003		107	93	78
4004		114	77	82
4005		105	85	79
4006		110	84	7 7
4007		116	90	81
4008		109	85	80
4009		114	84	80
4010		108	86	81
MEAN		100	0.4	70
		109	84	79
s.D.		3.7	6.5	1.8
N		10	10	10

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

FEMALES GR	OUP 1 0 N	IG/M3		INDIVIDUAL FEED CONSUMPTION VALUES (GRANS/ KG/ DAI)
	DAY	OF STU	DY	
ANIMAL#	0	7	13	
1501	100	84	79	
1502	111	83	88	
1503	96	80	84	
1504	103	84	81	
1505	101	87	81	
1506	103	88	78	
1507	99	88	71	
1508	98	84	86	
1509	106	76	82	
1510	97	82	97	
MEAN	101	84	83	
S.D.	4.6	3.6	6.9	
N	10	10	10	

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

FEMALES	GROUP 2	25	MG/M3		
		DAY	OF STU	ЛDY	
ANIMAL#		0	7	13	
2501	1	.03	86	82	·
2502	1	0.3	82	80	
2503		96	89	85	
2504		99	83	81	
2505	1	02	84	80	
2506		97	80	77	
2507	1	03	87	77	
2508	1	02	81	85	
2509		98	87	80	
2510	1	80	86	86	
MEAN	1	01	84	81	
S.D.	3	. 5	2.8	3.2	
N		10	10	10	

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES	GROUP 3 75	MG/M3		,, ,, ,, ,, ,, ,, ,, ,, ,, ,,
		OF ST	YDY	
ANIMAL#	0	7	13	
3501	110	86	81	
3502	96	86	74	
3503	97	81	80	
3504	99	83	83	
3505	106	86	81	
3506	106	89	89	
3507	99	82	72	
3508	SF	87	81	
3509	98	80	77	
3510	112	89	91	
MEAN	103	85	81	
s.b.	6.1	3.4	5.9	
N	9	10	10	

SF=Spilled Feeder

APPENDIX F

PETROLEUM COKE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES	GROUP 4	200	MG/M3	
	· • • • • • • • • • • • • • • • • • • •	DAY	OF STU	DY
ANIMAL#		0	7	13
4501		101	77	78
4502		95	83	78
4503		99	78	83
4504	1	L04	82	83
4505	1	L03	95	80
4506		105	80	75
4507		SF	90	89
4508	1	104	86	79
4509		103	81	82
4510	1	.02	82	78
MEAN	1	.02	83	80
S.D.		3.0	5.5	3.7
N		9	10	10

SF=Spilled Feeder

Individual Organ Weights	
 Preface	Appendix G

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Absolute Organ Weights	660
% Organ to Body Weight Ratios	
% Organ to Brain Weight Ratios	

Key to Abbreviations:

g = Grams wt. = Weight observ. = Observed

semis w/prostate = Seminal vesicles

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³

Summary statistics for absolute organ weights (g) Study number: 036147

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Term:	inal	Sacr:	ifice

	Cerminal	Admonal Glove	Brain		Heart		Liver
No/sex Subgroup Boo	ay wt. (g)	Adrenal Glands		Epididymides		Kidneys	
			Male	Animals			
1001/M 1/1	319.9	0.0483	1.9702	0.7815	1.3678	2.7428	11.466
1002/M 1/1	289.7	0.0485	1.9484	0.7857	1.1685	2.8161	9.974
1003/M 1/1	284.7	0.0591	1.9523	0.8559	1.2251	2.7197	9.833
1004/M 1/1	292.5	0.0634	1.8570	0.8648	1.0429	2.7511	11.392
1005/M 1/1	270.6	0.0573	1.8250	0.8472	1.0093	2.6815	9.49
1006/M 1/1	269.7	0.0562	1.9231	0.8116	1.1294	2.5673	9.78
1007/M 1/1	317.2	0.0648	2.0252	0.9830	1.2111	2.9328	12.54
1008/M 1/1	297.4	0.0565	1.9485	0.7584	1.1514	3.0385	9.519
1009/M 1/1	274.0	0.0592	1.8527	0.7753	1.1733	2.7526	10.449
1010/M 1/1	275.5	0.0673	1.9790	0.9086	1.2252	2.7236	12.079
Mean:	289.1	0.0581	1.9281	0.8372	1.1704	2.7726	10.653
tandard deviation:	18.2	0.0063	0.0638	0.0699	0.1005	0.1315	1,124
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
2001/M 2/1	307.7	0.0565	1.8802	0.8161	1.3126	2.8686	9.768
2002/M 2/1	296.5	0.0546	1.8071	0.7225	1.2523	2.8587	10.13
2003/M 2/1	304.1	0.0638	2.0010	1.0310	1.1720	3.0256	12.21
2004/M 2/1	266.1	0.0688	1.9329	0.7587	1.2320	2.5344	11.81
2005/M 2/1	305.0	0.0564	2.1437	0.7603	1.3025	2.6641	10.02
2006/M 2/1	277.3	0.0707	2.0010	0.8984	0.9958	2.7864	11.80
2007/M 2/1	282.1	0.0464	1.8279	0.6790	1.1066	2.6566	9.77
2008/M 2/1	283.0	0.0553	1.9752	0.7994	1.2010	2.8097	11.59
2009/M 2/1	257.5	0.0504	1.9694	0.7658	1.0874	2.4795	9.14
2010/M 2/1	321.9	0.0490	2.0168	0.7615	1.3761	3.2626	11.82
Mean:	290.1	0.0572	1.9555	0.7993	1.2038	2.7946	10.809
tandard deviation:	20.3	0.0082	0.0991	0.0999	0.1163	0.2322	1.13
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
3001/M 3/1	288.5	0.0638	2.0269	0.8293	1.3570	2.7493	11.085
3002/M 3/1	298.2	0.0586	1.9968	0.6986	1.1562	3.0225	11.36
3003/M 3/1	320.1	0.0620	1.9338	0.9149	1.3818	3.0349	11.970
3004/M 3/1	269.7	0.0545	1.8393	0.7296	1.1731	2.7165	9.444
3005/M 3/l	286.5	0.0712	1.8501	0.8232	1.1369	2.9925	10.199
3006/M 3/1	267.1	0.0522	1.8872	0.7999	1.0839	2.0783	8.763
3007/M 3/1	294.1	0.0651	1.9698	0.8093	1.1039	2.7958	10.183
3008/M 3/1	299.1	0.0651	1.9319	0.7704	1.1320	2.6381	
3009/M 3/1	310.4	0.0569	2.0017	0.8407	1.3304	3.1547	9.39
3010/M 3/1	290.7	0.0626	2.0418	0.7731	1.1765	2.9583	13.483
Mean:	292.4	0.0612	1.9479	0.7989	1.2032		11.767
andard deviation:	16.3	0.0057	0.0717	0.7989	0.1101	2.8141 0.3068	10.764
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	1.437 (10
4001/M 4/1	295.6	0.0485	2.0221	1.0172	1.2288	2.8610	10.363
4002/M 4/1	285.5	0.0490	2.0007	0.7239	1.1409	3.0231	10.363

Summary statistics for absolute organ weights (g) Study number: 036147

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Animal	Group/	Terminal		Brain		Heart		Liver
No/sex	Subgroup E	Body wt. (g)	Adrenal Glands	Ep	ididymides		Kidneys	
4004/M	4/1	324.5	0.0572	1.8993	0.8614	1.2099	2.8718	11.1187
4005/M	4/1	280.8	0.0630	1.8464	0.7368	1.1570	2.8852	10.1000
4006/M	4/1	282.4	0.0450	1.9523	0.8467	1.2587	2.8700	9.4641
4007/M	4/1	292.0	0.0645	1.9403	0.7572	1.3398	2.9926	9.5035
4008/M	4/1	296.9	0.0689	2.1083	0.7363	1.2500	3.1054	11.6208
4009/M	4/1	293.9	0.0577	1.9761	0.6478	1.4293	3.2957	10.0765
4010/M	4/1	270.1	0.0625	1.9492	0.8721	1.1415	2.4401	10.9720
•	Mean:	290.0	0.0569	1.9547	0.7858	1.2259	2.9085	10.4551
Standard d	eviation:	14.9	0.0079	0.0790	0.1131	0.1003	0.2266	0.6942
Number of	observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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rer	minai	Sacrifice

	ninal	Pituitary gland		Spleen		Thymus
No/sex Subgroup Body w	vt. (g) Lungs	Ser Ser	mis w/prostate	•	Testes	2
		Male	Animals			
	119.9 1.701	.5 0.0046	1.7575	0.5872	2.9025	0.4845
	289.7 1.563	.5 0.0053	1.6174	0.5887	2.8663	0.6950
	1.908	6 0.0096	1.9744	0.6424	3.4313	0.5580
	92.5 1.625	4 0.0047	1.5782	0.5342	2.7972	0.4449
The state of the s	270.6 1.490	5 0.0096	1.9836	0.5002	3.1518	0.4756
	69.7 1.462	6 0.0087	1.3910	0.5839	3.0392	0.444
	17.2 1.992	9 0.0097	2.0149	0.7765	3.3883	0.5218
1008/M 1/1 2	97.4 2.009	3 0.0073	2.1146	0.7378	2.9814	0.6412
1009/M 1/1 2	74.0 1.525	9 0.0093	1.5538	0.5773	3.0579	0.5320
1010/M 1/1 2	75.5 1.700	0.0098	1.5768	0.5774	3.0504	0.5151
Mean: 2	89.1 1.697	8 0.0079	1.7562	0.6106	3.0666	0.5312
Standard deviation:	18.2 0.205	5 0.0022	0.2477	0.0861	0.2086	0.0819
Number of observ. :	(10)) (10)	(10)	(10)	(10)	(10)
2001/M 2/1 3	07.7 1.920	5 0.0110	1.9658	0.6080	2.9682	0.4684
	96.5 2.170	7 0.0101	2.0448	0.6815	3.2605	0.4202
	04.1 2.128	7 0.0092	1.9646	0.5843	3.4823	0.6125
2004/M 2/1 2	66.1 1.776	5 0.0089	1.4767	0.5276	3.3298	0.4116
2005/M 2/1 3	05.0 1.933	1 0.0085	1.5521	0.6841	3.1019	0.942
2006/M 2/1 2	77.3 1.726	2 0.0112	1.6409	0.5818	2.8876	0.5228
2007/M 2/1 2	82.1 1.970	7 0.0103	1.8685	0.6275	3.2138	0.5578
2008/M 2/1 2	83.0 1.732	6 0.0078	1.4486	0.6050	3.0633	0.470
2009/M 2/1 2	57.5 1.661	5 0.0103	1.8172	0.5971	3.1515	0.3972
2010/M 2/1 3	21.9 1.946	4 0.0103	2.0566	0.7369	3.2743	0.4256
	90.1 1.896	7 0.0098	1.7836	0.6234	3.1733	0.5228
Standard deviation:	20.3 0.171	4 0.0011	0.2351	0.0612	0.1766	0.1629
Number of observ. :	(10)) (10)	(10)	(10)	(10)	(10)
	88.5 2.256	6 0.0099	1.6828	0.6315	3.4864	0.5943
3002/M 3/1 2	98.2 1.729	5 0.0100	2.0709	0.6905	2.3404	0.5828
3003/M 3/1 3	20.1 1.899	9 0.0103	1.8616	0.7495	3.2302	0.5202
3004/M 3/1 2	69.7 1.575	9 0.0112	1.9293	0.5662	3.1343	0.4806
3005/M 3/1 2	86.5 1.593	0.0099	1.9271	0.5068	2.6688	0.4323
3006/M 3/1 2	67.1 1.741	5 0.0071	1.9481	0.6907	3.1943	0.3669
3007/M 3/1 2	94.1 1.811	4 0.0103	1.5435	0.5899	3.3833	0.4207
3008/M 3/1 2	99.1 2.226	9 0.0095	2.0588	0.6273	3.0410	0.7622
3009/M 3/1 3	10.4 1.968		1.9368	0.6355	2.8372	0.5981
3010/M 3/1 2	90.7 2.326		1.6051	0.5860	2.9561	0.5117
Mean: 2	92.4 1.912		1.8564	0.6274	3.0272	0.5269
	16.3 0.274		0.1836	0.0702	0.3431	0.1138
Number of observ. :	(10)		(10)	(10)	(10)	(10)
4001/M 4/1 2	95.6 2.066	8 0.0098	2.0936	0.6022	3.5809	0.4691
4002/M 4/1 2	85.5 1.910		1.3814	0.6027	3.1258	0.5404
4003/M 4/1 2	77.8 1.778		1.5579	0.5268	2.6808	0.3823

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Animal Group/	Terminal	Pitui	Pituitary gland				Thymus
No/sex Subgroup Bo	dy wt. (g)	Lungs	Semis	w/prostate		Testes	
4004/M 4/1	324.5	2.0427	0.0107	1.5492	0.7050	3.0576	0.4650
4005/M 4/1	280.8	1.9301	0.0076	1.6691	0.5217	2.8036	0.5057
4006/M 4/1	282.4	1.8224	0.0098	1.6449	0.6120	3.2317	0.4105
4007/M 4/1	292.0	2.1308	0.0106	1.6724	0.6010	3.1275	0.4886
4008/M 4/1	296.9	1.9775	0.0100	2.1205	0.6415	3.3910	0.3713
4009/M 4/1	293.9	2.1594	0.0122	1.5137	0.7289	2.5908	0.6790
4010/M 4/1	270.1	2.0212	0.0107	1.6397	0.5668	2.9968	0.4719
Mean:	290.0	1.9841	0.0102	1.6842	0.6109	3.0587	0.4784
Standard deviation:	14.9	0.1249	0.0012	0.2396	0.0674	0.3078	0.0885
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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	Group/	Terminal		Brain		Kidneys		Lungs
No/sex S	Subgroup	Body wt. (g)	Adrenal Glands		Heart	-	Liver	~
				Female	Animal	6		·
1501/F	1/1	216.4	0.0733	1.9256	0.8082	2.0568	8.9642	1.549
1502/F	1/1	192.8	0.0685	1.8550	0.7760	1.7264	6.4086	1.477
1503/F	1/1	199.5	0.0540	1.9073	0.8332	1.7306	7.5774	1.604
1504/F	1/1	211.8	0.0739	1.8245	0.8925	2.1670	8.3446	1.731
1505/F	1/1	207.0	0.0781	1.8472	0.9006	1.8708	8.1067	1.456
1506/F	1/1	201.6	0.0609	1.9368	0.8314	1.7686	6.7711	1.855
1507/F	1/1	213.0	0.0597	1.8905	0.9473	2.0795	8.6789	1.402
1508/F	1/1	215.5	0.0732	1.9265	0.9649	1.8715	7.3124	1.523
1509/F	1/1	212.7	0.0814	1.9784	0.9114	2.0077	8.6891	1.759
1510/F	1/1	220.8	0.0705	1.7814	0.9501	1.9902	7.9233	1.355
	Mean:	209.1	0.0694	1.8873	0.8816	1.9269	7.8776	1.571
tandard de	viation:	8.7	0.0087	0.0596	0.0656	0.1558	0.8528	0.164
umber of c	bserv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
2501/F	2/1	208.7	0.0730	1.8548	0.9061	1.9257	8.9363	1.201
2502/F	2/1	202.0	0.0598	1.9304	0.9302	1.7906	6.9470	1.781
2503/F	2/1	191.6	0.0643	1.9385	0.8152	1.9775	8.1804	2.171
2504/F	2/1	216.6	0.0677	1.7856	0.8920	1.8672	7.7409	1.355
2505/F	2/1	191.7	0.0852	1.9719	0.8253	1.8099	8.5824	1.547
2506/F	2/1	216.1	0.0712	1.9305	0.9790	1.8581	7.8610	1.290
2507/F	2/1	201.3	0.0886	1.7554	0.7387	1.9166	8.0896	1.394
2508/F	2/1	202.0	0.0645	1.8879	0.8396	1.8661	8.1836	1.151
2509/F	2/1	223.8	0.0746	1.9046	0.8805	2.2801	9.5625	1.457
2510/F	2/1	198.5	0.0786	1.8613	0.8626	1.9007	8.3988	1.477
	Mean:	205.2	0.0728	1.8821	0.8669	1.9193	8.2483	1.482
tandard de	viation:	10.8	0.0093	0.0691	0.0671	0.1382	0.7047	0.301
umber of o	bserv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
3501/F	3/1	216.2	0.0885	1.7875	0.8539	1.9564	7.5783	1.380
3502/F	3/1	183.3	0.0587	1.9492	0.7960	1.7185	7.7056	1.555
3503/F	3/1	196.1	0.0808	1.8980	0.8636	1.8273	7.3667	1.599
3504/F	3/1	211.3	0.0745	1.8537	1.0043	2.2285	7.7690	1.579
3505/F	3/1	182.0	0.0732	1.9004	0.7862	1.5515	6.4190	1.476
3506/F	3/1	190.2	0.0572	1.8393	0.8330	1.7416	6.9452	1.478
3507/F	3/1	197.9	0.0689	1.8547	0.8533	1.6886	7.9822	1.175
3508/F	3/1	222.0	0.0862	1.7666	1.1726	2.2474	7.5411	1.691
3509/F	3/1	215.7	0.0854	1.8640	0.7837	1.7643	9.3634	1.873
3510/F	3/1	220.6	0.0725	1.9184	0.8995	2.0125	9.8290	1.981
	Mean:	203.5	0.0746	1.8632	0.8846	1.8737	7.8500	
andard de	viation:	15.4	0.0109	0.0566	0.1203	0.2322	1.0285	1.539 0.280
umber of o			(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	202.7	0.0635	1.8321	0.8716	2.0195	7.5482	1.630
4502/F	4/1	215.6	0.0719	1.9013	0.8688	2.1228	7.9559	1.6659
4503/F	4/1	195.0	0.0734	1.8931	0.7894	1.7643	7.4212	1.6838

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Number of observ. :

(10)

Animal	Group/	Terminal		Brain		Kidneys		Lungs
No/sex	Subgroup	Body wt. (g)	Adrenal Glands		Heart		Liver	
4504/F	4/1	221.6	0.0830	1.8545	0.9706	1.9654	8.1005	2.0181
4505/F	4/1	204.4	0.0727	1.8745	0.8429	1.9510	8.4828	1.9099
4506/F	4/1	216.7	0.0826	1.8396	0.9670	2.0389	8.8171	2.1384
4507/F	4/1	194.9	0.0680	1.7962	0.8557	1.9784	7.7237	1.7397
4508/F	4/1	193.8	0.0817	1.7975	0.8487	1.8827	8.4980	1.5245
4509/F	4/1	217.5	0.0738	1.7461	0.9466	1.7271	7.0907	1.7581
4510/F	4/1	210.2	0.0676	1.8769	0.7619	1.9916	7.6431	1.6146
	Mean:	207.2	0.0738	1.8412	0.8723	1.9442	7.9281	1.7683
Standard de	eviation:	10.5	0.0067	0.0494	0.0706	0.1219	0.5456	0.1944

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	rminal		itary gland		Thymus	
No/sex Subgroup Body	wt. (g)	Ovaries		Spleen		Uterus
			Female	Animal	s	
1501/F 1/1	216.4	0.1447	0.0122	0.5789	0.6601	0.7803
1502/F 1/1	192.8	0.0807	0.0065	0.5035	0.5820	0.4327
1503/F 1/1	199.5	0.0879	0.0111	0.5091	0.5129	0.5948
1504/F 1/1	211.8	0.1015	0.0129	0.6089	0.4232	0.4134
1505/F 1/1	207.0	0.0843	0.0143	0.4698	0.5460	0.5785
1506/F 1/1	201.6	0.0788	0.0108	0.4855	0.6241	0.5051
1507/F 1/1	213.0	0.0970	0.0154	0.5491	0.6274	0.7908
1508/F 1/1	215.5	0.0931	0.0149	0.4812	0.4714	0.4595
1509/F 1/1	212.7	0.0946	0.0129	0.5459	0.7104	0.8568
1510/F 1/1	220.8	0.0909	0.0078	0.4387	0.4183	0.5858
Mean:	209.1	0.0954	0.0119	0.5171	0.5576	0.5998
Standard deviation:	8.7	0.0188	0.0029	0.0527	0.1004	0.1589
Number of observ. :	(10)	(10)	(10)	(10)	(10)	
	(20)	(10)	(10)	(10)	(10)	(10)
2501/F 2/1	208.7	0.0934	0.0146	0.4447	0.6002	0.4783
2502/F 2/1	202.0	0.0793	0.0134	0.4697	0.5425	0.6289
2503/F 2/1	191.6	0.0846	0.0139	0.5807	0.4267	0.4599
2504/F 2/1	216.6	0.0819	0.0145	0.5153	0.4247	0.5259
2505/F 2/1	191.7	0.0855	0.0142	0.3968	0.5428	0.7475
2506/F 2/1	216.1	0.0914	0.0131	0.4845	0.4685	0.4450
2507/F 2/1	201.3	0.0965	0.0136	0.4010	0.5492	0.4832
2508/F 2/1	202.0	0.0728	0.0151	0.5728	0.5289	1.0848
2509/F 2/1	223.8	0.0922	0.0139	0.5679	0.6584	0.6500
2510/F 2/1	198.5	0.1040	0.0139	0.4511	0.4466	0.5462
Mean:	205.2	0.0882	0.0140	0.4885	0.5189	0.6050
Standard deviation:	10.8	0.0091	0.0006	0.0686	0.0770	0.1945
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2501/8 7/2	07.6	0.0000				
3501/F 3/1	216.2	0.0838	0.0156	0.5699	0.5318	0.8410
3502/F 3/1	183.3	0.0637	0.0161	0.3780	0.4403	0.5046
3503/F 3/1	196.1	0.0791	0.0147	0.4436	0.5226	0.7185
3504/F 3/1	211.3	0.0928	0.0141	0.5527	0.5258	0.4789
3505/F 3/1	182.0	0.0799	0.0114	0.4106	0.3517	0.5053
3506/F 3/1	190.2	0.0725	0.0101	0.5087	0.5955	0.5486
3507/F 3/1	197.9	0.0880	0.0117	0.4865	0.5323	0.3859
3508/F 3/1	222.0	0.0631	0.0124	0.5775	0.7038	0.5065
3509/F 3/1	215.7	0.0835	0.0131	0.4253	0.4497	0.5972
3510/F 3/1	220.6	0.0937	0.0141	0.5487	0.4782	0.8264
Mean:	203.5	0.0800	0.0133	0.4902	0.5132	0.5913
tandard deviation:	15.4	0.0108	0.0019	0.0722	0.0947	0.1537
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4501/F 4/1	202.7	0.0938	0.0159	0.4136	0.4640	0.7863
4502/F 4/1	215.6	0.1096	0.0112	0.4537	0.4900	0.4369
4503/F 4/1	195.0	0.0905	0.0142	0.4940	0.5796	0.7365

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Animal Group/	Terminal	Pitui	tary gland		Thymus		"
No/sex Subgroup Bo	ody wt. (g)	Ovaries		Spleen	_	Uterus	
4504/F 4/1	221.6	0.1122	0.0148	0.6962	0.4619	0.6759	
4505/F 4/1	204.4	0.1069	0.0122	0.5134	0.6419	0.6175	
4506/F 4/1	216.7	0.0696	0.0144	0.7022	0.5882	0.4913	
4507/F 4/1	194.9	0.0983	0.0097	0.4728	0.5084	0.5509	
4508/F 4/1	193.8	0.0889	0.0121	0.4526	0.2807	0.4589	
4509/F 4/1	217.5	0.0919	0.0109	0.4930	0.4558	0.9857	
4510/F 4/1	210.2	0.1044	0.0001	0.5573	0.4812	1.0426	
Mean:	207.2	0.0966	0.0116	0.5249	0.4952	0.6783	
Standard deviation:	10.5	0.0126	0.0045	0.0996	0.0985	0.2118	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	

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Terminal	Sacrifice	

		Terminal		Brain	Brain Heart				
No/sex Su	bgroup	Body wt. (g)	Adrenal Glands		Epididymides		Kidneys		
				Male	Animals				
1001/M	1/1	319.9	0.0151	0.6159	0.2443	0.4276	0.8574	3.584	
1002/M	1/1	289.7	0.0167	0.6726	0.2712	0.4033	0.9721	3.443	
1003/M	1/1	284.7	0.0208	0.6857	0.3006	0.4303	0.9553	3.454	
1004/M	1/1	292.5	0.0217	0.6349	0.2957	0.3565	0.9405	3.894	
1005/M	1/1	270.6	0.0212	0.6744	0.3131	0.3730	0.9909	3.507	
1006/M	1/1	269.7	0.0208	0.7131	0.3009	0.4188	0.9519	3.627	
1007/M	1/1	317.2	0.0204	0.6385	0.3099	0.3818	0.9246	3.954	
1008/M	1/1	297.4	0.0190	0.6552	0.2550	0.3872	1.0217	3.201	
1009/M	1/1	274.0	0.0216	0.6762	0.2830	0.4282	1.0046	3.813	
1010/M	1/1	275.5	0.0244	0.7183	0.3298	0.4447	0.9886	4.383	
M	iean:	289.1	0.0202	0.6685	0.2903	0.4051	0.9608	3.686	
Standard dev			0.0026	0.0331	0.0269	0.0292	0.0471	0.335	
Number of ob	serv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10	
2001/M	2/1	307.7	0.0184	0.6110	0.2652	0.4266	0.9323	3.174	
2002/M	2/1	296.5	0.0184	0.6095	0.2437	0.4224	0.9641	3.419	
2003/M	2/1	304.1	0.0210	0.6580	0.3390	0.3854	0.9949	4.017	
2004/M	2/1	266.1	0.0259	0.7264	0.2851	0.4630	0.9524	4.438	
2005/M	2/1	305.0	0.0185	0.7029	0.2493	0.4270	0.8735	3.288	
2006/M	2/1	277.3	0.0255	0.7216	0.3240	0.3591	1.0048	4.256	
2007/M	2/1	282.1	0.0164	0.6480	0.2407	0.3923	0.9417	3.464	
2008/M	2/1	283.0	0.0195	0.6980	0.2825	0.4244	0.9928	4.095	
2009/M	2/1	257.5	0.0196	0.7648	0.2974	0.4223	0.9629	3.549	
2010/M	2/1	321.9	0.0152	0.6265	0.2366	0.4275	1.0135	3.672	
М	ean:	290.1	0.0198	0.6767	0.2763	0.4150	0.9633	3.737	
tandard dev	iation:	20.3	0.0035	0.0537	0.0358	0.0288	0.0418	0.434	
umber of ob	serv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10	
3001/M	3/1	288.5	0.0221	0.7026	0.2875	0.4704	0.9530	3.842	
3002/M	3/1	298.2	0.0197	0.6696	0.2343	0.3877	1.0136	3.810	
3003/M	3/1	320.1	0.0194	0.6041	0.2858	0.4317	0.9481	3.739	
3004/M	3/1	269.7	0.0202	0.6820	0.2705	0.4350	1.0072	3.502	
3005/M	3/1	286.5	0.0249	0.6458	0.2873	0.3968	1.0445	3.560	
3006/M	3/1	267.1	0.0195	0.7066	0.2995	0.4058	0.7781	3.280	
3007/M	3/1	294.1	0.0221	0.6698	0.2752	0.3753	0.7781	3.462	
3008/M	3/1	299.1	0.0218	0.6459	0.2576	0.3785	0.8820	3.462	
3009/M	3/1	310.4	0.0183	0.6449	0.2708	0.4286	1.0163	4.343	
3010/M	3/1	290.7	0.0215	0.7024	0.2659	0.4047	1.0103	4.048	
•	ean:		0.0210	0.6674	0.2734	0.4114	0.9611	3.672	
tandard dev			0.0019	0.0328	0.0185	0.0298	0.0804	0.360	
umber of ob		(10)	(10)	(10)	(10)	(10)	(10)	(10)	
4001/M	4/1	295.6	0.0164	0.6841	0.3441	0.4157	0.9679	3.5060	
4002/M	4/1	285.5	0.0172	0.7008	0.2536	0.3996	1.0589	3.704	
4003/M	4/1	277.8	0.0190	0.6669	0.2370	0.3970	0.9865	3.7042	

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Summary Statistics for % Organ to Body Weight Study number: 036147

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•	Terminal		Brain		Heart		Liver
No/sex Subgroup Bo	dy wt. (g)	Adrenal Glands	Ep	Epididymides		Kidneys	
4004/M 4/1	324.5	0.0176	0.5853	0.2655	0.3729	0.8850	3.4264
4005/M 4/1	280.8	0.0224	0.6575	0.2624	0.4120	1.0275	3.5969
4006/M 4/1	282.4	0.0159	0.6913	0.2998	0.4457	1.0163	3.3513
4007/M 4/1	292.0	0.0221	0.6645	0.2593	0.4588	1.0249	3.2546
4008/M 4/1	296.9	0.0232	0.7101	0.2480	0.4210	1.0459	3.9140
4009/M 4/1	293.9	0.0196	0.6724	0.2204	0.4863	1.1214	3.4285
4010/M 4/1	270.1	0.0231	0.7217	0.3229	0.4226	0.9034	4.0622
Mean:	290.0	0.0197	0.6755	0.2713	0.4232	1.0038	3.6116
tandard deviation:	14.9	0.0029	0.0379	0.0390	0.0329	0.0712	0.2677
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

Summary Statistics for % Organ to Body Weight Study number: 036147

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Terminal	Sacrifice
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	Terminal	Pituitary gland			Spleen		Thymus	
No/sex Subgroup Bo	dy wt. (g)	Lungs	Sem	is w/prostate	-	Testes		
			Male	Animals				
1001/M 1/1	319.9	0.5319	0.0014	0.5494	0.1836	0.9073	0.1515	
1002/M 1/1	289.7	0.5390	0.0018	0.5583	0.2032	0.9894	0.2399	
1003/M 1/1	284.7	0.6704	0.0034	0.6935	0.2256	1.2052	0.1960	
1004/M 1/1	292.5	0.5557	0.0016	0.5396	0.1826	0.9563	0.1520	
1005/M 1/1	270.6	0.5508	0.0035	0.7330	0.1848	1.1647	0.1758	
1006/M 1/1	269.7	0.5423	0.0032	0.5158	0.2165	1.1269	0.1647	
1007/M 1/1	317.2	0.6283	0.0031	0.6352	0.2448	1.0682	0.1645	
1008/M 1/1	297.4	0.6756	0.0025	0.7110	0.2481	1.0025	0.2156	
1009/M 1/1	274.0	0.5569	0.0034	0.5671	0.2107	1.1160	0.1942	
1010/M 1/1	275.5	0.6171	0.0036	0.5723	0.2096	1.1072	0.1870	
Mean:	289.1	0.5868	0.0027	0.6075	0.2110	1.0644	0.1841	
Standard deviation:	18.2	0.0557	0.0008	0.0791	0.0237	0.0967	0.0285	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	
2001/M 2/1	307.7	0.6241	0.0036	0.6389	0.1976	0.9646	0.1522	
2002/M 2/1	296.5	0.7321	0.0034	0.6896	0.2298	1.0997	0.1417	
2003/M 2/1	304.1	0.7000	0.0030	0.6460	0.1921	1.1451	0.2014	
2004/M 2/1	266.1	0.6676	0.0033	0.5549	0.1983	1.2513	0.1547	
2005/M 2/1	305.0	0.6338	0.0028	0.5089	0.2243	1.0170	0.3089	
2006/M 2/1	277.3	0.6225	0.0040	0.5917	0.2098	1.0413	0.1885	
2007/M 2/1	282.1	0.6986	0.0037	0.6624	0.2224	1.1392	0.1977	
2008/M 2/1	283.0	0.6122	0.0028	0.5119	0.2138	1.0824	0.1661	
2009/M 2/1	257.5	0.6452	0.0040	0.7057	0.2319	1.2239	0.1543	
2010/M 2/1	321.9	0.6047	0.0032	0.6389	0.2289	1.0172	0.1322	
Mean:	290.1	0.6541	0.0034	0.6149	0.2149	1.0982	0.1798	
Standard deviation:	20.3	0.0434	0.0005	0.0701	0.0148	0.0929	0.0511	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	
3001/M 3/1	288.5	0.7822	0.0034	0.5833	0.2189	1.2085	0.2060	
3002/M 3/1	298.2	0.5800	0.0034	0.6945	0.2316	0.7848	0.1954	
3003/M 3/1	320.1	0.5935	0.0032	0.5816	0.2341	1.0091	0.1625	
3004/M 3/1	269.7	0.5843	0.0042	0.7154	0.2099	1.1621	0.1782	
3005/M 3/1	286.5	0.5560	0.0035	0.6726	0.1769	0.9315	0.1509	
3006/M 3/1	267.1	0.6520	0.0027	0.7294	0.2586	1.1959	0.1372	
3007/M 3/1	294.1	0.6159	0.0035	0.5248	0.2006	1.1504	0.1430	
3008/M 3/1	299.1	0.7445	0.0032	0.6883	0.2097	1.0167	0.2548	
3009/M 3/1	310.4	0.6342	0.0034	0.6240	0.2047	0.9140	0.1927	
3010/M 3/1	290.7	0.8002	0.0036	0.5522	0.2016	1.0169	0.1760	
Mean:	292.4	0.6543	0.0034	0.6366	0.2147	1.0390	0.1797	
Standard deviation:	16.3	0.0891	0.0004	0.0729	0.0225	0.1393	0.0350	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	
4001/M 4/1	295.6	0.6992	0.0033	0.7083	0.2037	1.2114	0.1587	
4002/M 4/1	285.5	0.6693	0.0039	0.4839	0.2111	1.0949	0.1893	
4003/M 4/1	277.8	0.6404	0.0036	0.5608	0.1896	0.9650	0.1376	

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Terminal Sacrifice

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Animal Group/	Animal Group/ Terminal		Pituitary gland			Spleen	
No/sex Subgroup Bo	dy wt. (g)	Lungs	Semis w/prostate		Testes		_
4004/M 4/1	324.5	0.6295	0.0033	0.4774	0.2173	0.9422	0.1433
4005/M 4/1	280.8	0.6874	0.0027	0.5944	0.1858	0.9984	0.1801
4006/M 4/1	282.4	0.6453	0.0035	0.5825	0.2167	1.1444	0.1454
4007/M 4/1	292.0	0.7297	0.0036	0.5727	0.2058	1.0711	0.1673
4008/M 4/1	296.9	0.6660	0.0034	0.7142	0.2161	1.1421	0.1251
4009/M 4/1	293.9	0.7347	0.0042	0.5150	0.2480	0.8815	0.2310
4010/M 4/1	270.1	0.7483	0.0040	0.6071	0.2098	1.1095	0.1747
Mean:	290.0	0.6850	0.0035	0.5816	0.2104	1.0561	0.1652
Standard deviation:	14.9	0.0421	0.0004	0.0815	0.0171	0.1049	0.0308
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal Gro		Terminal		Brain		Kidneys		Lungs
No/sex Sub	group	Body wt. (g)	Adrenal Glands		Heart		Liver	_
				Female	Animal	S	·	
	1/1	216.4	0.0339	0.8898	0.3735	0.9505	4.1424	0.716
	1/1	192.8	0.0355	0.9621	0.4025	0.8954	3.3240	0.766
	1/1	199.5	0.0271	0.9560	0.4176	0.8675	3.7982	0.804
	1/1	211.8	0.0349	0.8614	0.4214	1.0231	3.9398	0.817
	1/1	207.0	0.0377	0.8924	0.4351	0.9038	3.9163	0.703
	1/1	201.6	0.0302	0.9607	0.4124	0.8773	3.3587	0.920
•	1/1	213.0	0.0280	0.8876	0.4447	0.9763	4.0746	0.658
	1/1	215.5	0.0340	0.8940	0.4477	0.8684	3.3932	0.706
1509/F 1	1/1	212.7	0.0383	0.9301	0.4285	0.9439	4.0851	0.827
1510/F 1	1/1	220.8	0.0319	0.8068	0.4303	0.9014	3.5885	0.613
M €	a n:	209.1	0.0331	0.9041	0.4214	0.9208	3.7621	0.753
Standard devia		8.7	0.0038	0.0494	0.0219	0.0514	0.3205	0.091
Number of obse	erv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2501/F 2	2/1	208.7	0.0350	0.8887	0.4342	0.9227	4.2819	0.575
2502/F 2	2/1	202.0	0.0296	0.9556	0.4605	0.8864	3.4391	0.881
2503/F 2	2/1	191.6	0.0336	1.0117	0.4255	1.0321	4.2695	1.133
2504/F 2	2/1	216.6	0.0313	0.8244	0.4118	0.8620	3.5738	0.625
2505/F 2	2/1	191.7	0.0444	1.0286	0.4305	0.9441	4.4770	0.807
2506/F 2	2/1	216.1	0.0329	0.8933	0.4530	0.8598	3.6377	0.597
2507/F 2	2/1	201.3	0.0440	0.8720	0.3670	0.9521	4.0187	0.692
2508/F 2	2/1	202.0	0.0319	0.9346	0.4156	0.9238	4.0513	0.570
2509/F 2	2/1	223.8	0.0333	0.8510	0.3934	1.0188	4.2728	0.651
2510/F 2	2/1	198.5	0.0396	0.9377	0.4346	0.9575	4.2311	0.744
M e	a n:	205.2	0.0356	0.9198	0.4226	0.9360	4.0253	0.727
tandard devia		10.8	0.0053	0.0666	0.0275	0.0586	0.3546	0.175
umber of obse	erv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
3501/F 3	3/1	216.2	0.0409	0.8268	0.3950	0.9049	3.5052	0.638
3502/F 3	3/1	183.3	0.0320	1.0634	0.4343	0.9375	4.2038	0.848
3503/F 3	3/1	196.1	0.0412	0.9679	0.4404	0.9318	3.7566	0.815
3504/F 3	3/1	211.3	0.0353	0.8773	0.4753	1.0547	3.6768	0.747
3505/F 3	3/1	182.0	0.0402	1.0442	0.4320	0.8525	3.5269	0.8114
3506/F 3	3/1	190.2	0.0301	0.9670	0.4380	0.9157	3.6515	0.511
3507/F 3	3/1	197.9	0.0348	0.9372	0.4312	0.8533	4.0335	0.5938
3508/F 3	3/1	222.0	0.0388	0.7958	0.5282	1.0123	3.3969	0.762
3509/F 3	1/1	215.7	0.0396	0.8642	0,3633	0.8179	4.3409	0.762
3510/F 3	/1	220.6	0.0329	0.8696	0.4078	0.9123	4.4556	0.8984
Ме	an:	203.5	0.0366	0.9213	0.4345	0.9193	3.8548	
tandard devia		15.4	0.0041	0.0897	0.0445	0.9193	0.3761	0.7552
umber of obse		(10)	(10)	(10)	(10)	(10)	(10)	0.1173 (10)
4501/F 4	/1	202.7	0.0313	0.9038	0.4300	0.9963	3.7238	0.8044
	./1	215.6	0.0333	0.8819	0.4030	0.9846	3.6901	0.8044
	/1	195.0	0.0376	0.9708	0.4048	0.9048	3.8057	0.7725

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	•	Terminal		Brain		Kidneys		Lungs
No/sex Subg	No/sex Subgroup Body wt. (g)	Adrenal Glands		Heart	-	Liver	5	
4504/F 4	1/1	221.6	0.0375	0.8369	0.4380	0.8869	3.6555	0,9107
4505/F 4	1/1	204.4	0.0356	0.9171	0.4124	0.9545	4.1501	0.9344
4506/F 4	1/1	216.7	0.0381	0.8489	0.4462	0.9409	4.0688	0.9868
4507/F 4	1/1	194.9	0.0349	0.9216	0.4390	1.0151	3.9629	0.8926
4508/F 4	1/1	193.8	0.0422	0.9275	0.4379	0.9715	4.3849	0.7866
4509/F 4	1/1	217.5	0.0339	0.8028	0.4352	0.7941	3.2601	0.8083
4510/F 4	1/1	210.2	0.0322	0.8929	0.3625	0.9475	3.6361	0.7681
M e	an:	207.2	0.0357	0.8904	0.4209	0.9396	3.8338	0.8528
andard devia	ation:	10.5	0.0033	0.0495	0.0256	0.0645	0.3178	0.0760
mber of obse	erv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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	Terminal		itary gland		Thymus		
No/sex Subgroup Boo	•	Ovaries		Spleen		Uterus	
			Female	Animal	s		
1501/F 1/1	216.4	0.0669	0.0056	0.2675	0.3050	0.3606	
1502/F 1/1	192.8	0.0419	0.0034	0.2612	0.3019	0.2244	
1503/F 1/1	199.5	0.0441	0.0056	0.2552	0.2571	0.2981	
1504/F 1/1	211.8	0.0479	0.0061	0.2875	0.1998	0.1952	
1505/F 1/1	207.0	0.0407	0.0069	0.2270	0.2638	0.2795	
1506/F 1/1	201.6	0.0391	0.0054	0.2408	0.3096	0.2505	
1507/F 1/1	213.0	0.0455	0.0072	0.2578	0.2946	0.3713	
1508/F 1/1	215.5	0.0432	0.0069	0.2233	0.2187	0.2132	
1509/F 1/1	212.7	0.0445	0.0061	0.2567	0.3340	0.4028	
1510/F 1/1	220.8	0.0412	0.0035	0.1987	0.1894	0.2653	
Mean:	209.1	0.0455	0.0057	0.2476	0.2674	0.2861	
tandard deviation:	8.7	0.0079	0.0013	0.0255	0.0502	0.0713	
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	
		* *	••	·/	(20)	(20)	
2501/F 2/1	208.7	0.0448	0.0070	0.2131	0.2876	0.2292	
2502/F 2/1	202.0	0.0393	0.0066	0.2325	0.2686	0.3113	
2503/F 2/1	191.6	0.0442	0.0073	0.3031	0.2227	0.2400	
2504/F 2/1	216.6	0.0378	0.0067	0.2379	0.1961	0.2428	
2505/F 2/1	191.7	0.0446	0.0074	0.2070	0.2832	0.3899	
2506/F 2/1	216.1	0.0423	0.0061	0.2242	0.2168	0.2059	
2507/F 2/1	201.3	0.0479	0.0068	0.1992	0.2728	0.2400	
2508/F 2/1	202.0	0.0360	0.0075	0.2836	0.2618	0.5370	
2509/F 2/1	223.8	0.0412	0.0062	0.2538	0.2942	0.2904	
2510/F 2/1	198.5	0.0524	0.0070	0.2273	0.2250	0.2752	
Mean:	205.2	0.0430	0.0068	0.2382	0.2529	0.2962	
tandard deviation:	10.8	0.0049	0.0005	0.0333	0.0346	0.0996	
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	
3501/F 3/1	216.2	0.0388	0.0072	0.2636	0.2460	0.3890	
3502/F 3/1	183.3	0.0348	0.0088	0.2062	0.2402	0.2753	
3503/F 3/1	196.1	0.0403	0.0075	0.2262	0.2665	0.3664	
3504/F 3/1	211.3	0.0439	0.0067	0.2616	0.2488	0.2266	
3505/F 3/1	182.0	0.0439	0.0063	0.2256	0.1932	0.2776	
3506/F 3/1	190.2	0.0381	0.0053	0.2675	0.3131	0.2884	
3507/F 3/1	197.9	0.0445	0.0059	0.2458	0.2690	0.1950	
3508/F 3/1	222.0	0.0284	0.0056	0.2601	0.3170	0.2282	
3509/F 3/1	215.7	0.0387	0.0061	0.1972	0.2085	0.2769	
3510/F 3/1	220.6	0.0425	0.0064	0.2487	0.2168	0.3746	
Mean:	203.5	0.0394	0.0066	0.2403	0.2519	0.2898	
tandard deviation:	15.4	0.0050	0.0010	0.0251	0.0411	0.0668	
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	
4501/F 4/1	202.7	0.0463	0.0078	0.2040	0.2289	0 2020	
• • • • •			0.0078	0.2104		0.3879	
4502/F 4/1	215.6	0.0508	0.0059	0 2704	0.2273	0.2026	

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Ter	min	al.	Sacr	if	ice

* *			Pituitary gland		Thymus		
No/sex Subgroup Bo	ody wt. (g)	Ovaries		Spleen	-	Uterus	
4504/F 4/1	221.6	0.0506	0.0067	0.3142	0.2084	0.3050	
4505/F 4/1	204.4	0.0523	0.0060	0.2512	0.3140	0.3021	
4506/F 4/1	216.7	0.0321	0.0066	0.3240	0.2714	0.2267	
4507/F 4/1	194.9	0.0504	0.0050	0.2426	0.2609	0.2827	
4508/F 4/1	193.8	0.0459	0.0062	0.2335	0.1448	0.2368	
4509/F 4/1	217.5	0.0423	0.0050	0.2267	0.2096	0.4532	
4510/F 4/1	210.2	0.0497	0.0000	0.2651	0.2289	0.4960	
Mean:	207.2	0.0467	0.0056	0.2525	0.2392	0.3271	
Standard deviation:	10.5	0.0060	0.0022	0.0399	0.0489	0.0986	
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Terminal Sacrifice

- '	Terminal		Brain		Heart		Liver
No/sex Subgroup Bo	ody wt. (g)	Adrenal Glands		Epididymides		Kidneys	
			Male	Animals			
1001/M 1/1	319.9	2.4515	100.0000	39.6660	69.4244	139.2143	581.991
1002/M 1/1	289.7	2.4892	100.0000	40.3254	59.9723	144.5340	511.938
1003/M 1/1	284.7	3.0272	100.0000	43.8406	62.7516	139.3075	503.703
1004/M 1/1	292.5	3.4141	100.0000	46.5697	56.1605	148.1476	613.473
1005/M 1/1	270.6	3.1397	100.0000	46.4219	55.3041	146.9315	520.054
1006/M 1/1	269.7	2.9224	100.0000	42.2027	58.7281	133.4980	508.715
1007/M 1/1	317.2	3.1997	100.0000	48.5384	59.8015	144.8154	619.405
1008/M 1/1	297.4	2.8997	100.0000	38.9223	59.0916	155.9405	488.570
1009/M 1/1	274.0	3.1953	100.0000	41.8470	63.3292	148.5724	563.993
1010/M 1/1	275.5	3.4007	100.0000	45.9121	61.9101	137.6251	610.171
Mean:	289.1	3.0140	100.0000	43.4246	60.6473	143.8586	552.201
tandard deviation:	18.2	0.3344	0.0000	3.3229	4.0306	6.5480	51.212
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
2001/M 2/1	307.7	3.0050	100.0000	43.4050	69.8117	152.5689	519.535
2002/M 2/1	296.5	3.0214	100.0000	39.9812	69.2989	158.1927	561.070
2003/M 2/1	304.1	3.1884	100.0000	51.5242	58.5707	151.2044	610.594
2004/M 2/1	266.1	3.5594	100.0000	39.2519	63.7384	131.1191	611.050
2005/M 2/1	305.0	2.6310	100.0000	35.4667	60.7594	124.2758	467.878
2006/M 2/1	277.3	3.5332	100.0000	44.8976	49.7651	139.2504	589.800
2007/M 2/1	282.1	2.5384	100.0000	37.1465	60.5394	145.3362	534.712
2008/M 2/1	283.0	2.7997	100.0000	40.4719	60.8040	142.2489	586.816
2009/M 2/1	257.5	2.5592	100.0000	38.8849	55.2148	125.9013	464.126
2010/M 2/1	321.9	2.4296	100.0000	37.7578	68.2319	161.7711	586.111
Mean:	290.1	2.9265	100.0000	40.8788	61.6734	143.1869	553.169
tandard deviation:	20.3	0.4067	0.0000	4.6716	6.3917	13.1060	54.716
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
3001/M 3/1	288.5	3.1477	100.0000	40.9147	66.9495	135.6406	546.909
3002/M 3/1	298.2	2.9347	100.0000	34.9860	57.9027	151.3672	568.985
3003/M 3/1	320.1	3.2061	100.0000	47.3110	71.4552	156.9397	619.009
3004/M 3/1	269.7	2.9631	100.0000	39.6673	63.7797	147.6921	513.499
3005/M 3/1	286.5	3.8484	100,0000	44.4949	61.4507	161.7480	551.310
3006/M 3/1	267.1	2.7660	100.0000	42.3855	57.4343	110.1261	464.344
3007/M 3/1	294.1	3.3049	100.0000	41.0854	56.0412	141.9332	516.966
3008/M 3/1	299.1	3.3697	100.0000	39.8778	58.5952	136.5547	486.127
3009/M 3/1	310.4	2.8426	100.0000	41.9993	66.4635	157.6011	673.507
3010/M 3/1	290.7	3.0659	100.0000	37.8637	57.6207	144.8869	576.349
Mean:	292.4	3.1449	100.0000	41.0586	61.7693	144.4490	551.700
tandard deviation:	16.3	0.3151	0.0000	3.3991	5.1712	14.9485	62.266
umber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10
4001/M 4/1	295.6	2.3985	100.0000	50.3041	60.7685	141.4866	512.526
4002/M 4/1	285.5	2.4491	100.0000	36.1823	57.0250	151.1021	528.595
4003/M 4/1	277.8	2.8500	100.0000	35.5392	59.5326	147.9219	580.594

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Animal Group/	Terminal		Brain		Heart		Liver
No/sex Subgroup	Body wt. (g)	Adrenal Glands	E	pididymides		Kidneys	
4004/M 4/1	324.5	3.0116	100.0000	45.3536	63.7024	151.2031	585.4105
4005/M 4/1	280.8	3.4120	100.0000	39.9047	62.6625	156.2608	547.0105
4006/M 4/1	282.4	2.3050	100.0000	43.3694	64.4727	147.0061	484.7668
4007/M 4/1	292.0	3.3242	100.0000	39.0249	69.0512	154.2339	489.7954
4008/M 4/1	296.9	3.2680	100.0000	34.9239	59.2895	147.2940	551.1929
4009/M 4/1	293.9	2.9199	100.0000	32.7817	72.3293	166.7780	509.9186
4010/M 4/1	270.1	3.2064	100.0000	44.7414	58.5625	125.1847	562.8976
Mean	: 290.0	2.9145	100.0000	40.2125	62.7396	148.8471	535.2709
Standard deviation	: 14.9	0.4074	0.0000	5.5929	4.8524	10.7335	35.8176
Number of observ.	: (10)	(10)	(10)	(10)	(10)	(10)	(10)

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Terminal	Sacrifice

Animal Group/ Terminal		Pituitary gland			Spleen		Thymus
No/sex Subgroup Body	wt. (g)	Lungs	Sem	is w/prostate	-	Testes	•
			Male	Animals			
1001/M 1/1	319.9	86.3618	0.2335	89.2042	29.8041	147.3201	24.5914
1002/M 1/1	289.7	80.1427	0.2720	83.0117	30.2145	147.1105	35.6703
1003/M 1/1	284.7	97.7616	0.4917	101.1320	32.9048	175.7568	28.5817
1004/M 1/1	292.5	87.5283	0.2531	84.9865	28.7668	150.6301	23.9365
1005/M 1/1	270.6	81.6712	0.5260	108.6904	27.4082	172.7014	26.0603
1006/M 1/1	269.7	76.0543	0.4524	72.3311	30.3624	158.0365	23.0929
1007/M 1/1	317.2	98.4051	0.4790	99.4914	38.3419	167.3069	25.7654
1008/M 1/1	297.4	103.1204	0.3746	108.5245	37.8650	153.0100	32.9074
1009/M 1/1	274.0	82.3609	0.5020	83.8668	31.1599	165.0510	28.7149
1010/M 1/1	275.5	85.9020	0.4952	79.6766	29.1764	154.1385	26.0283
Mean:	289.1	87.9308	0.4080	91.0915	31.6004	159.1062	27.5349
Standard deviation:	18.2	8.9177	0.1147	12.5856	3.7230	10.4473	4.0340
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M 2/1	307.7	102.1434	0.5850	104.5527	32.3370	157.8662	24.9122
2002/M 2/1	296.5	120.1207	0.5589	113.1537	37.7124	180.4272	23.2527
2003/M 2/1	304.1	106.3818	0.4598	98.1809	29.2004	174.0280	30.6097
2004/M 2/1	266.1	91.9085	0.4604	76.3982	27.2958	172.2697	21.2944
2005/M 2/1	305.0	90.1759	0.3965	72.4029	31.9121	144.6984	43.9474
2006/M 2/1	277.3	86.2669	0.5597	82.0040	29.0755	144.3079	26.1269
2007/M 2/1	282.1	107.8122	0.5635	102.2211	34.3290	175.8193	30.5159
2008/M 2/1	283.0	87.7177	0.3949	73.3394	30.6298	155.0881	23.8001
2009/M 2/1	257.5	84.3658	0.5230	92.2718	30.3189	160.0234	20.1686
2010/M 2/1	321.9	96.5093	0.5107	101.9734	36.5381	162.3513	21.1027
Mean:	290.1	97.3402	0.5012	91.6498	31.9349	162.6879	26.5731
Standard deviation:	20.3	11.5398	0.0698	14.6122	3.3657	12.7244	7.1039
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M 3/1	288.5	111.3326	0.4884	83.0233	31.1560	172.0065	29.3206
3002/M 3/1	298.2	86.6136	0.5008	103.7110	34.5803	117.2076	29.1867
3003/M 3/1	320.1	98.2470	0.5326	96.2664	38.7579	167.0390	26.9004
3004/M 3/1	269.7	85.6793	0.6089	104.8932	30.7835	170.4072	26.1295
3005/M 3/1	286.5	86.1035	0.5351	104.1619	27.3931	144.2517	23.3663
3006/M 3/1	267.1	92.2796	0.3762	103.2270	36.5992	169.2614	19.4203
3007/M 3/1	294.1	91.9586	0.5229	78.3582	29.9472	171.7586	21.3575
3008/M 3/1	299.1	115.2700	0.4917	106.5687	32.4706	157.4098	39.4534
3009/M 3/1	310.4	98.3414	0.5345	96.7578	31.7480	141.7395	29.8796
3010/M 3/1	290.7	113.9289	0.5191	78.6120	28.7002	144.7791	25.0612
Mean:	292.4	97.9754	0.5110	95.5580	32.2136	155,5860	27.0076
Standard deviation:	16.3	11.6529	0.0583	11.3027	3.5249	18.2033	5.5834
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4001/M 4/1	295.6	102.2106	0.4846	103.5359	29.7809	177.0882	23.1987
4002/M 4/1	285.5	95.5066	0.5498	69.0458	30.1245	156.2353	27.0105
4003/M 4/1	277.8	96.0218	0.5398	84.0926	28.4357	144.7048	20.6359

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Animal (Animal Group/ Terminal		Pitui	tary gland		Spleen	Thymus	
No/sex Su	bgroup Bo	dy wt. (g)	Lungs	Semis	w/prostate	-	Testes	-
4004/M	4/1	324.5	107.5502	0.5634	81.5669	37.1189	160.9856	24.4827
4005/M	4/1	280.8	104.5331	0.4116	90.3975	28.2550	151.8414	27.3884
4006/M	4/1	282.4	93.3463	0.5020	84.2545	31.3476	165.5330	21.0265
4007/M	4/1	292.0	109.8181	0.5463	86.1929	30.9746	161.1864	25.1817
4008/M	4/1	296.9	93.7960	0.4743	100.5787	30.4274	160.8405	17.6113
4009/M	4/1	293.9	109.2759	0.6174	76.6004	36.8858	131.1068	34.3606
4010/M	4/1	270.1	103.6938	0.5489	84.1217	29.0786	153.7451	24.2099
N	lean:	290.0	101.5752	0.5238	86.0387	31.2429	156.3267	24.5106
tandard dev	riation:	14.9	6.4333	0.0572	10.2473	3.1972	12.3801	4.5774
number of ob	serv. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)

Number of observ. :

4501/F 4/1

4503/F 4/1

4/1

4502/F

(10)

202.7

215.6

195.0

(10)

3.4660

3.7816

3.8772

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Terminal Sacri	fice					7	Version 4.2.2
Animal Gro			Brain		Kidneys		Lungs
No/sex Subg	roup Body wt. (g)	Adrenal Glands		Heart		Liver	<u> </u>
			Female	Anima	l s		
	/1 216.4	3.8066	100.0000	41.9713	106.8135	465.5277	80.463
•	/1 192.8	3.6927	100.0000	41.8329	93.0674	345.4771	79.638
	/1 199.5	2.8312	100.0000	43.6848	90.7356	397.2841	84.145
	/1 211.8	4.0504	100.0000	48.9175	118.7723	457.3637	94.897
•	/1 207.0	4.2280	100.0000	48.7549	101.2776	438.8643	78.822
•	/1 201.6	3.1444	100.0000	42.9265	91.3156	349.6025	95.807
•	/1 213.0	3.1579	100.0000	50.1084	109.9974	459.0797	74.160
•	/1 215.5	3.7996	100.0000	50.0857	97.1451	379.5692	79.060
-	/1 212.7	4.1144	100.0000	46.0675	101.4810	439.1984	88.9309
1510/F 1	/1 220.8	3.9576	100.0000	53.3345	111.7211	444.7794	76.069
	an: 209.1	3.6783	100.0000	46.7684	102.2327	417.6746	83.199
Standard devia		0.4730	0.0000	4.0273	9.4727	45.8749	7.590
Number of obse	rv. : (10)	(10)	(10)	(10)	(10)	(10)	(10)
2501/F 2	/1 208.7	3.9357	100.0000	48.8516	103.8225	481.7932	64.767
•	/1 202.0	3.0978	100.0000	48.1869	92.7580	359.8736	92.260
2503/F 2	/1 191.6	3.3170	100.0000	42.0531	102.0119	421.9964	111.993
2504/F 2	/1 216.6	3.7914	100.0000	49.9552	104.5699	433.5182	75.890
2505/F 2	/1 191.7	4.3207	100.0000	41.8530	91.7846	435.2351	78.497
2506/F 2	/1 216.1	3.6882	100.0000	50.7123	96.2497	407.2002	66.832
2507/F 2	/1 201.3	5.0473	100.0000	42.0816	109.1831	460.8409	79.417
2508/F 2	/1 202.0	3.4165	100.0000	44.4727	98.8453	433.4764	60.983
2509/F 2	/1 223.8	3.9168	100.0000	46.2302	119.7154	502.0740	76.535
2510/F 2	/1 198.5	4.2229	100.0000	46.3440	102.1168	451.2331	79.358
	a n: 205.2	3.8754	100.0000	46.0741	102.1057	438.7241	78.653
Standard devia		0.5644	0.0000	3.3556	8.2196	39.5412	14.737
Number of obse	rv. : (10)	(10)	(10)	(10)	(10)	(10)	(10)
	/1 216.2	4.9510	100.0000	47.7706	109.4490	423.9609	77.2308
3502/F 3	/1 183.3	3.0115	100.0000	40.8373	88.1644	395.3212	79.8020
3503/F 3	/1 196.1	4.2571	100.0000	45.5005	96.2750	388.1296	84.267
3504/F 3	/1 211.3	4.0190	100.0000	54.1781	120.2190	419.1078	85.229
3505/F 3	/1 182.0	3.8518	100.0000	41.3702	81.6407	337.7710	77.704
3506/F 3	/1 190.2	3.1099	100.0000	45.2890	94.6882	377.6002	58.6582
3507/F 3	/1 197.9	3.7149	100.0000	46.0074	91.0444	430.3769	63.3634
3508/F 3	/1 222.0	4.8794	100.0000	66.3761	127.2161	426.8708	95.7659
3509/F 3	/1 215.7	4.5815	100.0000	42.0440	94.6513	502.3284	100.4936
3510/F 3	/1 220.6	3.7792	100.0000	46.8880	104.9051	512.3541	103.3048
Ме	an: 203.5	4.0155	100.0000	47.6261	100.8253	421.3821	82.5821
Standard devia	tion: 15.4	0.6668	0.0000	7.6307	14.4688	53.3788	14.6658
Number of obse	rv · (10)	(10)	(10)	(10)	(20)	(10)	

(10)

100.0000

100.0000

100.0000

(10)

47.5738

45.6951

41.6988

(10)

110.2287

111.6499

93.1964

(10)

411.9972

418.4453

392.0131

(10)

88.9962

87.5980

88.9441

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Animal Group			Brain		Kidneys		Lungs
No/sex Subgro	oup Body wt. (g)	Adrenal Glands		Heart	-	Liver	
4504/F 4/1	. 221.6	4.4756	100.0000	52.3376	105.9800	436.8024	108.8218
4505/F 4/1	204.4	3.8784	100.0000	44.9667	104.0811	452.5367	101.8885
4506/F 4/1	. 216,7	4.4901	100.0000	52.5658	110.8339	479.2944	116.2427
4507/F 4/1	. 194.9	3.7858	100.0000	47.6395	110.1436	430.0023	96.8545
4508/F 4/1	. 193.8	4.5452	100.0000	47.2156	104.7399	472.7678	84.8122
4509/F 4/1	. 217.5	4.2266	100.0000	54.2122	98.9119	406.0879	100.6873
4510/F 4/1	. 210.2	3.6017	100.0000	40.5935	106.1112	407.2194	86.0248
Меа	n: 207.2	4.0128	100.0000	47.4499	105.5877	430.7166	96.0870
andard deviati	on: 10.5	0.3917	0.0000	4.5366	5.8509	29.4381	10.6748
mber of observ	7. : (10)	(10)	(10)	(10)	(10)	(10)	(10)

Summary Statistics for % Organ to Brain Weight Study number: 036147

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	Terminal	Sacrifice
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	ninal		itary gland		Thymus	
No/sex Subgroup Body	wt. (g) 	Ovaries		Spleen		Uterus
			Female	Animal	s	
	216.4	7.5145	0.6336	30.0634	34.2802	40.5224
	192.8	4.3504	0.3504	27.1429	31.3747	23.3261
	199.5	4.6086	0.5820	26.6922	26.8914	31.1854
	211.8	5.5632	0.7070	33.3735	23.1954	22.6583
	207.0	4.5637	0.7741	25.4331	29.5583	31.3177
1506/F 1/1 :	201.6	4.0686	0.5576	25.0671	32.2233	26.0791
1507/F 1/1 :	213.0	5.1309	0.8146	29.0452	33.1870	41.8302
1508/F 1/1 :	215.5	4.8326	0.7734	24.9779	24.4692	23.8515
1509/F 1/1	212.7	4.7816	0.6520	27.5930	35.9078	43.3077
1510/F 1/1	220.8	5.1027	0.4379	24.6267	23.4815	32.8843
Mean: 2	209.1	5.0517	0.6283	27.4015	29.4569	31.6963
Standard deviation:	8.7	0.9632	0.1507	2.7680	4.6726	7.9027
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2501/F 2/1	208.7	5.0356	0.7871	23.9756	32.3593	25.7871
2502/F 2/1 2	202.0	4.1080	0.6942	24.3317	28.1030	32.5787
2503/F 2/1	191.6	4.3642	0.7170	29.9562	22.0119	23.7245
2504/F 2/1 2	216.6	4.5867	0.8121	28.8587	23.7847	29.4523
2505/F 2/1 1	191.7	4.3359	0.7201	20.1227	27.5268	37.9076
	216.1	4.7345	0.6786	25.0971	24.2683	23.0510
	201.3	5.4973	0.7748	22.8438	31.2863	27.5265
	202.0	3.8561	0.7998	30.3406	28.0153	57.4607
-	223.8	4.8409	0.7298	29.8173	34.5689	34.1279
	.98.5	5.5875	0.7468	24.2358	23.9940	29.3451
	205.2	4.6947	0.7460	25.9579	27.5918	32.0962
	10.8	0.5654	0.0457	3.5360	4.1516	10.0479
	(10)	(10)	(10)	(10)	(10)	(10)
3501/F 3/1 2	216.2	4.6881	0.8727	31.8825	29.7511	47.0490
•	.83.3	3.2680	0.8260	19.3926	22.5888	25.8875
	.96.1	4.1675	0.7745	23.3720	27.5343	37.8556
	211.3	5.0062	0.7606	29.8160	28.3649	25.8348
·	.82.0	4.2044	0.5999	21.6060	18.5066	26.5891
	.90.2	3.9417	0.5491	27.6573		
	.97.9	4.7447	0.6308	26.2307	32.3764	29.8266
	22.0	3.5718	0.7019	32.6899	28.7001 39.8392	20.8066
	15.7	4.4796	0.7019	22.8165		28.6709
	20.6	4.8843	0.7028	28.6020	24.1255	32.0386
	103.5	4.8843	0.7350		24.9270	43.0776
	15.4	0.5745		26.4065	27.6714	31.7636
	(10)	(10)	0.1008	4.4950	5.8310	8.3577
amber of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
	02.7	5.1198	0.8679	22.5752	25.3261	42.9180
	15.6	5.7645	0.5891	23.8626	25.7718	22.9790
4503/F 4/1 1	.95.0	4.7805	0.7501	26.0948	30.6165	38.9044

Huntingdon Life Sciences Princeton Research Center East Millstone, New Jersey Terminal Sacrifice

Summary Statistics for % Organ to Brain Weight Study number: 036147

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Version 4.2.2

	Froup/	Terminal	Pitui	tary gland		Thymus	·- · · · · · · · · · · · · · · · · · ·	
No/sex Su	bgroup B	Body wt. (g)	Ovaries		Spleen	-	Uterus	
4504/F	4/1	221.6	6.0501	0.7981	37.5411	24.9070	36.4465	
4505/F	4/1	204.4	5.7029	0.6508	27.3886	34.2438	32.9421	
4506/F	4/1	216.7	3.7834	0.7828	38.1713	31.9743	26.7069	
4507/F	4/1	194.9	5.4727	0.5400	26.3222	28.3042	30.6703	
4508/F	4/1	193.8	4.9458	0.6732	25.1794	15.6161	25.5299	
4509/F	4/1	217.5	5.2632	0.6242	28.2344	26.1039	56.4515	
4510/F	4/1	210.2	5.5624	0.0053	29.6926	25.6380	55.5491	
M	iean:	207.2	5.2445	0.6281	28.5062	26.8502	36.9098	
Standard dev	riation:	10.5	0.6444	0.2415	5.3351	5.0850	11.7942	
Number of ob	serv. :	(10)	(10)	(10)	(10)	(10)	(10)	

Huntingdon	Life Sciences
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Individual Animal Gross and	
Microscopic Observations	
Preface	Appendix H

Key to Abbreviation

LN = Lymph Node

Corresponding exposure levels for each group were as follows:

Group 1 - 0 mg/m³ Group 2 - 25 mg/m³ Group 3 - 75 mg/m³ Group 4 - 200 mg/m³

Notes: Unless otherwise specified in a histopathology note, the organ/tissue examined was the required (routine) section.

08-Jun-04; 17:43 Huntingdon Life Sciences, Inc. 036147

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Tissues without comment under Gross Observations were within normal limits at necropsy. The following tissues were unremarkable microscopically:

No tissues examined.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1002
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 1

Tissue Gross Observations/Comments Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Microscopic Observations/Comments

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male
PHASE DAY OF DEATH: 14
PHASE: Dosing phase
GROUP: 1

Tissue
Gross Observations/Comments
Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STA PHASE DAY OF DE	TUS: Final phase sacrifice ATH: 14	SEX: Male PHASE: Dosing phase	ANIMAL: 1005 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal. Minimal.	

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

	individual Animai Glos	ss and Microscopic Observations	
STA' PHASE DAY OF DE	TUS: Final phase sacrifice ATH: 14	SEX: Male PHASE: Dosing phase	ANIMAL: 1006 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.	

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male
PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

	That reduct million drops and microscopic observations		
PHASE DAY	STATUS: Final phase sacrifice OF DEATH: 14	SEX: Male PHASE: Dosing phase	ANIMAL: 1008 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPHAG Multifocal, Minimal. - SIX SECTIONS OF LUNG LOBE PRES	,

MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

Individual Inland Clobs and Metoscopic Observations			
PHASE DAY OF DEATH	8: Final phase sacrifice 1: 14	SEX: Male PHASE: Dosing phase	ANIMAL: 2001 GROUP: 2
Tissue		Microscopic Observations/Comments	
Mediastinal LN Enlarged, Slight		No micropathology observations on tissue.	
Lungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.	
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifoca Moderate.	1,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES Multifocal, Slight.	,
		BRONCHIOLAR ASSOCIATED LYMPHOID TI: BROWN-BLACK PIGMENT DEPOSITS, Foca. Moderate.	
		- FIVE SECTIONS OF LUNG LOBES PRES: MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR (TERMINAL BRONCHIOLE/ALVEOLAR DUCT; ALVEOLI) AND TEND TO BE CENTRIFUGA: DISTRIBUTION. PIGMENT PROMINENT IN LUNG LOBES.	SITES /CENTRAL L IN

08-Jun-04; 17:43

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Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

______ SEX: Male ANIMAL: 2002 STATUS: Final phase sacrifice GROUP: 2 PHASE DAY OF DEATH: 14 PHASE: Dosing phase ______ Gross Observations/Comments Microscopic Observations/Comments _______

Lungs

Discolored, All lobes, Pale, Severe

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

Discolored, All lobes, Black, Areas, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2003 PHASE: Dosing phase PHASE DAY OF DEATH: 14 GROUP: 2 Gross Observations/Comments Microscopic Observations/Comments Lungs Examined; 1 correlation found: Discolored, All lobes, Black, Slight

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2004 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2005 GROUP: 2 PHASE DAY OF DEATH: 14 PHASE: Dosing phase Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

SEX: Male STATUS: Final phase sacrifice ANIMAL: 2006 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 Gross Observations/Comments Microscopic Observations/Comments Discolored, All lobes, Black, Slight

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 2

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male
PHASE: Dosing phase

GROUP: 2

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 2009 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON

MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2

LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2010 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 - -Gross Observations/Comments Microscopic Observations/Comments Lungs Discolored, All lobes, Brown, Moderate Examined; 1 correlation found:

BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 3001 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES. Multifocal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES

LUNG LOBES.

(TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2

Petroleum Coke

A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male ANIMAL: 3002 PHASE: Dosing phase GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Epididymides		No micropathology observations on tissue.
Mediastinal LN	 Enlarged, Slight	No micropathology observations on tissue.
Lungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.
		BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Minimal.
		- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.
Prostate	Small, Ventral, Left, Slight	No micropathology observations on tissue.
Testes	Small, Left, Severe	No micropathology observations on tissue.
	Enlarged, Right, Moderate	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STA PHASE DAY OF DE	TUS: Final phase sacrifice	SEX: Male PHASE: Dosing phase	ANIMAL: 3002 GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3003
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUB: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Minimal.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male

ANIMAL: 3004

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 3

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Slight.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male
PHASE: Dosing phase

GROUP: 3

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found:

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 3006 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3006
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

-STATUS: Final phase sacrifice SEX: Male ANIMAL: 3007 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Gross Observations/Comments Microscopic Observations/Comments _ Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES. Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2

LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male PHASE: Dosing phase	ANIMAL: 3008 GROUP: 3
	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN		No micropathology observations on tis	sue.
Lungs	Discolored, All lobes, Black, Severe	Examined; 1 correlation found: BROWN-BLACK FIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. - SIX SECTIONS OF LUNG LOBE PRESENT O MICROSLIDE. PIGMENT DEPOSITS ARE PRIM AT BRONCHILOLAR-ALVEOLAR SITES (TERMI BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVE AND TEND TO BE CENTRIFUGAL IN	IARILY

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 3009 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Gross Observations/Comments Microscopic Observations/Comments ------Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Slight. OSSEOUS METAPLASIA, Focal, Slight. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Male
PHASE: Dosing phase

GROUP: 3

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs

Discolored, All lobes, Black, Severe

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Focal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male PHASE: Dosing phase	ANIMAL: 4001 GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN Enlarged, Slight		No micropathology observations on ti	issue.
	Discolored, Black, Slight		
Lungs	. Discolored, All lobes, Black, Severe	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Mode	erate.
		BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.	,
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.	,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.	
		- FIVE SECTIONS OF LUNG LOBES PRESEN MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR S	

LOBES.

(TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male PHASE: Dosing phase	ANIMAL: 4002 GROUP: 4
	Gross Observations/Comments	Microscopic Observations/Co	omments
Mediastinal LN Discolored, Black, Severe Enlarged, Slight		No micropathology observat	
Lungs	Discolored, All lobes, Black, Severe	Examined; 1 correlation for BROWN-BLACK PIGMENT DEPO	
		ALVEOLAR DUCT/ALVEOLAR EPI HYPERPLASIA/HYPERTROPHY, M Slight.	
		ALVEOLAR/INTRAALVEOLAR MAC	CROPHAGES,
		BRONCHIOLAR ASSOCIATED LYM	MPHOID TISSUE:

Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

BROWN-BLACK PIGMENT DEPOSITS, Focal,

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4002
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

-----STATUS: Final phase sacrifice SEX: Male ANIMAL: 4003 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 _ _ Gross Observations/Comments Microscopic Observations/Comments ------Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES, PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 4004 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Moderate Enlarged, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4004
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 4005 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Tissue Gross Observations/Comments Microscopic Observations/Comments -----Mediastinal LN . . . No micropathology observations on tissue. Discolored, Black, Severe Enlarged, Moderate Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. - SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL

BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI)

DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG

AND TEND TO BE CENTRIFUGAL IN

LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures dividual Animal Gross and Microscopic Observations

Individual Animal Gross and Microscopic Observations			
STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male pHASE: Dosing phase	ANIMAL: 4006 GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN .		No micropathology observations on t	issue.
	Enlarged, Slight		
Lungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.	
		BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal Slight.	.,
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal Moderate.	1,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.	
		BRONCHIOLAR ASSOCIATED LYMPHOID TIS BROWN-BLACK PIGMENT DEPOSITS, Multi Moderate.	
		- FIVE SECTIONS OF LUNG LOBES PRESI MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR (TERMINAL BRONCHIOLE/ALVEOLAR DUCT, ALVEOLI) AND TEND TO BE CENTRIFUGAL DISTRIBUTION. PIGMENT PRESENT IN AL LOBES. PIGMENT PROMINENT IN 1-2 LUI	SITES /CENTRAL L IN LL LUNG

LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

Tissue	Gross Observations/Comments	Microscopic Observations/Comme	
	ATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4006
	EATH: 14	PHASE: Dosing phase	GROUP: 4

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4007 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Moderate Lungs Discolored, All lobes, Black, Severe Examined: 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL

Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

HYPERPLASIA/HYPERTROPHY, Multifocal,

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 4008 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Severe Enlarged, Moderate Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

Moderate.

HYPERPLASIA/HYPERTROPHY, Multifocal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4008
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Bividual Animal Cross and Missaggeria Observation

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Male ANIMAL: 4009 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Enlarged, Slight Lungs Discolored, All lobes, Black, Severe Examined: 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

> ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal,

Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4009
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures dividual Animal Cross and Microscopic Observations

In the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations			
STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Male PHASE: Dosing phase	ANIMAL: 4010 GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN		No micropathology observations on t	issue.
Lungs	Discolored, All lobes, Red, Severe	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.	
		BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.	
	·	ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.	
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.	
		BRONCHIOLAR ASSOCIATED LYMPHOID TISS	SUE:

Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

BROWN-BLACK PIGMENT DEPOSITS, Multifocal,

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4010
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4

Tissue Gross Observations/Comments Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,

ALVEOLAR/INTRAALVEOLAR MACROPHAGES Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1502
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 1

Tissue Gross Observations/Comments Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS PHASE DAY OF DEATH	: Final phase sacrifice : 14	SEX: Female PHASE: Dosing phase	ANIMAL: 1503 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.	

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,
Multifocal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female
PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,

Multifocal, Minimal.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 1

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Lungs No gross observations on tissue.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES,

Multifocal, Slight.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

ST PHASE DAY OF D	ATUS: Final phase sacrifice EATH: 14	SEX: Female PHASE: Dosing phase	ANIMAL: 1507 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Commen	ts
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPH Multifocal, Slight.	ages,

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

ST PHASE DAY OF D	ATUS: Final phase sacrifice EATH: 14	SEX: Female PHASE: Dosing phase	ANIMAL: 1508 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.	

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

PHASE DAY	STATUS: Final phase sacrifice OF DEATH: 14	SEX: Female PHASE: Dosing phase	ANIMAL: 1509 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.	

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

	individual Allillai Gr	oss and microscopic observations	
STATUS	: Final phase sacrifice : 14	SEX: Female PHASE: Dosing phase	ANIMAL: 1510 GROUP: 1
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Lungs	No gross observations on tissue.	ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2501
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHIOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations -STATUS: Final phase sacrifice SEX: Female ANIMAL: 2502 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 . Gross Observations/Comments Microscopic Observations/Comments -Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES,

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Multifocal, Slight.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2503 PHASE: Dosing phase PHASE DAY OF DEATH: 14 _______ Microscopic Observations/Comments Gross Observations/Comments Lungs Examined; 1 correlation found:

Discolored, All lobes, Black, Moderate

BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

SEX: Female ANIMAL: 2504 STATUS: Final phase sacrifice GROUP: 2 PHASE DAY OF DEATH: 14 PHASE: Dosing phase Microscopic Observations/Comments Gross Observations/Comments Lungs Examined; 1 correlation found:

Discolored, All lobes, Brown, Severe

BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

08-Jun-04; 17:43

Huntingdon Life Sciences, Inc. 036147

Petroleum Coke

A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female
PHASE DAY OF DEATH: 14
PHASE: Dosing phase

GROUP: 2

Tissue
Gross Observations/Comments
Microscopic Observations/Comments

Discolored, All lobes, Brown, Moderate
Examined; 1 correlation found:

BROWN-BLACK PIGMENT DEPOSITS,
Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

-STATUS: Final phase sacrifice SEX: Female ANIMAL: 2506 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Minimal. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Female ANIMAL: 2507 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 ____ Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Minimal. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE

PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2

LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2508
PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2

Tissue Gross Observations/Comments Microscopic Observations/Comments

Lungs

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Minimal.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 2509 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 2 Tissue Gross Observations/Comments Microscopic Observations/Comments Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS,

> ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations

-ANIMAL: 2510 STATUS: Final phase sacrifice PHASE: Dosing phase PHASE DAY OF DEATH: 14 Microscopic Observations/Comments Gross Observations/Comments Tissue

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES, PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STA PHASE DAY OF DE	TUS: Final phase sacrifice ATH: 14	SEX: Female PHASE: Dosing phase	ANIMAL: 3501 GROUP: 3
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN	 Discolored, Black, Slight	No micropathology observations on tiss	ue.
Lungs			
	Discolored, All lobes, Black, Severe	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.	
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.	
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.	
		- FIVE SECTIONS OF LUNG LOBES PRESENT MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SIT (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CEN ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2	ES TRAL

LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations -STATUS: Final phase sacrifice SEX: Female ANIMAL: 3502 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

		•	
STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female PHASE: Dosing phase	ANIMAL: 3503 GROUP: 3
	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN	Discolored, Black, Slight	No micropathology observations on tissue	2.
Lungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES	

LUNG LOBES.

(TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

Thervillage Arrival Gloss and Milloscopic Observations			
STATUS: PHASE DAY OF DEATH:	** =	SEX: Female PHASE: Dosing phase	ANIMAL: 3504 GROUP: 3
Tissue	Gross Observations/Comments		
Mediastinal LN	 Discolored, Black, Slight	No micropathology observations on	tissue.
	Enlarged, Slight		
Lungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Mo	derate.
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifoca Moderate.	1,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES Multifocal, Moderate.	,
		BRONCHIOLAR ASSOCIATED LYMPHOID TI BROWN-BLACK PIGMENT DEPOSITS, Foca Minimal.	
		- FIVE SECTIONS OF LUNG LOBES PRES MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR (TERMINAL BRONCHIOLE/ALVEOLAR DUCT ALVEOLI) AND TEND TO BE CENTRIFUGA DISTRIBUTION. PIGMENT PROMINENT IN LUNG LOBES.	SITES /CENTRAL L IN

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 3505 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 - -Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

ANIMAL: 3506 STATUS: Final phase sacrifice SEX: Female PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 Gross Observations/Comments Microscopic Observations/Comments Tissue Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate Examined: 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Moderate.

Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal,

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 3507

PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3

Tissue Gross Observations/Comments Microscopic Observations/Comments

Discolored, All lobes, Black, Moderate

Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Focal, Minimal.

OSSEOUS METAPLASIA, Focal, Slight.

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 3508 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 3 _______ Gross Observations/Comments Microscopic Observations/Comments Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found:

BROWN-BLACK PIGMENT DEPOSITS, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PROMINENT IN 1-2 LUNG LOBES. DUE TO ARTIFACTUAL CHANGES, TISSUE IS DIFFICULT TO EVALUATE.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female PHASE: Dosing phase	ANIMAL: 3509 GROUP: 3
	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN Discolored, Black, Moderate		No micropathology observations on tissue.	
Lungs			
	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.	
		BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifoca Slight.	1,
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifoca Moderate.	1,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES Multifocal, Moderate.	,
		- FIVE SECTIONS OF LUNG LOBES PRESS MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR (TERMINAL BRONCHIOLE/ALVEOLAR DUCT, ALVEOLI) AND TEND TO BE CENTRIFUGAL DISTRIBUTION. PIGMENT PRESENT IN AL LOBES. PIGMENT PROMINENT IN 1-2 LUL LOBES.	SITES /CENTRAL L IN LL LUNG

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female	ANIMAL: 3510
		PHASE: Dosing phase	GROUP: 3
Cissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN Enlarged, Slight		No micropathology observations on tissue.	
ungs	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TIS BROWN-BLACK PIGMENT DEPOSITS, Focal Moderate.	SSUE:

LOBES.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures dividual Animal Cross and Microscopic Observations

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Female ANIMAL: 4501 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Tissue Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Enlarged, Slight Lungs Discolored, All lobes, Black, Moderate/ . Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

	TUS: Final phase sacrifice	SEX: Female PHASE: Dosing phase	ANIMAL: 4501 GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures dividual Animal Gross and Migrogonia Observation

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Female ANIMAL: 4502 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Moderate Lungs Discolored, All lobes, Black, Moderate Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL

HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 4

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4503 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 X -Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal,

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations				
STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female PHASE: Dosing phase	ANIMAL: 4504 GROUP: 4	
Tissue	Gross Observations/Comments	Microscopic Observations/Comme	ents	
Mediastinal LN Discolored, Black, Slight		No micropathology observation	ns on tissue.	
	Enlarged, Slight			
Lungs Discolored, All lobes, Black, Severe		Examined; 1 correlation found BROWN-BLACK PIGMENT DEPOSIT Multifocal, Moderate.		
		BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Mult Slight.	tifocal,	
		ALVEOLAR DUCT/ALVEOLAR EPITHI HYPERPLASIA/HYPERTROPHY, Mult Moderate.		

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. PIGMENT PROMINENT IN 1-2 LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: F: PHASE DAY OF DEATH: 1	mai phase sacrifice	SEX: Female PHASE: Dosing phase	ANIMAL: 4504 GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposure dividual Animal Gross and Migragoric Observation

Individual Animal Gross and Microscopic Observations STATUS: Final phase sacrifice SEX: Female ANIMAL: 4505 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Moderate Enlarged, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. BRONCHIOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

- FIVE SECTIONS OF LUNG LOBES PRESENTED ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHICLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. IN GENERAL, SEVERITY OF CHANGES ARE IN 2 OF 5 LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice

SEX: Female

PHASE DAY OF DEATH: 14

PHASE: Dosing phase

GROUP: 4

Tissue

Gross Observations/Comments

Microscopic Observations/Comments

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female PHASE: Dosing phase	ANIMAL: 4506 GROUP: 4	
Tissue	.ssue Gross Observations/Comments Microscopic (roscopic Observations/Comments	
Mediastinal LN Discolored, Black, Slight Enlarged, Slight		No micropathology observations on tissue.		
Lungs				
	Discolored, All lobes, Black, Moderate	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.		
		ALVEOLAR DUCT/ALVEOLAR EPITHELIA HYPERPLASIA/HYPERTROPHY, Multifo Moderate.		
		ALVEOLAR/INTRAALVEOLAR MACROPHAC	GES,	
		- FIVE SECTIONS OF LUNG LOBES PR	RESENT ON	

LOBES.

MICROSLIDES. PIGMENT DEPOSITS ARE
PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES
(TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL
ALVEOLI) AND TEND TO BE CENTRIPUGAL IN
DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4507 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Moderate Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

------STATUS: Final phase sacrifice SBX: Female ANIMAL: 4508 PHASE DAY OF DEATH: 14 PHASE: Dosing phase GROUP: 4 ------Tissue Gross Observations/Comments Microscopic Observations/Comments Mediastinal LN No micropathology observations on tissue. Discolored, Black, Slight Enlarged, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS. Multifocal, Moderate. ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate. BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Minimal. - FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. IN GENERAL, SEVERITY OF CHANGES ARE

IN 2 OF 5 LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures dividual Apimal Cross and Microscopia Chamberland

STATUS: Final phase sacrifice PHASE DAY OF DEATH: 14		SEX: Female PHASE: Dosing phase	ANIMAL: 4509 GROUP: 4
lissue	Gross Observations/Comments	Microscopic Observations/Comments	
Mediastinal LN Discolored, Black, Slight		No micropathology observations on t	tissue.
	Enlarged, Slight		
Lungs	Discolored, All lobes, Black, Severe	Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.	
		ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal slight.	ι,
		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.	
		BRONCHIOLAR ASSOCIATED LYMPHOID TIS BROWN-BLACK PIGMENT DEPOSITS, Multi Slight.	

- SIX SECTIONS OF LUNG LOBE PRESENT ON MICROSLIDE. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES. IN GENERAL, SEVERITY OF CHANGES ARE IN 2 OF 5 LOBES.

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures Individual Animal Gross and Microscopic Observations

STATUS: F	rinal phase sacrifice	SEX: Female	ANIMAL: 4509
PHASE DAY OF DEATH: 1	4	PHASE: Dosing phase	GROUP: 4
Tissue	Gross Observations/Comments	Microscopic Observations/Comments	

Petroleum Coke A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Nose-Only Exposures

Individual Animal Gross and Microscopic Observations ANIMAL: 4510 STATUS: Final phase sacrifice SEX: Female GROUP: 4 PHASE DAY OF DEATH: 14 PHASE: Dosing phase Gross Observations/Comments Microscopic Observations/Comments . No micropathology observations on tissue. Mediastinal LN Discolored, Black, Moderate Enlarged, Slight Lungs Discolored, All lobes, Black, Severe Examined; 1 correlation found: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Moderate.

ALVEOLAR DUCT/ALVEOLAR EPITHELIAL HYPERPLASIA/HYPERTROPHY, Multifocal, Slight.

ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Moderate.

BRONCHIOLAR ASSOCIATED LYMPHOID TISSUE: BROWN-BLACK PIGMENT DEPOSITS, Multifocal, Slight.

- FIVE SECTIONS OF LUNG LOBES PRESENT ON MICROSLIDES. PIGMENT DEPOSITS ARE PRIMARILY AT BRONCHILOLAR-ALVEOLAR SITES (TERMINAL BRONCHIOLE/ALVEOLAR DUCT/CENTRAL ALVEOLI) AND TEND TO BE CENTRIFUGAL IN DISTRIBUTION. PIGMENT PRESENT IN ALL LUNG LOBES.

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Exposure Chambers

40 Liter cast aluminum and alloy chamber with Polycarbonate nose-only tubes (ADG Limited, Inc.).

Compound Generator

Wright Dust Feeder, Model Mark II/WDF-II (small diameter cups) with a Wright Dust Feeder Speed Selector, Model E-352-BM (BGI, Inc.).

Compound Preparation

Stainless Steel Sieve, #60 opening, Fisher Scientific Co.

Flowmeters

Flowmeter, size 0 − 10, 0 − 20, 0 − 30, 0 − 40 Lpm (Dwyer[®]), calibrated prestudy with a Top Trak[™] Mass Flowmeter, Model 822-13-OV1 PV1-V1 (Sierra Instruments).

Chamber Static Pressure Gauges

Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.); calibrated prestudy with a Dwyer® Mark II Manometer, Model 25 (Dwyer® Instruments Inc.).

Pressure Gauges

USG backpressure gauge, PN 12672-1. Norgreen backpressure gauge, PN 9892K23. Ashcroft backpressure gauge, PN 733-47. Marshall Town backpressure gauge.

Regulators

Union Carbide, P/N SG 3800 30. Norgreen, PN 9892K23

Valves

Metering Valve, Model SS-4L Series (Nupro[®] Co.).

Tubing

Plastic, size ¼", ½", 1" (Norton, Baxter). Teflon®, size ½".
Y-Tube, plastic.
Stainless Steel, size ½".

Equipment List	Appendix I

Filter

Glass fiber filter paper, Type A/E, Size 3.7 cm, Lot No. 32928 and 13512 (Gelman Sciences Inc.).

Filter holder

Open-faced filter holder (Gelman Sciences Inc.).

Drying Unit

Drierite® Laboratory Gas Drying Unit (W. A. Hammond Drierite® Co.).

Particle Sizer/Analyzer

TSI Aerodynamic Particle Sizer, Model 331001 and a DELL computer, Model 486P/25, equipped with Epson Dot matrix printer, Model P630B.

Delron DCI-6 Cascade Impactor, Serial No. 695 with stainless steel slides, greased with lubricant (Dow-Corning) and a glass fiber filter paper, Type A/E, size 7.6 cm, Lot No. 00830 (Gelman Sciences, Inc.).

Vacuum Pump

Thomas Industries, Inc., Model 707CM50.

Timers

Gralab Universal Timer, Model 171.

Environmental Monitoring

Sunbeam and Springfield Temperature and Humidity Gauge, calibrated prestudy with Digital Hygrometer-Thermometer, ID No. LA (VWR).

Balances

Sartorius LC6200S (Sartorius Corporation). AND ER-182A.

Miscellaneous

Brass Cyclones #1, #2 and #3 (Intox). Carver Laboratory press model #C, serial # 32000-136.

 Chamber Distribution Records	Appendix J

Group (target)	Date	Port	Concentration (mg/m³)	Ratio to H-1
(targot)	Date	1 010	(1119/111)	Tradio to 11-1
2 (25 mg/m³)	26-Feb-04	H-1	11	1.00
		H-2	9.4	0.85
	1-Mar-04	H-1	17	1.00
		H-2	19	1.12
3 (75 mg/m³)	26-Feb-04	H-1	17	1.00
		H-2	18	1.06
	1-Mar-04	H-1	79	1.00
		H-2	70	0.89
4 (200 mg/m³)	28-Feb-04	H-1	200	1.00
		H-2	230	1.15
	1-Mar-04	H-1	200	1.00
		H-2	170	0.85

Appendix K

PROTOCOL

PETROLEUM COKE

A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA NOSE-ONLY EXPOSURES

CONFIDENTIAL

HLS Study No.:

Protocol No.:

Date:

03-6147

Final

17 February 2004

PROTOCOL SIGNATURES / PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title:

Petroleum Coke: A 2-Week Range-Finding Inhalation

Toxicity Study in the Rat via Nose-Only Exposures

HLS Study No.:

03-6147

This is the Final Protocol. It has been reviewed and approved by:

Huntingdon Life Sciences (HLS)

Address: 100 Mettlers Road

East Millstone, NJ 08875-2360

Phone No.: 732-873-2550 x2920

Fax No.: 732-873-3992

17 February, 2004 Date

American Petroleum Institute (API)

Address:

1220 L Street, Northwest

Washington, D.C. 20005-4070

Phone No.: 202-682-8480 Fax No.:

202-682-8270

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Huntingdon Life Sciences Study No. 03-6147

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1. INTRODUCTION

HLS Study No.

03-6147

Study Title

Petroleum Coke: A 2-Week Range-

Finding Inhalation Toxicity Study in the

Rat via Nose-Only Exposures

Testing Facility

Huntingdon Life Sciences

100 Mettlers Road

East Millstone, NJ 08875-2360

Purpose

This study is designed to provide a preliminary assessment of the toxicity of the test substance when administered via nose-only inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 421 inhalation study

03-4246.

2. STUDY PERSONNEL

Study Director

Gary M. Hoffman, B.A., DABT

Alternate Contact

Keith P. Hazelden, BSc, CBiol, MIBiol

Director of Reproductive Toxicology

Tel.: 732-873-2550 x2590

Additional personnel will be documented in the study file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation

Date Study Director signs protocol

Receipt of Test Animals

17 February 2004 (Experimental Start)*

First Day of Treatment

2 March 2004 (males) (Experimental

Last Day of Treatment

Start)**; 3 March 2004 (females)

16 March 2004 (females)

15 March 2004 (males);

Necropsy - Termination

16 March 2004 (males);

17 March 2004 (females)

Submission of Audited Draft Report

17 June 2004

Experimental Termination

Date of last data collection

Study Completion

Date final report is signed by Study

Director

^{*}as per OECD GLPs; ** as per EPA GLPs

4. EXPERIMENTAL DESIGN

4.1. STUDY SUMMARY

			Number of Animals			
Group	Group Designation	Exposure Level ^a	Initial		Necropsy ^b	
•		mg/m ³	М	F	M	F
1	Air Control	0.0	10	10	10	10
2	Low	5.0	10	10	10	10
3	Mid	20	10	10	10	10
4	High	50	10	10	10	10

^aExposures will be 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Exposure levels are expressed as mg/m³ of test substance. The exposures will be conducted via nose-only exposure because this regimen will minimize the dermal deposition, and possible oral absorption, of the test substance.

^bComplete postmortem evaluations will also be performed on animals which are found dead or euthanized in a moribund condition during the course of the study.

M = male; F = female.

The first day of exposures will be defined as Day 0 of the study.

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4.2. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures are considered to be the minimum necessary for determining exposure levels for a subsequent OECD 421 Study 03-4246.

4.3. JUSTIFICATION FOR TEST ANIMAL SELECTION

The rat is an animal model commonly utilized in toxicity studies as recommended in OECD and EPA guidelines. In addition, a historical data-base is available for comparative evaluation.

4.4. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in the protocol is considered to be the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

4.5. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels were selected, based on prior results (HLS study 97-6119) of pulmonary toxicity after 5 days of exposure at exposure levels greater than 50 mg/m³, in order to determine exposure levels for a subsequent OECD 421 Study 03-4246.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE: PETROLEUM COKE

Test Substance Category: Residual product from petroleum refining

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Sponsor. This documentation will be maintained by the Sponsor. The test substance will be stored (ambient conditions) in the inhalation laboratory and handled routinely while wearing gloves, dust-mask and labcoat.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and shipped to the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA, 703-435-8780 ext 201, attn: Sam Busey). If multiple studies are conducted with the same test substance, a common archival sample may be taken and appropriately labeled.

5.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered by nose-only inhalation exposure. The test substance will be administered as a dust (depending on the physical properties of the test substance) in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure (Wright Dust Feeder) determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure levels with a mass median aerodynamic diameter of 1.0 - 3.0 microns. The method will be described in the raw data of the study and in the report.

The nose-only exposure chambers will each have a volume of approximately 40 liters. Each chamber will be operated at a minimum flow rate of 8 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T₉₉ equilibrium time of at most 23 minutes. This chamber size and air flow rate is considered adequate to maintain the oxygen level at least 19%. At the end of the exposure, all animals will remain in the chamber for a minimum of 30 minutes. During this time the chamber will be operated at approximately the same flow rate using clean air only.

5.5. EXPOSURE CONCENTRATION DETERMINATION

A nominal exposure concentration will be calculated daily. The flow of air through the chamber will be monitored using appropriate calibrated equipment. The test substance consumed during the exposure will be divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.

During each exposure, measurements of airborne concentrations of test substance will be performed at least four times using a gravimetric sampling procedure. Also prior to initiation of animal exposures, additional samples will be taken to determine the distribution of the test substance in the exposure chamber.

If more than the normal amount of trial time is required because of test substance generation or monitoring problems (80 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

5.6. PARTICLE SIZE DISTRIBUTION ANALYSIS:

During each exposure, particle size determinations will be performed using a cascade impactor or other appropriate device, to characterize the aerodynamic particle size distribution of any aerosol present.

5.7. CHAMBER ENVIRONMENT:

Temperature, humidity and airflow rate will be recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the extent possible, between 20 to 24°C and 40 to 60%, respectively.

5.8. SUMMARY OF CHAMBER ACTIVITY:

The minimum frequency of chamber activity is summarized below.

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/day
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate	13X/day
Nominal Test Substance Concentration	1X/day
Rotation Pattern of Exposure Tubes	1X/day
Loading/Unloading Verification	1X/day

5.9. FREQUENCY AND DURATION OF ADMINISTRATION

The test substance will be administered for 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Test substance administration will continue through the day prior to necropsy.

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Study No. 03-6147

5.10. UNUSED TEST SUBSTANCE

The unused portion of the test substance as well as any empty test substance containers will be returned to the Archives of the Sponsor (see section 5.3) following completion of the in-life phase of the final study with this test substance. In the event the Sponsor wishes the Testing Facility to arrange for disposal, a cost for this service will be provided.

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus[®] Sprague-Dawley - derived (CD[®]) Crl: CD (SD) IGS BR

Female rats will be nulliparous and non-pregnant.

6.2. SUPPLIER

Charles River Laboratories Kingston, New York

Documentation of the specific breeding facility will be maintained in the study file.

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. NUMBER OF ANIMALS ON STUDY

<u>Total</u>	<u>Males</u>	Females	
80	40	40	

6.3.2. AGE

Young adult (approximately 6 weeks at receipt; approximately 8 weeks (and no more than 9 weeks) at initiation of exposures.

6.3.3. WEIGHT

Approximately 200 to 300 grams (males) and 150 to 250 grams (females) at first exposure. Animals outside of this range may be used at the discretion of the Study Director.

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6.4. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain suitability for study.

6.5. ANIMAL CARE AND HUSBANDRY

6.5.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry will be followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences Inc. is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.5.2. VETERINARY CARE

Animals will be monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.5.3. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5.4. HOUSING

Animals of the same sex will be individually housed in suspended, stainless steel wire mesh cages during the study.

6.5.5. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, MO) ad libitum.

6.5.6. WATER

Elizabethtown Water Company, Westfield, NJ; ad libitum, via automated watering system.

6.5.7. FEED ANALYSIS

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.5.8. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file. There are no known contaminants which are expected to interfere with the objectives of this study.

6.5.9. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Individual weights of animals placed on test shall be within $\pm 20\%$ of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

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6.5.10. IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be tailtattooed with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study number and animal number.

6.5.11. ANIMAL HUSBANDRY/EXPOSURE

Housing:

Individually in tubes.

Food:

None.

Water:

None.

7. IN-LIFE EVALUATIONS

7.1. CLINICAL OBSERVATIONS

7.1.1. VIABILITY CHECKS (CAGE-SIDE)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

7.1.2. PHYSICAL EXAMINATIONS

All animals will be observed as a group at least once during each exposure. This will routinely be performed near the middle of each exposure and may be performed more frequently if significant signs of toxicity are noted.

Each animal will be removed from its cage and examined at least once pretest and weekly during the study period. Examinations will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive

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circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded.

7.2. BODY WEIGHTS

Non-fasted body weights for animals will be recorded at least once pretest and once per week during the study period. Fasted weights will be obtained prior to necropsy.

7.3. FEED CONSUMPTION

Feed consumption will be measured (weighed) during the week prior to treatment initiation and once per week during the study period. Feed will be available without restriction 7 days/week except during exposures. Animals will be presented with weighed feeders at the scheduled intervals. After at least 5 days, the feeders will be reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal per day. The grams consumed per kilogram of body weight per day will then be calculated for each animal.

8. POSTMORTEM EVALUATIONS

8.1. MACROSCOPIC PATHOLOGY

A complete macroscopic examination will be performed on all animals, including animals euthanized in a moribund condition or found dead; all abnormal observations will be recorded. The necropsy will consist of an external examination, including identification of all clinically recorded lesions, as well as a detailed internal examination. Special attention should be paid to the organs of the reproduction system.

8.1.1. MORIBUND ANIMALS

Animals showing signs of severe debility, particularly if death appears imminent, will be euthanized to prevent loss of tissues through autolysis.

8.1.2. TERMINAL NECROPSY

Necropsy will be performed on all surviving animals after animals have been treated for at least 14 days. Necropsy schedules will be established in order to assure that approximately equal numbers from each group will be examined at similar times of each day of necropsy.

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8.2. METHOD OF EUTHANASIA

Exsanguination following carbon dioxide inhalation.

8.3. ORGAN WEIGHTS

Organs indicated below will be taken from all survivors at the scheduled necropsies, weighed, recorded and organ/body and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition during the course of the study. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissues in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired organs will be weighed together.

adrenals	liver	seminal vesicles
brain	lungs	spleen
epididymides	ovaries	testes
heart	pituitary	thymus
kidneys		uterus

8.4. TISSUE PRESERVATION

Tissues listed in Appendix A will be obtained at necropsy and preserved for all animals.

Eyes and testes and epididymides – modified Davidson's solution initially and then 10% neutral buffered formalin

All other tissues - 10% neutral buffered formalin

Note: Lungs (gravity method) and urinary bladder will be infused with formalin to ensure fixation.

8.5. MICROSCOPIC PATHOLOGY EVALUATIONS

The lungs from all animals will be examined. No other examinations are required. Authorization will be obtained from the Sponsor prior to performing any additional examinations.

Stains: Standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

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9. ARCHIVING OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond one year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

10. STATISTICAL ANALYSIS

10.1. ITEMS TO BE ANALYZED

The following will be compared for control and test substance-treated groups.

mean body weight values
mean feed consumption values
mean terminal organ weights, organ/body and organ/brain weight ratios

10.2. PROCEDURES

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. Organ weight data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964) or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated then Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in onecriterion 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 48: 907-911; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371.

11. REPORTING

11.1. STATUS REPORTS

Periodic written (weekly) updates on study progress will be provided by the Study Director.

11.2. FINAL REPORT

One unbound hard copy and one electronic copy of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

Compliance Statement (including Sponsor signature line)
Quality Assurance Statement
Summary
Introduction
Experimental Design

Materials and Methods

Discussion of Study Results

Conclusion (including NOAEL statement, if applicable)

Tables of Exposure Data

Mortality Data

Individual animal termination history

Summary of daily animal observations (as appropriate)

Summary of weekly physical examination data

Tables of mean and individual body weights

Tables of mean and individual feed consumption

Tables of mean and individual organ weights, organ/brain

and organ/body weight ratios

Individual and summary tables of macroscopic pathology findings

Individual and summary tables of microscopic pathology findings

References for experimental methodology

Senior personnel participating in the study

Copy of study protocol and associated amendments

12. REGULATORY REFERENCES

12.1. TESTING GUIDELINES

This study is not designed to meet or exceed any regulatory requirements. It is designed to assess the toxicity of the test substance in order to determine exposure levels for a subsequent OECD 421 inhalation study 03-4246.

12.2. GOOD LABORATORY PRACTICES

This study will be conducted in compliance with EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.

12.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991. The Sponsor should make particular note of the following:

- 1. The Sponsor's signature on this protocol documents that, for the study described, there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments in regard to species, test substance, route of administration or duration of treatment.
- 2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or written laboratory standard operating procedures.
- 3. Any procedures outlined in this study which cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing by the Sponsor and the Study Director, in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review Form.
- 4. Animals experiencing more than momentary or slight pain or distress due to test substance or injury or illness will be treated by the Testing Facility's veterinary staff with approved analgesics or agents to relieve pain after consultation with the Study Director and Sponsor. However, in emergency situations, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.
- 5. Methods of euthanasia used during this study are in conformance with the above-referenced regulations.

12.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with all appropriate regulations.

13. QUALITY ASSURANCE MONITORING

The Huntingdon Life Sciences Quality Assurance Unit will monitor the facilities, equipment, personnel, methods, practices, records and controls used in this study

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to assure that they are in conformance with this protocol, company SOPs, and the appropriate Good Laboratory Practice requirements.

14. ALTERATION IN STUDY DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by 2 members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A Tissues Preserved

Tissue	Preserved
adrenal gland	Х
aorta (thoracic)	Х
bone (sternum/femur)	Х
bone marrow (rib) a	X
brain (medulla/pons, cerebrum and cerebellum)	X
epididymides	X
esophagus	X
eye (with optic nerve)	X
heart	X
kidneys	Х
large intestine (cecum, colon, and rectum)	Х
lacrimal gland	Х
larynx	Х
liver	Х
lungs (with mainstem bronchi)	Х
lymph node (mesenteric and thoracic)	Х
mammary gland	X
muscle (biceps femoris)	X
nasopharyngeal tissue	X
nerve (sciatic)	X
ovaries	Х
pancreas	х
pituitary	х
prostate	х

Huntingdon Life Sciences

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Study No. 03-6147

Tissue	Preserved
salivary gland with submandibular lymph node	X
seminal vesicles	X
skin	Х
small intestine (duodenum, jejunum, ileum)	X
spinal cord (cervical, thoracic, lumbar)	Х
spleen	X
stomach	X
testes	X
thymic region	X
thyroid (with parathyroids)	X
trachea	X
uninary bladder	X
uterus (body/horns with cervix)	X
Zymbal's gland	X
gross lesions	X
target organs ^b	X

^aBone marrow smears will be prepared and archived. They will only be evaluated (Sponsor approval, additional cost) if needed.

^bTarget organs will be designated by the Study Director, Pathologist and/or Sponsor based on experimental findings.

Huntingdon Life Sciences Study No. 03-6147

Page 1 of 1 Final Protocol

Protocol Amendment No. 1

ID.

Study Title: Petroleum Coke: A 2-Week Range-Finding Inhalation Toxicity
Study in the Rat via Nose-Only Exposures

Changes

1. Study Summary, page 2:

Revise Exposure Levels: Group 2 = 25 5 mg/m³

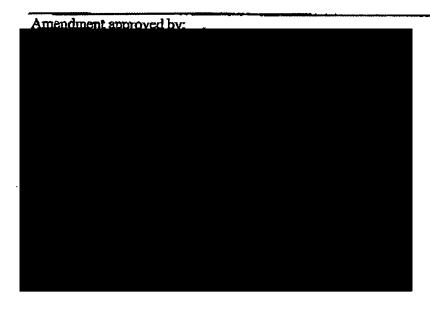
Group $3 = 75.20 \text{ mg/m}^3$

Group $4 = 200 \pm 0 \text{ mg/m}^3$

2.Justification for Exposure Level Selection, page 3: Add as below.

Reasons for Changes

1. and 2. Based on a subsequent re-review of the prior data for the test substance (e.g. slight pulmonary toxicity and body weight effects after 5 days of exposure to 50 mg/m³) and review of the purpose of this study as a range-finding study for a subsequent reproduction assessment OECD 421 study 03-4246, it was decided that the initially selected high exposure level of 50 mg/m³ was not high enough to sufficiently assess a maximum tolerated exposure level. Therefore, the high exposure level was increased to 200 mg/m³ (expected to result in marked pulmonary toxicity and body weight effects). This will result in an essentially 12 times higher exposure than the prior 5 days study since the exposure level will be increased by a factor of 4 (from 50 to 200 mg/m³) and the duration of the exposures will be increased by a factor of 3 (from 5 to 14 days). The lower exposures levels were also proportionately adjusted.



1 Mar oy

Date

OIMAR DA

Date

1meres 4

Date

03 Much, 2004

Date

Protocol Amendment No. 2

Study Title: Petroleum Coke: A 2-Week Range-Finding Inhalation Toxicity
Study in the Rat via Nose-Only Exposures

Changes

1. Organ Weights, page 11:

Revise:seminal vesicles and prostate...

2. Statistical Analysis, page 12:

Revise:Bartlett's test (....;Snedecor, G.W. and Cochran, W.G. 1967. Statistical Methods. 6th edition. Ames: Iowa State University Press) will be performed....

3. Tissues Preserved, page 17:

Revise:lymph node (mesenteric and mediastinal thoracie)...

Reasons for Changes

- 1. The prostate is also weighed as attached to the seminal vesicles.
- 2. Clarification of the references for the Bartlett's Test.
- 3. Clarification of the terminology for the lymph nodes collected at necropsy.

Amendment approved by:



18 Jue 04

Date

Date

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	Certificate of Analysis	Appendix L



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Page 1 of 2

Lancaster Laboratories Sample No. SW 4073302

Collected: 06/26/2003 00:00

Submitted: 06/27/2003 10:40 Reported: 07/09/2003 at 11:42

Discard: 08/09/2003

Pet Coke Micronized Solid Sample

Cost Center# ENG-4066 HPV Petroleum Cake Account Number: 10863

Chevron Products Company 940 Hensley St. Bldg. 210

Richmond CA 94801

MICPC

CAT			As Receiv	red	As Received Method		Dilution
Mc.	Analysis Name	CAS Number	Result		Detection Limit	units	Factor
07804	PARS in Soil by GC/MS						
01191	Acenaphthene	83-32-9	и.в.		1,000.	ug/kg	10
01195	Pyrene	129-00-0	8,600.	J	1,000.	ug/kg	10
02751	1-Methylnaphthalene	90-12-0	10,000.		1,000.	ug/kg	10
03761	Naphthalene	91-20-3	11,000.		1,000.	ug/kg	10
03765	Acenaphthylene	208-96-8	N.D.		1,000.	ug/kg	10
03768	Fluorens	86-73-7	1,500.	J	1,000.	ug/kg	10
03775	Phonanthrone	85-01-8	7,800.	J	1,000.	ug/kg	10
03776	Anthracene	120-12-7	3,300.	J	1,000.	ug/kg	10
03778	Fluoranthene	206-44-0	1,400.	J	1,000.	ug/kg	10
03781	Bonzo (a) anthracene	56-55-3	7,100.	J	1,000-	ug/kg	10
03782	Chrysene	218-01-9	9,400.	J	1,000.	ug/kg	10
03786	Benzo (b) fluoranthene	205-99-2	3,800.	J	1,000.	ug/kg	.10
03787	Benzo(k) fluorantheno	207-08-9	N.D.		1,000.	ug/kg	10
03788	Benzo(a) pyzene	50-32-8	11,000.		1,000.	ug/kg	10
03789	Indeno(1,2,3-cd)pyrene	193-39-5	3,500.	J	1,000.	ug/kg	10
03790	Dibenz (a, h) anthraceno	53-70-3	4,100.	3	1,000.	ug/kg	10
03791	Benzo(g,h,i)perylene	191-24-2	8,700.	J	1,000.	ug/kg	10
04694	2-Methylnaphthalene	91-57-6	26,000.		1,000.	ug/kg	10
			· · · · · · · · · · · · · · · · · · ·	 .		_	

Due to sample matrix interferences observed during the extraction, the normal reporting limits could not be obtained.

Due to the sample matrix an initial dilution was necessary to perform the analysis. Therefore, the reporting limits for the GC/MS semivolatile compounds were raised.

State of California Lab Certification No. 2116

Laboratory Chronicle

Analysis
Analysis Wasa Hethod Trials Date and T

SW-846 8270C

Trial# Date and Time 1 07/02/2003 18:34 5

Analyst Susan L Scheuering Dilution Factor 10

MEMBER

PAHs in Soil by GC/MS

CAT

No.

07804



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Page 2 of 2

Lancaster Laboratories Sample No. SW 4073302

Collected: 06/26/2003 00:00

Submitted: 06/27/2003 10:40 Reported: 07/09/2003 at 11:42

Discard: 08/09/2003

Pet Coke Micronized Solid Sample

Cost Center# ENG-4066 HPV Petroleum Cake

MICPC

07806 BMA Soil Extraction

SW-846 3550B

Account Number: 10863

Chevron Products Company 940 Hensley St. Bldg. 210

Richmond CA 94801

06/30/2003 20:00 Sally L Appleyard

.

Testing Facility Personnel	Appendix M

TITLE/DEPARTMENT NAME/DEGREE SENIOR VICE PRESIDENT, SAFETY ASSESSMENT DIRECTOR, DEVELOPMENTAL AND REPRODUCTIVE TOXICOLOGY DIRECTOR, TOXICOLOGY **OPERATIONS** DIRECTOR, ANALYTICAL SERVICES DIRECTOR, QUALITY ASSURANCE STUDY DIRECTOR **PATHOLOGIST** STUDY MONITOR **VETERINARIAN** MANAGER/SUPERVISOR Rodent/Inhalation Toxicology Pharmacy Necropsy Histology

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	Report Amendments	Appendix N

There are no amendments for this report at this time.

Studies 831

Test Article: Analytical

Test Article: Analytical Before and After Summary Tables

Concentrations of Selected Metals in Petroleum Coke Sample Analyzed Before and After Toxicology Studies^{1, 2}

		Pre-Test Micronized ³	Post-Test Micronized 3, 4
	Units	Result	Result
AL	mg/kg	300.2	250.7
AS	mg/kg	<29.61	<2.31246
В	mg/kg	<29.61	
BA	mg/kg	<29.61	6.87
BE	mg/kg	<14.805	
BI	mg/kg	<29.61	
CA	mg/kg	121.6	158.7
CD	mg/kg	<14.805	
co	mg/kg	<14.805	1.7
CR	mg/kg	<14.805	4.58
CU	mg/kg	<17.766	2.25
FE	mg/kg	247	276.1
к	mg/kg	<44.414	20.5
LI	mg/kg	<14.805	<1.15623
MG	mg/kg	60.85	65.46
MN	mg/kg	<29.61	7.27
МО	mg/kg	<29.61	15.99
NA	mg/kg	114.6	99.03
NI	mg/kg	351.7	304.6
Р	mg/kg	30.3	25.01
PB	mg/kg	<29.61	7.38
PD	mg/kg		<6.937379
PT	mg/kg		4.48
s	mg/kg	58060	
SB	mg/kg	<74.024	
SE	mg/kg	<29.61	
SI	mg/kg		204
SN	mg/kg		<2.31246
TI	mg/kg	<14.805	14.35
٧	mg/kg	1805	1580
ZN	mg/kg	<14.805	11.19

Analyses performed by ChevronTexaco Energy Technology Company Elemental Spectroscopy Laboratory
 Original data and reports stored at ChevronTexaco Energy Technology
 Lot number M05369A
 Data from the environmental post study analysis

Concentrations of Selected Polyaromatic Hydrocarbon Compounds in Petroleum Coke Sample Analyzed Before and After Toxicology Studies ¹

Analysis Name		Pre-Test Micronized ²		Post-Test Micronize	
	Units	Result	MDL	Result	MDL
Acenaphthene	ug/kg	N.D.	1,000	690. J	200.
Pyrene	ug/kg	8,600 J	1,000	7,400	200.
1-Methylnaphthalene	ug/kg	10,000	1,000	10,000.	200.
Naphthalene	ug/kg	11,000	1,000	10,000.	200.
Acenaphthylene	ug/kg	N.D.	1,000	N.D.	200.
Fluorene	ug/kg	1,500 J	1,000	1,300. J	200.
Phenanthrene	ug/kg	7,800 J	1,000	7,000	200.
Anthracene	ug/kg	3,300 J	1,000	3,300.	200.
Fluoranthene	ug/kg	1,400 J	1,000	1,300.	200.
Benzo(a)anthracene	ug/kg	7,100 J	1,000	7,800.	200.
Chrysene	ug/kg	9,400 J	1,000	7,900.	200.
Benzo(b)fluoranthene	ug/kg	3,800 J	1,000	3,900.	200.
Benzo(k)fluoranthene	ug/kg	N.D.	1,000	1,600.	200.
Benzo(a)pyrene	ug/kg	11,000	1,000	13,000.	200.
Indeno(1,2,3-cd)pyrene	ug/kg	3,500 J	1,000	3,600.	200.
Dibenz(a,h)anthracene	ug/kg	4,100 J	1,000	4,700.	200.
Benzo(g,h,i)perylene	ug/kg	8,700 J	1,000	14,000.	200.
2-Methylnaphthalene	ug/kg	26,000	1,000	27,000.	1000

 $^{^{\}rm 1}$ Analysis performed by Lancaster Laboratories $^{\rm 2}$ Lot number M05369A

Laboratory Report for Concentrations of Selected Metals in Petroleum Coke Samples Analyzed Before Toxicology Studies Laboratory Report for Concentrations of Selected Metals in Petroleum Coke Samples Analyzed Before Toxicology Studies

CHEVRONTEXACO ENERGY TECHNOLOGY COMPANY ELEMENTAL SPECTROSCOPY LABORATORY PROJECT SUMMARY

For:

Patrick Beatty

Location:

Richmond

Phone:

CTN242-7037

Reported:

February 18, 2004

1. Project Title:

Determination of metals by microwave digestion and ICP-AES (modified EPA Methods)

2. Sample Description:

Petroleum coke

3. Analytical Approach:

Conventional ashing and air-refluxing methods have been widely used in Petroleum industry analytical laboratories for many years. These traditional methods are always time-consuming, labor-intensive, tedious, and cumbersome. Additionally, contamination or loss is very likely to occur from the acids (especially sulfuric acid) and/or vessels used during the sample preparation. Moreover, sulfur determination may not be achieved because sulfuric acid is always used in these methods.

Utilizing a high pressure microwave system, many innovative and rapid analytical methods were developed in our atomic spectroscopy lab recently. The high operating temperature and pressure attainable in this microwave digestion system ensures total decomposition of complex petroleum crudes and petrochemical products, with no residual organic content. Sample preparation time has been shortened from days (or, in some cases, even more than a week) to minutes. Our analytical methods can now also be applied to the determination of metals in crudes and polymer samples because sulfuric acid is no longer required in the microwave digestion process. The microwave digestion system also eliminates contamination previously due to the use of more traditional digestion vessels, and from airborne particulates in the lab environment.

Samples were digested by modified EPA 3052 (closed vessel microwave digestion) and analyzed by modified EPA 6010 (ICP-AES).

4. Analytical Results:

3030999 PETROLEUM COKE 2NM

M	ICROWAVE DIGST	/ICP PLUS	REPORTED		
ΑL	300.200 PPM	AS	<29.61 PPM	В	<29.61 PPM
BA	<29.61 PPM	BE	<14.805 PPM	ВІ	<29.61 PPM
CA	121.600 PPM	CD	<14.805 PPM	CO	<14.805 PPM
CR	<14.805 PPM	CU	<17.766 PPM	FE	247.000 PPM
K	<44.414 PPM	LI	<14.805 PPM	MG	60.850 PPM
MN	<29.61 PPM	MO	<29.61 PPM	NA	114.600 PPM
NI	351.700 PPM	Р	30.300 PPM	PB	<29.61 PPM
S	58060.000 PPM	SB	<74.024 PPM	SE	<29.61 PPM
SI	554.600 PPM	SN	<44.414 PPM	TI	<14.805 PPM
V	1805.000 PPM	ZN	<14.805 PPM		

3030251 PETROLEUM COKE

		~~ ~~~~~~~~			
MICRO	DWAVE DIGST/ICI	P PLUS REF	PORTED		
AL	321.000 PPM	AS	<19.279 PPM	В	<19.279 PPM
BA	<19.279 PPM	BE	<9.639 PPM	BI	<19.279 PPM
CA	178.000 PPM	CD	<9.639 PPM	CO	<9.639 PPM
CR	<9.639 PPM	CU	<11.567 PPM	FE	310.000 PPM
K	<28.918 PPM	LI	<9.639 PPM	MG	77.370 PPM
MN	<19.279 PPM	MO	<19.279 PPM	NA	133.000 PPM
NI	367.100 PPM	P	<19.279 PPM	PB	<19.279 PPM
S	73920 PPM	SB	<48.197 PPM	ŞE	<19.279 PPM
SI	743.200 PPM	SN	<28.918 PPM	TI	12.910 PPM
V	1938,000 PPM	ZN	12.010 PPM		

Analyzed and Reported by: J. David Hwang and David Leong

Laboratory Report for Concentrations of Selected Metals in Petroleum Coke Samples Analyzed After Toxicology Studies

Concentration of Selected Metals in Petroleum Coke Samples Analyzed After Toxicology Studies^{3,4,5}

	WIL6485A (2 mm) ¹	WIL6484A (3.3 micron) ²
AL	205.1	250.7
AS	<2.306273	<2.31246
BA	7.74	6.87
CA	81.73	158.7
CO	1.9	1.7
CR	3.94	4.58
CU	. 1.83	2.25
FE	215.9	276.1
K	10.91	20.5
ĻI	<1.153137	<1.15623
MG	50.34	65.46
MN	. 5.31	7.27
MO	16.58	15.99
NA	87.84	99.03
NI	319.6	304.6
Р	19.75	25.01
PB	4.88	7.38
PD	<6.918819	<6.937379
PT	3.81	4.48
SI	86.75	204
SN	<2.306273	<2.31246
TI	11.66	14.35
V	1559.00	1580
ZN	8.87	11.19

Also identified as "pellet" petcoke; lot number M05369B
 Also identified as micronized petcoke; lot number M05369A
 Samples were shipped from Wildlife International to ChevronTexaco Energy Technology Company Elemental Spectroscopy Laboratory

⁴ Samples were digested by modified EPA 3052 (closed vessel microwave digestion) and analyzed by modified EPA 6010 (ICP-AES)

⁵ Original data stored at ChevronTexaco Energy Technology Company

Huntingdon Life Sciences Study No. 03-4246

Page 1 of 1 Final Protocol

Protocol Amendment No. 5

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

Identification of Test Substance, page 5:

Revise: At the end of the study, a 200 gram sample of the test substance will be shipped for analysis to ChevronTexaco Energy Research and Technology Corp., 100 Chevron Way, Richmond, CA 94802, 510-242-7037, atm: Patrick Beatty. Since this analysis was not conducted using the same methods as the pre-study analysis and therefore was not valid for a comparison to the pre-study data, the data from an analysis of a sample from the same lot number stored at Wildlife International will instead be reported for this study.

Reasons for Changes

Clarification of the data to be reported for test substance stability analysis.

Additional Cost Required: No

Amendment approved by:

160,000

1/200

Not used for pre and post study stability assessment due to deviation in Chevron analysis (calcinated) rendering the results inappropriate for comparison to original data

CHEVRONTEXACO ENERGY TECHNOLOGY COMPANY ELEMENTAL SPECTROSCOPY LABORATORY PROJECT SUMMARY

For: Location: Richmond

Phone: CTN242-7038 Reported: February 7, 2006

1. Project Title:

Determination of metals by microwave digestion and ICP-AES (modified EPA Methods)

2. Sample Description:

Petroleum coke

3. Analytical Approach:

Conventional ashing and air-refluxing methods have been widely used in Petroleum industry analytical laboratories for many years. These traditional methods are always time-consuming, labor-intensive, tedious, and cumbersome. Additionally, contamination or loss is very likely to occur from the acids (especially sulfuric acid) and/or vessels used during the sample preparation. Moreover, sulfur determination may not be achieved because sulfuric acid is always used in these methods.

Utilizing a high pressure microwave system, many innovative and rapid analytical methods were developed in our atomic spectroscopy lab recently. The high operating temperature and pressure attainable in this microwave digestion system ensures total decomposition of complex petroleum crudes and petrochemical products, with no residual organic content. Sample preparation time has been shortened from days (or, in some cases, even more than a week) to minutes. Our analytical methods can now also be applied to the determination of metals in crudes and polymer samples because sulfuric acid is no longer required in the microwave digestion process. The microwave digestion system also eliminates contamination previously due to the use of more traditional digestion vessels, and from airborne particulates in the lab environment.

The sample was calcinated at 600 °C for 3 hours and then digested by modified EPA 3052 (closed vessel microwave digestion) and analyzed by modified EPA 6010 (ICP-AES).

4. Analytical Results:

AL	40360	PPM
AS	<185.642	PPM
ВА	1008	PPM
BI	<185.642	PPM
CA	22650	PPM
В	<185.642	PPM
со	241	PPM
CR	708	PPM
CU	303	PPM
FE	35720	PPM
K	3216	PPM
BE	<92.821	PPM
Ц	155	PPM
MG	8936	PPM
MN	1085	PPM
МО	2137	PPM
NA	14510	PPM
CD	<92.821	PPM
NI	43500	PPM
Р	2056	PPM
PB	1035	PPM
\$	15240	PPM
SB	<464.105	PPM

SE	<185.642 PPM
SI	32000 PPM
SN	<185.642 PPM
TI	1686 PPM
V	233600 PPM
ZN	1497 PPM

Analyzed and Reported by:

Laboratory Report for Concentrations of Selected Polyaromatic Hydrocarbon Compounds in Petroleum Coke Sample Analyzed Before Mammalian Toxicology Studies



ANALYTICAL RESULTS

Prepared for:

Chevron Products Company 940 Hensley St. Bldg. 210

> Richmond CA 94801 510-242-8191

> > Prepared by:

Lancaster Laboratories 2425 New Holland Pike Lancaster, PA 17605-2425

SAMPLE GROUP

The sample group for this submittal is \$57532. Samples arrived at the laboratory on Friday, June 27, 2003. The PO# for this group is 99011184 and the release number is BEATTY.

Client Description

Pet Coke 2mm Solid Sample Pet Coke Micronized Solid Sample Lancaster Labs Number 4073301 4073302

I COPY TO

Lancaster Laboratories

1 COPY TO

Chevron CRTC

Questions? Contact your Client Services Representative Alison M O'Comor at (717) 656-2300.

Respectfully Submitted,

A4200 3:66





Page 1 of 2

Lancaster Laboratories Sample No. SW 4073302

Collected: 06/26/2003 00:00

Account Number: 10863

Submitted: 06/27/2003 10:40 Reported: 07/09/2003 at 11:42 Chevron Products Company 940 Hensley St. Bldg. 210

Discard: 08/09/2003

Pet Coke Micronized Solid Sample

Cost Center# ENG-4066 HPV Petroleum Cake Richmond CA 94801

MICPC

CAS No.	Analysis wasa	As Received CAS Sumber Result		red.	As Received Nativod Detection Limit	uni ta	Dilution Factor	
07804	PAHs in Soil by GC/MS							
01191	Acensphthene	83~32~9	N.D.		1,000.	ug/kg	10	
01195	Pyrene	129-00-0	8,600.	J	1,000.	ug/kg	10	
02751	1-Methylnaphthalene	90-12-0	10,000.		1,000.	ug/kg	10	
03761	Naphthalene	91-20-3	11,000.		1,000.	ug/kg	10	
03765	Acensphthylene	208-96-8	N.D.		1,000.	ug/kg	10	
03768	Fluorene	86-73-7	1,500.	J	1,000.	ug/kg	10	
03775	Phenanthrene	85-03-8	7,800.	3	1,000.	ug/kg	10	
03776	Anthracene	120-12-7	3,300.	Į	1,000.	ug/kg	10	
03778	Fluozanthene	206-44-0	1,600.	J	1,000.	ug/kg	10	
03781	Bonzo (a) anthracons	56-55-3	7,100.	J	1,000-	ug/kg	10	
03782	Chrysens	218-01-9	9,400.	J	1,000.	ug/kg	10	
03786	Bengo (b) fluoranthene	205-99-2	3,600.	J	1,000.	ng/kg	10	
03787	Benzo (k) fluorantheno	207-08-9	N.D.		1,000.	ug/kg	10	
03788	Benzo (a) pyrene	50~32~8	11,000.		1,000.	ug/kg	18	
03789	Indeno(1,2,3=cd)pyrene	193-39-5	3,500.	J	1,000.	ug/kg	10	
03790	Dibenz (a, h) anthracene	53-70-3	4,100.	J	1,000.	ug/kg	10	
03791	Benzo(g,h,i)perylene	191-24-2	9,700.	J	1,000.	ug/kg	10	
04694	2-Methylnaphthalene	91-37-6	26,000.		1,000.	ug/kg	10	

Due to sample matrix interferences observed during the extraction, the normal reporting limits could not be obtained.

Due to the sample matrix an initial dilution was necessary to perform the analysis. Therefore, the reporting limits for the GC/MS semivolatile compounds were raised.

State of California Lab Cartification No. 2116

Laboratory Chronicle

CAT Analysis Name Hethod . Trials Date and Time Analyst Fadeor 07804 PAHs in Soil by GC/MS SE-846 8270C 1 07/02/2003 18:34 Susan L Schewaring 10





Page 2 of 2

Lancaster Laboratories Sample No. SW 4073302

Collected:06/26/2003 00:00

Account Number: 10863

Submitted: 06/27/2003 10:40 Reported: 07/09/2003 at 11:42 Chevron Products Company 940 Hensley St. Bldg. 210

Discard: 08/09/2003

Richmond CA 94801

Pet Coke Micronized Solid Sample

Cost Center# ENG-4066 HPV Petroleum Cake

MICPC

07806 MMA Soil Extraction

5W-846 3550B

1 06/30/2003 20:00 Sally L Appleyard

1

Analysis Resort



Page 1 of 1

Lancaster Laboratories Sample No. SW 4073301

Collected:06/26/2003 00:00

Account Number: 10863

Submitted: 06/27/2003 10:40 Reported: 07/09/2003 at 11:42 Chevron Products Company 940 Hensley St. Bldg. 210

Discard: 08/09/2003 Pet Coke 2mm Solid Sample Cost Center# ENG-4066 HPV Petroleum Cake

Richmond CA 94801

ZMMPC

Cat

Xo.

07804

97806

					As Received		and Surand and
Cat			As Race	i.vecl	bodsess		Dilutica
No.	Amplyois Mame	CAS Aumber	Rocult		Detection Limit	unite	Factor
07804	PAHs in Soil by GC/MS						
01191	Acenaphthene	83-32-9	N.D.		330.	ug/kg	10
01195	Pyrone	129-00-0	1,300.	3	330.	ug/kg	10
02751	1-Mathylnaphthalene	90-12-0	2,780.	3	330.	ug/kg	10
03761	Naphthalene	91-20-3	3,600.		330.	ug/kg	10
03765	Aconophthylono	208-96-8	N.D.		330.	ug/kg	10
03768	Pluorene	85-73-7	340.	J	330.	ug/kg	30
03775	Phenanthrene	85-01-8	690.	J	330.	ug/kg	10
03776	Anthracene	120-12-7	N.D.		330.	ug/kg	10
03778	Fluoranthono	205-44-0	N.D.		330.	ug/kg	10
03781	Benzo (a) anthracene	56~55~3	580.	រ	330.	ug/kg	10
03782	Chrysena	218-01-9	880.	J	330.	ug/kg	10
03786	Benzo (b) fluoranthene	205-99-2	520.	J	330.	ug/kg	10
03787	Benzo (k) fluoranthene	207-08-9	N.D.		330.	ug/kg	10
03788	Benzo (a) pyrone	50-32-8	1,800.	3	330.	ug/kg	10
03789	Indeno (1, 2, 3-cd) pyrene	193-39-5	340.	J	330.	ug/kg	10
03790	Dibenz (a, h) anthracene	53-70-3	490.	3	330.	ug/kg	10
03791	Benzo(g,h,i)perylene	191-24-2	1,100.	ď	330.	ug/kg	10
04694	2-Methylnaphthalene	91-57-6	11,000.	•	330.	ng/kg	10
	The to the semple matrix an		• • •			-99	

Due to the sample matrix an initial dilution was necessary to perform the analysis. Therefore, the reporting limits for the GC/MB semivolatile compounds were raised.

SH-846 3550B

State of California Lab Certification No. 2116

Laboratory Chronicle

Analysis

Mathod Stiel Date and Time Analysis

SW-846 82700 1 07/02/2003 15:41 Susan L Schouoring 10

06/30/2003 20:00

Sally L Appleyard



Analysis Name

PARs in Soil by GC/MS

DNA Soil Extraction



Page 1 of 2

Quality Control Summary

Client Name: Chevron Products Company

Group Number: 857532

Reported: 07/09/03 at 11:42 AM

Laboratory Compliance Quality Control

inalysis Femo	Blank Result	Blank MDL	Report Units	ics rec	lcsd sokc	ics/icsd Limits	2000	RPD Haw
Botch number: 03181SLA026	Sample ni	mber(s):	4073301-40	73302				
Acenaphthene	N.D.	33.	ug/kg	91		76-109		
Pyzene	R.D.	33.	ug/kg	89		71-110		
1-Methylnaphthaleno	N.D.	33.	ug/kg	87		76-101		
Maphthalene	N.D.	33.	ug/kg	87		73-103		
Aconaphthylone	N.D.	33.	ug/kg	94		73-106		
Pluozena	N.D.	33.	ug/kg	93		66-115		
Phenanthrone	N.D.	33.	ug/kg	88		70-107		
Anthracene	N.D.	33.	ug/kg	86		71-107		
Fluoranthens	N.D.	33.	ug/kg	90		69-107		
Benzo (a) anthracene	u.d.	33.	ug/kg	93		74-107		
Chrysone	N.D.	33.	ug/kg	89		72-109		
Benzo (b) fluoranthene	N.D.	33.	ug/kg	95		71-113		
Banzo(k) fluoranthene	N.D.	33.	ug/kg	97		75-112		
Benzo (a) pyrane	w.n.	33.	ug/kg	94		79-111		
Indeno(1,2,3-cd)pyrene	N.D.	33.	ug/kg	93		74-113		
Dibanz (m, h) sothracene	N.D.	33.	ug/kg	95		81-118		
senzo(g,h,i)perylene	N.D.	33.	ug/kg	92		74-114		
2-Methylnaphthalene	n.d.	33.	ug/kg	90		70-102		

Sample Matrix Quality Control

	386	MSD	1/8/143D		RED	aug	DUP	DUR	Dog RPD
Analysis Yeżs	PREC	AREC	Linico	RED	HAT	Conc	Cong	RED	Mack
Batch number: 031818LA026	Sample	redmya e	(8): 40733	01-40733	302				
Acensphthana	107	93	48-132	14	30				
Fyrene	92	68	28-144	12	30				
1-Methylnaphthalene	75	67×	72-100	5	30				
Paphthalene	77	61	38-132	9	30				
Acenephthylane	108	91	46-128	18	30				
Fluorene	88	75	39-137	14	30				
Phonanthrene	88	74	29-143	13	30				
Anthracene	101	85	35-138	17	30				
Fluoranthens	67	72	19-148	11	30				
Benzo (a) anthracene	89	75	26-144	14	30				
Chrysens	101	90	23~150	9	30				
Senzo (b) fluoranthens	30	74	32-140	16	30				
Bonzo (k) fluorantheno	103	68	36-143	16	30				
Benzo(a) pyrone	90	72	23-154	13	30				
Indeno(1,2,3-cd)pyrane	92	78	13-155	15	30				
Dibens (a, h) anthracens	110	88	19-169	19	30				
Benzo(g,h,i)perylene	99	83	17-152	13	30				
2-Methylnaphthalene	39	19±	32-133	6	30				

^{*-} Outside of specification

- (1) The result for one or both determinations was less than five times the LOQ.
- (2) The background result was more than four times the spike added.





Page 2 of 2

Quality Control Summary

Client Name: Chevron Products Company

Group Number: 857532

Reported: 07/09/03 at 11:42 AM

Sample Matrix Quality Control

	MS	ASSED .	X8/1550		JUPO	WKG	DOP	DUD	Dup RPO
Bantygie Name	AREC	AREC	Linico	RPD	MAX	Conc	Cone	RIO	Max

Surrogate Quality Control

Analysis Name: PAHs in Soil by GC/MS Batch number: 031818LA026 Bitrobentene-d5

	erttobeuzeus-do	5-ArmoropibusuAt	TarbusuAr-ars
4073301	101	108	92
4073302	101	99	84
Blank	87	95	83
LCS	94	92	93
MS	105	107	98
msd	90	90	78
100			
Limits:	47-129	55-123	39-128
			•

* Outside of specification

⁽²⁾ The background result was more than four times the spike added.



⁽¹⁾ The result for one or both determinations was less than five times the LOQ.

Laboratory Report for Concentrations of Selected Polyaromatic Hydrocarbon Compounds in Petroleum Coke Sample Analyzed after Mammalian Toxicology Studies

Anglysis Report



ANALYTICAL RESULTS

Prepared for:

Chevron Products Company 940 Hensley St. Bldg. 210

> Richmond CA 94801 510-242-8191

> > Prepared by:

Lancaster Laboratories 2425 New Holland Pike Lancaster, PA 17605-2425

SAMPLE GROUP

The sample group for this submittal is 927702. Samples arrived at the laboratory on Tuesday, January 11, 2005. The PO# for this group is 0015000452 and the release number is RUSSELL WHITE.

Client Description Pet Cake Micronized Post Study Grab Solid Sample Lancaster Labs Number 4443909

1 COPY TO

Lancaster Laboratories

1 COPY TO

Chevron CRTC

Questions? Contact your Client Services Representative Andres Amaya at (717) 656-2300.

Respectfully Submitted,



VANDUVSIKE KE DIDINI



Page 1 of 1

Lancaster Laboratories Sample No. SW 4443909

Pet Cake Micronized Post Study Grab Solid Sample

Cost Center#

HPV Petroleum Cake Collected:11/08/2004

Submitted: 01/11/2005 09:00

Account Number: 10863

Chevron Products Company 940 Hensley St. Bldg. 210

Reported: 01/24/2005 at 14:00 Discard: 02/24/2005

Richmond CA 94801

PETCA

				As Received		
CAT			As Received	Method		Dilution
No.	Analysis Name	CAS Number	Result	Detection Limit	Units	Factor
07804	PAHs in Soil by GC/MS					
01191	Acenaphthene	83-32-9	690. J	200.	ug/kg	1
01195	Pyrene	129-00-0	7,400.	200.	ug/kg	1
02751	1-Methylnaphthalene	90-12-0	10,000.	200.	ug/kg	1
03761	Naphthalene	91-20-3	10,000.	200.	ug/kg	1
03765	Acenaphthylene	208-96-8	N.D.	200.	ug/kg	1
03768	Fluorene	86-73-7	1,300. J	200.	ug/kg	1
03775	Phenanthrene	85-01-8	7,000.	200.	ug/kg	1
03776	Anthracene	120-12-7	3,300.	200.	ug/kg	ı
03778	Fluoranthene	206-44-0	1,300. J	200.	ug/kg	1
03781	Benzo (a) anthracene	56-55-3	7,800.	200.	ug/kg	1
03782	Chrysene	218-01-9	7,900.	200.	ug/kg	1
03786	Benzo(b) fluoranthene	205-99-2	3,900.	200.	ug/kg	1
03787	Benzo(k) fluoranthene	207-08-9	1,600. J	200.	ug/kg	1
03788	Benzo(a)pyrene	50-32-8	13,000.	200.	ug/kg	1
03789	Indeno(1,2,3-cd)pyrene	193-39-5	3,600.	200.	ug/kg	1
03790	Dibenz (a, h) anthracene	53-70-3	4,700.	200.	ug/kg	1
03791	Benzo(g,h,i)perylene	191-24-2	14,000.	200.	ug/kg	1
04694	2-Methylnaphthalene	91-57-6	27,000.	1,000.	ug/kg	5
	Due to insufficient sample, th	e reporting lim	its for the GC/MS	5		

State of California Lab Certification No. 2116

semivolatile compounds were raised.

Laboratory Chronicle

CAT				Analysis		Dilution
No.	Analysis Nama	Method	Trial#	Date and Time	Analyst	Factor
07804	PAHs in Soil by GC/MS	SW-846 8270C	1	01/13/2005 03:29	Ryan P Byrne	1
07804	PAHs in Soil by GC/MS	SW-846 8270C	1	01/13/2005 06:00	Ryan P Byrne	5
07806	BNA Soil Extraction	SW-846 3550B	ı	01/12/2005 16:30	Ashley B Zook	1



Analysis Request/ Environmental Services Chain of Custody For Lancaster Laboratories use only Acct # 108103 Group# 927702 Sample # 4443909 COC# O) 1005 - 13 Please print. Instructions on reverse side correspond with circled numbers. Matrix (5) Anzivees Requested For Lab Use Only FSC: ___ SCR #: Project Namer#: HPU Patroleum Coke PWSID #: Project Manager: Type Here. PAHS Quote #: Sampler: Type Here..... Type Here..... Tyroe Here..... Туре Неге..... Type Here.... Name of state where samples were collected: Composite Type Here. Type Here. (2) Date Time Grab Othe 300 Collected Collected Sample Identification Remarks oke Micronized 11-8-04 242-2028 Turnaround Time Requested (TAT) (please circle): Normal Date Time Received by Date Inme (Rush TAT is subject to Lancaster Laboratories approval and surcharge.) 1 2150 PM -100 14051450 Date results are needed: Rollinguishadhu } Date Time Received by: Date Time Rush results requested by (please circle): Phone Fax E-mail 1000 Phone #: Fax #: Relinguished by: Date Time Received by: Date Time E-mail address: Oata Package Options (please circle if required) SDG Complete? QC Summary Type VI (Raw Data) Yes Relinquished by: Date Time Received by: Date lime Type I (Tier I) Site-specific QC required? Yes No Type II (Tier II) Other (ffyes, indicate QC sample and submit triplicate volume.) Relinguished by: Date Time Received by: Date Time Internal Chain of Custody required? Yes No Type III (NJ Red. Del.)

Lancaster Laboratories, Inc., 2425 New Holland Pike, PO Box 12425, Lancaster, PA 17605-2425 (717) 656-2300 Copies: White and yellow should accompany samples to Earcaster Laboratories. The pink copy should be retained by the client.

Type IV (CLP)

2102 Rey, 6/6/03

1051090A

03-4246

Page 835 Final Report

		T IIIai Teport
	Certificates of Analysis	Appendix Z
Feed Certificates	of Analysis	836
Water Certificates	of Analysis	846
Bedding Certificat	es of Analysis	856



Returnsto Certified Analysis Retrieval

Product Code:

5002M

Product Desc:

CERTIFIED RODENT DIET MEAL

Lab Number: Lot Code: L0413099-2 FEB 25 04 1B

Entered:

Trithion

3/9/2004

Assay		Analy	/sis Units	
PROTEIN		2	20.8 %	
FAT ACID (HYDRO.)		5.34 %		
FIBER (CRUDE)		4	1.93 %	
ARSENIC		LESS THAN	0.2 PPM	
CADMIUM		0.0	051 PPM	
CALCIUM		3.0	879 %	
LEAD		0.	172 PPM	
MERCURY		LESS THAN 0.0	025 PPM	
PHOSPHORUS		0.6	634 %	
SELENIUM		0.3	300 PPM	
ORGANOPHOSPHATES	РРМ	ORGANOPHOSPHATES	PPM	
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02	
Ethion	on LESS THAN 0.02		LESS THAN 0.02	
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02	
Thimet LESS THAN		Thiodan	LESS THAN	

PESTICIDES AND PCB	РРМ	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
	1		

LESS THAN

0.02

Mirex	LESS THAN 0.02	РСВ	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS T	HAN 5 PPB

No notes.

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
 2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation
 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.

The use of the term "Less Than" does not imply that traces of analyte were present.



Return to Certified Analysis Retrieval.

Product Code:

5002M

Product Desc:

CERTIFIED RODENT DIET MEAL L0413666-3 MAR 08 04 1B

Lab Number: Lot Code: Entered:

3/22/2004

Assay	Analysis	Units
PROTEIN	20.8	%
FAT ACID (HYDRO.)	5.42	%
FIBER (CRUDE)	4.37	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	LESS THAN 0.05	PPM
CALCIUM	0.926	%
LEAD	0.181	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.702	%
SELENIUM	0.440	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	ו אווז בו בוו אוו	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	iiParathion i	LESS THAN 0.02
Thimet	LESS THAN 0.02	I I niodan I	LESS THAN 0.02
Trithion	LESS:THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
	1		11

Mirex	LESS THAN 0.02	РСВ	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS T	HAN 5 PPB

No notes.

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
- 2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.

The use of the term "Less Than" does not imply that traces of analyte were present.



Return to Centified Analysis Retrieval

5002M

CERTIFIED RODENT DIET MEAL

Product Code:

Product Desc:

Lab Number: Lot Code:

L0416157-1 APR 21 04 3A

Entered:

5/4/2004

Assay	Analysis	Units
PROTEIN	21	%
FAT ACID (HYDRO.)	6.06	%
FIBER (CRUDE)	4.25	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.055	PPM
CALCIUM	0.831	%
LEAD	0.240	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.642	%
SELENIUM	0.239	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	III IIGI IITOTOD I	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	0.02
Methyl Parathion	LESS THAN 0.02	iiParatnion i	LESS THAN 0.02
Thimet	LESS THAN 0.02	II I DIAMAN I	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	РРМ
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
	1	7	1

000 ---

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS	THAN 5 PPB

No notes.

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
 2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation
 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.

The use of the term "Less Than" does not imply that traces of analyte were present.



Return to Certified Analysis Retrieval

Product Code:

Product Desc:

5002M CERTIFIED RODENT DIET MEAL L0416157-3

Lab Number: Lot Code:

APR 21 04 3C

Entered: 5/4/2004

Assay	Analysis	Units
PROTEIN	21.4	%
FAT ACID (HYDRO.)	5.82	%
FIBER (CRUDE)	4.4	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.058	PPM
CALCIUM	0.898	%
LEAD	0.233	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.651	%
SELENIUM	0.225	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	BI BELUTATAD I	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	0.03
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	РРМ	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
	1]

Mirex	LESS THAN 0.02	РСВ	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS 7	THAN 5 PPB

No notes.

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
 2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation
 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.

The use of the term "Less Than" does not imply that traces of analyte were present.



Return to Certified/Analysis:Retrieval

Product Code:

Product Desc:

5002M CERTIFIED RODENT DIET MEAL

Lab Number: Lot Code: Entered:

L0416691-2 APR 30 04 2B 5/18/2004

Assay	Analysis	Units
PROTEIN	20.9	%
FAT ACID (HYDRO.)	5.61	%
FIBER (CRUDE)	4.52	%
ARSENIC	0.393	PPM
CADMIUM	0.056	PPM
CALCIUM	0.869	%
LEAD	0.173	PPM
MERCURY	LESS THAN 0.025	РРМ
PHOSPHORUS	0.645	%
SELENIUM	0.257	PPM

ORGANOPHOSPHATES PPM		ORGANOPHOSPHATES PPM	
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	0.03
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	НСВ	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
		il — — — — — — — — — — — — — — — — — — —	

Mirex	LESS THAN 0.02	РСВ	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS	THAN 5 PPB

No notes.

- For additional information, please contact:

 1) Customer Service at (314) 982-1310 -- for assay methodology

 2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation

 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.

The use of the term "Less Than" does not imply that traces of analyte were present.

PHONE (610) 974-8100

•		FA	X (610) 974-8	3104				
SEND DATA TO: VAME:	Terry Kusznir	o :	, ,		INV#:	335841-3	35843	•
COMPANY: ADDRESS:	Huntingdon Life PO Box 2360, M East Millstone, I	lettlers Road	60		PAGE:	1 OF 6		
PHONE:	(732) 873-2550	v 2100			PO#:			
FAX:	(732) 873-3992		TEST REPORT		PWS ID#:			
PROJECT NAME: SAMPLED BY: LOCATION: DATE: FIME:	ANIMAL DRINK KINGA PALL SEE BELOW 07/13/04 SEE BELOW	ING WATER		GRAB SAMI COMPOSIT DATE RECE TIME RECE RECEIVED	E SAMPLES EIVED BY L IVED BY LA	AB: AB:	335841-3: NONE 07/14/04 0900 J. ALTEM	
SAMPLE:	SITE #1, V-2 R	OOM 908			TIME:	1503		
FEST	RESULT	UNITS	METHOD	INV#	START DATE	START TIME	END DATE	INIT.
COPPER	0.06	MG/L	SM#18 3111 B	335841	07/15/04	0730	07/19/04	GR
_EAD	<0.001	MG/L	EPA 200.9	335841	07/15/04	0730	07/15/04	KW
SAIVIPLE:	SITE #2, V-3 R0	OOM 956			TIME:	1512		
<u>rest</u>	RESULT	UNITS	METHOD	INV#	START DATE	START TIME	END DATE	INIT.
COPPER	0.03	MG/L	SM#18 3111 B	335842	07/15/04	0730	07/19/04	GR
_EAD	<0.001	MG/L	EPA 200.9	335842	07/15/04	0730	07/15/04	KW

SAMPLE:	SITE #3, V-1 R0	OOM 722			TIME:	1520		
					START	START	END	
<u>rest</u>	RESULT	UNITS	METHOD	INV#	DATE	TIME	DATE	INIT.
COPPER	<0.020	MG/L	SM#18 3111 B	335843	07/15/04	0730	07/19/04	GR
_EAD	<0.001	MG/L	EPA 200.9	335843	07/15/04	0730	07/15/04	KW

REMARKS:

THE ABOVE TEST RESULTS MEET	ALL	THE REQUIREMENTS OF NELAC.
-----------------------------	-----	----------------------------

MANAGER:	tiplane	Oleca	DATE: Qu	la 27 AM
. •	//	, , , , , , , , , , , , , , , , , , , ,		7

PHONE (610) 974-8100 FAX (610) 974-8104

SEND DATA TO:

NAME:

Terry Kusznir

COMPANY:

Huntingdon Life Sciences

ADDRESS:

PO Box 2360, Mettlers Road

East Millstone, NJ 08875-2360

PAGE: PO#:

INV#:

PHONE: FAX:

(732) 873-2550 x 2100

(732) 873-3992

TEST REPORT

PWS ID#:

TIME:

PROJECT NAME: SAMPLED BY:

LOCATION:

ANIMAL DRINKING WATER

KINGA PALL

SEE BELOW

07/13/04 SEE BELOW

GRAB SAMPLES:

COMPOSITE SAMPLES: DATE RECEIVED BY LAB:

TIME RECEIVED BY LAB:

RECEIVED FOR LAB BY:

335844-335846

NONE 07/14/04

335844-335846

2 OF 6

0900 J. ALTEMOSE

KW

SAMPLE:

COPPER

DATE:

TIME:

TEST

-EAD

TEST

.EAD

SITE #4, F WING ROOM 550

RESULT **UNITS METHOD** 0.04 MG/L SM#18 3111 B < 0.001 MG/L

EPA 200.9 ·

INV# 335844 335844

START START DATE TIME 07/15/04 0730 07/15/04 0730

1527

END DATE INIT. 07/19/04 GR 07/15/04

SAINPLE:

COPPER

SITE #5, L WING ROOM 455

RESULT UNITS **METHOD** 0.04 MG/L SM#18 3111 B < 0.001 MG/L EPA 200.9

INV# 335845 335845

TIME: **START** DATE 07/15/04 07/15/04 0730

TIME:

START

1534 START END TIME 0730

DATE INIT. 07/19/04 GR 07/15/04 KW

SAMPLE:

OPPER

EST

EAD

SITE #6, INHALATION ROOM 809 RESULT

UNITS METHOD < 0.020 MG/L SM#18 3111 B < 0.001 MG/L **EPA 200.9**

INV# 335846 335846

DATE TIME 07/15/04 0730 07/15/04 0730

1603

START

DATE INIT. 07/19/04 GR 07/15/04 KW

END

!EMARKS:

HL ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

PHONE (610) 974-8100 FAX (610) 974-8104

SEND DATA TO:

INV #:

335848-335849

VAME:

Terry Kusznir

335855-335856

COMPANY:

Huntingdon Life Sciences

335862-335863

\DDRESS:

PO Box 2360, Mettlers Road

PAGE:

3 OF 6

East Millstone, NJ 08875-2360

PO#:

PHONE: FAX:

(732) 873-2550 x2100

(732) 873-3992

TEST REPORT

PWS ID#:

PROJECT NAME:

ANIMAL DRINKING WATER

335848-335849

SAMPLED BY:

KINGA PALL

GRAB SAMPLES:

335855-335856

.OCATION:

SEE BELOW

COMPOSITE SAMPLES:

335862-335863

DATE:

07/13/04

NONE

ΓIME:

DATE RECEIVED BY LAB:

07/14/04

SEE BELOW

TIME RECEIVED BY LAB: RECEIVED FOR LAB BY:

0900

J. ALTEMOSE

SAMPLE:	$SII \succeq #1, V-2$	ROOM 908			TIME:	1503		
	ĺ				START	START	END	
EST	RESULT	UNITS	METHOD	INV#	DATE	TIME	DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	335848	07/14/04	1425	07/15/04	JLS
ST)ARD PLATE COUNT SPC. Afron	4	CFU/ML	SM#19 9215 B	335855	07/14/04	1220	07/16/04	JLS
FOTAL COLIFORM	0	PER 100 ML	EPA 600-R-00-013	335862	07/14/04	1300	07/15/04	KBF
= COLL	٥	PER 100 M	EDA 600 D 00 013	335963	07/14/04	1200	07/45/04	NDE.

SAMPLE:	SITE #2, V-3	ROOM 956			TIME:	1512		
					START	START	END	
rest	RESULT	UNITS	METHOD	INV#	DATE	TIME	DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	335849	07/14/04	1425	07/15/04	JLS
STANDARD PLATE COUNT	3	CFU/ML	SM#19 9215 B	335856	07/14/04	1220	07/16/04	JLS
FOTAL COLIFORM	0	PER 100 ML	EPA 600-R-00-013	335863	07/14/04	1300	07/15/04	KBF
E. COLI	0	PER 100 ML	EPA 600-R-00-013	335863	07/14/04	1300	07/15/04	KBF

REMARKS:

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

WANAGER:	Stephani	O luca	DATE:	Order 27, Jung
	/ //	 		

PHONE (610) 974-8100 FAX (610) 974-8104

SEND DATA TO:

NAME:

Terry Kusznir

KINGA PALL

SEE BELOW

SEE BELOW

RESULT

<1

2

0

RESULT

<1

2

07/13/04

Huntingdon Life Sciences

COMPANY: ADDRESS:

PHONE:

FAX:

PO Box 2360, Mettlers Road

East Millstone, NJ 08875-2360

ANIMAL DRINKING WATER

(732) 873-2550 x2100

PROJECT NAME:

SAMPLED BY:

LOCATION:

DATE:

TIME:

TEST

(732) 873-3992

TEST REPORT

PWS ID#:

INV #:

PAGE:

PO#:

GRAB SAMPLES:

335850-335851 335857-335858 335864-335865

335850-335851

335857-335858

335864-335865

4 OF 6

COMPOSITE SAMPLES: DATE RECEIVED BY LAB: NONE 07/14/04

TIME RECEIVED BY LAB: 0900 RECEIVED FOR LAB BY:

J. ALTEMOSE

SAMPLE:

SITE #3, V-1 ROOM 722

TIME: START 1520 START

END INV# DATE TIME DATE INIT. 335850 07/14/04 07/15/04 1425 JLS

1220

S DARD PLATE COUNT SPC A Amon

TOTAL COLIFORM E. COLI

PSEUDOMONAS

0 PER 100 ML

UNITS

PER 100 ML

CFU/ML

UNITS

PER 100 ML

CFU/ML

EPA 600-R-00-013 PER 100 ML EPA 600-R-00-013

METHOD

SM#19 9215 B

SM#19 9215 B

335864 07/14/04 335864 07/14/04

TIME:

START

DATE

335857 07/14/04

1300 1300

1527

07/15/04 KBF 07/15/04 KBF

07/16/04 JLS

SAMPLE:

PSEUDOMONAS

STANDARD PLATE

TEST

SITE #4, F-WING ROOM 550

SM#19 9215 B SM#19 9215 B

METHOD

335858 07/14/04

335851 07/14/04

INV#

1425 1220

START

TIME

07/16/04 JLS

END

DATE

07/15/04

INIT.

JLS

COUNT **TOTAL COLIFORM** E. COLI

0 PER 100 ML EPA 600-R-00-013 0 PER 100 ML EPA 600-R-00-013

335865 07/14/04 335865 07/14/04

1300 1300

07/15/04 KBF 07/15/04 KBF

REMARKS:

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

MANAGER:

REVIEWED

PHONE (610) 974-8100 FAX (610) 974-8104

SEND DATA TO:

335852-335853

NAME:

Terry Kusznir

335859-335860

COMPANY:

Huntingdon Life Sciences

335866-335867

ADDRESS:

PO Box 2360, Mettlers Road

5 OF 6

East Millstone, NJ 08875-2360

PAGE:

INV#:

PHONE:

(732) 873-2550 x2100

PO#:

FAX:

(732) 873-3992

TEST REPORT

PWS ID#:

PROJECT NAME:

ANIMAL DRINKING WATER

GRAB SAMPLES:

335852-335853

SAMPLED BY:

KINGA PALL

335859-335860

LOCATION:

SEE BELOW

COMPOSITE SAMPLES:

335866-335867

DATE:

07/13/04

NONE 07/14/04

TIME:

SEE BELOW

DATE RECEIVED BY LAB:

0900

TIME RECEIVED BY LAB:

RECEIVED FOR LAB BY:

J. ALTEMOSE

							0. 7 (III 1 II II II	
SAMPLE:	SITE #5, L-V	VING ROOM 45	55		TIME:	1534		
•	İ				START	START	END	
TEST	RESULT	UNITS	METHOD	INV#	DATE	TIME	DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	335852	07/14/04	1425	07/15/04	JLS
ST JARD PLATE COUNT SPC	>3,000	CFU/ML	SM#19 9215 B	335859	07/14/04	1220	07/16/04	JLS
TOTAL COLIFORM E. COLI	0 0	PER 100 ML PER 100 ML	EPA 600-R-00-013 EPA 600-R-00-013	335866 335866	07/14/04 07/14/04	1300 1300	07/15/04 07/15/04	KBF KBF

SAMPLE:	SITE #6, INH	IALATION ROC	OM 809		TIME:	1603		
					START	START	END	
ΓEST	RESULT	UNITS	METHOD	INV#	DATE	TIME	DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	335853	07/14/04	1425	07/15/04	JLS
STANDARD PLATE COUNT	<1	CFU/ML	SM#19 9215 B	335860	07/14/04	1220	07/16/04	JLS
FOTAL COLIFORM	0	PER 100 ML	EPA 600-R-00-013	335867	07/14/04	1300	07/15/04	KBF
E. COLI	0	PER 100 ML	EPA 600-R-00-013	335867	07/14/04	1300	07/15/04	KBF

REMARKS:

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

PHONE (610) 974-8100 FAX (610) 974-8104

SEND DATA TO:

INV#: 335854

VAME:

Terry Kusznir

335861

COMPANY:

Huntingdon Life Sciences

335868

ADDRESS:

PO Box 2360, Mettlers Road

PAGE:

6 OF 6

East Millstone, NJ 08875-2360

PO#:

PHONE:

FAX:

(732) 873-2550 x2100

TEST REPORT

PWS ID#:

PROJECT NAME:

ANIMAL DRINKING WATER

(732) 873-3992

335854

SAMPLED BY:

KINGA PALL

GRAB SAMPLES:

335861 335868

LOCATION:

SEE BELOW

COMPOSITE SAMPLES:

DATE:

07/13/04

NONE

TIME:

DATE RECEIVED BY LAB:

07/14/04 0900

SEE BELOW

TIME RECEIVED BY LAB: RECEIVED FOR LAB BY:

J. ALTEMOSE

SAMPLE:

TEST

E. COLI

SITE #7, PHARMACY

TIME: 1556

START START END DATE TIME DATE INIT.

1425

PSEUDOMONAS <1 PER 100 ML SM#19 9215 B)ARD PLATE . 16 CFU/ML SM#19 9215 B COUNT SPC MANON

0

0

RESULT

335861 07/14/04

335854 07/14/04

INV#

1220 07/16/04 JLS

07/15/04 JLS

TOTAL COLIFORM

PER 100 ML PER 100 ML

UNITS

EPA 600-R-00-013 EPA 600-R-00-013

METHOD

335868 07/14/04 335868 07/14/04 1300 1300

07/15/04 KBF 07/15/04 KBF

REMARKS:

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

PHONE (610) 974-8100 FAX (610) 974-8104

S	FI	N	n	D	Δ٦	ГΔ	T	Λ.	

NAME:

Terry Kusznir

COMPANY:

Huntingdon Life Sciences

ADDRESS:

PO Box 2360, Mettlers Road

East Millstone, NJ 08875-2360

PAGE: PO#:

INV #:

340365

1 OF 1

PHONE: FAX:

(732) 873-2550 x2100

(732) 873-3992

TEST REPORT

PWS-ID#:

PROJECT NAME:

SAMPLED BY:

ANIMAL DRINKING WATER

LOCATION:

KINGA PALL

SEE BELOW

08/16/04

1533

GRAB SAMPLES:

COMPOSITE SAMPLES:

DATE RECEIVED BY LAB: TIME RECEIVED BY LAB:

NONE 08/17/04 0845

340365

RECEIVED FOR LAB BY:

K. BROWN

SAMPLE:

DATE:

TIME:

SITE #1, L-WING ROOM 455

START START **END TEST** RESULT **UNITS METHOD** INV# DATE TIME DATE INIT. STANDARD PLATE COUNT SM#19 9215 B CFU/ML 340365 08/17/04 1052 08/19/04 KBF

REMARKS:

HE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

Suphanie

DATE: <u>Leigos, mi</u>

Elizabethtown Water Company Physical & Chemical Analyses

Page 853

Date May 6, 2004 Raritan-Millstone Plant **General Source** Plant Delivered Water - 6:30 a.m. .5-6-04, MT Sample No. 1 Sample No. 2 Sample No. 3 Sample No. 4 Sample No. 5 Sample No. 6 Sample No. 7 Sample No. 8 Parameter MCL (mg/l) 4.0 5.0 6.0 7.0 8.0 Temperature ° F 60 0.10 Turbidity (NTU) 0.3 NTU 10 * 1 Color Threshold Odor 40 ° C 3 TON * 3/2cc 3 3 TTN * Threshold Taste 333 Conductivity (micromhos / cm) Hardness, Total (as mg / I CaCO3) 96 250 mg / 1* Alkalinity 44 pН 6.5-8.5 * 7.1 Chlorine, Free / Total (mg / I Cl) <0.05/0.94 74 Calcium (as mg / I CaCO3) Magnesium (as mg / I CaCO3) 22 0.3 mg/ l* < 0.05 iron, Total (mg / I Fe) Sulfates (mg / I SO4) 250 mg/ l * 42.5 250 mg/ i * 44.2 Chlorides (mg / i Cl) 0.10 Fluoride (mg / I F) 2 mg/l* 500 mg / 1* 146 Total Dissolved Solids (mg / 1) < 0.10 Total Suspended Solids (mg / I) <0.05 Ammonia Nitrogen (mg / I N) 1.05 Nitrate Nitrogen (mg / I N) 10 mg/l 10.1 Dissolved Oxygen (mg / I O2) BOD 5 (mg / 1 O2) -1.41 Langelier Index +/- 1.0 Surfactants (mg / I LAS) 0.5 mg / 1* 0 Hydrogen Sulfide (mg / I H2S as S) Nitrite Nitrogen (mg / I N) <.01 1 mg / 1 0.09 Phosphate (mg / 1 PO3) Manganese (mg / I MN) < 0.05 0.05 mg / l* Zinc 0.05 5 mg/l * T.O.C. (mg / I) 5 mg/l * 1.6 Laboratory Analyst: JP

REVIEWED

^{*} Secondary or Recommended MCL

Elizabethtown Water Company Physical & Chemical Analyses

Date June 2, 2004

General Source	Raritan-Millsto	ne Plant	•							
Sample No. 1 Sample No. 2	Plant Delivered	Water - 7:30 a.	m. 6-2-04, ken							
Sample No. 3										
Sample No. 4										
Sample No. 5										
Sample No. 6			•							
Sample No. 7										
Sample No. 8										
Faran	neter	MCL (mg/l)	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0
Temperature * F		-	68							
Turbidity (NTU)		0.3 NTU	80,0							
Color		10 *	1						• •	
Threshold Odor 40 'C		3 TON *	3,2/2cc							
Threshold Taste	ט	3 TTN *	3.1							
Conductivity (micromh	nos / cm)	-	367							
Hardness, Total (as mo	g / I CaCO3)	250 mg / i *	102							
Alkalinity		•	45							
рH		6.5-8.5 *	7.0							
Chlorine, Free / Total (mg / I Cl}	-	<0.05/1.10							
Calcium (as mg / I CaC	:03)	-	74							
Magnesium (as mg / I	CaCO3)	-	28							
Iron, Total (mg / I Fe)		0.3 mg/l*	<0.05		•					
Sulfates (mg / I SO4)		250 mg/ l *	49.7							
Chlorides (mg / I Cl)		250 mg/1*	44.3							
Fluoride (mg / I F)		2 mg/l*	<0.1							
Total Dissolved Solids	(mg / I)	500 mg / l *	174							
Total Suspended Solid	is (mg / i)	•	<0.10							
Ammonia Nitrogen (m	g/1N)	-	0.1							
Nitrate Nitrogen (mg/	IN)	10 mg / I	1.15							
Dissolved Oxygen (mg	g / I O2)	•	9.8							
BOD 5 (mg / I O2)		-								
Langelier Index		+/- 1.0	-1.40							
Surfactants (mg / I LAS	5)	0.5 mg / *	-			•				
Hydrogen Sulfide (mg	/ I H2S as S)	•								
Nitrite Nitrogen (mg / I		1 mg/i	<.01							
Phosphate (mg / I PO3	3)	-	0.2							
Manganese (mg / i MN	1)	0.05 mg /1*	<0.05							
Zinc		5 mg/l *	0.46					-		
T.O.C. (mg / I)		: 5 mg/l *	1.3							

Laboratory Analyst: MT/JP

* Secondary or Recommended MCL

Any questions please call Water Quality Specialist- (908) 301-3163

1) Taste and olar hast regulated by Elizabetholm

REVIEWED m 21 Tueon

Elizabethtown Water Company Physical & Chemical Analyses

Page 855 July 7, 2004 Date

Seneral Source Raritan-Millstone	Plant								
iample No. 1 Plant Delivered	Water - 7:30 a.m.	7-7-04, Ken							
ample No. 2									
lample No. 3 lample No. 4	• • • • • • • • • • • • • • • • • • • •							•	
iample No. 5									
lample No. 6									
ample No. 7		•		•				•	
iample No. 8	1	1							
'arameter - ··	MCL (mg/l)	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0
emperature ° F	-	78.0							
urbidity (NTU)	0.3 NTU	0.1							
Polor	. 10 *	1.0		•					
hreshold Odor 40 ° C	3 TON *	2.9/2cc							
hreshold Taste	3 TTN *	2.9							
Conductivity (micromhos / cm)	-	379.0						•	
lardness, Total (as mg / I CaCO3)	250 mg / l *	110.0							
\lkalinity	-	49.0							
ı H	6.5-8.5 *	7.0							
Chlorine, Free / Total (mg / I Cl)	-	<0.05/0.90							
Calcium (as mg / I CaCO3)	-	74.0							
/lagnesium (as mg / I CaCO3)	-	36.0							
ron, Total (mg / I Fe)	0.3 mg/1*	<0.05			•				
Sulfates (mg / I SO4)	250 mg/ (*	50.5							
Chlorides (mg / i Cl)	250 mg/ l *	40.1							
fluoride (mg / I F)	2 mg/1*	<0.1							
otal Dissolved Solids (mg / I)	500 mg / 1 *	194.0							
otal Suspended Solids (mg / 1)	-	<0.10							
\mmonia Nitrogen (mg / I N)	-	<0.05							
litrate Nitrogen (mg / I N)	10 mg / l	0.7							
Dissolved Oxygen (mg / I O2)	-	8.0		٠			•		
3OD 5 (mg / 1 O2)	-								
_angelier Index	+/- 1.0	-1.2							
Surfactants (mg / I LAS)	0.5 mg / 1*	-						:	
lydrogen Sulfide (mg / I H2S as S)	-	0.0			÷				
√itrite Nitrogen (mg / I N)	1 mg / l	<.01			in the second				
Phosphate (mg / I PO3)	-	<0.05			<i>:</i> .				
vlanganese (mg / I MN)	0.05 mg / 1*	<0.05							
Zinc	5 mg/l *	0.6							
F.O.C. (mg / i)	5 mg/i *	1.7						:	
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'Secondary or Recommended MCL							···· • • • • • • • • • • • • • • • • •	· · . 	\cap
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Any questions please call Water Quality Specialist- (908) 301-3163

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Corp. Hidgits: 2261 Trany Road, Northwood, OH 43619-1397 / 419.666.9455 / Fex 419.666.2954 3400 Cobb International Blvd., Kennesaw, GA 30152-7601 / 770.427.3101 / Fex 770.426.5692 Page 856 9 Morgan, Ivrino, CA 92618-2078 / 949.951.3110 / Fox 949.951.3280

9 Morgan, Irvino, CA 92618-2078 / 949.951.3110 / Fox 949.951.3260 Affiliates: France • Germany • Israel • Taiwen • United Kingdom

Ensuring Medical Device Safety and Compliance

Confidential MS005_00P

Ted Weaver
The Andersons
P.O. Box 119
Maurace, OH 43537

Lab No.

04T_38507_0

P.O. No. Test Facility: TED WEAVER NAMSA

6750 Wales Road

Northwood, OH 43619

STERILITY TEST

Test Article:

"425URB" - Bed O' Cobs Lot #DD084

ID No.

Lot DD084

Procedure/Test Method:

S-20431-01-00/Immersion

Test Article Received:

June 8, 2004

Test Start Date:

June 8, 2004

Test Termination Date:

June 22, 2004

Number of Products Tested:

1

STERILITY TEST RESULTS

Test Article Identity Maintained as Submitted by Client

Articles Tested	Number of Articles Tested	Type of Media	Incubation Temperature (Degrees C)	Number of Days Incubated	Number of Positive Articles
Product Section	1	SCDB-400 ml	20-25	14	0
Product Section	1	FTM-400 ml	30-35	14	0

SCDB = Soybean Casein Digest Broth

FTM = Fluid Thioglycollate Medium

Results and conclusions apply only to the test article tested. No further evaluation of these results is made by NAMSA. Any extrapolation of these data to other samples is the responsibility of the sponsor. All procedures were conducted in conformance with good laboratory practice and ISO 17025.

Record Storage: All raw data pertaining to this study and a copy of the final report are to be retained in designated NAMSA archive files for a period of 5 years.

A-12-03-4246

cal Date Completed

Approved B

Michelle R. Pierce

Manager, Microbiology

Certificate of Processing

Facility:

Westerville

Cell: Production A

Customer Name: Customer PO #:

04/23/04

The Anderson Inc.

Run Date: Run Number:

AND01 AND 6040009

Date Format: MM/DD/YY Customer Ref:

Total Pallets:

MATERIALS PROCESSED:

Qty	Product	Description	Lot Number	LOT #
1,713	BED'O COB 1/4" BAG	10/TOTE 23.75 X 11.75 X 8"	DD084	425RB
1	SAMPLE-506	11./5 A 6	DD084	425RB

1,714 Bags

Total

Minimum Dose:

28.9 kGy

Maximum Dose:

53.9 kGy

Sterigenics certifies that the materials listed above (as described by its Manufacturer) received the indicated doses within the precision and accuracy of the dosimetry system employed:

Certified By

Date: 04/26/04

ISO 9001:2000 REGISTERED

Page 1 of 1

Original

PROTOCOL

PETROLEUM COKE

REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING STUDY IN RATS VIA NOSE-ONLY INHALATION EXPOSURES

CONFIDENTIAL

HLS Study No.:

Protocol No.:

Date:

03-4246

Final

4 May 2004

PROTOCOL PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title:

Petroleum Coke: Reproduction/Developmental Toxicity

Screening Study in Rats via Nose-Only Inhalation Exposures

HLS Study No.:

03-4246

This is the Final Protocol. It has been reviewed and approved by:

Huntingdon Life Sciences (HLS) Address: 100 Mettlers Road

East Millstone, NJ 08875-2360

Phone No.: 732-873-2550 x2920

Fax No.: 732-873-3992

11 May 2009
Date

American Petroleum Institute (API)

Address:

1220 L Street, Northwest

Washington, D.C. 20005-4070

Phone No.:

202-682-8480

Fax No.:

202-682-8270

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1. INTRODUCTION

HLS Study No.

03-4246

Title

Petroleum Coke:

Reproduction/Developmental Toxicity Screening Study in Rats via Nose-Only

Inhalation Exposures

Testing Facility

Huntingdon Life Sciences

100 Mettlers Road

East Millstone, NJ 08875-2360

Purpose

This study is designed to assess possible effects on reproductive performance, in male and female rats when the test substance is administered by nose-only inhalation exposure. The study should permit detection of effects on gonadal function, mating behavior, conception, development of the conceptus, parturition and pup survival to postnatal day 4. However, it will not provide complete information on all aspects of reproduction and development and will not allow for definite claims of no reproductive/developmental effects.

2. STUDY PERSONNEL

Study Director

Alternate Contact



Additional personnel will be documented in the project file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation Date

Date Study Director Signs Protocol

Receipt of Test Animals

11 May 2004 (Experimental Start)*

Initiation of Exposures

25 May 2004 (Experimental Start)**

Initiation of Mating

8 June 2004

Termination of Mating

22 June 2004

Termination of Exposures

Male Rats:

21 June 2004

Female Rats: 10 July 2004

Necropsy:

Male Rats:

25 June 2004

Female Rats: 3-17 July 2004

Submission of Draft Final Report:

18 October 2004

Experimental Termination:

Date of last data collection

Study Completion Date:

Date final report is signed

by Study Director

^{*}as per OECD GLPs; ** as per EPA GLPs

4. EXPERIMENTAL DESIGN

			Treatment Schedule Pre-mating Period		Number of Animals		
Group	Group	Exposure Levels	Male	Female	Male	Female	
}	Designation	(mg/m ³)	Rats ^b	Rats ^c	Rats	Rats	
1	Air Control ^a	0	2 weeks	2 weeks	12	12	
2	Low	25	2 weeks	2 weeks	12	12	
3	Mid	75	2 weeks	2 weeks	12	12	
4	High	200	2 weeks	2 weeks	12	12	

^a Control animals will be exposed to air only with the same treatment regimen as the test substance exposed groups.

The first day of exposures will be defined as Day 0 of the study. The day of detection of mating will be designated GD 0. The day of birth of the litter will be designated LD 0 = PND 0.

4.1. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures are as recommended in the referenced guidelines. Daily exposure for 6 hours per day provides an adequate model for potential human exposure during a typical work-day, while continuous (7 days per week) exposure is necessary to maximize the likelihood of detecting effects within a relatively short exposure period and is essential for proper evaluation of effects on the process of development. The combination of a pre-mating exposure period of 2 weeks with an overall exposure period of at least 4

b Male rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 2 weeks prior to mating initiation. Exposure of male rats will continue during the mating and post-mating periods until euthanized on the day after a minimum exposure of 28 days.

Female rats (12/group) will be exposed once daily (6 hours/day), seven days/week for at least two weeks prior to mating initiation. Female rats will continue to be treated once daily (6 hours/day) during the mating period, but will be separated from their male partners during exposure. Once mated, female rats will be treated once daily (6 hours/day) during gestation (Days 0-19). Sacrifice will be on lactation day 4 = postnatal day 4. Female rats without evidence of mating will continue to be treated for up to 19 days (6 hours/day) following completion of the mating period and then held for up to an additional 7 days prior to sacrifice. In the event that female rats without evidence of mating appear pregnant (based on observations and body weights), exposure will be terminated on the estimated Gestation Day 19 with sacrifice 7 days later.

weeks, with mating/fertility assessments in both sexes and detailed histopathology of the male gonads, is considered sufficient for detection of most effects on fertility and gametogenesis. The 2-week pre-mating exposure period, continuing for females through gestation, also allows for evaluation of possible effects on the estrous cycle, implantation and development of the conceptus, on subsequent parturition and early offspring viability and growth.

4.2. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model acceptable under OECD and EPA testing guidelines for reproductive toxicity studies. In addition, an historical database for this strain of rat is available in the Testing Facility for comparative evaluation.

4.3. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in this study is considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD and EPA guidelines. Eight-10 pregnancies per group is considered an adequate number for screening for reproductive and developmental toxicities. The group size of 12 males and 12 females used in this study, retaining a one male to one female pairing ratio, with expected pregnancy rates of 80-90%, is anticipated to provide at least 8-10 pregnancies per group for evaluation.

4.4. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels are based on results of a 2-week range-finding study 03-6147 which showed slight to moderate pulmonary toxicity (but not systemic toxicity) at exposure levels of 25, 75 and 200 mg/m³. Therefore, the same exposure levels were accepted as appropriate for this study.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE:

Petroleum Coke

The test substance is labeled as "3.3 Micron Mean Petroleum Coke" based on preparation by AVEKA, 2045 Wooddale Drive, Woodbury, MN 55125 and their particle size evaluation using the Horiba LA-910 with the test substance suspended in water.

TEST SUBSTANCE CATEGORY:

Residual product from petroleum refining

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability, and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Sponsor. This documentation will be maintained by the Sponsor. The test substance will be stored (ambient conditions) in the inhalation laboratory and handled routinely while wearing gloves, dust-mask and labcoat.

At the end of the study, a 200 gram sample of the test substance will be shipped for analysis to ChevronTexaco Energy Research and Technology Corp., 100 Chevron Way, Richmond, CA 94802, 510-242-7037, attn: Patrick Beatty.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and shipped to the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA, 703-435-8780 ext 201, attn: Sam Busey). Since multiple studies are conducted with the same test substance, a common archival sample will be taken and appropriately labeled.

5.4. UNUSED TEST SUBSTANCE

The unused portion of test substance as well as any empty test substance containers will be returned to the Archives of the Sponsor (see Section 5.3 above) following completion of the study.

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus® Sprague-Dawley - derived (CD®) Crl: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories Kingston, New York

Note: males and females will be supplied from separate colony rooms to ensure that there is no mating of male-female siblings.

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. Number

Male RatsFemaleRatsTotal484896

6.3.2. Age and Weight

Animals will be ordered with body weight stipulations to allow all rats of the same sex to be within \pm 20% of the mean weight at the time of randomization. Male rats will be approximately 6 weeks at receipt and approximately 8 weeks (200-300 grams) at initiation of treatment. Female rats will be approximately 6 weeks at receipt and approximately 8 weeks (150-250 grams) at initiation of treatment. Female rats will be nulliparous and non-pregnant. Animals outside this weight range will be used at the discretion of the Study Director.

6.4. ANIMAL HUSBANDRY

6.4.1. Facilities Management/Animal Husbandry

Currently acceptable practices of good animal husbandry will be followed, e.g., Guide for the Care and Use of Laboratory Animals; National Academy Press 1996. Huntingdon Life Sciences is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.4.2. Veterinary Care

Animals are monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.4.3. Housing

All animals will be housed individually in stainless steel suspended cages with wire mesh floors and fronts except for the mating period when one male and one female rat will be housed together. Cages will be arranged in such a way that possible effects due to placement are minimized. During cohabitation (when female rats will be brought to the male rats' cages), male and female rats will then be housed in stainless steel cages of appropriate size for group housing animals. Each cage will be fitted to secure a glass feeder jar with a stainless steel lid. Clean feeder jars and fresh feed will be provided at least weekly. From Day 18 of gestation and during

lactation, the dam will be housed with her litter in plastic "shoebox" cages with bedding. Clean feed jars and fresh feed will be provided at least weekly for periods when feed consumption is not being recorded and at each interval when feed consumption will be recorded.

6.4.4. Feed and Feed Analysis

Certified Rodent Diet, No. 5002; (Meal) supplied by PMI Nutrition International (St. Louis, MO) and provided *ad libitum*.

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.4.5. Water and Water Analysis

Facility water is supplied by Elizabethtown Water Company (Westfield, NJ) and will be provided *ad libitum* to individual animal cages via an automated watering system.

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file at the Testing Facility. There are no known contaminants which are expected to interfere with the objectives of this study.

6.4.6. Bedding Article

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) will be provided for each mated female rat on Gestation Day 18. Fresh bedding will be provided weekly or as needed throughout lactation. There are no known contaminants in the bedding which are expected to interfere with the results of this study.

6.4.7. Environmental Conditions

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain their suitability.

6.6. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Disposition of all animals not utilized in the study will be maintained in the study file.

6.7. ANIMAL IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be tail-tattooed with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study number and animal number.

6.8. MATING PROCEDURE

Within each treatment group, the male and female rats will be co-housed (1:1 in the male's cage) until evidence of mating is seen or for 14 consecutive days. Female rats will be observed at approximately the same time each morning for the presence of a vaginal plug or sperm in the vaginal smear. If not mated, the stage of the estrous cycle will instead be recorded. The day on which evidence of mating is observed will be defined as day 0 of gestation. Once mated, the female rat will be removed from the mating cage and housed individually for the remainder of the

study. After the mating period is over, female rats without evidence of copulation will be removed from the mating cage and housed individually for the remainder of the study (up to 26 days) and monitored for visible signs of pregnancy with corresponding body weight gain.

6.9. ANIMAL HUSBANDRY DURING EXPOSURE

Housing - individually in tubes Feed - none Water - none

7. TEST SUBSTANCE ADMINISTRATION

7.1. ROUTE OF ADMINISTRATION

Inhalation via nose-only exposure.

7.2. DURATION AND FREQUENCY OF ADMINISTRATION

Male rats will be exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of male rats will continue during the mating and post-mating periods until euthanized on the day after a minimum exposure of 28 days. Female rats (12/group) will be exposed once daily, seven days/week for at least two weeks prior to mating initiation. Female rats will continue to be treated once daily during the mating period, but will be separated from the males during actual exposure. Once mated, female rats will be treated once daily during gestation (days 0-19). Female rats without evidence of mating will continue to be treated for up to 19 days (6 hours/day) following completion of the mating period and then held for up to an additional 7 days. In the event that female rats without evidence of mating appear pregnant (based on observations and body weights), exposure will be terminated on the estimated Gestation Day 19.

7.3. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered as a **dust** in the breathing air of the animals by nose-only inhalation exposure. The test atmosphere will be generated by an appropriate procedure (Wright Dust Feeder with or without cyclone pre-collectors) determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to select the optimal set of conditions to generate a stable and uniform atmosphere at the target exposure levels with a mass median aerodynamic diameter of 1.0 - 3.0 microns. The method will be described in the raw data of the study and in the report.

The nose-only exposure chambers will each have a volume of approximately 40 liters. Each chamber will be operated at a minimum flow rate of 8 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time of at most 23 minutes. This chamber size and air-flow rate is considered adequate to maintain the oxygen level at least 19%. At the end of the exposure, all animals will remain in the chamber for a minimum of the T_{99} equilibrium time. During this time the chamber will be operated at approximately the same flow rate using clean air only.

7.4. EXPOSURE CONCENTRATION ADMINISTRATION

A nominal exposure concentration will be calculated daily. The flow of air through the chambers will be monitored using appropriate calibrated equipment. The test substance consumed during the exposure will be divided by the total volume of air having passed through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.

During each exposure, measurements of airborne concentrations of test substance will be performed at least 4 times using an appropriate sampling procedure (drawing from the exposure chamber a measured volume of air through a pre-weighed glass fiber filter) and gravimetric analytical procedure (post-weighing the glass fiber filter and dividing the weight gain by the measured volume of sampled air). If more than the normal amount of trials is required because of test substance generation or monitoring problems (50 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

7.5. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each week of exposure, particle size determinations will be performed using a TSI APS (for Group 1) and a cascade impactor (for Groups 2-4) to characterize the aerodynamic particle size distribution of the aerosolized test substance.

7.6. CHAMBER ENVIRONMENT

Temperature, humidity and airflow rate will be recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the extent possible, at 20 to 24°C and 40 to 60%, respectively.

7.7. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/Chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/week
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate	13X/day
Nominal Test Substance Concentration (excluding the air control chamber)	1X/day
Rotation Pattern of Exposure Tubes	1X/day
Loading/Unloading Verification	1X/day

8. EXPERIMENTAL EVALUATION

8.1. OBSERVATIONS

8.1.1. Viability Checks (Cageside)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

8.1.2. Detailed Physical Observations

All animals will be observed as a group at least once during each exposure. This will routinely be performed near the middle of each exposure and may be performed more frequently if signs of toxicity are noted.

Each animal will be removed from its cage and a detailed physical observation performed prior to randomization. Male rats will have a detailed physical observation performed once weekly beginning during the premating period and continuing through euthanasia. Female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 21 and Lactation Days 0, 1 and 4. Female rats without evidence of mating will continue to be observed weekly during the mating and post-mating period until euthanized.

Examinations during non-exposure periods will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of

clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded. Pertinent behavioral changes, signs of difficult or prolonged parturition and all signs of toxicity, including mortality, will be recorded. These records will include, as appropriate, time of onset, degree and duration.

8.2. BODY WEIGHTS

Body weights of the male rats and the female rats will be recorded at the time of randomization into test groups, on the day treatment is initiated and at least weekly thereafter throughout the study until euthanized. Mated female rats will be weighed on Gestation Days 0, 7, 14 and 20 and female rats that deliver litters will be weighed on Lactation Days 1 and 4. Female rats without evidence of mating will continue to be weighed weekly during the mating and post-mating period until euthanized. A terminal body weight will also be recorded for each animal.

8.3. FEED CONSUMPTION

Feed consumption for the male rats and the female rats will be measured pretest and weekly during the pre-mating treatment period. Feed consumption will not be measured during the mating period when male rats are being co-housed with female rats. Feed consumption for the male rats will be measured weekly, and if not mated, for the female rats, during the post-mating period. For pregnant or confirmed mated female rats, feed consumption will be measured on Gestation Days 0-7, 7-14 and 14-20 and on Lactation Days 1-4.

8.4. PARTURITION AND LACTATION

On Gestation Day 18, several days prior to expected parturition, female rats will be transferred to solid, plastic cages with bedding article provided. Thereafter, examination for signs of parturition will be made twice daily (morning and afternoon). The duration of gestation will be calculated. Evidence of difficult or prolonged parturition will be recorded. The day on which parturition initiates will be defined as Lactation Day 0. Litters will be observed as soon as possible after parturition completion for the number of live and dead pups, runts and pup abnormalities. Each pup will be sexed. Thereafter, litters will be observed twice daily (morning and afternoon). All pups in the litter will be uniquely identified by toe tattoo after parturition completion. The presence of dead pups will be recorded, and these will be removed from the litter as found and necropsied. Unusual observations and the absence of milk in the stomach will be noted. Any abnormalities observed in maternal behaviour (particularly relating to maternal care of the litter) will be recorded.

8.5. F_1 PUP EVALUATIONS

8.5.1. Pup Physical Examinations

Each pup will be given a gross physical examination on Lactation Days 0 and 4. Pups will also be observed for any abnormal behavior.

8.5.2. Body Weights and Sexing Data

Individual pup body weights data will be recorded on Lactation Days 1 and 4. Pups will be sexed on Lactation Day 0 and sex verified on Lactation Day 4.

9. POSTMORTEM

9.1. METHOD OF EUTHANASIA

All animals (except Lactation Day 4 pups) will be euthanized by exsanguination following an overexposure of inhaled carbon dioxide. Lactation Day 4 pups will be euthanized using an intraperitoneal injection of sodium pentobarbital.

9.2. POSTMORTEM EXAMINATION – ADULT ANIMALS DYING DURING THE STUDY

Animals that die during the study will be given a macroscopic postmortem examination and gross lesions will be saved and preserved in 10% neutral buffered formalin. Reproductive tissues as indicated below will also be saved but no organ weights will be recorded. Female rats dying during the study will have the number of any implantation sites and corpora lutea recorded.

9.3. EUTHANASIA SCHEDULE

9.3.1. Adult Male Rats

Male rats will be euthanized after at least 28 days of exposure. Necropsy schedules will be established in order to assure that approximately equal numbers from each group will be examined at similar times of each day of necropsy.

9.3.2. Adult Female Rats

Mated female rats will be euthanized on Lactation Day 4. Female rats in which evidence of mating was detected but failed to deliver will be sacrificed 26 days after evidence of mating.

Female rats where no evidence of mating was detected and who failed to deliver a litter will be euthanized 26 days after the completion of the mating period. Female rats with total litter loss (all pups found dead prior to scheduled sacrifice) will be euthanized on Lactation Day 4.

9.4. MACROSCOPIC EXAMINATION – ADULT MALE RATS

Macroscopic postmortem examinations will be performed on all male rats, including those dying spontaneously or euthanized in a moribund condition. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. Special attention will be paid to the organs of the reproductive system. Gross lesions will be preserved in 10% neutral buffered formalin with the exception of testes and epididymides which will be preserved in a modified Davidson's fixative for at least 24 hours and then stored in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.5. MACROSCOPIC EXAMINATIONS – ADULT FEMALE RATS

Macroscopic postmortem examinations will be performed on all female rats, including those dying spontaneously or euthanized in a moribund condition. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. Special attention will be paid to the organs of the reproductive system. The number of implantation sites and corpora lutea will be recorded for each female rat. Gross lesions will be preserved in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.6. ORGAN WEIGHTS - ADULT RATS

Organs indicated below will be collected at the scheduled necropsy, weighed wet, recorded and organ/body weight ratios and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition and for those female rats not delivering pups. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissue in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired reproductive organs will be weighed separately.

Male Rats	Female Rats	<u>All Rats</u>
Epididymides	Ovaries with Oviducts	Adrenal Glands
Prostate	Uterus with Vagina	Brain
Seminal Vesicles with		Lungs
Coagulating Gland		Pituitary
Testes		Thymus

9.7. TISSUES PRESERVED - ADULT RATS

Tissues listed in Appendix A will be obtained at necropsy for all male and all female rats from each exposure group and preserved in 10% neutral buffered formalin with the exception of testes and epididymides which will be preserved in a modified Davidson's fixative for at least 24 hours and then stored in 10% neutral buffered formalin. Lungs (gravity method) will be infused with 10% neutral buffered formalin for optimal preservation.

9.8. MICROSCOPIC PATHOLOGY EVALUATIONS - ADULT RATS

Microscopic examinations for control and high exposure group male and female animals will be performed on tissues and organs as designated in Appendix A. During the microscopic examination of the testes, special emphasis will be placed on the stages of spermatogenesis and the interstitial testicular cell structure. Histopathological examination of the ovary will detect qualitative depletion of the primordial follicle population. Any abnormalities not noted during macroscopic postmortem examinations that are seen during histological processing will be recorded. If treatment-related changes are observed in the high exposure group, microscopic examinations will be performed on the low and mid exposure groups upon approval of the Sponsor (additional cost).

Stains: Standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

9.9. MACROSCOPIC POSTMORTEM EXAMINATION - F₁ PUPS

Macroscopic postmortem examinations (internal and external) will be performed on all F_1 pups found dead during lactation. Unusual observations, including gross abnormalities and the absence of milk in the stomach, will be noted and then the carcasses will be discarded. F_1 pups found dead at birth will be identified (lung floatation test) as stillborn or alive but found dead. Macroscopic postmortem examinations (external only) will be performed on all F_1 pups on Lactation Day 4 for pups surviving

to that interval. Unusual observations, including gross abnormalities, will be noted and then the carcasses will be discarded.

10. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond 1 year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

11. STATISTICAL EVALUATIONS

11.1. CONTINUOUS DATA - to include but not be limited to:

- Body weights
- Body weight changes
- Feed consumption values
- Gestation length
- Number of implantation sites and corpora lutea
- Pre- and post-implantation loss
- F₁ pup weights (each weighing interval during lactation)
- Number of pups per litter
- Number of male and female pups
- Pup weight distinguished by sex and as a composite for both sexes (litter as experimental unit)
- Absolute organ weights, organ weight to body weight ratios and organ weight to brain weight ratios

Evaluation of equality of group means will be made by the appropriate statistical method. For all parameters except for organ weights, the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance will be used (Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional testing will be performed using Dunnet's t-test to determine which means are significantly different from the control (Dunlap et al., 1981). Organ weight data will be analyzed only by parametric methods. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995; Snedecor and Cochran, 1967) will be performed to determine if groups have equal variances. The standard

one-way analysis of variance (ANOVA) using the F ratio to assess significance will be used (Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's t-test (Dunlap et al., 1981; Dunnett, 1955, 1964) for homogeneous data, or Cochran and Cox's modified t-test (Cochran and Cox, 1959) for non-homogeneous data. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Snedecor, G.W. and Cochran, W.G. 1967. Statistical Methods. 6th edition. Ames: Iowa State University Press; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.

11.2. INCIDENCE DATA - to include but not be limited to:

- Mortality rate
- Mating indices, male and female fertility indices
- Litter survival indices
- Gestation indices
- Incidence of dams with no viable pups
- Mean pup survival indices (Days 0 and 4)

A Fisher Exact Test with Bonferonni correction (Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.) will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

12. REPORTING

12.1. STATUS REPORTS

The Testing Facility will furnish progress reports to the Sponsor at least weekly.

12.2. FINAL REPORT

One unbound hard copy and one electronic copy of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

12.2.1. Body of Report

- Compliance Statement (including Sponsor signature line)
- Quality Assurance Statement
- Abstract
- Introduction
- Experimental Design (including justification for exposure levels)
- Materials and Methods
- Results and Discussion
- Conclusion (including NOAEL statement, if applicable)
- Statistical Procedures
- Protocol deviations and study impact statements

12.2.2. Summary Tables

- Exposures
- Mortality
- Mating indices and male and female fertility indices
- Physical in-life observations
- Mean body weight data male and female rats premating; male rats during mating and postmating; female rats during gestation and lactation
- Mean animal weight gain data male and female rats premating; male rats during mating and postmating; female rats during gestation and lactation
- Mean feed consumption data male and female rats premating; female rats during gestation and lactation

- Mean gestation length
- Mean number of implantation sites and corpora lutea
- Mean pre- and post-implantation loss
- Mean female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Litter survival indices
- Mean litter pup survival indices (Lactation Days 0 and 4)
- Mean pup weights (Lactation Days 1 and 4)
- Mean pup sex ratio (Days 0 and 4)
- Macroscopic postmortem examination (male rats, female rats, F₁ pups)
- Mean absolute organ weights, organ weight to body weight ratios and organ weight to brain weight ratios
- Microscopic Pathology

12.2.3. Appendix Tables (Individual data)

- Mortality
- Physical in-life observations
- Individual body weight data male and female rats premating;
 male rats during mating and postmating; female rats during gestation and lactation
- Individual animal weight gain data male and female rats premating; male rats during mating and postmating; female rats during gestation and lactation
- Individual feed consumption data male and female rats premating; female rats during gestation and lactation
- Individual mating and pre-coital interval data
- Individual gestation length
- Individual number of implantation sites and corpora lutea
- Individual pre- and post-implantation loss
- Individual female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Individual litter survival indices
- Individual litter pup survival indices (Days 0 and 4)
- Individual pup weights (Days 1 and 4)
- Individual macroscopic postmortem examination (male rats, female rats, F₁ pups)
- Individual absolute organ weights, organ weight to body weight ratios and organ weight to brain weight ratios
- Individual Microscopic Pathology

12.2.4. Appendices

- Analyses of feed, water and bedding
- Personnel involved in the study
- Protocol and Amendments

12.3. ROBUST SUMMARY

This report will be separately provided by the Testing Facility's UK office in both IUCLID and WORD® electronic formats.

13. REGULATORY REFERENCES

13.1. TEST GUIDELINE

This study will comply with the

- 1. Organization for Economic Cooperation and Development (March 22, 1996) OECD Guidelines for Testing of Chemicals; OECD Guideline 421: Reproduction/Developmental Toxicity Screening Test, pp. 1-10.
- 2. EPA Health Effects Test Guidelines (July 2000) OPPTS 870.3550: Reproduction/Developmental Toxicity Screening Test, pp. 1-11.

13.2. GOOD LABORATORY PRACTICES

This study will be conducted in compliance with

- 1. Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17.
- 2. EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA).

13.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all appropriate parts of the Animal Welfare Act regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991. The Sponsor should make particular note of the following:

1. The Sponsor's signature on this protocol documents for the study described, that there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments.

- 2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or in written laboratory standard operating procedures.
- 3. Any procedures outlined in this study protocol which are expected to cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing, by the Sponsor and the Study Director and approved by the IACUC; in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review form.
- 4. Animals experiencing more than momentary or slight pain or distress due to test substance or emergency situations such as injury or illness will be treated by the Testing Facility's veterinarian staff with approved analgesics or agents to relieve pain. If possible, the Study Director will be consulted prior to treatment; however, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.
- 5. Methods of euthanasia used during this study are in conformance with the above referenced regulations.

13.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with appropriate animal welfare regulations.

14. QUALITY ASSURANCE MONITORING

The Quality Assurance Unit of Huntingdon Life Sciences (East Millstone, NJ) will monitor the facilities, equipment, personnel, methods, practices, records, raw data, draft and final reports and controls used in this study to assure that they are in conformance with this protocol, company Standard Operating Procedures and the referenced Good Laboratory Practice regulations.

15. ALTERATION OF DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by two members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A TISSUES PRESERVED/EXAMINED

Tissue	Tissues	Microscopic ^a
	Preserved	Examination
Adrenal glands	X	
Brain	X	
Epididymides	X	X
Larynx ^b	X	X
Lungs (with mainstem bronchi)	X	X
Lymph nodes (mediastinal)	X	·
Nasopharynx ^c	X	X
Ovary with oviducts	X	X
Pituitary	X	
Prostate	X	X
Seminal Vesicles	X	X
Testes	X	X
Thymus	X	
Trachea	X	X
Uterus with Vagina	X	X
Macroscopic Lesions	X	X

^aControl and high exposure male and female animals. If a treatment-related change is observed in the high exposure group, microscopic examinations will be performed on the low and mid exposure groups upon Sponsor approval (additional cost).

^bThe laryngeal mucosa shall be examined. Sections of the larynx to be examined include the epithelium covering the base of the epiglottis, the ventral pouch and the medial surfaces of the vocal processes of the arytenoid cartilages.

Four sections of the nasopharyngeal tissue shall be examined. This shall include sections through the nasal cavity and examinations of the squamous, transitional, respiratory and olfactory epithelia.

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

1. Proposed Study Dates, page 2:

Revise: Termination of Exposures Male Rats: 24 21 June 2004

Female Rats: 10 July 2004

2. Experimental Design, page 3:

Add to revise: The exposure levels for Groups 2, 3 and 4 will be 30, 100 and 300 mg/m³, respectively.

3. Justification for Exposure Level Section, page 4:

Replace:

The exposure levels are based primarily upon findings in a two-week range-finding study (03-6147) in which exposure to the test substance resulted in alveolar and/or bronchiolar epithelial hyperplasia/hypertrophy at exposure levels of 25, 75 and 200 mg/m³. Both the severity (slight to moderate) and the incidence (0 to 100%) were exposure level-responsive. Absolute lung weight was increased by approximately 12 to 16% at the highest concentration. The highest exposure concentration chosen for this reproduction screen, 300 mg/m³, was selected as a balance between the above pulmonary effects, the longer exposure period of this study and greater respiratory demands of pregnancy.

4. Detailed Physical Observations, page 11:

Revise:....Female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 21 and Lactation Days 0, 1 and 4.....

5. Macroscopic Postmortem Examination - F₁ Pups, page 15:

Replace: Macroscopic post-mortem examinations (internal and external) will be performed on all F_1 pups found dead during lactation. Unusual observations, including gross abnormalities and the absence of milk in the stomach, will be noted and then the carcasses will be discarded. The day of death of any pup found dead will be recorded. Intact F_1 pups found dead on the day of birth will be identified by the lung floatation test, examination of the lungs or ductus arteriosus, or other appropriate method as stillborn or alive at birth. F_1 pups found dead on the day of birth that are autolyzed, partially cannibalized or otherwise unsuitable for this determination will be so noted and reported. Macroscopic post-mortem examinations (external only) will be performed on all F_1 pups on Lactation Day 4 for pups surviving

to that interval. Unusual observations, including gross abnormalities, will be noted and then the carcasses will be discarded.

Reasons for Changes

- 1. Correction of scheduled date since animals will be exposed until day before sacrifice.
- 2. A re-examination of the data from the range-find study 03-6147 resulted in a decision that the animals could tolerate a higher exposure level than 200 mg/m³ since only slight to moderate pulmonary toxicity was seen.
- 3. See #2.
- 4. Correction of the observation intervals during the gestation period.
- 5. Clarification of the procedures for examining dead pups.

Additional Cost Required: Yes

Amendment approved by:

Date

21 MAY 04

Date

Date

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

1. Proposed Study Dates, page 2:

Revise: Termination of Exposures

Terminal Sacrifice

Female Rats: 11 July 2004

Female Rats: 5-16 July 2004

2. Detailed Physical Observations, page 11:

Add: ...Female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 and Lactation Days 0 (except if parturition doesn't complete on the same day as it initiates), 1 and 4...

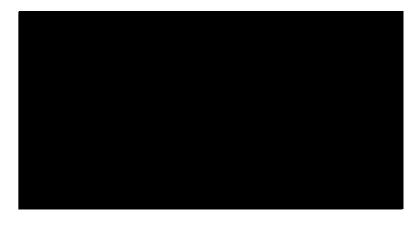
3. Final Report, Appendices, page 20:

Add: Final report for the Range-Find study 03-6147.

Reasons for Changes

- 1. Correction of scheduled dates.
- 2. Clarification of the lactation period observations intervals.
- 3. Request of the Sponsor.

Additional Cost Required: No Amendment approved by:



27 Sec. 04
Date

12/23/04 Date

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

Microscopic Pathology Evaluations-Adult Rats, page 15 and Appendix A, page 22: Add: The respiratory tract (nasopharynx, larynx, trachea and lungs) will also be examined for the Groups 2 and 3 test animals.

Reasons for Changes

Effects of exposure (including proliferative and/or inflammatory responses in the lungs) were noted in the Group 4 high exposure test animals compared to the Group 1 air control test animals. Therefore, an evaluation of the lower level exposed test animals is considered of interest.

Additional Cost Required: Yes

Amendment approved by:



27 100 d

12/23/04 Date

Page 1 of 1 Final Protocol

Protocol Amendment No. 4

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

Microscopic Pathology Evaluations-Adult Rats, page 15 and Appendix A, page 22: Add: The mediastinal lymph nodes will also be examined for all test animals.

Reasons for Changes

Effects of exposure (marked to severe increase in lymphoid cellularity caused by an expansion of the paracortical/T-lymphocyte population) were noted in the Group 4 high exposure test animals compared to known normal morphology of this node. Therefore, an evaluation of the control and all exposed test animals is considered of interest.

Additional Cost Required: Yes

Amendment approved by:

Barcos

4/13/05 Date Huntingdon Life Sciences Study No. 03-4246

Page 1 of 1 Final Protocol

Protocol Amendment No. 5

Study Title: Petroleum Coke: Reproduction/Developmental Toxicity Screening
Study in Rats via Nose-Only Inhalation Exposures

Changes

Identification of Test Substance, page 5:

Revise: At the end of the study, a 200 gram sample of the test substance will be shipped for analysis to ChevronTexaco Energy Research and Technology Corp., 100 Chevron Way, Richmond, CA 94802, 510-242-7037, attn: Patrick Beatty. Since this analysis was not conducted using the same methods as the pre-study analysis and therefore was not valid for a comparison to the pre-study data, the data from an analysis of a sample from the same lot number stored at Wildlife International will instead be reported for this study.

Reasons for Changes

Clarification of the data to be reported for test substance stability analysis.

Additional Cost Required: No

Amendment approved by:

1/16 /2008

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	Testing Facility Personnel	Appendix BB

TITLE/DEPARTMENT

SENIOR VICE PRESIDENT, SAFETY ASSESSMENT

DIRECTOR, DEVELOPMENTAL AND REPRODUCTIVE TOXICOLOGY

DIRECTOR, ANALYTICAL SERVICES

DIRECTOR, TOXICOLOGY OPERATIONS

DIRECTOR, QUALITY ASSURANCE

STUDY DIRECTOR

PATHOLOGIST

STUDY MONITOR

VETERINARIAN

MANAGER/SUPERVISOR

Rodent and Reproductive Toxicology Inhalation Toxicology Pharmacy Necropsy and Fetal Pathology Histology

NAME/DEGREE



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Historical Control Data	
CD Rat - Mating, Fertility and Gestation	
Preface	Appendix CC

Data used for historical control purposes was obtained from inhalation studies run prior to this study (from April 2001 to August 2002).

Historical Control Data	
CD Rat - Mating, Fertility and Gestation	Appendix CC

					Females			
Study ID	Initiation Date	Paired w/ Males No.	Mated No.	Mating Index %	Pregnant No.	Fertility Index %	No. with Liveborn No.	Gestation Index %
00-4208 P0 00-4208 F1	12-Jun-01	26 26	24 23	92.3 88.5	23 21	95.8 91.3	23 21	100.0 100.0
00-4207 P0 00-4207 F1	30-Apr-01	26 26	25 25	96.2 96.2	24 25	96.0 100.0	24 25	100.0 100.0
00-4206	20-Aug-02	26	24	92.3	21	87.5	21	100.0
00-4205	20-May-02	26	25	96.2	22	88.0	22	100.0
00-4204	19-Mar-02	26	26	100.0	25	96.2	25	100.0
00-4203	21-Jan-02	26	26	100.0	25	96.2	25	100.0
00-4202	22-Aug-01	26	26	100.0	24	92.3	24	100.0
		MEAN SD N	25 1.1 9	95.7 4.05 9	23 1.7 9	93.7 4.19 9	23 1.7 9	100.0 - 9
		MIN MAX	23 26	88.5 100.0	21 25	87.5 100.0	21 25	100.0 100.0

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	Final Report
Report Amendments	Appendix DD

There are no amendments for this report at this time.