



RECEIVED
OCT 1 2008

08 JUL 31 AM 11:33

Howard J. Feldman
Director

Regulatory and Scientific Affairs

1220 L Street, NW
Washington, DC 20005-4070
USA
Telephone 202-682-8340
Fax 202-682-8270
Email Feldman@api.org
www.api.org



NON-CONFIDENTIAL INFORMATION

July 31, 2008

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Coke (Petroleum) Study Findings



Dear Sir or Madam:

The American Petroleum Institute (API) manages a testing program for the Petroleum HPV Testing Group (membership list attached). The Testing Group is an unincorporated group of 60 manufacturers affiliated by contractual obligation to API to participate in EPA's HPV Challenge Program. This notice is submitted pursuant to Section 8(e) of the Toxic Substances Control Act for the substance, Coke (Petroleum), CAS Number 64741-79-3.

The Testing Group recently received a revised draft study report; Petroleum Coke: Reproduction/Developmental Toxicity Screening Study in Rats via Nose-Only Inhalation Exposures. The study followed the OECD 421 testing protocol and was conducted to fulfill the guidelines of EPA's HPV Challenge Program. The test material was petroleum green coke milled to a median diameter of 3.3 microns. Nominal exposure concentrations of 0, 30, 100, and 300 mg/m³ were tested.

The first and second drafts of the study report indicated that there were no statistically significant differences in fertility (no. pregnant/no. cohabited) or gestation (no. live litters/no. confirmed pregnant) indices among the groups and the NOAEL was reported as the highest exposure concentration, 300 mg/m³. While there was no change in the originally reported data, the third draft of the study report now finds that the fertility and gestation indices of the 300 mg/m³ group are outside the testing facility's historical control lower ranges and now notes a low number of implantation sites with no viable fetuses for one female in the 300 mg/m³ group. The 300 mg/m³ group had a fertility index of 75% versus a historical control value of 87.5% and concurrent control value of 91.7%, and a gestational index of 88.9% versus a historical control value of 95.2% and concurrent control value of 100%. Reproductive performance values are shown below.

Contains No CBI **CONTAINS NO CBI**

An equal opportunity employer

313279

	Control	30 mg/m3	100 mg/m3	300 mg/m ³
A - No. Cohabited	12	12	12	12
B - No. Mated	11	12	12	11
C - No. Pregnant	11	12	12	9
D - Fertility Index (C/A)	91.7%	100%	100%	75%
E - No. Live Litters	11	12	12	8
F - Gestation Index (E/C)	100%	100%	100%	88.9%

Therefore the NOAEL for reproductive effects in the revised report is 100 mg/m³. The Summary section of the laboratory's third draft report is attached to provide additional study details. [Please note that the laboratory's Summary erroneously reports the control fertility index as 100%.]

Based on EPA's published TSCA 8(e) guidance we are submitting this finding of reduced fertility in rats in the 300 mg/m³ group for your review. For all other measurements of reproductive performance, such as mating index, days to mating, gestation length, pre-/post-implantation loss, or number of litters with still born pups, responses in treated groups were not different from control. No developmental or post-parturition effects were observed in the study. The NOAEL for other parental systemic and developmental toxicity in the study was considered to be 300 mg/m³. Because of the lack of statistical significance associated with the reduction in fertility, small group sizes used in the OECD 421 study, and the absence of effects on other reproductive parameters, we believe the findings to be of uncertain relationship to petroleum coke exposure.

If you have any questions or require further information regarding this submission please contact Thomas Gray at API (202-682-8480 or grayt@api.org).

Sincerely,



Howard J. Feldman

Attachments: Petroleum HPV Testing Group Membership List
Data Summary

cc. Oscar Hernandez, USEPA
Diane Sheridan, USEPA
Mark Townsend, USEPA

Petroleum HPV Testing Group Member Companies

Alcoa Inc.
Amerada Hess Corporation
ATOFINA Petrochemicals, Inc.
Big West Oil LLC/Flying J Inc.
BP p.l.c.
Calcasieu Refining Company
ChevronTexaco Corporation
CHS Inc.
CITGO Asphalt Refining Company
CITGO Petroleum Corporation
ConocoPhillips
Countrymark Refinery
Cross Oil Refining & Marketing, Inc.
Crown Central Petroleum Corporation
Dakota Gasification Company
Dynergy Liquids MKTG & Trade
Edgington Oil Company
Elkhorn Operating Company
Equilon Enterprises LLC/Motiva Enterprises LLC
Ergon Refining, Inc.
Ergon West Virginia Inc
ExxonMobil Americas Refining and Supply Company
Farmland Industries, Inc.
Flint Hills Refineries
Formosa Hydrocarbons Co., Inc.
Giant Industries, Inc.
Holly Corp/Navajo Refining Co
Honeywell International
Hovensa, LLC
Hunt Refining Co
Kern Oil & Refining Company
La Gloria Oil & Gas Company
Lion Oil Company
Lyondell-CITGO Refining LP
Marathon Ashland Pipeline, LLC
Merichem Chemicals & Refinery Serv LLC
Murphy Oil Corporation
National Cooperative Refinery Association
Neville Chemical Company
PDV Midwest Refining, LLC
Placid Refining Company LLC
Premcor Refining Group Inc. (TN)
Safety-Kleen Oil Recovery
Sasol North America Inc.
Shell Oil Company
Sid Richardson Gasoline Co.
Silver Eagle Refining, Inc. (UT)
Silver Eagle Refining, Inc. (WY)
Sinclair Oil Corporation
South Hampton Refining Company
Sunoco, Inc.
Tesoro Petroleum Corporation
The Goodyear Tire & Rubber Company
The Premcor Refining Group Inc. (CT)
True Oil Co/88 Oil Co/Equit. Oil Purch. Co
Unocal International Supply and Trading Co.
US Oil & Refining Co.
Valero Energy Corp
Williams Energy Services
Wynnewood Refining Company

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

This study was designed to screen possible effects on reproductive performance, in male and female Sprague Dawley CD[®] rats when petroleum coke was administered as a dust, via nose-only inhalation exposure. It also was designed to detect effects on gonadal function, which may not be evident from histological examination of the reproductive organs. In addition, this study can detect effects on mating behavior, conception, development of the conceptus, parturition, lactation, and pup survival to postnatal day 4.

Male and female Sprague-Dawley CD[®] rats (12/sex/group) were exposed to petroleum coke once daily (6 hours/day), 7 days/week for 2 weeks prior to mating initiation, at levels of 0 (air only), 30, 100 or 300 mg/m³. In addition, male rats were exposed during the mating and post-mating periods for a minimum exposure of 28 days until euthanized and necropsied. Female rats continued to be treated once daily (6 hours/day) during the mating period. Once mated, female rats were treated once daily (6 hours/day) during gestation days 0 through 19, and euthanized on lactation day 4 and necropsied.

The following parameters were evaluated in all animals: viability, clinical observations, body weights, feed consumption, organ weights, and macroscopic observations. Macroscopic postmortem examinations (external only) were performed on all surviving F₁ pups on postnatal day 4. Histopathological evaluations were conducted on all air control and test substance exposed adult animals. Exposure levels were determined using a gravimetric sampling procedure four times per chamber per day. Particle size distribution measurements were also made once per chamber per week.

The mean (\pm standard deviation) exposure concentrations of petroleum coke were determined to be 31.2 ± 4.6 , 99.4 ± 13.9 , and 300.7 ± 34.7 mg/m³ for the three exposed groups, respectively. Chamber environmental conditions averaged 20°C temperature and 44% relative humidity. The average mass median diameter was determined to be 2.287 μ m with an average geometric standard deviation of 2.848 indicating that the particles for the test substance exposed groups were highly respirable to the test animals.

There was no effect of treatment on survival. All animals survived until the termination of the study. The test animals were generally unremarkable during the non-exposure period. There were no exposure-related differences in absolute body weights, body weight changes or feed consumption in the remaining test substance exposed animals, compared to the air control animals.

Mating, fertility, and gestation indices were unaffected by the exposures for the lower two exposure groups. In the 300 mg/m³ group, four pairings either did not result in pregnancy (3/12) or did not result in delivery of viable fetuses (1/12). Of the three females that were not pregnant, one was acyclic (one control female was also acyclic).

SUMMARY

Both of the other non-pregnant dams mated but neither had corpora lutea or implantations. Consequently, the overall fertility index for the 300 mg/m³ group was slightly decreased when compared with control values ([75% [9/12] versus 100% [11/11]), however the difference was not statistically significant. A fourth dam was pregnant, but had only two corpora lutea, two implantation sites, and no viable fetuses. The gestation index at 300 mg/m³ (88.9% [8/9]) was reduced but not statistically different from the controls (100% [11/11]). However the fertility and gestation indices observed in the 300 mg/m³ group were outside the testing facility's historical control data minimum (fertility index of 87.5% and gestation index of 95.2%). There were no exposure-related inter-group differences for delivery parameters, including the duration of gestation and the proportion with live litters and/or with stillborn pups. Parturition data for the female rats treated with the test substance were comparable to the air control group. The pups were unremarkable during the early postnatal period until termination at postnatal day 4. There were no meaningful differences in pup body weights or weight gains, up to postnatal day 4, in the pups feeding from dams exposed to test substance during gestation compared to the pups feeding from air control dams. The decreased fertility and gestation indices in the 300 mg/m³ coupled with the single female with a low number of implantation sites and no viable fetuses were considered exposure-related.

Except for the low exposure males, there were exposure-related increases (up to 37% in males and 58% in females) in absolute lung weights compared to the air control animals. Lungs from all test substance-treated rats were slightly to severely discolored black. Inhalation of petroleum coke was associated with the presence of pigment deposits, probably representing test substance, in the lungs, mediastinal lymph nodes and nasal olfactory epithelium of most male and female rats, and in the lumens of the nasal turbinates and pharynx of male rats. Test substance-related changes characterized by proliferative and/or inflammatory responses were observed in the lungs at all exposure levels. In the mediastinal lymph nodes draining the lungs of the animals at all exposure levels, hyperplasia of the paracortical T lymphocyte population accompanied the deposition of pigment. In the larynx, minimal squamous metaplasia of the respiratory epithelium occurred and was considered to be an adaptive response to inhalation of particulates. These effects were considered to be in response to inhalation of particulate matter, and histological findings were considered to be adaptive. There were no exposure-related differences in the incidence of macroscopic postmortem evaluations in the pups from test substance exposed animals as compared to the pups from air control animals.

In conclusion, exposure of male and female rats to target concentrations of 30, 100 or 300 mg/m³ of petroleum coke by nose-only inhalation for 4-6 weeks resulted in discolored lungs, increased lung weight, and proliferative and/or inflammatory responses in the lungs and mediastinal lymph nodes, in all test substance exposed groups. Decreased fertility and gestation indices coupled with the single female with a low number of implantation sites and no viable fetuses were observed in the 300 mg/m³ exposure group. There were no effects observed on offspring survival and weight

SUMMARY

development up to postnatal day 4. Therefore, the no-observed-adverse-effect level (NOAEL) for adult males and females for systemic toxicity was 300 mg/m³. A NOAEL for the portal of entry was not established for females; the female lowest-observed-adverse-effect level (LOAEL), based on lung weight increases, was 30 mg/m³. The portal of entry NOAEL for males, based on increased lung weights, was 100 mg/m³. Based on the lower fertility and gestational indices, and low number of implantation sites with no viable fetuses for one female in the 300 mg/m³ exposure group, the reproductive NOAEL was 100 mg/m³. The developmental NOAEL was 300 mg/m³.