

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

* replicate data

Conclusion: (FT - CL)

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

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). Olefins Panel HVP Stream: Pyrolysis Gasoline. Typical composition ranges for Pyrolysis Gasoline are shown in Table 2 of the Test Plan.</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>Dripolene. Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93329). Olefins Panel HVP Stream: Pyrolysis Gasoline. Typical composition ranges for Pyrolysis Gasoline are shown in Table 2 of the Test Plan.</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 Rabbit, New Zealand White Males and females 3 None dermal</p>
<p>Test Conditions</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 40-85% 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><u>Results</u> LD₅₀ with confidence limits.</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: decreased fecal output, decreased fecal pellet size, soft stool, and decreased food consumption. No gross pathological findings were noted at necropsy.</p>
<p>Remarks</p>	<p></p>
<p><u>Conclusions</u> (study author)</p>	<p>The LD₅₀ was not reached at 2g/kg.</p>
<p><u>Data Quality</u> Reliability</p>	<p>1. Reliable without restriction.</p>
<p><u>References</u></p>	<p>Rodriguez, S.C. and Dalbey, W.E. 1994. Dermal toxicity of dripolene in the New Zealand White rabbit. Study #65643. Stonybrook Laboratories, 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</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> 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 change</p>	<p>Hydrogenated Pyrolysis Gasoline CAS# 68410-97-9. Clear liquid, aromatic odor. Olefins Panel HVP Stream: Hydrotreated C6-C8.</p> <p>Standard method (not referenced) with doses based on a limit test and range-finding study</p> <p>Acute LD50</p> <p>Yes</p> <p>1984</p> <p>Rat, Fischer 344</p> <p>Males and females</p> <p>5</p> <p>None</p> <p>Oral</p> <p>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.</p> <p>LD50 = 5.17g/kg (95% confidence limits: 5.02-5.45g/kg)</p> <p>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).</p> <p>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.</p> <p>1. Reliable without restrictions.</p> <p>Rausina, G.A. 1984. Acute oral toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2091. Gulf Life Sciences Center, Pittsburgh, PA</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

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 /dose Vehicle Route of administration</p> <p>Test Conditions</p> <p><u>Results</u> LC₅₀ 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 change</p>	<p>Hydrogenated Pyrolysis Gasoline CAS# 68410-97-9. Clear liquid, aromatic odor. Olefins Panel HVP Stream: Hydrotreated C6-C8.</p> <p>Standard method (not referenced) Acute LC50 Yes 1984 Rat, Fischer 344 Males and females 5 Filtered air Inhalation</p> <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^oF (75.5^oF 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> <p>LC50>12,408ppm 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> <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> <p>1. Reliable without restrictions.</p> <p>Rausina, G.A. 1984. Acute inhalation toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2092. 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

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><u>Results</u> Genotoxic effects</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>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. Olefins Panel HVP Stream: Hydrotreated C6-C8.</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-Nitrosoguanidine (5µg/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>
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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>Hydrogenated Pyrolysis Gasoline, CAS #68410-97-9. clear liquid with aromatic odor. Composition, purity and stability referred to sponsor. Olefins Panel HVP Stream: Hydrotreated C6-C8.</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 37°C 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. Olefins Panel HVP Stream: Hydrotreated C6-C8.</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. Olefins Panel HVP Stream: Hydrotreated C6-C8.</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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<p><u>Data Quality</u> <i>Reliabilities</i></p> <p><u>References</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>1. Reliable without restriction</p> <p>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</p> <p>5/7/2001 (Prepared by a contractor to the Olefins Panel)</p>
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<p><u>Reference</u></p> <p><u>Other</u> <i>Last changed</i></p>	<p>Haworth, S.R. 1978. Bacterial DNA repair assay of Mobil Chemical Company Compound MCTR-125-78 (MRI #110). E. G. and G. Mason Research Institute, Rockville, MD. for Mobil Chemical Co, Edison, NJ</p> <p>Slater, E.E. et al. 1971. Cancer Res. 31: 970-973.</p> <p>Green, M.H.L. and Muriel, W.J. 1976. Mutat. Res. 38:3-32</p> <p>Ames, B.N. et al. 1973. Proc. Natl. Acad. Sci., USA 70: 782-786.</p> <p>2/28/2002 (Prepared by a contractor to the Olefins Panel)</p>
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