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211 (b) Research Group

Via Overnight Mail

NON-CONFIDENTIAL INFORMATION

February 26, 2002

TSCA Document Processing Center
U.S. Environmental Protection Agency
EPA East Bldg, Room 6428 (Mail Code 7407M)
ATTN: Document Control Officer TSCA Section 8(e)
1201 Pennsylvania Ave., NW
Washington, DC 20460-0001

Contain NO CBI

Re: TSCA (8e) Submission for Clean Air Act Section 211(b) Gasoline/TAME Vapor Condensate (Lot # API 01-04)

Dear Sir/Madam:

The 211(b) Research Group (see attached membership list) is an unincorporated group of US fuel and fuel additive manufacturers affiliated by contractual obligation to meet the testing requirements of Section 211(b)(2) and 211(e) of the Clean Air Act. The 211(b) Research Group, on behalf of its member companies, is submitting this notice pursuant to TSCA Section 8(e). This notice is based on preliminary results from a study to evaluate reproductive toxicity in rats after inhalation exposure to vapors of unleaded gasoline blended with tertiary-amyl methyl ether (TAME). The study found that exposure to this gasoline/TAME vapor condensate significantly depressed rat pup weights at postnatal days 14 and 21.

As part of the 211(b) Alternative Tier II test program on gasoline (CAS No. 86290-81-5) containing 15% TAME (CAS No. 994-05-8), a One Generation Reproductive Toxicity study was conducted (OPPTS Guidelines 870.3800). In this study, Sprague-Dawley-derived CD® rats were exposed to the test substance by inhalation for 6 hour/day, 7 day/week for ten weeks of premating exposure and throughout mating, gestation and lactation (beginning on day postnatal day 4) until weaning on postnatal day 28. Exposure levels were 0, 2000, 10000, and 20,000 mg/m^3 total vapor concentration (estimated TAME concentrations of 290, 1450, and 2900 mg/m^3). Potential toxicity was evaluated by clinical observations, body weight/gain, and food consumption during all intervals. Mating, fertility, and gestation indices were compared across exposure groups, as were semen analyses, duration of gestation, stillbirth, litter size, pup survival, and postnatal growth. At necropsy on postnatal day 28, organ weights (brain, thymus, and spleen) were recorded. Statistical analysis of body weight and weight gain data was performed by one-way analysis of variance (ANOVA); where the ANOVA was statistically significant, multiple group comparisons were performed using Dunnett's test. Microscopic evaluation of preserved tissues is ongoing.

Statistically significant decreases in pup weight gain postnatal day 7-14 occurred at the 10,000 and 20,000 mg/m^3 exposure levels. Pup weight was statistically reduced at these exposure levels on postnatal day 14 and continued to be statistically smaller for male pups and combined sexes (males + females) in the 20,000 mg/m^3 exposure level on postnatal day 21. At the lowest exposure level, 2000 mg/m^3, pup weight was statistically reduced on postnatal day 21 for male and combined-sex pups, as was weight gain for the interval postnatal day 4-21 and 14-21. However, mid-dose male and low-, mid- and high-dose female pup weights were not significantly different from control at day 21. There were no statistically significant differences between control and any exposure group for pup body weight or pup organ weight on postnatal day 28. There were no differences from control for reproductive parameters, semen analyses, average litter size, birth weight, stillbirths or pup survival. Although the study director considers the weight decrement observed in the mid- and high-exposure groups to be exposure-related, the relationship between the findings in the low-exposure group and exposure are considered questionable.

Preliminary results from a similar study with unoxygenated gasoline vapor in rats were negative. Reduced pup weight during lactation was previously reported to the EPA under TSCA Section 8(e) in January 1997 based upon an inhalation two-generation reproduction study conducted with neat TAME at exposure levels of 1040, 6250, and 12,500 mg/m^3.

The significance of the current results for potential human health hazard assessment is unknown at this time.

When the final report of the One Generation Reproductive study is complete, it will be submitted to the EPA Office of Transportation and Air Quality, Fuels and Energy Division, as part of the requirements of Clean Air Act Section 211(b)(2) and 211(e) (Docket No. A-90-07). If you require further information, please contact Lorraine Twerdok at 202-682-8344, or by mail at this address.

Regards,

Lorraine E. Twerdok

Lorraine Twerdok, Ph.D., DABT
Administrator, 211(b) Research Group

Cc: John Brophy, EPA
Mike Davis, EPA
Tom Goldsworthy, ILS
Rich Schlesinger, NYU
211(b) Research Group Member Companies

Sponsor Study No: 211-TAME-1G

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

		GROUP		I	II	III	IV
		DOSE LEVEL(MG/M3)		0	2000	10000	20000
day	1	males	MEAN	7.4	7.3	7.3	7.1
			S.D.	0.54	0.44	0.77	1.00
			N	23	25	24	23
	1	females	MEAN	7.1	6.9	7.0	6.7
			S.D.	0.49	0.44	0.74	1.01
			N	22	25	24	23
	1	males+females	MEAN	7.2	7.1	7.2	6.9
			S.D.	0.52	0.45	0.78	0.96
			N	23	25	24	23
day	4	males	MEAN	10.6	10.2	10.4	9.8
		preculling	S.D.	1.05	1.03	1.52	1.59
			N	22	25	24	23
	4	females	MEAN	10.1	9.8	10.0	9.3
		preculling	S.D.	0.92	1.00	1.39	1.72
			N	22	25	24	23
	4	males+females	MEAN	10.4	10.0	10.2	9.6
		preculling	S.D.	1.03	1.02	1.49	1.62
			N	22	25	24	23
day	4	males	MEAN	10.6	10.2	10.4	9.8
		postculling	S.D.	1.09	1.06	1.52	1.56
			N	22	25	24	23
	4	females	MEAN	10.1	9.8	10.0	9.3
		postculling	S.D.	0.93	1.00	1.41	1.78
			N	22	25	24	23
	4	males+females	MEAN	10.4	10.0	10.2	9.6
		postculling	S.D.	1.00	1.02	1.49	1.63
			N	22	25	24	23

No statistically significant differences

Sponsor Study No: 211-TAME-16

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY
INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

	GROUP		I	II	III	IV
	DOSE LEVEL(MG/M3)		0	2000	10000	20000
day 7	males	MEAN	14.9	14.0	14.3	13.9
		S.D.	1.33	1.33	1.55	1.92
		N	22	25	24	23
7	females	MEAN	14.1	13.4	13.7	13.2
		S.D.	1.15	1.41	1.41	2.01
		N	22	25	24	23
7	males+females	MEAN	14.5	13.7	14.0	13.5
		S.D.	1.23	1.35	1.48	1.91
		N	22	25	24	23
day 14	males	MEAN	26.5	24.9	24.6*	24.2**
		S.D.	1.82	2.48	2.32	2.82
		N	22	25	24	23
14	females	MEAN	25.6	24.2	23.9*	23.1**
		S.D.	1.67	2.46	2.19	2.93
		N	22	25	24	23
14	males+females	MEAN	26.0	24.6	24.3*	23.7**
		S.D.	1.68	2.42	2.22	2.81
		N	22	25	24	23
day 21	males	MEAN	43.3	39.3*	40.1	39.3*
		S.D.	4.21	4.36	4.75	6.11
		N	22	25	24	23
21	females	MEAN	41.5	38.7	39.1	37.8
		S.D.	3.72	4.64	4.84	6.16
		N	22	25	24	23
21	males+females	MEAN	42.5	39.0*	39.7	38.5*
		S.D.	3.87	4.38	4.65	6.02
		N	22	25	24	23

Statistical key: * = p<0.05 ** = p<0.01

Sponsor Study No: 211-TAME-1G

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

	GROUP		I	II	III	IV
	DOSE LEVEL(MG/M3)		0	2000	10000	20000
day 28	males	MEAN	81.6	78.0	77.6	76.6
		S.D.	5.90	7.07	8.25	10.53
		N	22	25	24	23
28	females	MEAN	75.8	73.3	72.3	70.8
		S.D.	4.63	6.68	7.68	9.04
		N	22	25	24	23
28	males+females	MEAN	78.8	75.6	75.1	73.6
		S.D.	5.12	6.60	7.66	9.36
		N	22	25	24	23

No statistically significant differences

Sponsor Study No: 211-TAME-1G

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY
INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS

GROUP		I	II	III	IV
DOSE LEVEL(MG/M3)		0	2000	10000	20000
day 1- 4 males	MEAN	3.2	2.9	3.0	2.7
	S.D.	0.77	0.80	1.01	1.08
	N	22	25	24	23
females	MEAN	3.0	2.9	3.0	2.6
	S.D.	0.63	0.73	0.92	1.13
	N	22	25	24	23
males+females	MEAN	3.1	2.9	3.0	2.7
	S.D.	0.70	0.75	0.96	1.10
	N	22	25	24	23
day 4- 7 males	MEAN	4.2	3.8	3.9	4.1
	S.D.	0.63	0.77	0.76	1.01
	N	22	25	24	23
females	MEAN	4.1	3.6	3.8	3.9
	S.D.	0.59	0.77	0.74	0.97
	N	22	25	24	23
males+females	MEAN	4.1	3.7	3.8	4.0
	S.D.	0.59	0.76	0.73	0.97
	N	22	25	24	23
day 4-21 males	MEAN	32.7	29.0*	29.8	29.5*
	S.D.	3.59	3.65	4.14	5.10
	N	22	25	24	23
females	MEAN	31.4	28.9	29.1	28.5
	S.D.	3.41	4.06	4.34	5.02
	N	22	25	24	23
males+females	MEAN	32.1	28.9*	29.5	29.0*
	S.D.	3.41	3.84	4.09	4.96
	N	22	25	24	23

Statistical key: * = p<0.05

Sponsor Study No: 211-TAME-1G

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS

GROUP		I	II	III	IV
DOSE LEVEL(MG/M3)		0	2000	10000	20000
day 4-28 males	MEAN	71.0	67.8	67.2	66.7
	S.D.	5.27	6.75	7.66	9.47
	N	22	25	24	23
females	MEAN	65.7	63.6	62.3	61.5
	S.D.	4.36	6.30	7.26	7.84
	N	22	25	24	23
males+females	MEAN	68.4	65.6	64.9	64.0
	S.D.	4.67	6.27	7.11	8.26
	N	22	25	24	23
day 7-14 males	MEAN	11.6	10.9	10.3*	10.3*
	S.D.	1.16	1.81	1.33	1.63
	N	22	25	24	23
females	MEAN	11.5	10.8	10.1**	9.9**
	S.D.	1.20	1.71	1.46	1.47
	N	22	25	24	23
males+females	MEAN	11.5	10.9	10.2**	10.1**
	S.D.	1.14	1.73	1.36	1.49
	N	22	25	24	23
day 7-28 males	MEAN	66.8	64.0	63.3	62.7
	S.D.	4.95	6.40	7.22	8.91
	N	22	25	24	23
females	MEAN	61.6	60.0	58.6	57.6
	S.D.	3.95	5.96	6.85	7.37
	N	22	25	24	23
males+females	MEAN	64.2	61.9	61.1	60.0
	S.D.	4.31	5.92	6.71	7.74
	N	22	25	24	23

Statistical key: * = p<0.05 ** = p<0.01

Sponsor Study No: 211-TAME-1G

GASOLINE TAME VAPOR CONDENSATE: A ONE-GENERATION WHOLE-BODY INHALATION REPRODUCTION TOXICITY STUDY IN RATS

SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS

GROUP DOSE LEVEL(MG/M3)		I 0	II 2000	III 10000	IV 20000
day 14-21 males	MEAN	16.9	14.3*	15.6	15.0
	S.D.	2.74	2.23	2.91	3.75
	N	22	25	24	23
females	MEAN	15.8	14.5	15.2	14.7
	S.D.	2.64	2.56	2.97	3.61
	N	22	25	24	23
males+females	MEAN	16.4	14.4	15.4	14.8
	S.D.	2.60	2.30	2.85	3.62
	N	22	25	24	23
day 14-28 males	MEAN	55.2	53.1	53.0	52.3
	S.D.	4.35	5.02	6.33	8.01
	N	22	25	24	23
females	MEAN	50.2	49.2	48.4	47.7
	S.D.	3.27	4.70	5.79	6.44
	N	22	25	24	23
males+females	MEAN	52.7	51.1	50.8	49.9
	S.D.	3.72	4.61	5.78	6.83
	N	22	25	24	23
day 21-28 males	MEAN	38.3	38.8	37.5	37.3
	S.D.	2.79	3.90	3.93	5.13
	N	22	25	24	23
females	MEAN	34.3	34.7	33.2	33.0
	S.D.	2.41	3.37	3.29	3.26
	N	22	25	24	23
males+females	MEAN	36.3	36.7	35.4	35.0
	S.D.	2.45	3.44	3.44	3.81
	N	22	25	24	23

Statistical key: * = p<0.05

SECTION 211(b) RESEARCH GROUP MEMBERSHIP YEAR 2002

Organization
3M Automotive Aftermarket Division
A.E. Staley Manufacturing Company
Aectra Refining & Marketing
AGP Corn Processing
Akzo Nobel Chemicals Inc.
Albemarle Corporation
Amerada Hess Corporation
ANGUS Chemical Co. a subsidiary of Dow Chem. Co.
Archer Daniels Midland Company
Astra Oil Company, Inc.
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Baker Petrolite
BASF Corporation
Bayer Corporation *(new member)*
Belvieu Environmental Fuels/Enterprise Products
Betz Process Chemicals
Big West Oil/Flying J Inc.
Blue Coral Inc.-Slick 50 Products Corp.
BP p.l.c. [BP, AMOCO, ARCO]
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Buckman Laboratories, Inc.
Calcasieu Refining Company
Calumet Lubricants (own Pennzoil's Rouseville Refinery)
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CITGO Petroleum Corporation
Coastal States Management
Conoco, Inc.
Countrymark Cooperative, Inc.
CRC Industries, Inc./K&W Products
Crompton Corp. (was Witco Corp.)
Crown Central Petroleum Corp.
Ecofuel S.p.A. (American AGIP)
Enron Liquid Fuels
Eott Energy Operating LTD Partnership
Equistar Chemicals/Lyondell Chem. Co.
Equiva Services LLC
Ergon, Inc.
Ethyl Corporation
ExxonMobil Biomedical. Sciences. Inc. (*was Mobil Corp*)
ExxonMobil Refining & Supply Company
Farmland Industries, Inc.
Farstad Oil, Inc.
First Brands Corporation
Fortum Oil and Gas (was Neste Oy)
George E. Warren Corporation
Giant Industries Arizona, Inc.
Global Octanes Corporation

Organization
Global Petroleum
Gold Eagle Company
Grain Processing Corporation
Griffith Oil Co. Inc.
Guardsman Products/Valspar
Gulf Oil Limited Partnership
Halron Oil Co., Inc. *(new member)*
Holly Corporation/Navajo Refining Company
Hunt Refining Company
Huntsman Corporation
Infineum USA LP
Inland Refining Inc.
Irving Oil Corporation/Irving Oil Terminals, Inc.
Irving Oil Transportation Company
Kern Oil & Refining Company
Kerr-McGee Corp.
Kinder MorganEnergy Partners/Kinder Morgan Operating LP "A"
Koch Industries
Kop-Coat, Inc./Valvtect Petroleum/Alox Chem**
Lion Oil Company
LL&E Petroleum Marketing, Inc. c/o Equiva
Lyondell-CITGO Refining LP
Marathon Ashland Petroleum LLC (MAPLLC)
Mid-America Dairymen, Inc./Golden Cheese Co. of California
Midwest Grain Products, Inc.
Minnesota Corn Processing
Murphy Oil Corporation

Organization
Nalco Chemical Company/Exxon Energy Chemicals, LP
National Cooperative Refining Association/Cooperative Refining, LLC
NCH Corporation/Systems General
New Energy Corp.
Noco Energy Corp.
Northville Industries Corporation
Octel America, Inc.
Paramount Petroleum Corporation
Pekin Energy Company
Petro Diamond Incorporated
Petrochemical Products, Inc.
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Placid Refining Company
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Reid Petroleum Corp.
Rohm and Haas Company/Morton International
Sabic Americas, Inc.
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Sinclair Oil Corporation
SNPE North America Inc.
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Statoil Marketing & Trading (US) Inc.
Sun Company, Inc.
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Technical Chemical Company

Organization
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Tesoro Hawaii Petroleum
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Turtle Wax, Inc.
Ultramar Diamond Shamrock
Unichem A Division of BJ Services Co., U.S.A.
United Color Manufacturing Inc.
United Refining Company
UOP LLC
US Oil & Refining Co./ Time Oil Company
Valero Energy Corp./Valero Refining
Valvoline Company
Vitol S.A. Inc.
Warren Distribution
Wescourt Group Inc.
Western Petroleum Company
Williams Refining, LLC (was Mapco, Inc.)
Wynnewood Refining Company
Wyoming Refining Company