

CAS No.: 71-43-2
Robust Summary No.: OP E-002

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Biodegradation

Test Substance: CAS No. 71-43-2; Benzene

Method/Guideline: OECD 301F

Year (guideline): 1993

Type (test type): Ready Biodegradability, Manometric Respirometry Test

GLP: Yes

Year (study performed): 2000

Inoculum: Domestic activated sludge

Exposure Period: 28 days

Test Conditions: (FT - TC)

- Note: Concentration prep., vessel type, replication, test conditions.**

Activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride, EDTA). Test vessels were 500 mL dark glass bottles placed on a magnetic stirrer and electronically monitored for oxygen consumption. Test material and blanks were tested in triplicate, controls were tested in duplicate. Test material (benzene) concentration was 17mg/L. Sodium benzoate (positive control) concentration was 30mg/L. Toxicity control with benzene and Na Benzoate concentrations at 17 and 30 mg/L, respectively. Test temperature was 22 +/- 2 Deg C. All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.

Results: (FT - RS)

Units/Value:

- Note: Deviations from protocol or guideline, analytical method.**

Test material was readily biodegradable. Half-life was <2 weeks. By day 28, 63.0% degradation of the test material was observed. 10% biodegradation was achieved in less than 5 days, 50% biodegradation on approximately day 5. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

<u>Sample</u>	% Degradation* <u>(day 28)</u>	Mean % Degradation <u>(day 28)</u>
Benzene	54, 72, 63	63
Na Benzoate	65, 75	70
Toxicity Control	59, 65	62

* replicate data

Conclusion: (FT - CL)

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Biodegradation

Reliability: (FT - RL)

(1) Reliable without restriction

Reference: (FT - RE)

Brixham Environmental Laboratory. 2001. OECD 301F, Ready biodegradability: Manometric respirometry. Study # AH0378/A.

Other (source): (FT - SO)

Olefins Panel, American Chemistry Council

* IUCLID field abbreviations include:

FT - Freetext

TC - Test Conditions

RS - Results

CL - Conclusion

RL - Reliability

RE - Reference

SO - Source

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p>	<p>Dripolene. Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93329)</p>
<p><u>Method</u> Method/guideline followed Type (test type) GLP Year Species/Strain Sex No. of animals per sex per dose Vehicle Route of administration</p>	<p>Not specified Acute, limit test Yes 1994 Rat, Sprague-Dawley Males and females 5 None Oral gavage</p>
<p>Test Conditions</p>	<p>Sprague Dawley rats (180-350g) were individually housed in stainless steel suspended cages and fasted overnight prior to administration of 2g/kg neat dripolene. The study room was maintained at 68-72⁰F with a relative humidity of 35-63% and a 12 hr light-dark cycle. Water and chow diet were available ad lib after dosing. Test article was administered once on day 1 by oral gavage through a blunted needle. Rats were observed for clinical signs approx. 30 min, 1hr, and 4hr, after dosing, and daily thereafter until sacrifice on day 15. Rats were checked once a day for mortality and moribundity. Observations were not made on weekends. Body wts were recorded prior to fasting and on days 1, 8 and 15.</p>
<p><u>Results</u> LD₅₀ with confidence limits.</p>	<p>The LD₅₀ was not reached at 2g/kg. There were no deaths and all rats gained some weight during the study. Clinical signs noted in one or more rats were salivation, decreased activity, rales, lacrimation, chromodacryorrhea, ataxia, head shaking, chromorhinorrhea, miosis, slight tremors, mydriasis, hyperactivity, hypothermia, urogenital discharge, nasal discharge, decreased food consumption, decreased fecal output, vocalization, and decreased stool size. No gross pathological findings were noted at necropsy.</p>
<p>Remarks</p>	<p>The LD₅₀ was not reached at 2g/kg.</p>
<p><u>Conclusions</u> (study author)</p>	<p>1. Reliable without restriction.</p>
<p><u>Data Quality</u> Reliability</p>	<p>Rodriguez, S.C. and Dalbey, W.E. 1994. Acute oral toxicity of dripolene in Sprague Dawley Rats. Study #65642. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p>
<p><u>References</u></p>	<p>10/23/2001 (Prepared by a contractor to the Olefins Panel)</p>
<p><u>Other</u> Last changed</p>	

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Type (test type) GLP Year Species/Strain Sex No. of animals per sex per dose Vehicle Route of administration Test Conditions</p>	<p>Dripolene. Yellow, homogeneous liquid. Stable for 5 years at ambient temperature (CRU #93329)</p> <p>Not specified. Acute irritation Yes 1994 Rabbit, New Zealand White Males and females 3 None Dermal</p> <p>Three males and 3 female rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a room maintained at 69-72⁰F with relative humidity of 38-85% and 12hr light-dark cycle. Water and chow diet were available ad lib. One 1sq. inch test site was selected on the right anterior flank of 4 animals and the left anterior flank of 2 animals. The sites were designated as anterior flank (1-hr occlusion) test sites. A second 1 sq. inch test site was selected on the right posterior flank of 4 animals and the left posterior flank of 2 animals. The sites were designated as posterior flank (4-hr occlusion) test sites. The test sites were not abraded. 0.5ml of test substance was applied to the posterior test site under 1 sq. inch Webril patch. The patch was secured to the skin with an occlusive rubber dam followed by surgical tape. 0.5ml of test substance was applied to the anterior test site under a 1 sq. inch patch and similarly secured. Following 1hr exposure, the anterior patch was removed and the site evaluated for DOT corrosion. This site was reevaluated at 48hrs post-dosing. After the initial evaluation, residual test substance was removed by gently wiping the site with saline dampened cotton. Following a 4hr exposure, the posterior patch was removed and the site evaluated for DOT corrosion and OSHA Primary Irritation Index (PII). This site was reevaluated at 48hrs post-dosing. After the initial evaluation, the residual test substance was removed by gently wiping the site with saline dampened cotton. The posterior test site was also evaluated for dermal irritation according to the Draize method at 4.5, 28, 52, and 76hrs and at 7, 10 and 14 days post-dosing. Clinical observations were recorded at approx. 1hr and 4hr post-dosing and daily thereafter. The condition of each animal was checked once daily in the morning. The rabbits in this study were concurrently evaluated for ocular irritation to reduce the number of animals used. (Study 65644, see separate summary)</p>
<p><u>Results</u></p> <p>Remarks</p>	<p>The test material was negative for DOT corrosion after 1hr and 4hr occlusions and 48hr post-dose. After the 4hr occlusion, rabbits showed well-defined erythema (Draize score 2.2) and slight edema (Draize score 2.2) that cleared almost completely after 14 days (Draize scores <1.0). The OSHA PII score was 3.9, corresponding to a rating of "non-irritant". Skin flaking in 4 rabbits and skin cracking in 2 rabbits were observed on day 7.</p>
<p><u>Conclusions</u> (study author)</p>	<p>The test article was rated non-corrosive by DOT criteria after 1hr and 4hr occlusions, and non-irritating by OSHA PII criteria.</p>
<p><u>Data Quality</u> Reliability</p>	<p>1. Reliable without restrictions.</p>
<p><u>References</u></p>	<p>Rodriguez, S.C. and Dalbey, W.E. 1994. Acute dermal irritation/corrosion of dripolene in the New Zealand White rabbit. Study #65644. Stonybrook Laboratories, Inc., Princeton, NJ. for Mobil Chemical Co., Edison, NJ</p>
<p><u>Other</u> Last changed</p>	<p>10/23/2001 (Prepared by a contractor to the Olefins Panel)</p>

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Type (test type) GLP Year Species/Strain Sex No. of animals per sex per dose Vehicle Route of administration</p> <p>Test Conditions</p> <p><u>Results</u> Remarks</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u> Reliability</p> <p><u>References</u></p> <p><u>Other</u> Last changed</p>	<p>Dripolene. Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93329)</p> <p>Not specified Acute irritation Yes 1994 Rabbit, New Zealand White Males and females 3 None Instillation into conjunctival sac</p> <p>Rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a study room maintained at 69-72⁰F with relative humidity of 40-85% and a 12 hr light-dark cycle. Water and chow diet were available ad lib. The left eye was designated as the test eye and the right eye served as untreated control; 0.1ml of test article was instilled into the left conjunctival sac of 3 males and 3 females. Both eyes were grossly examined and the test eye was scored according to the Draize method at 1, 24, 48 and 72 hrs post-dose. The rabbits tested in this study were also concurrently evaluated for dermal irritation/corrosion to reduce the number of animals used (Study #65645 - see separate summary).</p> <p>Slight irritation of the iris was seen at 1 hr., which gradually resolved over 10 days; conjunctivae and cornea were irritated to a much greater extent but the effect also resolved over the 10-day post-dose period. One hour Draize scores were cornea, 16.7; iris, 2.5 and conjunctivae, 15.3. Total scores were: 1 hr. 34.5; 24 hr. 15.3; 48 hr, 10.7; 72 hr 9.9; 7 days, 4.5; 10 days, 1.7. Four rabbits had corneal ulceration; conjunctival redness and swelling; two of these rabbits had corneal opacity and iritis.</p> <p>Total Draize scores were: 1 hr. 34.5; 24 hr. 15.3; 48 hr, 10.7; 72 hr 9.9; 7 days, 4.5; 10 days, 1.7. Four rabbits had corneal ulceration; conjunctival redness and swelling; two of these rabbits had corneal opacity and iritis.</p> <p>1. Reliable without restriction.</p> <p>Rodriguez, S.C. and Dalbey, W.E. 1994. Ocular irritation of dripolene in the New Zealand White rabbit. Study #65644. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ. Rodriguez, S.C. and Dalbey, W.E. 1994. Acute dermal irritation/corrosion of dripolene in the New Zealand White rabbit. Study #65645. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p> <p>10/23/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<u>Test Substance</u>	Hydrogenated Pyrolysis Gasoline CAS# 68410-97-9. Clear liquid, aromatic odor
<u>Method</u> Method/guideline followed	Standard method (not referenced) with doses based on a limit test and range-finding study
Type (test type)	Acute LD50
GLP	Yes
Year	1984
Species/Strain	Rat, Fischer 344
Sex	Males and females
No. of animals per sex per dose	5
Vehicle	None
Route of administration	Oral
Test Conditions	Rats (99.9-134.0 g; 57 days old) were individually housed in screen-bottomed cages in a room with 70.6°F temperature, relative humidity of 59% and a 12 hr light/dark cycle. Chow diet and tap water from an automatic watering system were available ad lib. Rats were fasted for 24 hours prior to dosing at 4.2, 4.6, 5.0, and 5.4g/kg and observed at 1 and 4 hrs after dosing on day 1, and daily thereafter, over 14 days for clinical signs, morbidity and mortality. Gross necropsies were performed on all rats. LD50 was calculated by Probit analysis.
<u>Results</u> LD ₅₀ with confidence limits.	LD50 = 5.17g/kg (95% confidence limits: 5.02-5.45g/kg)
Remarks	On day 1, males and females showed dose responsive increases in ataxia, harsh respiratory sounds, and a non-dose responsive increase in red ocular discharge. Soft feces were observed in treated males and females on day 2. Frequency of clinical signs decreased by day 3 and signs were absent by day 5. There were no changes in body weight gain among the groups. Male and female mortalities were combined to calculate an LD50. Mortality from a previously performed limit test, conducted at 5.0g/kg was combined with results from the 5.0g/kg dose in this definitive study, raising that group number to 20. Mortalities were: 0/10 at 4.2, and 4.6g/kg, 7/20 at 5.0g/kg, 7/10 at 5.4g/kg. Gross necropsies revealed red lungs, gas-filled stomach and intestine, mottled liver, discoloration of kidney, and opaque eyes in rats that died during the study. These observations, with the exception of opacity in the left eye of one 5.4g/kg female, were absent in rats sacrificed at study termination (day 15).
<u>Conclusions</u> (study author)	The acute median lethal dose (LD50) for Hydrogenated Pyrolysis Gasoline in male and female rats was 5.17g/kg. A descriptive classification of Practically Non-toxic for acute oral exposure was assigned.
<u>Data Quality</u> Reliability	1. Reliable without restrictions.
<u>References</u>	Rausina, G.A. 1984. Acute oral toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2091. Gulf Life Sciences Center, Pittsburgh, PA
<u>Other</u> Last change	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p>	Hydrogenated Pyrolysis Gasoline CAS# 68410-97-9. Clear liquid, aromatic odor
<p><u>Method</u> Method/guideline followed Type (test type) GLP Year Species/Strain Sex No. of animals per sex /dose Vehicle Route of administration</p>	Standard method (not referenced) Acute LC50 Yes 1984 Rat, Fischer 344 Males and females 5 Filtered air Inhalation
<p>Test Conditions</p>	Rats (8 wks. old, 100-172g at initiation) were individually housed in stainless steel, screen-bottomed cages in a room maintained at 73.0 ^o F (75.5 ^o F during exposure) temperature, relative humidity of 51% (40% during exposure) and a 12 hr light/dark cycle. Rats received chow diet and tap water ad lib, except during exposure. One group of 10 rats was exposed to aerosolized test article generated by a ball jet nebulizer for 4 hrs. A condensing flask was used to prevent large particles from entering the chamber. Actual average chamber concentration was 12,408ppm (range 8,642-17,371ppm) determined by gas chromatography. Particulate phase was negligible. Rats were observed for clinical signs at 1 and 4 hrs after dosing on day 1 and daily thereafter over 14 days, and for morbidity and mortality twice daily on weekdays, once daily on weekends. Body wt. was determined at initiation and on days 8 and 15. Gross necropsies were performed on all rats at termination on day 15.
<p><u>Results</u> LC₅₀ with confidence limits.</p>	LC50>12,408ppm
<p>Remarks</p>	There were no deaths during the study, no effects on body wt gain, and no gross alterations were seen at necropsy. Immediately after exposure, all rats exhibited lethargy, increased and labored respiration, and ocular discharge; most animals showed twitching and dry red material around nose/mouth. There were a few instances of harsh respiratory sounds, trembling, and perianal soiling. These clinical signs decreased in frequency by 4 hr post-exposure and disappeared by day 2.
<p><u>Conclusions</u> (study author)</p>	No deaths occurred at the dose of 12,408ppm of test article, indicating a descriptive classification of Practically Non-toxic for acute inhalation exposure. Clinical signs noted immediately after exposure (increased/labored respiration, twitching, trembling, lethargy, ocular discharge) were not observed by day 2 and thereafter.
<p><u>Data Quality</u> Reliability</p>	1. Reliable without restrictions.
<p><u>References</u></p>	Rausina, G.A. 1984. Acute inhalation toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2092. Gulf Life Sciences Center, Pittsburgh, PA
<p><u>Other</u> Last change</p>	Revised 7/27/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

<p><u>Test Substance</u> <i>Test substance</i></p> <p><u>Method</u> Method/guideline followed Type System of testing GLP Year Species/Strain Metabolic activation Species and cell type Quantity Induced or not induced Concentrations tested Statistical Methods</p> <p>Remarks for Test Conditions</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. clear liquid with aromatic odor, negligible solubility in water, contains <55.0% benzene, <25% toluene, <10% dimethyl benzene/xylene, <7% pentane, <7% ethylbenzene, <3% cyclohexane, <2% hexane</p> <p>Standard method per Ames et al Reverse mutation bacterial assay Salmonella typhimurium, Escherichia coli with and without metabolic activation Yes 1991 S. typh. TA1535, TA1537, TA98, TA100; E. coli WP2(uvrA) Yes Male Sprague Dawley rat liver (S9 fraction), Molecular Toxicology, Inc., Annapolis, MD 20% S9 fraction in 0.5ml S9 mix/plate Aroclor 1254 induced, rats given a single 500mg/kg ip dose 0, 33, 100, 333, 1000, 3333, 10,000µg/plate ± S9. All diluted in acetone (200mg/ml) None specified. Test article considered mutagenic when it induces a reproductive, dose-related increase in number of revertants in one or more strains at 3 consecutive dose levels. A non-mutagen does not induce a dose-related increase in at least 2 independent tests.</p> <p>Hydrogenated pyrolysis gasoline (HPG) was prepared in acetone immediately prior to use. At end of the study, an aliquot of the stock dilution was sent to PTRL West, Richmond, CA to confirm concentration. Salmonella (approx. 10⁸ cells/ml) were exposed to either test material or acetone in 3 plates/dose ± S9 by the plate incorporation method. Six dose levels from 33-10,000µg/plate were employed in both the range-finding trial using TA100 and the mutagenicity test with all strains of Salmonella and E. coli. Optimum level of S9 for the mutagenicity assay was determined by testing the highest non-toxic dose, 10,000µg per plate with metabolic activation systems containing 4, 20 or 80% S9 fraction. No noteworthy increases in revertants or cytotoxicity was observed at any S9 concentration; 20% S9 was used in the mutagenicity test. All plates were incubated at 37⁰C for 48 hrs then revertant colonies were counted. Positive control compounds were: cultures-S9, sodium azide (5µg/plate) for TA1535, TA100; 9-aminoacridine (50µg/plate) for TA1537; 2-nitrofluorene (5µg/plate) for TA98; N-ethyl-N'-Nitro-N-Nitrosoguanidene (5ug/plate) for E. coli WP2, and cultures+S9, 2-anthramine (4µg/plate) for TA1535, TA1537, (2µg/plate) for TA98, TA100, and (20µg/plate) for E. coli WP2. Two independent assays were performed.</p> <p>HPG did not induce increases in number of revertant colonies and no toxicity was observed in any Salmonella strain or E. coli WP2 with or without 20% S9 metabolic activation in both studies. Positive control compounds performed appropriately.</p> <p>Hydrogenated pyrolysis gasoline is not mutagenic to bacteria under conditions of this assay.</p> <p>1. Reliable without restriction</p> <p>Riccio, E.S. and Stewart, K.R. 1991. Salmonella-Escherichia coli/microsome plate incorporation assay of Hydrogenated Pyrolysis Gasoline. SRI Study #2545-A03-91, Sponsor study #91-66. SRI International, Menlo Park, CA for Chevron Environmental Health Center, Richmond, CA</p> <p>5/7/2001 (Prepared by a contractor to the Olefins Panel)</p>
<p><u>Results</u> Genotoxic effects</p>	<p>HPG did not induce increases in number of revertant colonies and no toxicity was observed in any Salmonella strain or E. coli WP2 with or without 20% S9 metabolic activation in both studies. Positive control compounds performed appropriately.</p>
<p><u>Conclusions</u> (contractor)</p>	<p>Hydrogenated pyrolysis gasoline is not mutagenic to bacteria under conditions of this assay.</p>
<p><u>Data Quality</u> <i>Reliabilities</i></p>	<p>1. Reliable without restriction</p>
<p><u>Reference</u></p>	<p>Riccio, E.S. and Stewart, K.R. 1991. Salmonella-Escherichia coli/microsome plate incorporation assay of Hydrogenated Pyrolysis Gasoline. SRI Study #2545-A03-91, Sponsor study #91-66. SRI International, Menlo Park, CA for Chevron Environmental Health Center, Richmond, CA</p>
<p><u>Other</u> <i>Last changed</i></p>	<p>5/7/2001 (Prepared by a contractor to the Olefins Panel)</p>

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

<p><u>Test Substance</u> <i>Test substance</i></p> <p><u>Method</u> Method/guideline followed Type System of testing GLP Year Species/Strain Metabolic activation Species and cell type Quantity Induced or not induced Concentrations tested</p> <p>Exposure period Statistical Methods</p> <p>Remarks for Test Conditions</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. clear liquid with aromatic odor. Composition, purity and stability referred to sponsor.</p> <p>Standard method based on Cortesi et al (1983), Dunkel et al (1981), Reznikoff et al (1973) In vitro cell transformation Mouse embryo cells Yes 1984 BALB/3T3-A31 -1-1 from T. Kakunaga, National Cancer Inst., 1983 No NA NA NA Cytotoxicity: 8, 16, 32, 64, 128, 256, 512, 1024, 2048, and 5000µg/ml; Transformation: 100, 250, 500, 1500µg/ml, all diluted in 10% Pluronic[®] polyol F68 (prepared in deionized water, mol. wt. 8350, 80% hydrophilic). 2 days None employed. Criteria for positive response were a two-fold increase in type III foci at the highest dose over vehicle control (at least 2 type III foci if vehicle control had none) with or without a dose related response, or a two-fold increase at two or more consecutive doses. Test is equivocal if two-fold increase occurred at any one level other than the highest acceptable dose.</p> <p>Sufficient Hydrogenated Pyrolysis Gasoline (HPG) was weighed separately for each dose level, 0.40ml of 10% F68 added per ml of final volume and medium (Eagles MEM with 10% heat-inactivated fetal calf serum) added as required to achieve final volume for testing. Test preparations were mixed just prior to addition to cultures at 50µl to each 5 ml culture. All cultures were incubated at 37⁰C in 5% CO₂ enriched humidified atmosphere. For cytotoxicity, 2 cultures/dose group, 2 cultures for vehicle F68 or medium negative control were seeded with 1x10⁴ cells/plate in day 1, exposed on days 2-3, trypsinized and counted with a Coulter Model ZB on day 4 for at least 20% survival. For transformation, 15 cultures (1x10⁴ cells/flask/dose group) and two colony-forming cultures (100 cells/plate/dose group) were seeded on day 1, exposed on days 2-3 and culture medium changed on day 4. For transformation cultures, medium continued to be changed weekly to day 29. Positive control was 3-methylcholanthrene (1µg/ml). Colony forming cultures were fixed, stained, and counted visually on day 10 to determine cloning efficiency (avg. number colonies/plate ÷ 100 cells seeded). Transformation cultures were fixed and stained on day 29 for focus counting and evaluation. Transformation frequency = total type III foci ÷ total flasks/dose group.</p>
<p><u>Results</u> Genotoxic effects</p>	<p>HPG induced toxicity in BALB/3T3 cells after two days exposure beginning at 128 µg/ml (45.4% relative survival) with relative survivals of 26.7, 25.6, 3.2 and 0% at 512, 1024, 2048 and 5000µg/ml, respectively. In the transformation assay, toxicity was seen at all dose levels (relative cloning efficiencies of 53.7, 67.8, 78.5 and 0% at 100, 250, 500 and 1500µg/ml). At 1500µg/ml, the highest dose level, HPG induced 5 Type III foci; no other dose levels produced a positive response. Transformation frequencies were 0.13, 0, 0, 0.07 and 0.36 for medium control, vehicle control, 100, 250, 500 and 1500µg/ml, respectively. Positive and negative controls gave appropriate responses.</p>
<p><u>Conclusions</u> (contractor)</p>	<p>Hydrogenated Pyrolysis Gasoline induced transformation in BALB/3T3 cells under conditions of this assay. Cytotoxicity and impairment of cloning efficiency were also observed. The positive response was observed only at the highest dose level, a level that appeared to be too toxic for cells to recover and form colonies (0% relative colony forming efficiency)</p>

<p><u>Data Quality</u> <i>Reliabilities</i></p> <p><u>Reference</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>1. Reliable without restriction</p> <p>Brecher, S. 1984. Transformation test of Hydrogenated Pyrolysis Gasoline. Proj. #2098. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co, Houston, TX</p> <p>Cortesi, E. et al. 1983. Teratogenesis, Carcinogenesis, Mutagenesis 3: 101-110.</p> <p>Dunkel, V.A. et al. 1981. J. Nat'l Cancer Inst. 67: 1303-1315.</p> <p>Reznikoff, C.A. et al. 1973. Cancer Res. 3239-3249.</p> <p>Revised 8/27/2001 (Prepared by a contractor to the Olefins Panel).</p>
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Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

<p><u>Test Substance</u> <i>Test substance</i></p> <p><u>Method</u> Method/guideline followed Type System of testing GLP Year Species/Strain Metabolic activation Species and cell type Quantity Induced or not induced Concentrations tested</p> <p>Exposure period Statistical Methods</p> <p>Remarks for Test Conditions</p> <p><u>Results</u> Genotoxic effects</p> <p><u>Conclusions</u> (contractor)</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. clear liquid with aromatic odor. Composition, purity and stability referred to sponsor.</p> <p>Standard method based on Williams et al (1977, 1982) In vitro mammalian DNA repair assay Unscheduled DNA synthesis (UDS) in primary hepatocyte cultures Yes 1984 Fischer 344 male rat (10 wks old) No NA NA NA 8, 16, 32, 64, 128, 256, 512, 1024µg/ml diluted in 10% Pluronic F68 (prepared in deionized water, mol. wt 8350, 80% hydrophilic) 18 hrs. None specified. Criteria for positive response are incorporation of radioactive precursor (³H-thymidine) in cells that are not normally synthesizing DNA, indicating repair of damage. A positive response is defined as a mean net nuclear grain count at any treatment level that exceeds concurrent negative control by at least 6 grains/nucleus; negative control value must not exceed 5 grains. If this criterion is not met, a positive response can be identified if there is a significant difference (p<0.01) in % cells in repair at any dose level and negative control value. This indicator defines whether a small fraction of cells is undergoing repair (Casciano & Gaylor, 1983). A positive response need not be dose related.</p> <p>Sufficient Hydrogenated Pyrolysis Gasoline (HPG) was weighed separately for each dose level, 0.40ml of 10% F68 added per ml of final volume and sufficient medium (Williams Medium E with 10% fetal bovine serum and insulin) added to achieve final volume. Test preparations were mixed just prior to addition at 20µl to each 2ml culture. The conc. of ³H-thymidine (½ life 12.4 yrs.) used in these assays was 1mCi/ml. All cultures were incubated at 37°C in 5% CO₂ enriched humidified atmosphere. No range finding assay was performed. In the UDS assay, 2x10⁵ cells/ml were seeded into coverslip cultures, exposed to ³H-thymidine and test substance for 18 hours (3 cultures/dose level, 8 dose levels), untreated controls, vehicle F68 control and positive control, 2-acetyl aminofluorene (0.01µg/ml). Cells growing on coverslips were rinsed, fixed and glued to microscope slides on day 2. On day 3, slides were dipped in autoradiographic emulsion and stored in the dark at 2-8°C. Autoradiographs were developed, stained and coverslipped on day 10. Numbers of grains overlying 50 randomly selected nuclei/slide were counted. The highest of 3 cytoplasmic grain counts/cell were subtracted and this number was divided by a conversion factor (unspecified) to obtain net nuclear grain count. Avg. net nuclear grain count/slide (sum of net nuclear grain count ÷ 50) and mean net nuclear grain count (avg. net nuclear grain count/slide ÷ 3) were calculated. In addition, % cells in repair were determined for each dose level.</p> <p>HPG induced toxicity in primary hepatocytes following 18 hr exposure that left too few cells for UDS analysis at doses of 512 and 1024µg/ml. HPG did not induce unscheduled DNA synthesis at any dose level with sufficient cells to be analyzed. Positive and negative controls gave appropriate responses.</p> <p>Hydrogenated Pyrolysis Gasoline did not induce unscheduled DNA synthesis in primary cultures of rat hepatocytes under conditions of this assay.</p>
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<p><u>Data Quality</u> <i>Reliabilities</i></p> <p><u>Reference</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>2. Reliable with restrictions. No table of cell counts/viability. No individual data to verify calculations and identify conversion factor. Statistical criteria are mentioned but method is not cited.</p> <p>Brecher, S. 1984. Hepatocyte primary culture/DNA repair test of Hydrogenated Pyrolysis Gasoline. Proj. # 2097. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX</p> <p>Williams, G.M. 1977. Cancer Res. 37: 1845-1851</p> <p>Williams et al. 1977. In Vitro 13: 809-817</p> <p>Williams et al. 1982. Mut. Res. 97:359-370</p> <p>Casciano, D.A. and Gaylor, D.W. 1983. Mut. Res. 122:81-86</p> <p>5/7/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vivo

<p><u>Test Substance</u> Remarks</p> <p><u>Method</u> Method/guideline followed Type GLP Year Species Strain Sex</p> <p>Route of administration Doses/concentration levels Exposure period</p> <p>Statistical methods</p> <p>Remarks for Test Conditions.</p> <p><u>Results</u> Genotoxic effects NOAEL (NOEL) LOAEL (LOEL)</p> <p><u>Conclusions</u> (study authors)</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. Clear liquid with aromatic odor. Compositional analysis, purity and stability referred to sponsor.</p> <p>None specified. Comparable to standard assay. Mammalian bone marrow erythrocyte micronucleus assay Yes 1984 Mice Crl:CD-1(ICR)BR Swiss Male and female. Range-finding 2M, 2F (10 wks old)/group; 3 groups; Micronucleus test 10M, 10F (11 wks old)/group in 4 groups, 15M, 15F in one group. Oral gavage 0, 0.5, 1.0, 2.0g/kg (2doses), 2.0g/kg (1 dose) undiluted 1 dose/day for 2 days: one group- 1 dose, 1 day only</p> <p>Values from treated groups for daily mean body weights, group means and std. dev. for polychromatic erythrocytes (PCEs) with micronuclei (MN) , and group mean ratios of PCE to normochromatic erythrocytes (NORMs) were calculated and compared with vehicle control values by Student's t-test. Positive response was indicated by statistically significant (p<0.05) increases in micronucleated PCE at any dose level with a dose related response evident. Results were considered equivocal if only one of these criteria was met.</p> <p>Animals in the range-finding study (2M, 2F/group), 3 treated groups (no control group) were given 1.25, 2.5, and 5.0g/kg neat hydrogenated pyrolysis gasoline (HPG) by gavage once each day for two days. Eighty percent of the dose level that produced ~50% mortality was selected for the maximum dose in the micronucleus study. In the micronucleus study, three groups of mice were given undiluted HPG by oral gavage daily for two days at doses of 0.5, 1.0, 2.0g/kg, negative control mice were given corn oil (5g/kg). One-half of each treated group and negative control (5M, 5F) was killed on day 3 and the remainder on day 4. One group (15M, 15F), given 2.0 g/kg by gavage in a single dose for 1 day only, was killed on days 2, 3, 4 (5/sex/day). Positive control mice (4M, 4F) given cyclophosphamide (75 mg/kg) ip daily for 2 days were killed on day 3. Survival, body wt, and clinical signs were observed and recorded daily. Slides of femoral bone marrow smears were prepared, stained with May-Grunewald/Giemsa stain and examined microscopically. For each mouse, 1000 PCE and all associated mature erythrocytes (NORMs) were counted. Data collected included group mean body weights for each day, total PCEs, total NORMs, PCEs with MN, and NORMs with MN.</p> <p>NOAELmortality = 1.0g/kg; NOELgenetics > 2.0g/kg (Assigned by reviewer) In the range-finding study, half of the animals given HPG at conc of 5.0g/kg died on or before day 2. Gross necropsy of dead mice was unremarkable. In the micronucleus test, 1/10 males given 2.0g/kg (2 doses) died on day 2. No other mortality or significant wt changes were observed. Lethargy was observed among high dose mice. Surviving mice treated with HPG did not show any significant increase in micronucleus formation in PCE and no significant changes in ratio of PCE/NORM compared to negative controls. Negative and positive controls gave appropriate results.</p> <p>Oral treatment of mice with Hydrogenated Pyrolysis Gasoline for 1-2 days at doses up to 2.0g/kg/day had no effect on frequency of micronucleated polychromatic erythrocytes in bone marrow under these test conditions. HPG did not induce cytogenetic damage.</p>
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<u>Data Quality</u> <i>Reliabilities</i>	1. Reliable without restriction
<u>References</u>	Khan, S.H. 1984. Micronucleus test of Hydrogenated Pyrolysis Gasoline. Proj. #2096. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX
<u>Other</u> <i>Last changed</i>	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Repeated Dose Toxicity

<p><u>Test Substance</u> Remarks</p> <p><u>Method</u> Method/guideline followed Test type GLP Year Species Strain Route of administration Duration of test Doses/concentration levels Sex Exposure period Frequency of treatment Control group and treatment Post exposure observation period Statistical methods</p> <p>Test Conditions</p> <p><u>Results</u> NOAEL (NOEL) LOAEL (LOEL) Remarks</p> <p><u>Conclusions</u> (study authors)</p> <p><u>Quality</u> Reliabilities</p> <p><u>References</u></p> <p><u>Other</u> Last changed</p>	<p>Hydrogenated Pyrolysis Gasoline CAS #68410-97-9, Clear liquid with aromatic odor.</p> <p>Standard method, method not referenced Subacute Yes 1984 Rat Fischer 344 Inhalation 8 days 0, 4869±470, 9137±917ppm±SD, actual exposure conc. Males and females (5/sex/group) 6 hrs. once daily for 5 days (d1-5) 5M, 5F; filtered air 2 days Body wt variance compared by Bartlett's test and one way analysis of variance. Group mean body wt compared either with Dunnett's test or a modified t-test to assess significance.</p> <p>Rats (9 wks old, 113-195g at initiation) were housed individually in stainless steel, screen-bottomed cages. Rooms were maintained at 72.2°F (exposure chamber 75°F) with relative humidity of 54% (exposure chamber 50%), and 12 hr light/dark cycle. Rats received chow diet and tap water ad lib throughout the study, except during exposure. Three groups of 10 rats (5M, 5F/group) each, were exposed to test article or air. Test article was aerosolized with a ball jet nebulizer; an in-line condensing flask was used to prevent large particles from entering the exposure chamber. Chamber concentration of test article was measured by gas chromatography. Rats were observed twice daily on weekdays and once daily on weekends for morbidity/mortality, and once daily for clinical signs immediately after exposure on days 1-5. Surviving rats were sacrificed on day 8. Gross necropsies were performed on all rats.</p> <p>NOAEL< 4869ppm (estimated by reviewer) LOAEL= 4869ppm (estimated by reviewer) based on clinical observations, reduced wt gain. Two rats (1M, 1F) from group 3 (9137ppm) died on day 2; one female from group 3 died during exposure on day 1. Rats in groups 2 and 3 showed ocular discharge throughout d1-5. Rats in group 2 showed increased respiratory rate and dry red material around nose and mouth. All rats in group 2 were lethargic and showed labored respiration. Many rats in group 3 were lethargic and exhibited twitching and harsh respiratory sounds during days 1-5. All rats in group 2 and all but one survivor in group 3 appeared normal on day 8. Group mean body wt was significantly decreased in a dose related manner. No test article related effects were seen at gross necropsy on day 8; the male rat that died during the study showed gas in the G.I. tract and red-tinged fluid in the stomach.</p> <p>Exposure to test article caused a significant decrease in group mean body wt of male and female rats of low and high dose groups that was correlated with exposure level. Three deaths occurred in the high dose group during exposure. Major clinical signs were lethargy, twitching, harsh respiratory sounds and ocular discharge. No gross alterations were found in rats surviving to sacrifice.</p> <p>1. Reliable without restrictions</p> <p>Rausina, G.A. 1984. Five-day repeated dose inhalation toxicity study in rats of Hydrogenated Pyrolysis Gasoline. Proj. #2099. Gulf Life Sciences Center, Pittsburgh, PA</p> <p>Revised 7/27/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary – Group 5: High Benzene Naphthas

Fish Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Year (guideline) Type (test type) GLP Year (study performed) Species Analytical Monitoring</p> <p>Exposure Period Statistical Methods</p> <p>Test Conditions</p> <p>Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, supplier of organisms, age, size, weight, loading</p> <p><u>Results</u> Units/Value: Note: Deviations from protocol or guideline, analytical method, biological observations, control survival</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u> Reliabilities</p> <p><u>Reference</u></p> <p><u>Other</u> Last changed</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. 100% pure, colorless liquid.. Composition and stability referred to sponsor.</p> <p>OECD Guideline #203, US EPA 40CFR, Part 797.1400 1992 Static Fish Acute Toxicity- Water Accommodated Fraction (WAF) Yes 1993 Rainbow trout (<i>Oncorhynchus mykiss</i>) from Westacre Trout Farm, Norfolk, UK Total carbon analysis using Ionics TC/TOC Model 555 with infra-red gas analyzer to verify concentrations of 0,32, and 320mg/L(WAF) 96 hrs LC50 and 95% confidence limits were calculated by method of Thompson and Weil (1952, Biometrics 8: 51-54).</p> <p>Individual test material exposure solutions were prepared as WAFs by adding ratios of test material to dilution water equivalent to 32, 56, 100, 180, and 320mg/L, stirring with a propeller stirrer for 24 hr at 14°C. After settling for approx. 1hr, WAFs were withdrawn via a siphon into 2 replicate 20liter test vessels/dose group. Ten juvenile fish were introduced into each vessel containing 19cm of either test media or diluent water, an initial loading rate of 0.46g body wt/liter. Animals were exposed for 96 hrs without renewal. Fish were not fed for 48 hrs prior to or during exposure; supplementary aeration was not provided. Average size of fish was determined by measuring control fish at end of exposure: mean std. length= 4.3±0.23cm, mean wt.= 0.92±0.14g. Exposure temperature was 14±1°C, photoperiod was 16hr light/8hr dark (light intensity not specified); pH increased from 7.5 to 7.9 with increasing dose; mg dissolved O₂/liter was 7.8-8.2 in controls and doses up to 180mg/L, and 9.6-9.8 at 320mg/L (WAF). TC/TOC analysis was not performed at 96 hr since values obtained at 0 hr indicated that TC(dissolved) analysis was not appropriate for verification of HPG(WAF) concentrations; exposure media results were similar to control levels. Criteria for death were absence of respiratory movement and absence of response to physical stimulation of caudal peduncle.</p> <p>24 hr LC₅₀ = 230mg/L; 48 hr and 72 hr LC₅₀ = 180mg/L 96 hr LC₅₀ = 170mg/L. 100% mortality occurred at 320mg/L by 24 hrs. Other marked reactions to exposure at 180 and 320mg/L were lethargy, loss of equilibrium and moribundity.</p> <p>The 96 hr LC₅₀ for Hydrogenated Pyrolysis Gasoline WAF in rainbow trout is 170mg/L (95% CL= 150-200) based on nominal values. The no observed effect level (NOEL) is 100 mg/L (WAF)</p> <p>2. Reliable with restriction. Analytical method was inappropriate.</p> <p>Douglas, M.T. 1993. Hydrogenated pyrolysis gasoline (Water accommodate fraction) Acute toxicity to Rainbow trout (<i>Oncorhynchus mykiss</i>). CRTC Ref. #92-79. Huntingdon Research Centre, Ltd., Cambridgeshire, England, for Chevron Research and Technology Co., Richmond, CA</p> <p>Revised 7/27/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary – Group 5: High Benzene Naphthas

Algal Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Year (guideline) Type (test type) GLP Year (study performed) Species</p> <p>Analytical Monitoring</p> <p>Exposure Period</p> <p>Statistical Methods</p> <p>Test Conditions</p> <p>Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, age.</p> <p>Results Units/Value: Measurement (cells/growth)</p> <p>Note: Deviations from protocol or guideline, analytical method, biological observations, control survival</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u> Reliabilities</p> <p><u>Reference</u></p> <p><u>Other</u> Last changed</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. 100% pure, colorless liquid.. Composition and stability referred to sponsor.</p> <p>OECD Guideline #201, US EPA 40CFR 797.1050 1992 Algae acute toxicity- Water accommodated fraction (WAF) Yes 1993 Fresh water green algae (<i>Selenastrum capricornutum</i>), strain # CCAP278/4 from Freshwater Biological Assoc. Cumbria, UK Yes. Total carbon analysis using Ionics TC/TOC Model 555 with infrared gas analyzer to verify test conc. at 0, 62.5 and 1000mg/L (WAF) at 0 and 96 hrs. 96 hrs None specified</p> <p>Individual test material solutions were prepared as WAF by adding ratios of test material to dilution water equivalent to 62.5, 125, 250, 500 and 1000mg/L, stirred on a magnetic stirrer for 24 hr at 24^oC. After settling for approx. 1hr, WAFs were withdrawn by siphon and 100ml measured into 250 ml conical flasks. Two ml of algal suspension in log phase (0.802 absorbance at 665nm) were added to each of 3 flasks/dose level. Cultures were incubated without media renewal for 96 hrs under continuous illumination of approx. 7000 lux, provided by 7x30W “warm white “ 1 meter fluorescent tubes in a Gallenkamp Illuminated Orbital Incubator at 24±1^oC and oscillation of 120 cycles/min. Samples were taken at 0, 24, 48, 72 and 96 hr and absorbance measured in a spectrophotometer at 665nm wavelength. Cell densities of control cultures were counted with a haemocytometer at initiation and study termination. pH values ranged from 7.8-8.0 at initiation and 7.6-8.4 at 96 hrs. Index of growth was calculated from the area under the growth curve; percent inhibition of growth at each dose was calculated by comparing the area under test curve with control. Median effective conc. for inhibition of growth (EbC₅₀) is based on comparison of areas under growth curves after 72 and 96 hrs. Avg. max growth rate is calculated from the log phase of growth curve for each culture. ErC₅₀ is the median effective conc. for inhibition of growth based on comparison of max growth (24-48 hrs).</p> <p>Mean cell densities of control cultures at initiation (0 hr)= 8.91x10⁴ cells/ml and at termination (96 hrs) = 2.41x10⁶ cells/ml. No cultures were contaminated and no abnormalities were seen in any culture upon microscopic examination at 96 hrs. Total dissolved carbon was 7.1, 7.0, 17.2 mg/L at initiation and 9.7, 7.9 and 13.0mg/L at 96hrs for 0(control), 62.5 and 1000 mg/L (WAF) respectively. Biomass: EbC₅₀ (72 hr) >1000 mg/L (WAF); EbC₅₀ (96 hr) >1000 mg/L (WAF) Growth rate: ErC₅₀ (24-48hr) >1000mg/L (WAF) NOAEL = 125mg/L</p> <p>Hydrogenated pyrolysis gasoline is not inhibitory to the growth of <i>Selenastrum capricornutum</i> at conc of 125mg/L (WAF). EbC₅₀ (96hr) and ErC₅₀ (24-48hrs) are both >1000mg/L (WAF).</p> <p>1. Reliable without restriction</p> <p>Douglas, M.T. 1993. Hydrogenated pyrolysis gasoline (Water accommodated fraction) Algal Growth Inhibition. CRTC Ref. #92-81. Huntingdon Research Centre, Ltd, Cambridgeshire, England, for Chevron Research and Technology Co, Richmond, CA</p> <p>5/10/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary – Group 5: High Benzene Naphthas

Biodegradation

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Year (guideline) Type (test type) GLP Year (study performed) Inoculum</p> <p>Exposure Period</p> <p>Test Conditions</p> <p>Note: Concentration prep., vessel type, replication, test conditions.</p> <p><u>Results</u> Units/Value:</p> <p>Note: Deviations from protocol or guideline, analytical method.</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u> Reliabilities</p> <p><u>Reference</u></p> <p><u>Other</u> Last changed</p>	<p>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9 100% pure, colorless liquid.. Composition and stability referred to sponsor.</p> <p>OECD guideline 301D; EEC directive 67/548 Annex V part C.6 (84/449/EEC) 1984 Aerobic Aquatic Biodegradation (Closed Bottle Test) Yes 1993 Domestic activated sewage sludge bacteria from Huntingdon Research Centre sewage treatment plant.</p> <p>28 days</p> <p>Hydrogenated pyrolysis gasoline (HPG, 2mg/L) was added, via a Hamilton microliter syringe to reduce loss of volatile constituents, to culture bottles containing inorganic nutrient medium with or without activated sewage sludge bacteria. The nutrient medium consisted of aerated reverse osmosis purified, deionized water, phosphate buffer, magnesium sulfate, calcium chloride and ferric chloride. Activated sewage sludge filtrate was added at a rate of 1 drop of inoculum/liter. Glass 500ml culture bottles covered in foil, fitted with plastic screw caps and PTFE faced sealing discs of ethylene propylene, were filled by siphon and tightened to exclude all air bubbles. Duplicate bottles were prepared in each test and control series to allow single oxygen determination/bottle at 0, 5, 15, and 28 days. Sodium benzoate (3mg/L), the standard substance, was dispensed directly into sludge-inoculated nutrient medium, or added to a sludge-inoculated medium containing 2mg/L HPG. The bottles containing HPG+sodium benzoate were sampled on day 0 and 28 only to examine inhibitory effects. All bottles were incubated in a water bath at 20±1⁰C; measurements of dissolved oxygen conc. were made with a Yellow Springs BOD meter. Concentrations of HPG or sodium benzoate as mg carbon/L were not provided.</p> <p>Percent biodegradation values were calculated as % of Theoretical Oxygen Demand (NO₃); TOD_(NO₃) was 3.15mgO₂/mg for HPG and 1.67mgO₂/mg for sodium benzoate. Hydrogenated pyrolysis gasoline attained 68% biodegradation within 28 days but did not degrade 60% within 10 days of exceeding the 10% degradation level. HPG is thus not readily biodegradable. Sodium benzoate degraded 86% within 28 days. Cultures containing both HPG and sodium benzoate showed an oxygen depletion value 5% lower than separate cultures. HPG is not considered to have an inhibitory effect on sewage bacteria.</p> <p>Hydrogenated pyrolysis gasoline is not readily biodegradable but is considered ultimately biodegradable. No inhibitory effects on sewage bacteria were observed in this assay.</p> <p>1. Reliable without restriction</p> <p>Douglas, M.T. 1993. Hydrogenated Pyrolysis Gasoline Ready Biodegradability (Closed Bottle Test). CRTC Ref. #92-82. Huntingdon Research Centre Ltd. Cambridgeshire England for Chevron Research and Technology Co., Richmond, CA</p> <p>5/10/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u> Method/guideline followed Type (test type) GLP Year Species/Strain Sex No. of animals per sex per dose Vehicle Route of administration</p> <p>Test Conditions</p> <p><u>Results</u> LD₅₀ with confidence limits.</p> <p>Remarks</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u> Reliability</p> <p><u>References</u></p> <p><u>Other</u> Last changed</p>	<p>Pyrolysis gasoline (Rerun Tower Overheads) Yellow, homogeneous liquid, stable for 5 years at ambient temperature.</p> <p>Not specified Acute, limit test Yes 1994 Rat, Sprague-Dawley Males and females 5 None Oral gavage</p> <p>Sprague Dawley rats (180-350g) were individually housed in stainless steel suspended cages and fasted overnight prior to administration of 2g/kg neat pyrolysis gasoline. The study room was maintained at 68-72⁰F with a relative humidity of 35-63% and a 12 hr light-dark cycle. Water and chow diet were available ad lib after dosing. Test article was administered once on day 1 by oral gavage through a blunted needle. Rats were observed for clinical signs approx. 30 min, 1hr and 4hr, after dosing, and daily thereafter until sacrifice on day 15. Rats were checked once a day for mortality and moribundity. Observations were not made on weekends. Body wts were recorded prior to fasting and on days 1, 8 and 15.</p> <p>The LD₅₀ was not reached at 2g/kg. There were no deaths and all rats gained some weight during the study. Clinical signs noted in one or more rats were salivation, decreased activity, rales, lacrimation, chromodacryorrhea, ataxia, chromorhinorrhea, miosis, slight tremors, mydriasis, hyperactivity, hypothermia, urogenital discharge, nasal discharge, decreased food consumption, decreased fecal output, vocalization, and penile discharge. No gross pathological findings were noted at necropsy.</p> <p>The LD₅₀ was not reached at 2g/kg.</p> <p>1. Reliable without restriction.</p> <p>Rodriguez, S.C. and Dalbey, W.E. 1994. Acute oral toxicity of pyrolysis gasoline in Sprague Dawley Rats. Study #65636. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p> <p>10/16/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u></p> <p>Method/guideline followed</p> <p>Type (test type)</p> <p>GLP</p> <p>Year</p> <p>Species/Strain</p> <p>Sex</p> <p>No. of animals per sex per dose</p> <p>Vehicle</p> <p>Route of administration</p> <p>Test Conditions</p> <p><u>Results</u></p> <p>LD₅₀ with confidence limits.</p> <p>Remarks</p> <p><u>Conclusions</u></p> <p>(study author)</p> <p><u>Data Quality</u></p> <p>Reliability</p> <p><u>References</u></p> <p><u>Other</u></p> <p>Last changed</p>	<p>Pyrolysis gasoline (Rerun Tower Overheads). Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93328)</p> <p>Not specified</p> <p>Acute, limit test</p> <p>Yes</p> <p>1994</p> <p>Rabbit, New Zealand White</p> <p>Males and females</p> <p>3</p> <p>None</p> <p>dermal</p> <p>Rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a study room maintained at 69-72⁰F with a relative humidity of 38-85% and a 12 hr light-dark cycle. Water and chow diet were available ad lib. The dorsal skin surface extending down from the front to rear legs and from left to right lower flanks was clipped free of hair the day prior to test article administration. Test article was spread evenly over the clipped area (approx. 10% of body surface area) at a dose of 2g/kg. A layer of 8-ply gauze was placed on the dorsal site, and a rubber dam sleeve was fitted snugly over the gauze pad and around the trunk. Edges of the dam were taped in place. An Elizabethan collar was affixed to the neck to prevent oral ingestion of test article and mechanical irritation of the test site. After 24 hrs, the collar and wrappings were removed and residual test article was wiped off. Body wts were recorded on days 1, 8 and 15. Rabbits were observed for toxicity at about 1 and 2 hr post-dose and daily thereafter on weekdays through day 14. Observations for mortality/moribundity were made daily. Rabbits were sacrificed on day 15 and necropsies were performed.</p> <p>The LD₅₀ was not reached at 2g/kg. There were no deaths during the study and rabbits either gained some weight or remained at day 1 body wt. Signs that might have resulted from treatment in one or more rabbits were: soft stool, decreased fecal pellet size, nasal discharge, and test site erythema. No gross pathological findings were noted at necropsy.</p> <p>The LD₅₀ was not reached at 2g/kg.</p> <p>1. Reliable without restriction.</p> <p>Rodriguez, S.C. and Dalbey, W.E. 1994. Dermal toxicity of pyrolysis gasoline in the New Zealand White rabbit. Study #65637. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p> <p>10/16/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p>	<p>Pyrolysis gasoline (rerun tower overhead). Yellow, homogeneous liquid. Stable for 5 years at ambient temperature. (CRU #93328)</p>
<p><u>Method</u></p> <p>Method/guideline followed</p> <p>Type (test type)</p> <p>GLP</p> <p>Year</p> <p>Species/Strain</p> <p>Sex</p> <p>No. of animals per sex per dose</p> <p>Vehicle</p> <p>Route of administration</p> <p>Test Conditions</p>	<p>Not specified.</p> <p>Acute irritation</p> <p>Yes</p> <p>1994</p> <p>Rabbit, New Zealand White</p> <p>Males and females</p> <p>3</p> <p>None</p> <p>Dermal</p> <p>Three males and 3 female rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a room maintained at 69-72⁰F with relative humidity of 38-85% and 12hr light-dark cycle. Water and chow diet were available ad lib. One 1sq. inch test site was selected on the right anterior flank of 4 animals and the left anterior flank of 2 animals. The sites were designated as anterior flank (1-hr occlusion) test sites. A second 1 sq. inch test site was selected on the right posterior flank of 4 animals and the left posterior flank of 2 animals. The sites were designated as posterior flank (4-hr occlusion) test sites. The test sites were not abraded. 0.5ml of test substance was applied to the posterior test site under 1 sq. inch Webril patch. The patch was secured to the skin with an occlusive rubber dam followed by surgical tape. 0.5ml of test substance was applied to the anterior test site under a 1 sq. inch patch and similarly secured. Following 1hr exposure, the anterior patch was removed and the site evaluated for DOT corrosion. This site was reevaluated at 48hrs post-dosing. After the initial evaluation, residual test substance was removed by gently wiping the site with saline dampened cotton. Following a 4hr exposure, the posterior patch was removed and the site evaluated for DOT corrosion and OSHA Primary Irritation Index (PII). This site was reevaluated at 48hrs post-dosing. After the initial evaluation, the residual test substance was removed by gently wiping the site with saline dampened cotton. The posterior test site was also evaluated for dermal irritation according to the Draize method at 4.5, 28, 52, and 76hrs and at 7, 10 and 14 days post-dosing. Clinical observations were recorded at approx. 1hr and 4hr post-dosing and daily thereafter. The condition of each animal was checked once daily in the morning. The rabbits in this study were concurrently evaluated for ocular irritation to reduce the number of animals used. (Study 65638, see separate summary)</p>
<p><u>Results</u></p>	<p>The test material was negative for DOT corrosion after 1hr and 4hr occlusions, and 48hr post-dose. After the 4hr occlusion, the 4.5hr to 14day post-dose Draize scores for erythema and edema varied between 2.2 and 3.2, and 1.5 to 3.3, respectively, with no trend over time. The OSHA PII score was 4.7, corresponding to a rating of "non-irritant". Diarrhea, soft stool, decreased fecal pellet size and nasal discharge were observed during the study.</p>
<p>Remarks</p>	
<p><u>Conclusions</u> (study author)</p>	<p>The test article was rated non-corrosive by DOT criteria after 1hr and 4hr occlusions, and non-irritating by OSHA PII criteria.</p>
<p><u>Data Quality</u></p> <p>Reliability</p>	<p>1. Reliable without restrictions.</p>
<p><u>References</u></p>	<p>Rodriguez, S.C. and Dalbey, W.E. 1994. Acute dermal irritation/corrosion of pyrolysis gasoline in the New Zealand White rabbit. Study #65639. Stonybrook Laboratories, Inc., Princeton, NJ. for Mobil Chemical Co., Edison, NJ</p>
<p><u>Other</u></p> <p>Last changed</p>	<p>10/23/2001 (Prepared by a contractor to the Olefins Panel)</p>

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

<p><u>Test Substance</u></p> <p><u>Method</u></p> <p>Method/guideline followed</p> <p>Type (test type)</p> <p>GLP</p> <p>Year</p> <p>Species/Strain</p> <p>Sex</p> <p>No. of animals per sex per dose</p> <p>Vehicle</p> <p>Route of administration</p> <p>Test Conditions</p> <p><u>Results</u></p> <p>Remarks</p> <p><u>Conclusions</u> (study author)</p> <p><u>Data Quality</u></p> <p>Reliability</p> <p><u>References</u></p> <p><u>Other</u></p> <p><i>Last changed</i></p>	<p>Pyrolysis gasoline (Rerun Tower Overheads). Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93328)</p> <p>Not specified</p> <p>Acute irritation</p> <p>Yes</p> <p>1994</p> <p>Rabbit, New Zealand White</p> <p>Males and females</p> <p>3</p> <p>None</p> <p>Instillation into conjunctival sac</p> <p>Rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a study room maintained at 69-72⁰F with relative humidity of 38-85% and a 12 hr light-dark cycle. Water and chow diet were available ad lib. The left eye was designated as the test eye and the right eye served as untreated control; 0.1ml of test article was instilled into the left conjunctival sac of 3 males and 3 females. Both eyes were grossly examined and the test eye was scored according to the Draize method at 1, 24, 48 and 72 hrs post-dose. The rabbits tested in this study were also concurrently evaluated for dermal irritation/corrosion to reduce the number of animals used (Study #65639- see separate summary).</p> <p>Cornea and iris were not affected by treatment, however conjunctivae yielded Draize scores of 13.7 (1hr); 3.7 (24hr); 2.3 (48hr) and 0.7 (72hr).</p> <p>Pyrolysis gasoline produced conjunctival irritation shortly after instillation that cleared almost completely by 72 hrs.</p> <p>1. Reliable without restriction.</p> <p>Rodriguez, S.C. and Dalbey, W.E. 1994. Ocular irritation of pyrolysis gasoline in the New Zealand White rabbit. Study #65638. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p> <p>Rodriguez, S.C. and Dalbey, W.E. 1994. Acute dermal irritation/corrosion of pyrolysis gasoline in the New Zealand White rabbit. Study #65639. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.</p> <p>10/16/2001 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

<p><u>Test Substance</u> <i>Test substance</i></p>	<p>Rerun Tower Overheads from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% C4, C6-C8 and xylene.</p>
<p><u>Method</u> Method/guideline followed Type System of testing GLP Year Species/Strain Metabolic activation Species and cell type Quantity Induced or not induced Concentrations tested</p>	<p>Standard method based on Ames et al, 1975 Reverse mutation bacterial assay Salmonella typhimurium with and without metabolic activation Yes 1981 S. typhimurium TA 98, TA100, TA1535, TA1537, and TA1538. Yes Sprague Dawley male rat liver (S9 fraction) from Litton Bionetics, Kensington, MD 50ul S9 fraction in 0.5ml S9 mix/plate Aroclor 1254-induced, rats were given a single ip 500mg/kg dose, 5 days prior to sacrifice. 0, 0.029, 0.094, 0.30, 0.97µl/plate –S9, and 0.094, 0.30, 0.97, and 3.1µl/plate + S9; samples diluted in dimethyl sulfoxide (DMSO). Negative control 50µl DMSO</p>
<p>Statistical Method</p>	<p>None. Criteria for a positive response were an increase in revertant colonies at least two-fold that of negative control at the lowest active dose, and a dose response curve. Positive results must be reproducible in an independent repeat assay.</p>
<p>Remarks for Test Conditions</p>	<p>Rerun tower overheads test solutions were prepared in DMSO immediately prior to use. Salmonella (Approx. 1.4×10^8 cells/ml) were exposed to either test solution or DMSO ±S9 by the preincubation method. Doses of 0.029-0.97µl/plate-S9 and 0.094-3.1µl/plate +S9 were determined by a pretest toxicity test in TA 100 and TA1537±S9 using incremental doses from 0.01-10µl/plate. Culture tubes containing 50µl test solution or DMSO, 0.1ml Salmonella and 0.5 ml phosphate buffer or S9 mix were combined and incubated with shaking (150 rpm) for 20 minutes at 37°C. At the end of the preincubation period, top agar was added, mixed and cultures were overlaid on minimal agar plates, 3 plates/dose/strain. Plates were incubated at 37°C for 48 hrs, then counted automatically (Biotran II) and background lawn evaluated by stereomicroscope. Positive control compounds were: -S9, 2-nitrofluorene (2-NF, 20µg/plate) for TA98 and TA1538; N-methyl-N'-nitro-N-nitrosoguanidine (MNNG, 2.0µg/plate) for TA100 and TA1535; 9-aminoacridine (9-AA, 25µg/plate) for TA1537; +S9 2-aminoanthracene (2µg/plate) for all strains except TA1537.</p>
<p><u>Results</u> Genotoxic effects</p>	<p>The preliminary toxicity test exhibited severe toxicity at 10µl/plate with activation and at 3.1 and 10µl/plate without activation (individual data not shown). In the mutagenicity test, none of the 5 strains of Salmonella exhibited revertant frequencies substantially different from the solvent or spontaneous controls at any dose level with or without metabolic activation (e.g. TA98-S9: 16, 15, 12, 12, and 0 average revertants/plate and TA100-S9: 111, 115, 107, 94, and 0 at 0[DMSO], 0.029, 0.094, 0.30, and 0.97µl/plate, respectively; TA98+S9: 33, 26, 26, 22, and 0 revertants/plate, and TA100+S9: 128, 161, 128, 118, and 0 revertants/plate at 0[DMSO], 0.094, 0.30, 0.97 and 3.1µl/plate, respectively). Clearing of background lawn and microcolonies were observed at the maximum doses (0.97µl/plate-S9; 3.1µl/plate+S9). Positive control compounds (2 plates/strain) performed appropriately (-S9: MNNG 1906, 1883 revertants/plate in TA 100 and TA1535, respectively; 9-AA 586 revertants/plate in TA1537; 2-NF 2114, 1214 revertants/plate in TA98 and TA1538, respectively; and +S9 2-aminoanthracene 406-2307 revertants/plate for all strains except TA1537). The results of this assay indicate that rerun tower overheads had no mutagenic activity in this test system. (Reviewer's note: Due to toxicity, tests were performed over a low dose range; 3 of 4 doses were non-toxic and showed sufficient growth to evaluate mutagenicity. Testing at any lower doses was impractical).</p>
<p><u>Conclusions</u></p>	<p>Rerun Tower Overheads did not induce an increase in revertant colonies in any Salmonella</p>

<p>(contractor)</p> <p><u>Data Quality</u> <i>Reliabilities</i></p> <p><u>Reference</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>strain, tested at any dose level with or without metabolic activation in this single Ames test.</p> <p>1. Reliable without restriction</p> <p>Blackburn, G.R. 1981. An Ames Salmonella/mammalian microsome mutagenesis assay for the determination of potential mutagenicity of Rerun Tower Overheads from an olefins/aromatics plant. Study No. 1781-80. Mobil Environmental and Health Sciences Laboratory, Princeton, NJ.</p> <p>Ames B. N. et al. 1975. Mutat. Res. 31: 347-364.</p> <p>10/02/2001 (Prepared by a contractor for the Olefins Panel)</p>
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Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

<p><u>Test Substance</u> <i>Test substance</i></p>	Rerun tower overheads (RT0, 0818805). Compositional analysis, stability and purity referred to sponsor
<p><u>Method</u> Method/guideline followed Type System of testing GLP Year Species/Strain Metabolic activation Species and cell type Quantity Induced or not induced Concentrations tested</p>	<p>Standard method, no guideline specified Cell transformation Mouse embryo cells Yes 1981 BALB-c/3T3 mouse cell line No NA NA NA Initial cytotoxicity: 0, 0.01, 0.1, 1.0, 10.0, 100.0µg/ml medium; Transformation: 0, 0.8, 4.0, 20.0 and 100µg/ml, diluted in dimethyl sulfoxide. Negative control was DMSO at 2.5% vol. concentration.</p>
<p>Statistical Method</p>	T-test specified. Standard criteria for positive response is a two fold increase in type III foci at highest dose over vehicle control with or without a dose related response or a 2 fold increase at 2 or more consecutive doses.
<p>Remarks for Test Conditions</p>	<p>Routine procedures were referred to Appendix 1 Standard Operating Procedures, which was not included with this report. Only specifics unique to this assay are presented. Due to the volatile nature of test material, the cytotoxicity assay and transformation assays were conducted in tightly capped T-25 flasks in sealed plastic bags. The pH of medium during the 72hr exposure period was maintained at 7.4 by 0.02M Hepes buffer in flasks. RTO was prepared as a 1% stock solution in DMSO, which, when added to culture medium at a 2.5% vol. conc. was a suspension. Despite limited solubility, RTO produced a dose-dependent cytotoxic effect after a 3-day exposure period. In the initial toxicity assay, RTO was added to flasks, seeded with BALB-c/3T3 cells, at concentrations of 0, 0.01, 0.1, 1.0, 10.0 and 100.0µg/ml, incubated for 3 days at 37°C in a CO₂ in air incubator, after which cells were counted for survival. In the transformation assay, RTO was tested at 0, 0.8, 4.0, 20.0 and 100µg/ml. In a standard BALB-c/3T3 transformation assay, colony formation cultures (approx. 100 cells/culture) and transformation cultures (approx. 10⁷ cells/culture, 20 cultures/dose) were seeded on day 1, exposed to test material for 2-3 days, and culture medium was changed on day 4. For transformation cultures, medium continued to be changed weekly to day 29. Colony formation cultures were fixed, stained and counted visually on day 8 to determine cloning efficiency; transformation cultures were fixed and stained on day 29 for focus counting and evaluation. Transformation frequency = total type III foci ÷ total cultures/dose. Positive control compound was 3-methyl cholanthrene (2µg/ml).</p>
<p><u>Results</u> Genotoxic effects</p>	<p>RTO induced toxicity in BALB-c/3T3 cells after 3 days exposure at concentrations of 10µg/ml (59% viability) and at 100µg/ml (18% viability). In the transformation assay, inhibition of cloning efficiency (CE, clones/100 cells) occurred at 4.0µg/ml (89% CE), 20.0µg/ml (81% CE) and 100µg/ml (65% C.E.); cell toxicity was somewhat less than in the initial cytotoxicity assay [40% viability at 100µg/ml]. RTO did not induce statistically significant increased incidence of transformed foci compared to negative controls at any dose level. Values were 0.10 foci/flask, 2/20 flasks with foci at 100µg/ml, 0.0 foci/flask, 0/20 flasks with foci at 20.0µg/ml, 0.15 foci/flask, 3/20 flasks with foci at 4.0µg/ml, 0.10 foci /flask, 2/20 flasks with foci at 0.8µg/ml compared to 0.05 foci/flask, 1/20 flasks with foci in negative control group. [Reviewer's note: Negative control value of 1 focus/20 flasks was lower than control values in other concurrent studies on 2 other compounds in this series where negative controls had 4 foci in 20 flasks (0.20 foci/flask)]. Positive control compound, 3 methyl cholanthrene, induced 56 foci/19 flasks (2.95 foci/flask),</p>

<p><u>Conclusions</u> (contractor)</p> <p><u>Data Quality</u> <i>Reliabilities</i></p> <p><u>Reference</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>18/19 flasks with foci.</p> <p>Rerun tower overheads did not induce neoplastic transformation in BALB-c/3T3 cells and was not active in this test system.</p> <p>2. Reliable with restrictions. Complete details of assay methods are not included in the report. Specifics of statistics are not supplied.</p> <p>Tu, A.S. and Sivak, A. 1981. BALB-c/3T3 Neoplastic transformation assay on 0818802, 08188003 and 08188005 (Rerun tower overheads). ALD Ref. #86374. Arthur D. Little, Inc. Cambridge, MA for Mobil Oil Corp, Study #1771-80, Princeton, NJ</p> <p>Roy, T.A., 1981. Analysis of rerun tower bottom oil by combined capillary gas chromatography/mass spectrometry. Study #1272-81-. Toxicology division, Mobil Oil Co., Princeton, NJ</p> <p>12/07/01 (Prepared by a contractor to the Olefins Panel)</p>
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Robust Summary – Group 5: High Benzene Naphthas

Developmental Toxicity/Teratogenicity

<p><u>Test Substance</u> Remarks</p> <p><u>Method</u> Method/guideline followed Test type GLP Year Species Strain Route of administration Concentration levels Sex Exposure period Frequency of treatment Control group and treatment Duration of test Statistical methods</p> <p>Remarks for Test Conditions.</p>	<p>Rerun Tower Overheads, light thermal cracked naphtha, CAS #64741-74-8. Unsaturated hydrocarbons in C4-C8 range; boiling over 20-120⁰C (68⁰-248⁰F); approximately 40% benzene, 26% C5, 13% toluene, 20% C4, C6-C8 and xylene.</p> <p>Standard method, no guidelines specified</p> <p>Teratology Yes 1981 Rabbit New Zealand white Oral gavage 0,10, 25 and 50mg/kg/day in Mazola® corn oil Female; 16 pregnant rabbits/group Days 6-28 of gestation Once/day 16 pregnant rabbits; 0.5ml corn oil/kg/day 32 days (from artificial insemination to Caesarean section on day 29 of gestation) Chi-square test with Yates's correction for 2x2 contingency tables and/or Fisher's exact probability test used for male/female sex distribution and number of litters with malformations. Mann-Whitney U test to compare number of early and late resorptions, and postimplantation losses. Analysis of variance (one-way), Bartlett's test and T-test (for equal and unequal variance) with Dunnett's multiple comparison tables used to compare mean number of viable fetuses, total implantations, corpora lutea and mean fetal body weights. All comparisons at p<0.05.</p> <p>Sixty-four sexually mature, virgin NZW female rabbits (7 months old, 3.4 - 4.2kg) were ear-tagged and individually housed in suspended wire cages in a room with temperature and humidity control (data not presented), a 12 hr light-dark cycle and special ventilation due to volatility of test sample. Purina Certified Rabbit Chow® and tap water were available ad lib. Sperm was collected from each of 6 proven NZW breeder males, using an artificial vagina. Semen was immediately evaluated for motility and used for insemination only if motility was =55%. Useable ejaculate was diluted with 0.9%NaCl at 35⁰C; 0.25-0.50ml of dilute semen introduced into the anterior vagina. Ovulation was induced by injection of 100 units of chorionic gonadotropin (Ayerst, NY) in the marginal ear vein of the female immediately after insemination. Semen from each male was used to inseminate an equal number of females in each group. Insemination was performed over 2 days; day of insemination was designated day 0 of gestation.</p> <p>Rerun tower overhead test solutions were prepared daily in corn oil and shaken by hand to ensure proper mixing. No analysis of dosing solution compositions was provided. Dosage levels of 0, 10, 25 and 50mg/kg/day were administered at a constant volume of 0.5ml/kg by oral gavage once daily from day 6-28 of gestation. Individual doses were determined from body wt recorded on gestation day 6. Dams were observed daily for mortality, overt changes in appearance and behavior, and clinical signs of toxicity during treatment. Maternal body wts were recorded on gestation days 0, 6, 12, 18, 24 and 29. On gestation day 29, all females were sacrificed by an overdose of sodium pentobarbital in the marginal ear vein; the uterus was excised and weighed prior to removal of fetuses. Number and location of viable and non-viable fetuses, early and late resorptions, total implantations and corpora lutea were recorded. Abdominal and thoracic cavities and organs of dams were examined grossly and the carcasses discarded. Uteri from females that appeared non-gravid were opened and placed in 10% ammonium sulfide solution to confirm pregnancy status. All fetuses were weighed individually and examined for external malformations and variations. Each fetus was dissected, internally sexed and examined for visceral malformations and variations, including brain by a mid-coronal slice and heart by Staples technique (Staples, 1974). Eviscerated, skinned fetuses were</p>
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<p><u>Results</u> NOAEL maternal toxicity NOAEL developmental toxic ity</p> <p>Maternal effects</p> <p>Embryo/fetal effects</p> <p><u>Conclusions</u> (study authors)</p> <p><u>Data Quality</u> Reliabilities</p> <p><u>References</u></p> <p><u>Other</u> Last changed</p>	<p>numbered and tagged for identification, fixed, mascerated and stained with Alizarin Red S for skeletal evaluation..</p> <p>NOAEL maternal= 25mg/kg (based on one female aborting on gestation day 19) NOAEL developmental = 50mg/kg (based on 2 malformations) Assigned by reviewer. In a preliminary study, rerun tower overheads was administered undiluted to 16 mated female rabbits/group at 0, 10, 25 and 50mg/kg/day. Forty-two rabbits died between day 8-29 of gestation, of which 6 aborted prior to death and 6 aborted and were sacrificed. Total dead or aborted and sacrificed animals were 14/16, 11/16, 10/16, and 13/16 in 0(untreated control), 10, 25, and 50mg/kg/day, respectively. Intubation errors or respiratory disorders were determined to be probable cause of deaths; extremely high mortality in control group negated any meaningful comparisons of any parameters with treated groups. Study was repeated at same doses of rerun tower overheads diluted in corn oil.</p> <p>Maternal survival was 100% in all groups. Slight increase in occurrence of matted hair coat (nasal region) and slight reduction in fecal material was noted in 50mg/kg group only. One rabbit (50mg/kg) aborted on gestation day 19 and remained on study until scheduled sacrifice; aborted material was discarded. At Caesarean section, congested consolidated or emphysematous lungs and hydrocele(s) on the oviduct(s) were noted with similar frequency in all groups including controls. There were no biologically meaningful differences in mean maternal body wt, body wt gain or adjusted mean body wt (body wt exclusive of uterus and contents) in any treated group compared to controls. [Reviewer’s comment: Maternal body wt data did not appear to be statistically analyzed.]</p> <p>There were no biologically meaningful or statistically significant differences in mean number of corpora lutea, total imp lants, early and late resorptions, postimplantation loss, viable fetuses, fetal sex distribution or mean fetal body wts in any treated group compared to controls. No significant differences were present in number of litters with malformations or genetic or developmental variations in treated groups compared with controls. In the 50mg/kg./day group, 1 pup in 1 litter had an atlas-occipital anomaly of the skeleton and one pup in 1 litter had an enlarged heart with an interventricular spetal defect, interrupted aortic arch and retroesophophageal left subclavian vessel (sexes not specified). Scoliosis was observed in all groups including controls. All malformations were within historical ranges for the laboratory.</p> <p>Rerun Tower Overheads did not induce significant maternal or fetal toxicity or significant malformations/variations in offspring of New Zealand White rabbits treated with oral doses of 10, 25, and 50mg/kg/day in corn oil from day 6-28 of gestations.</p> <p>2. Reliable with restrictions. No analysis of dosing solution to verify correct test material volume was performed.</p> <p>Miller, L.G. and Schardein, J.L. 1981. Rerun Tower Overheads: Teratology study in rabbits (MCTR-171-79). IRDC study #450-011a. International Research and Development Corp., Mattawan, Mich. for Mobil Oil Corp., Princeton, NJ Staples, R.E. 1974. Teratology 9: A37-A38.</p> <p>10/09/2001 (Prepared by a contractor to the Olefins Panel)</p>
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