AR201-13434B

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6. approx. 97% endo- and approx. 1% cyclopentadiene. Clear colorless liquid at room temperature.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute
GLP	Yes
Year	1981
Species/Strain	Rat, Fischer 344
Sex	Males and females
No. of animals per sex per dose	6
Vehicle	Air
Route of administration	Whole Body Inhalation
Test Conditions	Animals were housed 2/cage in stainless steel cages and received water and powdered chow diet ad lib except during exposure. A 12hr light/dark photoperiod cycle was maintained. Animals were kept in their respective cages during exposure. Exposure was for a single 6hr period on day 1 and sacrifice was on day 15. DCPD vapor was generated inside a heated pyrex tube to achieve complete vaporization while keeping temperature below the point (35^0C) at which fracturing to monomer occurred. Chamber concentrations of DCPD and cyclopentadiene (CPD) were monitored by gas chromatography/flame ionization detection with detection limit of 0.05ppm for both compounds. The actual exposure concentrations were 46, 130, 260 and 557ppm. This study was conducted to obtain a definitive LC_{50} value for DCPD exposure that was not confounded by fracturing of DCPD. Previous publications give conflicting LC_{50} values that might have been caused by loss of DCPD via fracturing. In the present study, CPD was below the detection limit. Animals were observed daily for clinical signs. All rats were necropsied for gross lesions. LC_{50} was calculated by the method of moving averages.
Results	
LC_{50} with confidence limits.	LC_{50} males: 284 (236-341)ppm; females 353 (322-387)ppm
Remarks	Rats of both sexes in the 557ppm group showed loss of righting reflex, impaired gait, stereotypic behavior, labored breathing, nasal discharge, convulsions and death. At 260ppm, both sexes showed stereotypic behavior, respiratory difficulty and nasal discharge. In rats dying from exposure, convulsions were observed immediately before death. At 130ppm, the only sign observed in both sexes, was a somewhat sluggish movement. No treatment-related clinical signs were observed in rats exposed to 46ppm. In rats that did not die during the study, all clinical signs cleared by day 2. There were no gross pathological effects noted at necropsy.
Conclusions (study author)	LC_{50} males: 284 (236-341)ppm; females 353 (322-387)ppm The LC_{50}s reflect the effects of DCPD. Results were not confounded by fracturing of DCPD into CPD.
Data Quality	
Reliability	**2.** Reliable with restrictions. The actual numbers of rats dying at the various exposure levels were not presented in the report.
References	Gad, S.C., Snellings, W.M., Egan, G.F., Nachreiner, D.J., Evancheck, R.E. and Dickey, C.L. 1981. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Doc. #81-MR-R2694. Bushy Run Research Center, Export, PA for Exxon Chemical Corp. Snellings, W.M. 1981. 9-day rat and mouse inhalation study. Report #43-527. Bushy Run Research Center, Export PA for Exxon Corp., Linden, NJ (test article description) Gad, S.C., Egan, G.F., Nachreiner, D.J., and Evancheck, R.E. 1980. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Abst. #130 from the 19th

	Annual meeting of the Society of Toxicology Bevan, C., Snellings, W.M., Dodd, D.E. and Egan, G.F. 1992. Subchronic toxicity study of dicyclopentadiene vapor in rats. Toxicol. and Ind. Health 8:353-367. (detailed discussion of results)
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6. approx. 97% endo- and approx. 1% cyclopentadiene. Clear colorless liquid at room temperature.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute
GLP	Yes
Year	1981
Species/Strain	Mouse, B6C3F1
Sex	Males and females
No. of animals per sex per dose	6
Vehicle	Air
Route of administration	Whole Body Inhalation
Test Conditions	Animals were housed 2/cage in stainless steel cages and received water and powdered chow diet ad lib except during exposure. A 12hr light/dark photoperiod cycle was maintained. Animals were kept in their respective cages during exposure. Exposure was for a single 6hr period on day 1 and sacrifice was on day 15. DCPD vapor was generated inside a heated pyrex tube to achieve complete vaporization while keeping temperature below the point (35^0C) at which fracturing to monomer occurred. Chamber concentrations of DCPD and cyclopentadiene (CPD) were monitored by gas chromatography/flame ionization detection with detection limit of 0.05ppm for both compounds. The actual exposure concentrations were 46, 130, 260 and 557ppm. This study was conducted to obtain a definitive LC_{50} value for DCPD exposure that was not confounded by fracturing of DCPD. Previous publications give conflicting LC_{50} values that might have been caused by loss of DCPD via fracturing. In the present study, CPD was below the detection limit. Animals were observed daily for clinical signs. All mice were necropsied for gross lesions. LC_{50} was calculated by the method of moving averages.
Results	
LC_{50} with confidence limits.	LC_{50} males: 143 (130-157)ppm; females 130 (103-153)ppm
Remarks	Mice of both sexes in the 557ppm group showed loss of righting reflex, impaired gait, stereotypic behavior, labored breathing, clear nasal discharge, and deaths. At 260ppm, mice of both sexes showed stereotypic behavior, respiratory difficulty, impaired gait, loss of coordination and convulsions prior to death. At 130ppm, mice displayed irregular breathing and stereotypic behavior; females also showed loss of coordination and slight tremors. No treatment-related clinical signs were observed in mice exposed to 46ppm. There were no gross pathological effects noted at necropsy.
Conclusions (study author)	LC_{50} males: 143 (130-157)ppm; females 130 (103-153)ppm The LC_{50}s reflect the effects of DCPD. Results were not confounded by fracturing of DCPD into CPD.
Data Quality	
Reliability	**2.** Reliable with restrictions. The actual numbers of mice dying at the various exposure levels were not presented in the report.
References	Gad, S.C., Snellings, W.M., Egan, G.F., Nachreiner, D.J., Evancheck, R.E. and Dickey, C.L. 1981. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Doc. #81-MR-R2694. Bushy Run Research Center, Export, PA for Exxon Chemical Corp. Snellings, W.M. 1981. 9-day rat and mouse inhalation study. Report #43-527. Bushy Run Research Center, Export PA for Exxon Corp., Linden, NJ (test article description) Gad, S.C., Egan, G.F., Nachreiner, D.J., and Evancheck, R.E. 1980. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Abst. #130 from the 19th

	Annual meeting of the Society of Toxicology Bevan, C., Snellings, W.M., Dodd, D.E. and Egan, G.F. 1992. Subchronic toxicity study of dicyclopentadiene vapor in rats. Toxicol. and Ind. Health 8:353-367. (detailed discussion of results)
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Genetic Toxicity - in Vitro

Test Substance	Dicyclopentadiene resin grade (DCPD), CAS #77-73-6, purity 75%; stable at room temperature; clear light yellow liquid
Test substance	
Method	
Method/guideline followed	OECD guideline 471 (adopted 7/21/97);EEC Annex V of Directive 67/548/EEC, Part B 13/14: Mutagenicity: reverse mutation assay using bacteria (draft Brussels 7/23/99)
Type µ	Bacterial reverse mutation
System of testing	Salmonella typhimurium and Escherichia coli with and without metabolic activation
GLP	Yes
Year	2000
Species/Strain	S. typhimurium TA98, TA100, TA1535, TA1537 and E. coli WP2uvrA.
Metabolic activation	Yes
Species and cell type	Wistar male rat liver (S9 fraction) prepared at Notox
Quantity	5% S9 fraction in 1st experiment; 10% S9 fraction in 2nd experiment
Induced or not induced	Aroclor 1254 induced, rats were given 500mg/kg ip 5 days prior to sacrifice
Concentrations tested	1st exp.:-S9 0, 1 (Sal.only, except TA100), 3, 10, 33, 100, (TA100 and E.coli only) 333, 1000, 3330 and 5000µg/plate; +S9 (5%) 0, 3, 10, 33, 100, 167 (Sal. only except TA100), (TA100 and E.coli) 333, 1000, 3330 and 5000µg/plate. 2nd exp.:-S9 0, 1 (Sal only) 3, 10, 33, 66 (E.coli only) and 100µg/plate; +S9 (10%) 0, 3 (Sal. only), 10, 33, 100 167 (Sal. only); (E. coli only) 333 and 666µg/plate
Statistical Methods	None. Criteria for positive response were at least a 3-fold (TA1535, TA 1537, TA98, E.coli WP2) or 2-fold (TA100) dose related increase over solvent control values for the respective strains with or without metabolic activation. Positive or negative responses should be reproducible in at least one independent repeat experiment.
Remarks for Test Conditions	Dicyclopentadiene test solutions were prepared in ethanol immediately prior to use. Salmonella strains and E. coli WP2 (approx. 10^9 cells/ml) were exposed to either test solution or ethanol ±S9 in 3 plates/dose/strain by the preincubation method. The range-finding test in TA100 and E. coli WP2 over a range of 3-5000µg/plate ±S9 was incorporated into the 1st experiment. TA98, TA1535 and TA1537 were tested at 1-100µg/plate –S9 and 3-167ug/plate +S9 (5%) in the 1st experiment. The highest concentration of test solution used in the 2nd experiment was the level at which there was significant inhibition of bacterial growth in TA100 and E.coli WP2. Culture vessels containing 0.1ml bacterial culture, 0.05ml test substance in ethanol or ethanol alone for the control, and 0.5ml S9 mix (5% S9 in exp.1 and 10% S9 in exp. 2) or 0.5ml of 0.1M phosphate buffer were combined and incubated with shaking (70rpm) for 30 min at 37^0C. After preincubation, solutions were added to 3ml molten (45^0C) top agar and poured on minimal agar plates. Plates were incubated upside down in the dark at 37^0C for 48 hrs. Revertant colonies were counted automatically (Protos model 50000) or manually if < 40 colonies/plate were present, and conditions of background lawn were evaluated. Positive control compounds were: -S9 sodium azide (NaA, 1ug/plate) for TA1535; 9-aminoacridine (9-AC, 60µg/plate) for TA1537; daunomycine (DM, 4µg/plate) for TA98; methyl methanesulfonate (MMS, 650µg/plate) for TA100 and 4-nitroquinoline N-oxide (4-NQO, 1µg/plate) for E.coli WP2; +S9: 2-aminoanthracene (2-AA) 2.5, 1.0, 5.0 and 10.0µg/plate for TA1535 & TA1537, TA98, TA100 and E. coli WP2, respectively.
Results	In the range-finding test presented as part of experiment 1, using TA100 and E.coli WP2 uvrA at concentrations of 3-5000µg/plate with 5% S9in mix, or no metabolic activation, DCPD precipitate in top agar at concentrations of 1000µg and above+S9. . Precipitate was present +S9 at 3330 and 5000µg/plate at the beginning of incubation but was not apparent at the end of incubation. In TA100 plates±S9, extreme inhibition of background lawn and appearance of microcolonies occurred from 333-500µg/plate; in E. coli WP2, extreme inhibition began at 100µg/plate-S9 and at 333µg/plate+S9. No increase in revertant colonies was observed at any non-toxic doses ±S9 (e.g. TA100-S9: 82, 84, 87, 71 and 37
Genotoxic effects	

	avg. revertants/plate and +S9: 97, 100, 89, 92,and 58 avg. revertants/plate at 0, 3, 10, 33 and 100ug/plate, respectively). Salmonella strains TA1535, TA1537 and TA98 were tested at concentrations of 0, 1, 3, 10, 33 and 100µg/plate–S9 and 0, 3, 10, 33, 100 and 167µg/plate +S9 (5% in mix). No precipitate was observed in top agar or on plates at any dose level. Extreme toxicity to background lawns was observed at 100µg/plate-S9 and at 167µg/plate+S9 for all strains. No increase in number of revertant colonies compared to solvent controls was observed (e.g. TA98 –S9: 14, 13, 14, 16 and 8 avg. revertants/plate at 0, 1, 3, 10 and 33µg/plate; +S9: 20, 13, 19, 19 and 10 avg. revertants/plate at 0, 3, 10, 33 and 100µg/plate, respectively). In experiment 2, 10% S9 fraction (v/v) was employed in metabolically activated cultures. Salmonella strains TA1535, TA1537, TA98, TA100 were exposed to 1-100µg/plate –S9 and 3-167µg/plate +S9; E.coli WP2 was exposed to 3-100µg/plate –S9 and 10-666µg/plate +S9. No precipitate was observed in top agar solutions or on plates. Toxicity to background lawn and reduction in revertant colonies was observed at 100µg/plate at a moderate level in Salmonella strains and slightly in E. coli WP2 –S9; slight inhibition of background lawn was observed at 167µg/plate in Salmonella stains and slight to moderate inhibition was observed in E. coli WP2 at 333 and 666ug/plate +S9. No increase in revertant colonies was observed at any dose level. (e.g. TA100-S9: 96, 107, 88, 99, 78 and 57 avg. revertants/plate at 0, 1, 3, 10, 33 and 100µg/plate; +S9: 105, 117, 100, 112, 82 and 90 avg. revertants/plate at 0, 3, 10, 33, 100 and 167µg/plate. E.coli WP2 -S9: 8, 6, 13, 8, 8 and 10 avg. revertants/plate at 0, 3, 10, 33, 66 and 100µg/plate; +S9: 8, 8, 10, 9, 10 and 7 avg. revertants/plate at 0, 10, 33, 100 and 333 and 666µg/plate). Positive control compounds responded appropriately: -S9: NaA 118, 139; 9-AC 95, 160; DM 404, 421; MMS 629, 589; 4-NQO 857,644 avg. revertants/plate in experiments 1 and 2, respectively, and +S9: 2-AA 198, 217; 206,146; 494, 385; 1089, 581; 287, 189 avg. revertants/plate in experiments 1 and 2 for strains TA1535, TA1537, TA98, TA100 and E.coli WP2). DCPD resin grade did not induce a dose-related or 2-fold or 3-fold increase in the number of revertant colonies in any Salmonella strain or in E. coli WP2 uvrA ±S9 in two independent assays.
Conclusions (contractor)	Dicyclopentadiene resin grade did not induce a significant increase in revertant colonies in Salmonella strains or in E. coli WP2 uvrA with or without rat liver metabolic activation at any dose level and is not considered a mutagen in this test system.
Data Quality *Reliabilities*	**1.** Reliable without restrictions
Reference	Verspeek-Rip, C.M. 2000. Evaluation of the mutagenic activity of dicyclopentadiene resin grade in the Salmonella typhimurium reverse mutation assay and the Escherchia coli reverse mutation assay (Preincubation test) with independent repeat. Proj. #284265. Notox B.V., The Netherlands. For Dow Chemical Co., Dow Europe S.A. – Horgen
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Genetic Toxicity - in Vitro

Test Substance	
Test substance	Dicyclopentadiene, CAS # 77-73-6 (3a, 4, 7, 7a-Tetrahydro-4, 7-methanoindene), purity 95%.
Method	
Method/guideline followed	Japan: Guidelines for Screening Mutagenicity Testing on Chemicals
Type	Mammalian chromosomal aberration
System of testing	Chinese hamster lung cells
GLP	Yes
Year	1998
Species/Strain	Chinese hamster lung (CHL/IU) cells
Metabolic activation	Yes
Species and cell type	Rat liver (Strain not specified)
Quantity	Not specified
Induced or not induced	Phenobarbital and 5,6-benzoflavone induced (Treatment not specified)
Concentrations tested	0.0, 0.014, 0.029, 0.057mg/ml –S9 24 hr continuous treatment; or short-term treatment (duration not specified); 0.0, 0.03, 0.05, 0.10mg/ml +S9 short-term treatment.
Statistical Methods	Not specified. Japanese guidelines state "test substance is considered to be positive when assay cultures show a significantly higher incidence of cells with chromosomal aberrations as compared with the negative control, and when this effect is reasonably reproducible or dose-dependent."
Remarks for Test Conditions	Summarized information only. Test material was prepared in acetone and administered to Chinese hamster lung cells with and without metabolic activation in 2 cultures per dose level. The test material was incubated with CHL cells in growth phase (usually 10^5 cells/ml growth medium) for 24 hrs continuous treatment without metabolic activation and for a shorter duration (Japanese guidelines indicate 3-6 hrs) with and without metabolic activation from rat liver S9, at 37^0C in a 5% CO_2 in air humidified atmosphere. In accordance to Japanese guidelines, the dose range was selected to produce 50% or greater inhibition of cell growth or mitosis at the maximum dose level. Following short-term exposure, cultures containing S9 mix were washed and fresh medium added. All cultures were treated with Colcemid® approximately 2 hrs prior to harvest to arrest dividing cells in metaphase. Cells were fixed and slides prepared for chromosome analysis (Giemsa is a standard stain for metaphase chromosome spreads). All slides, including positive and negative controls were coded before microscopic analysis. Japanese guidelines specify that 100 metaphase spreads should be counted and analyzed for structural aberrations (gaps, breaks, exchanges) and polyploids, and the percentage of cells with aberrations (with and without gaps) calculated. The negative control vehicle was acetone; positive control compounds were mitomycin C –S9 and cyclophosphamide + S9 (doses not specified).
Results	
Genotoxic effects	Dicylcopentadiene did not induce structural chromosomal aberrations or polyploidy in CHL/IU cells up to a concentration causing more than 50% cell growth inhibition with or without metabolic activation. Structural chromosomal aberrations were marginally induced at the highest dose –S9, 0.057mg/ml, after 24 hr continuous exposure.
Conclusions	
(contractor)	Dicyclopentadiene did not induce significant cytogenetic damage to mammalian cells in vitro under conditions of this assay. Although some marginal chromosome damage occurred at the highest –S9 dose after 24 hrs continuous exposure, the test material was confirmed to be negative for clastogenicity in an in vitro micronucleus assay (details not cited).
Data Quality	
Reliabilities	**2.** Reliable with restrictions. Limited detail; summary information sheet only provided by Japan Chemical Industry Ecology-Toxicology and Information Center (JETOC). Study was performed according to Japanese test guidelines for mutagenicity and GLP at a reputable laboratory.

Reference	JETOX 1998. Special Issue #3; No. 32 (March, 1998), Tokyo, Japan. Study performed at Hatano Research Institute, Food and Drug Safety Center, Hadanishi, Kanagawa, Japan. Handbook of Existing and New Chemical Substances, 8th Ed. 1999. Supervised by Chemical Products Safety Division, Basic Industries Bureau, The Ministry of International Trade and Industry, Japan.
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6, >95% endo-DCPD, 0.5%iso-DCPD and approx. 1% cyclopentadiene (CPD). Clear colorless liquid at room temperature.
Remarks	
Method	
Method/guideline followed	Not specified
Test type	Subchronic
GLP	Yes
Year	1982
Species	Rat
Strain	Fischer 344
Route of administration	Inhalation
Duration of test	26 wks
Doses/concentration levels	0, 1.0, 5.1 and 51ppm (actual)
Sex	Males and females
Exposure period	2, 6 and 13 wks
Frequency of treatment	6hr/day, 5 days/wk
Control group and treatment	Male and female rats, Filtered air
Post exposure observation period	4 and 13 wks
Statistical methods	Analysis of variance, Bartlett's test, Duncan's multiple range test, F-test, Student's t-test, Cochran t-test (applied when appropriate)
Test Conditions	Rats (30-34 days of age) were individually housed in stainless steel wire mesh suspended cages and maintained on a 12hr light/dark cycle. Chow diet and water were provided ad lib. Room temperature and relative humidity were maintained between 68-72^{0}F and 40-60%, respectively; during exposure, ranges were 70-79^{0}F and 39-68%, respectively. DCPD vapor was generated by heating the liquid in a Pyrex tube using a minimum amount of heat to prevent decomposition and formation of CPD. Filtered air was used to dilute the vapor prior to introduction into the chamber. Chamber concentrations were monitored by gas chromatography/flame ionization detection. Each dose group consisted of 51 rats/sex. Nine rats/sex/dose were scheduled for sacrifice the day after 2, 6, and 13 wks of exposure and 4 and 13 wks post-exposure. In addition, 3 rats/sex/dose were sacrificed after 13 wk exposure and 3/sex/dose after 13 wks post-exposure for electron microscopy of the kidneys. Rats were observed for clinical signs before and after each exposure, and daily during the recovery period. Body wt was recorded at initiation, weekly during both the exposure period and the first 5 wks of recovery, and then every 2 wks. High dose rats received opthalmoscopic examination before sacrifice. Hematology and serum chemistry analyses were performed on all rats prior to sacrifice after 2, 6 and 13wk exposure and 4 and 13wk post-exposure with blood from the orbital sinus. Erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin and concentration, and total/differential white blood cell counts were determined. Serum was analyzed for creatinine, urea nitrogen, calcium, phosphrous, chloride, alanine aminotransferase, aspartate aminotransferase, total protein, albumin, total bilirubin, alkaline phosphatase, glucose and osmolality. Urinalysis was performed weekly for the first 4 wks of the study and prior to sacrifice. Semi-quantitative assessments were made of pH, protein, glucose, bilirubin, urobilinogen and blood, and quantitative assessment of volume, specific gravity, osmolality, color, turbidity, creatinine, calcium, phosphorous, chloride, sodium and potassium. Food and water consumption were also measured. A urine concentration test was performed on day 6 (males and females) and on day 83 (males only) in rats deprived of water for 16 hrs. Necropsies were conducted on all rats. Kidneys, lungs, liver and testes were weighed. Adrenals, bone and bone marrow (sternum), brain, epididymides, eyes, heart, kidneys, larynx, liver, lungs, lymph nodes (mediastinal), muscle (gastrocnemeous), nasal turbinates, parathyroids, pituitary, sciatic nerve, spleen, testes, thymus, thyroids, trachea, urinary bladder and gross lesions were preserved for microscopic evaluation. All rat kidneys and urinary bladders were examined microscopically; other organs were only examined microscopically in control and high dose rats sacrificed after 13 wks of exposure. Electron

	microscopic examination was performed on rat kidneys fixed in gluteraldehyde/formaldehyde for 24hr and post-fixed in 1% osmium tetroxide, and embedded in Epon 812.
Results	
NOAEL (NOEL)	Males<1.0ppm (renal tubule hyperplasia, epithelial cell casts); Females=51ppm
LOAEL (LOEL)	Males=1.0ppm (renal tubule hyperplasia, epithelial cell casts); Females: not reached at 51ppm
Remarks	No treatment related mortality occurred. No consistent pattern of clinical signs was observed during the study, and during exposure, all rats appeared normal. There were no treatment related changes in body wt or food consumption. Males in the 51ppm group had a significant decrease in urine specific gravity and osmolality, occasionally associated with increased urine volume and/or increased water consumption; these effects were exposure, dose and time-related. Analysis of urine sediment uncovered epithelial cells indicative of renal damage in all test article dose groups. Dose-related epithelial cell casts were found at all DCPD levels during the study but not during recovery. These effects were not seen in females. At 51ppm, males showed altered excretion rates for calcium (decrease), sodium (decrease) and potassium (increase). Urine concentrating ability was also decreased at 51ppm in males but not in females. Serum chemistries were minimally altered: calcium (increase at 51 and 5.1ppm), alanine aminotransferase (decrease at 51 and 5.1ppm). No biologically significant changes in hematological parameters were seen. Mild conjunctivitis was seen in several rats during DCPD exposure in the 51 and 5.1ppm groups. No significant effects were seen at necropsy. Male rats at 51ppm had significant increases in relative liver wt and both absolute and relative kidney wts; these effects cleared during recovery. DCPD related organ wt changes were not seen in females. The only histopathological finding related to DCPD exposure was in male rat kidney. At 5.1 and 51ppm males accumulated hyaline droplets in the proximal convoluted tubular epithelial cells by the 10th DCPD exposure, and resolved during recovery. Males exposed to 5.1 and 51ppm had tubular hyperplasia, tubule proteinosis and basement membrane thickening. The frequency of kidney tubular protein accumulation after 30 exposures increased significantly in 1.0ppm males. On several occasions, parameters measured in the 1.0ppm males changed in the same direction as in the higher dose groups but the magnitude of change was lower, and hence, not significant. Examples of occurrences were for relative kidney wt., decreased urine osmolality, decreased sodium, increased potassium excretion, and kidney tubular hyperplasia. Electron microscopy supported the light microscopy observations.
Conclusions (study authors)	The only major effect observed was a male rat specific nephropathy, characteristic of the hyaline droplet nephropathy produced by a diverse group of compounds.
Quality Reliabilities	**1.** Reliable without restrictions
References	Dodd, D.E., Longo, L.C. and Eisler, D.L. 1982. Ninety-day vapor inhalation study on rats and mice. Report #44-520. Bushy Run Research Center, Export, PA, for Exxon Corp. East Millstone, NJ Bevan, C., Snellings, W.M., Dood, D.E. and Egan, G.F. 1992. Subchronic toxicity study of dicyclopentadiene vapor in rats. Toxicol. and Ind. Health 8: 353-67. Gad, S.C., Snellings, W.M., Egan, G.F., Nachreiner, D.J., Evanscheck, R.E. and Dickey, C.L. 1981. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Doc. #81-MR-R2694. Bushy Run research Center, Export, PA for Exxon Chemical Corp. Snellings, W.M. 1981. 9-day rat and mouse inhalation study. Report #43-527. Bushy Run Research Center, Export PA for Exxon Corp., Linden, NJ (test article description). Gad, S.C., Egan, G.F., Nachreiner, D.J., and Evanscheck, R.E. 1980. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Abst. #130 from the 19th Annual meeting of the Society of Toxicology
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6, >95% endo-DCPD, 0.5%iso-DCPD and approx. 1% cyclopentadiene (CPD). Clear colorless liquid at room temperature.
Remarks	
Method	
Method/guideline followed	Not specified
Test type	Subchronic
GLP	Yes
Year	1982
Species	Mouse
Strain	B6C3F1
Route of administration	Inhalation
Duration of test	26 wks
Doses/concentration levels	0, 1.0, 5.1 and 51ppm (actual)
Sex	Males and females
Exposure period	2, 6 and 13 wks
Frequency of treatment	6hr/day, 5 days/wk
Control group and treatment	Male and female mice, Filtered air
Post exposure observation period	4 and 13 wks
Statistical methods	Analysis of variance, Bartlett's test, Duncan's multiple range test, F-test, Student's t-test, Cochran t-test (applied when appropriate)
Test Conditions	Mice (30-34 days of age) were individually housed in stainless steel wire mesh suspended cages and maintained on a 12hr light/dark cycle. Chow diet and water were provided ad lib. Room temperature and relative humidity were maintained between 68-72^{0}F and 40-60%, respectively; during exposure, ranges were 70-79^{0}F and 39-68%, respectively. DCPD vapor was generated by heating the liquid in a Pyrex tube using a minimum amount of heat to prevent decomposition and formation of CPD. Filtered air was used to dilute the vapor prior to introduction into the chamber. Chamber concentrations were monitored by gas chromatography/flame ionization detection. Each dose broup consisted of 45 mice/sex. Nine mice/sex/dose were scheduled for sacrifice after 2, 6, and 13 wks of exposure and 4 and 13 wks post-exposure.. Mice were observed for clinical signs before and after each exposure, and daily during the recovery period. Body wt was recorded at initiation, weekly during both the exposure period and the first 5 wks of recovery, and then every 2 wks. High dose mice received opthalmoscopic examination before sacrifice. Hematology and serum chemistry analyses were performed on all mice prior to sacrifice after 2, 6 and 13wk exposure and 4 and 13wk post-exposure with blood from the orbital sinus. Erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin and concentration, and total/differential white blood cell counts were determined. Serum was analyzed for creatinine, urea nitrogen, calcium, phosphrous, chloride, alanine aminotransferase, aspartate aminotransferase, total protein, albumin, total bilirubin, alkaline phosphatase, glucose and osmolality. Necropsies were conducted on all mice. Kidneys, lungs, liver and testes were weighed. Adrenals, bone and bone marrow (sternum), brain, epididymides, eyes, heart, kidneys, larynx, liver, lungs, lymph nodes (mediastinal), muscle (gastrocnemeous), nasal turbinates, parathyroids, pituitary, sciatic nerve, spleen, testes, thymus, thyroids, trachea, urinary bladder and gross lesions were preserved for microscopic evaluation. Organs were only examined microscopically in control and high dose mice sacrificed after 13 wks of exposure.
Results	
NOAEL (NOEL)	Males and Females = 5.1ppm
LOAEL (LOEL)	Males and Females = 51.0ppm (deaths)
Remarks	Ten males and 9 female mice exposed to 51ppm DCPD died during the study; whereas no more than 2 mice died at any other level. No significant clinical signs or body wt changes were noted prior to death. The likely cause of death appeared to be pulmonary congestion and possibly renal failure. These effects were not seen in mice sacrificed at the end of the

	study. During exposure, a few of the mice at 51 and 5.1ppm showed coordination loss and/or decreased activity. Males and females in the 51ppm group showed significant elevation in body wt gain that returned to control values during recovery. No consistent changes in serum chemistry values were found. No biologically significant effects on hematology and no alterations in blood cell differential counts were observed. Mild conjunctivitis was seen in one male mouse at 51ppm. No lesions were found at gross necropsy. No exposure related changes in organ wt were observed and no histopathological effects were noted in either sex.
Conclusions (study authors)	Approximately 20% of both sexes of mice died at 51ppm, apparently of pulmonary congestion, but similar effects were not seen in mice sacrificed on schedule. A significant body wt gain was also observed, only in female mice, at 51ppm (40% of the LD_{50}). No other biologically significant effects were observed.
Quality Reliabilities	**1.** Reliable without restrictions
References	Dodd, D.E., Longo, L.C. and Eisler, D.L. 1982. Ninety-day vapor inhalation study on rats and mice. Report #44-520. Bushy Run Research Center, Export, PA, for Exxon Corp. East Millstone, NJ Gad, S.C., Snellings, W.M., Egan, G.F., Nachreiner, D.J., Evancheck, R.E. and Dickey, C.L. 1981. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Doc. #81-MR-R2694. Bushy Run Research Center, Export, PA for Exxon Chemical Corp. Snellings, W.M. 1981. 9-day rat and mouse inhalation study. Report #43-527. Bushy Run Research Center, Export PA for Exxon Corp., Linden, NJ (test article description). Gad, S.C., Egan, G.F., Nachreiner, D.J., and Evancheck, R.E. 1980. Acute and subacute inhalation toxicity of dicyclopentadiene in rats and mice. Abst. #130 from the 19th Annual meeting of the Society of Toxicology
Other Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Developmental Toxicity/Teratogenicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6, $C_{10}H_{12}$, purity 98%
Remarks	
Method	
Method/guideline followed	Standard method, no guidelines specified
Test type	Developmental toxicity – Range finding study
GLP	Yes
Year	1993
Species	Rat
Strain	Sprague Dawley (VAF), CD(SD)BR
Route of administration	Oral gavage
Concentration levels	0, 50, 200, 300, 400 and 500mg/kg/day in corn oil
Sex	Female; timed pregnancies: 11 rats/group for 50-400mg/kg; 10 rats in 500mg/kg group
Exposure period	Days 6-15 of gestation
Frequency of treatment	Once/day in the morning
Control group and treatment	11 timed pregnant rats; 5ml corn oil/kg/ day
Duration of test	Day 5 - 20 of gestation
Statistical methods	Data analyzed using non-parametric statistical methods to identify dose response trends among treatment groups and differences between control and treatment groups. Kruskal-Wallis one-way analysis of variance used for all parameters except gestation day 5-20 body wts, gravid uterus wt and average fetal wts. Mann-Whitney Wilcoxan U test was used when Kruskal-Wallis was significant ($p<0.05$). Jonckheere's test for k independent samples was used for dose-response trends for gestation day 5 to day 20 body wt data. If no trend was found, Dunn's test was used for differences among dose groups; if a trend was present Shirley's test was applied. Body wt data from non-pregnant rats were not included.
Remarks for Test Conditions.	Sixty-five timed-pregnant rats (approx. 77 days old), received on day 5 of gestation (plug date=day 0 of gestation), were individually housed (room environmental information not presented) and identified by tail tattoo. Animals were assigned to control or one of 5 treatment groups using a stratified randomization method. [Reviewer's note: Actual number of animals/group was not specified but was estimated from subsequent data to be 11 rats each/treatment group 50-400mg/kg and vehicle control, and 10 rats/500mg/kg group.] All animals found dead prior to scheduled necropsies were examined for gavage injury and pregnancy. Non-pregnant animals were excluded from body wt data and all subsequent tabulations. Doses of 50-500mg/kg were selected based on the reported LD_{50} range for DCPD in rats of 378-820mg/kg. Test solutions were formulated in corn oil (w/v) and administered at a standard volume of 5ml/kg body wt. for all dose levels. Dosages were adjusted based on body wt on gestation days 6, 8, 10, 12 and 14. Dosage solutions were analyzed by capillary gas chromatography for concentration accuracy and stability. Corn oil solutions containing 10mg/ml of DCPD were stable when stored for 30 days in sealed glass bottles at room temperature. Body wts were recorded on gestation days 5, 6, 8, 10, 12, 14, 16 and 20 (termination). Clinical signs of toxicity or mortality were evaluated twice daily during and post-dosing. At Caesarean section, the following data were collected: terminal body wt of dams, gravid uterine wt, live litter wt, number of implantation sites, resorptions, dead fetuses and live fetuses.
Results	
NOAEL maternal toxicity	NOAELmaternal was not determined.
NOAEL developmental toxicity	NOAELfetal = 50mg/kg (Assigned by reviewer)
Maternal effects	Signs of systemic toxicity beginning at day 7 of gestation were observed in all animals dosed at 200mg/kg and above. Clinical signs included dried material around nose and mouth, rough hair coat, and lethargy increasing in severity with increasing dose; convulsions (1 rat in 200mg/kg group), hunched posture (6 rats in 300mg/kg group)and ataxia (5 rats in 300mg/kg, 11rats in 400mg/kg and 9 rats in 500mg/kg/day groups). All

	animals in the 400 and 500mg/kg/day groups were found dead by gestation day 9; 3/7 and 8/9 pregnant rats in groups 200 and 300mg/kg/day were found dead or were sacrificed for humane reasons by gestation day 9. Body wts of treated pregnant rats were decreased in a dose-related manner beginning at gestation day 8. Statistically significant differences from vehicle control (9 total rats) were observed on gestation days 8 and 10 in the 50mg/kg/day group (10 rats; 6% lower on both days), gestation days 8-20 in 200mg/kg (4 rats; 16-21% lower during treatment, 9% lower post-treatment) and 300mg/kg (1 rat) groups, and gestation day 8 in the 400 and 500mg/kg groups (all animals died on day 9). Dose-related decreases were also noted for body wt gain: statistically significant decreases during treatment (25 and 60% less than controls, respectively) in the 50 and 200mg/kg groups, wt gain during gestation (20% less) and corrected wt gain (23% less) were significantly decreased in the 200mg/kg group. The single pregnant female in the 300mg/kg/day group was excluded from wt gain calculations.
Embryo/fetal effects	At the gestation day 20-caesarean section, average fetal wt was significantly lower by 10% compared to controls in the 200mg/kg group; the single rat in the 300mg/kg group resorbed her litter. All other fetal parameters, including live fetuses/litter, dead fetuses/litter, resorptions/litter, completely resorbed litter, dead implants/litter and total implants/litter in the 50 and 200mg/kg/day dose groups did not differ from vehicle controls.
Conclusions (study authors)	In this range-finding study, dicyclopentadiene treatment caused maternal toxicity and lethality at doses of 200mg/kg/day and above with 100% mortality of animals treated at 400 and 500mg/kg/day. Body wt and wt gain were decreased at all dose levels, reductions being greater with increasing doses. The only developmental toxicity in surviving litters was decreased fetal wt. in the 200mg/kg/day group.
Data Quality *Reliabilities*	**2.** Reliable with restrictions. Actual number of animals/group not specified. Room environmental conditions not reported.
References	Gulati, D.K. et al. 1993. Range-finding studies: Developmental toxicity of dicyclopentadiene when administered via gavage to CD Sprague-Dawley rats. Study No. NTP-92-RF/DT-038. Environmental Health Research and Testing, Inc. Lexington, KY. for National Toxicology Program, NIEHS, Research Triangle Park, NC
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Developmental Toxicity/Teratogenicity

Test Substance	Dicyclopentadiene (DCPD), CAS #77-73-6, C10H12, purity 98%
Remarks	
Method	
Method/guideline followed	Standard method, no guidelines specified
Test type	Developmental toxicity – Range finding study
GLP	Yes
Year	1993
Species	Rabbits
Strain	New Zealand White
Route of administration	Oral gavage
Concentration levels	0, 25, 100, 200, 300 and 400mg/kg/day in corn oil
Sex	Female; presumed pregnant: 10/group
Exposure period	Days 6-19 of gestation
Frequency of treatment	Once/day in the morning
Control group and treatment	10 presumed pregnant rabbits; 1ml corn oil/kg/ day
Duration of test	Day 2 - 30 of gestation
Statistical methods	Data analyzed using non-parametric statistical methods to identify dose response trends among treatment groups and differences between control and treatment groups. Kruskal-Wallis one-way analysis of variance used for all parameters except gestation day 3--30 body wts, gravid uterus wt and average fetal wts. Mann-Whitney Wilcoxan U test was used when Kruskal-Wallis was significant ($p<0.05$). Jonckheere's test for k independent samples was used for dose-response trends for gestation day 3 to day 30 body wt data. If no trend was found, Dunn's test was used for differences among dose groups; if a trend was present Shirley's test was applied. Body wt data collected after animals aborted were not included.
Remarks for Test Conditions.	Sixty presumed-pregnant rabbits (approx. 22 wks old), received on day 2 of gestation (breeding date=day 0 of gestation), were individually housed (room environmental information not presented) and identified by ear tattoo. Animals were assigned to control or one of 5 treatment groups using a stratified randomization method. Doses of 25-400mg/kg were selected based on the reported LD_{50} range for DCPD in rats of 820mg/kg, as no rabbit data were available. Test solutions were formulated in corn oil (w/v) and administered at a standard volume of 1ml/kg body wt. for all dose levels. Dosages were adjusted based on body wt on gestation days 6, 8, 10, 12, 14, 16 and 18. Dosage solutions were analyzed by capillary gas chromatography for concentration accuracy and stability. Corn oil solutions containing 10mg/ml of DCPD were stable when stored for 30 days in sealed glass bottles at room temperature. Body wts were recorded on gestation days 3, 6, 8, 10, 12, 14, 16 18, 20, 25 and 30 (termination). Clinical signs of toxicity or mortality were evaluated twice daily during and post-dosing. At Caesarean section, the following data were collected: terminal body wt of dams, gravid uterine wt, number of implantation sites, resorptions, dead fetuses and live fetuses.
Results	
NOAEL maternal toxicity	NOAELmaternal =25mg/kg. (based on abortion by 1 dam at 100mg/kg/day)
NOAEL developmental toxicity	NOAELfetal = 300mg/kg (Assigned by reviewer)
Maternal effects	Signs of systemic toxicity (decreased food and water consumption) were noted in all animals in the 300 and 400mg/kg/day groups beginning on gestation day 9; 1/9 and 3/9 rabbits in the 300 and 400mg/kg groups, respectively, died prior to scheduled necropsy. In the 100mg/kg/day group, one rabbit aborted her litter beginning on gestation day 18; another had bloody vaginal discharge beginning on day 26 of gestation but was pregnant at scheduled necropsy. In the 300mg/kg group, 1 rabbit had a bloody vaginal discharge beginning on day 19 of gestation, aborted 4 kits on day 21 with an additional 9 masses on gestational day 22. Three animals in the 400mg/kg/day group had blood vaginal discharges; 2 recovered over several days, one was dead on gestation day 23. Body wts

Embryo/fetal effects	taken after abortions and developmental toxicity data from the 2 animals that aborted were not included in data analysis. Maternal body wt decreased in a generally dose-related manner beginning on gestation day 8, becoming statistically significant ($p<0.05$) from controls from day 10 through gestation day 18 for the 300mg/kg group and day 8-30 for the 400mg/kg group. Maternal wt gain during treatment was also statistically significantly decreased compared to controls in the 200mg/kg/day and higher groups. At Caesarean section, the number of resorptions and non-live implants/litter were higher, and the number of fetuses was lower, in the 400mg/kg group compared to controls but were not statistically significant. Two litters from this group showed gross deformities of kits – one with eyes open and 1 with eyes open and deformed hind limbs in one litter of 3 total live kits, and eyes open in all 12 kits from another 400mg/kg litter. No other developmental parameters were adversely affected.
Conclusions (study authors)	Dicyclopentadiene caused maternal toxicity at 200mg/kg/day and higher dose levels and abortion of 1 litter at 100mg/kg in this range-finding study. Gross deformities were evident in two litters from dams given 400mg/kg/day but no other developmental endpoints were significantly affected at any other maternally toxic or non-toxic dose level.
Data Quality *Reliabilities*	**1.** Reliable without restrictions.
References	Gulati, D.K. et al. 1993. Range-finding studies: Developmental toxicity of dicyclopentadiene when administered via gavage to New Zealand White rabbits. Study No. NTP-92-RF/DT-044. Environmental Health Research and Testing, Inc. Lexington, KY. for National Toxicology Program, NIEHS, Research Triangle Park, NC
Other L*ast changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Developmental Toxicity/Teratogenicity

Test Substance	Dicyclopentadiene (DCPD) CAS #77-73-6, purified
Remarks	
Method	
Method/guideline followed	Standard method, no guideline specified
Test type	Teratogenesis
GLP	Not specified
Year	1978
Species	Rat
Strain	Sprague Dawley [CRL:COBS CD(SD)BR]
Route of administration	Diet (Purina Laboratory Meal Chow)
Concentration levels	0, 80, 250, 750ppm
Sex	Female, pregnant (20/treatment group)
Exposure period	Days 6-15 of gestation
Frequency of treatment	Ad lib exposure to treated diet
Control group and treatment	21 pregnant females; diet containing 300ml corn oil/10kg meal
Duration of test	Day 0-19 of gestation
Statistical methods	Dunnett's t-test used for body wts and food consumption of dams, mean pup wts based on litter averages. ($p<0.05$). Ratios (e.g. sex, pregnancy) analyzed by 2x2 contingency table with Yates' correction. Discontinuous parameters (e.g. number of abnormal fetuses in a litter) were evaluated by Wilcoxon Rank Sum. The litter was the basic sampling unit.
Remarks for Test Conditions.	Female rats were acclimated for 12 days then paired with sexually mature males (1:1) of the same strain and supplier. Females were examined daily for evidence of mating and the presence of a copulatory plug was considered day 0 of gestation. Mated female rats, approximately 11 wks old at time of first dose (day 6 of gestation) were assigned sequentially to treatment groups and identified by cage cards. Females were individually housed in wire cages in a temperature-controlled room (Temp. and humidity ranges not reported) with a 12hr light/dark cycle. Appropriate diets and fresh water (acidified pH 2.5) were provided ad lib. DCPD was incorporated in basal diet daily on days 6-15 of gestation. Test material (0.8, 2.5, and 7.5g) was suspended in 300ml corn oil and blended with 10kg basal diet in a twin shell blender for 15 min. Vehicle control diet contained 300ml corn oil in 10kg meal. Mated females were weighed on day 0, 6, 16 and 19 of gestation. Food consumption was measured during period 0-6, 6-16 and 16-19 of gestation. Animals were observed daily for changes in general appearance, behavior and condition. On day 19 of gestation, adult females were sacrified by chloroform anesthesia, visceral and thoracic regions were examined, and the uterus removed and opened. Number of implantation sites, placement in uterine horns, live and dead fetuses, and resorption sites were recorded. Fetuses were removed, examined extemally for abnormalities and weighed. One third of fetuses from each litter were fixed in Bouin's fluid for soft tissue examination of head, thoracic and visceral organs. Remaining fetuses were eviscerated and stained with Alizarin Red S for skeletal examination. Uterus and ovaries of adult females were preserved in 10% formalin.
Results	
NOAEL maternal toxicity	NOAELmaternal and embryo/fetal toxicity = 750ppm. Assigned by reviewer.
NOAEL developmental toxicity	
Maternal effects	No adult females died during the study and all appeared normal on day 19 of gestation, except for 1 rat in the 80ppm group that was emaciated, had an arched back and red crust around the mouth and nose. Mean body wts and food consumption indicated no significant differences between control and treated pregnant rats (Data cited in Appendix 1, not included with report). Test material did not produce any adverse effects on uterine contents on day 19 of gestation. Pregnancy ratios were: 19/21, 20/20, 19/20 and 19/20 in 0, 80, 250 and 750ppm groups, respectively. All dams in all groups had live litters.
Embryo/fetal effects	Incidence of litters with resorptions was 74%, 40%, 58% and 42%; live fetuses/implantation site was 94%, 93%, 93% and 96% and mean live litter size was 15.5,

	13.9, 14.4 and 14.7pups/litter in 0, 80, 250 and 750ppm groups, respectively. There were no litters with dead fetuses. Average fetal wt and length (combined sexes), and sex ratio were comparable to controls. Examination of offspring at delivery revealed subcutaneous hematomas in some fetuses from litters at all groups including controls. In the control group, one fetus had swelling of the right hind limb, and one fetus from a different control litter had intestines protruding from the umbilicus. Bouin's fixed specimens revealed only the absence of left kidney in one control fetus, enlarged kidney in one 80ppm fetus, and unilateral anophthalmia in one 750ppm fetus; no other soft tissue effects were seen. Results of skeletal examination demonstrated commonly encountered changes in all dose groups. A few instances of retarded bone ossification were observed in 2, 3, 0 and 2 litters in control, 80, 250 and 750ppm groups, respectively but variation and incidences were within historical range for the laboratory and did not indicate adverse effect on fetal growth and development, or teratogenic potential.
Conclusions (study authors)	Administration of dicyclopentadiene to female rats from day 6-15 of gestation by incorporation in the diet at 80, 250 and 750ppm produced no adverse effect on pregnant dams and did not induce terata, variations in fetal sex ratio, embryotoxicity or inhibition of fetal growth and development.
Data Quality *Reliabilities*	**2.** Reliable with restrictions. Analysis of test material in diet was not performed. Although diet was prepared daily, accuracy of blending was not verified. Food consumption data was not presented and actual volume of test material ingested/group was not calculated. Adherence to GLP was not indicated.
References	Beliles, R.P. 1978. Teratology study in rats using dicyclopentadiene in diet. LBI Proj. #10734-05. Litton Bionetics, Inc., Kensington, MD, for US Army Medical Bioengineering Research and Development Command, Washington, DC Contract No. DAMD17-77-C-7003 (1980)
Other L*ast changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Toxicity to Reproduction

Test Substance	Dicyclopentadiene, CAS # 77-73-6 (3a, 4, 7, 7a-Tetrahydro-4, 7-methanoindene), purity 94.65%.
Remarks	
Method	
Method/guideline followed	OECD Guideline 422:
Test type	Combined repeated dose toxicity study with reproduction/ developmental toxicity screening
GLP	Yes
Year	1998
Species	Rats
Strain	Sprague Dawley (Crj:CD[SD]) from Charles River Japan, Inc
Route of administration	Oral gavage
Duration of test	Males 44 days; Females from 14 days before mating through gestation and parturition until day 3 of lactation
Concentration levels	0, 4, 20, 100mg/kg/day in olive oil
Sex	Males and females; 10M, 10F/group (ages not specified)
Exposure period	Maximum 45 consecutive days
Frequency of treatment	Once/day
Control group and treatment	Males and females; olive oil, once/day
Statistical methods	None specified
Remarks for Test Conditions.	No study details provided. In OECD guideline 422, test substance is administered to male and female rats daily by oral gavage from 2 weeks prior to mating and during mating (approx. 2 weeks). Male rats continue to be dosed for at least another two weeks post-mating or, as in this study, until sacrifice of females after day 3 of lactation. Females continue to be dosed through gestation to day 3 of lactation. Females are sacrificed on day 4 of lactation and males on day 45 of the study.
Results	
NOAEL	NOELrepeat dose toxicity: Males < 4/mg/kg/day; Females = 20mg/kg/day NOELreproduction: Parental Males = 100mg/kg/day; Dams and offspring = 20mg/kg/day Repeat dose toxicity: Two females in the high dose (100mg/kg) group died; males and surviving females showed slight suppression of body wt gain and decreased food consumption. Blood chemistry of high dose males showed increase in GOT and GPT; no test material related changes occurred in hematology parameters for any treatment group. Increased weight of liver and kidneys of male rats given 100mg/kg were accompanied by single cell necrosis in liver, and hyaline droplets and basophilic changes in tubular epithelium of kidneys under microscopic examination. Increase in fatty droplets in fascicular zone of adrenals was observed in both males and females in the 100mg/kg group. Similar histopathologic changes were seen in kidneys of 4, 20mg/kg group male rats and in adrenals of 20mg/kg group male rats. Reproduction/Developmental toxicity: Dicyclopentadiene had no effect on mating, fertility, gestation, implantation, or delivery indices, or on gestation length, number of corpora lutea, implantations, or parturition. Two females in the 100mg/kg group lost 100% of their litters during lactation (days 1-4). [Reviewer's note: It is likely that these are the females that died, but not specified in summary]. A low viability index and tendency to lower birth wt and body wt gain was observed in neonates in the highest dose group (100mg/kg). No significant differences in number of offspring, live offspring at birth, sex ratio or live birth index were found. No abnormal findings were observed in external features, clinical signs in dams or during life of offspring, or at necropsy of offspring.
Conclusions (contractor)	Dicyclopentadiene induced systemic toxicity in male and female rats including death of two females at the 100mg/kg/day dose level. No compound related effects were seen on reproductive parameters although two females in the 100mg/kg group lost 100% litters

	during lactation. Effects on neonates included low viability index, lower birth wt and body wt gain in the 100mg/kg group, but no effects were seen on other parameters in neonates at any dose level.
Data Quality *Reliabilities*	**2.** Reliable with restriction. Limited study design detail; no analytical data on dosing solutions, no numerical or statistical data available. Summary information sheet provided by Japan Chemical Industry Ecology-Toxicology and Information Center (JETOC). Study performed according to OECD Guideline 422 and GLP by a reputable laboratory.
References	JETOC 1998. Special Issue #3; No. 32 (March 1998), Tokyo, Japan. Study performed at Mitsubishi Chemical Safety Institute, Ltd., Kashimagun, Ibaraki, Japan
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Toxicity to Reproduction

Test Substance	Dicyclopentadiene (DCPD) CAS #77-73-6, purified
Remarks	
Method	
Method/guideline followed	Standard method, no guideline specified
Test type	Three generation Reproduction
GLP	Not specified
Year	1979
Species	Rat
Strain	Sprague Dawley [CRL:COBS CD(SD)BR]
Route of administration	Diet (Purina Laboratory Meal Chow)
Duration of test	3 generations (approx. 45-50wks)
Concentration levels	0, 80, and 750ppm nominal concentrations (0, 69.3, 693ppm actual concentrations)
Sex	Males and females (10M, 20F/group in F0 generation)
Exposure period	F0-approx 28 wks; F1a, F2a and F3- in utero, birth to weaning; F1b, F2b- in utero and approx. 31 wks.
Frequency of treatment	Ad lib exposure to treated diet
Control group and treatment	10M, 20F/group in F0 generation; diet containing 300ml corn oil/10kg meal
Statistical methods	No methods specified
Remarks for Test Conditions.	Weanling albino rats were acclimated for 11 days, then assigned randomly to three groups. These F0 generation rats were identified by ear tag and cage cards, housed individually in shoe-box cages on AB-SORB-DRI bedding, except when mating. Food and water were provided ad lib. Room temperature, humidity and light/dark cycle intervals were not specified. Fresh diets were prepared weekly of appropriate quantity of DCPD dissolved in 300ml corn oil, added to 10kg diet and mixed for at least 15min in a twin shell blender. Control diet was prepared in the same way of 300ml corn oil/10kg diet. Dietary batches were analyzed by gas-liquid chromatography. Seven weeks after initiation of treated diet, F0rats were mated, 1 male: 2 females, within a dose group for 2 wks. At the end of 2 weeks, rats were returned to individual cages and females were allowed to deliver. One week after weaning the first litter (F1a), F0 parents were re-mated- each male with 2 different females within the group. One week after weaning the second litter (F1b), F0 parents were killed and gross necropsies were performed. F1b pups (1M, 2F) from each litter, where possible, were selected to be parents for the next generation, and were caged, fed and watered just as the F0 rats. When F1b rats were approx. 100 days old, they were mated to produce the F2a litters and subsequently the F2b litters. Selected F2b pups were used to produce F3 litters. For each litter, observations included gross abnormalities of pups, mean body wt by sex at birth, number of pups/sex at day 4 of lactation, number of pups/sex and body wts at day 21 of lactation (weaning). At day 4 of lactation, each litter was reduced to 8 pups (4/sex if possible). At weaning, gross necropsies were performed on approx. 1/3 of the first litter (a) from all three generations and on 1/3 of F3b litters.
Results	
NOAEL	NOAEL parental and offspring =750ppm (693ppm actual) [all generations]. Assigned by reviewer
General information	Weekly feed analyses showed a 69.3ppm (87%) average value for 80ppm diet level and 693ppm (92%) for the 750ppm level. Body wt and food consumption data were cited in appendices that were not included in this report.
First generation	F0 parents, F1a and F1b offspring: One F0 female in the 80ppm group was found dead in wk. 28; all other F0 rats survived in good condition. Body wt and food consumption were comparable to controls at each interval. Necropsy findings of F0 parents were unremarkable. Reproductive data for F1a mating indicated 100% fertility for males in control and 80ppm groups and 90% in the 750ppm group. All females mated; Fertility index(F1a litters produced/mated F0 females) was 95%, 90% and 80% in 0, 80 and 750ppm groups, respectively. Gestation index (live litter/pregnant females) was 100% and newborn

	viability was 99% for F1a litters in all groups. Number of live pups/litter was 11, 12, and 12 in 0, 80 and 750ppm; pup sex ratio on day 0 of lactation and pup body wt at day 0 and day 21 of lactation were comparable in all groups. F1a pup viability on day 4 of lactation was 98%, 99% and 98% in 0, 80 and 750ppm groups, and at end of lactation (day 21/day 4 after litters reduced to 8 pups) was 100% in all groups. In F1a litters, one pup in an 80ppm litter had a opaque left eye and 1 pup in a 750ppm litter had a crooked tail. In the 2nd mating of F0 parents to produce litters F1b, male fertility was 100%; female fertility was 90% in control and 80ppm groups and 95% in 750ppm group. Gestation index was 100% in all groups. F1b newborn viability was 99%, 97% and 99%, pup viability on day 4 of lactation was 97%, 95% and 94%, and viability on day 21 (weaning) was 97%, 97% and 96% in 0, 80 and 750ppm groups, respectively. Live pups/litter, sex ratio and pup body wt at day 0 and day 21 of lactation were comparable to controls and to F1a data. One pup in an 80ppm litter had a deformed hind foot.
Second generation	F1b parents, F2a and F2b offspring: Body wt of F1b parent rats were comparable or greater than controls except for 80ppm females at wk 20 (just prior to 2nd mating) when a slightly lower mean body wt (not statistically significant) was seen. Food consumption was also comparable except during wk 20 when both males and females in the 750ppm group had statistically significant reduced food intake ($p<0.05$, Students t-test). At necropsy, no gross lesions were found in F1b parents. Male fertility was 100%, 100% and 90% for F2a and F2b mating in 0, 80 and 750ppm groups; female fertility was 95%, 90% and 70% in F2a and 95%, 95% and 85% in F2b mating. Reduction in female fertility at 750ppm was not statistically significantly (chi square) different from the 95% control values and may be attributable to failure of one 750ppm male to sire a litter in either mating, resulting in 2/6 and 2/3 non-productive females in F2a and F2b mating, respectively. Gestation index was 100% for all groups in both matings. Newborn viability indices were 100%, 97% and 100% in F2a litters and 99%, 100% and 98% in F2b litters for 0, 80 and 750ppm groups. Pup viability on day 4 of lactation for F2a litters was 98%, 94% and 98%, and at day 21 after reduction (weaning) was 98%, 97% and 98%; for F2b litters, viability at day 4 was 95%, 98% and 93% and at day 21 was 99%, 98% and 99% for 0, 80 and 750ppm groups, respectively. Live pups/litter were 13, 14; 12, 15 and 12, 14 in litters F2a and F2b in 0, 80 and 750ppm groups, respectively. Sex ratios and pup wts on day 0 and day 21 of lactation were comparable to controls and between F2a and F2b mating for both dose groups, and similar to F1 data. One male pup in 80ppm group had hydrocephalus.
Third generation	F2b parents, F3a and F3b offspring: Body wt and food consumption of F2b parent rats were comparable to controls. Necropsy findings were unremarkable. Male fertility indices were 90%, 100% and 89% in the F3a mating and 90%, 100% and 100% in F3b mating for 0, 80 and 750ppm groups. Female fertility was lower than previous generations in all groups: F3a 65%, 80% and 85%; F3b 85%, 80% and 83% for 0, 80 and 750ppm groups, respectively. Gestation indices were 100% and newborn viability was 99% in F3a litters and 97-98% in F3b litters for all groups. Pup viability at day 4 of lactation was 96% and 98%; 96% and 100%; 99% and 98% in lF3a and F3b litters and at day 21 was 92% and 99%; 100% and 99%; 98% and 97% in F3a and F3b litters for 0, 80 and 750ppm groups, respectively. Live pups/litter ranged from 12-14 in both F3a and F3b mating and were comparable in all groups and with previous generations. Sex ratios were also comparable. A slight reduction in mean pup wt at day 21 (weaning) compared to controls was seen in both treated groups in the F3b litters, only the 750ppm female mean pup wt value was statistically significant. The 80ppm female mean pup wt value was the same but not statistically significant probably due to a slightly larger standard deviation. F3b mean pup wt at day 21 of lactation were: males 49±10g, 44±11g and 43±11g; females 48±9.3g, 41±12g and 41±9.5g for 0, 80 and 750ppm groups, respectively. F3a mean pups wt at day 21, ranged from 46-48g for males and 42-45g for females in all groups. Since mean weanling pup wts in other generations and in the F3a mating were not appreciably different within generations, this F3b occurrence was not considered biologically significant. Pup general observations and necropsy data were unremarkable.
Conclusions (contractor)	Dietary administration of dicyclopentadiene at nominal concentrations of 80 and 750ppm to three successive generations of male and female albino rats had no deleterious effects on reproductive performance or general condition of the animals compared to concurrent controls. No evidence of dose-related teratogenic effects was seen in pups of any generation.

Data Quality	
Reliabilities	**2.** Reliability with restrictions. Actual body wt, food consumption data and details of necropsy of adults not included in the report. Adult organs were not reported to have been weighed or examined h istopathologically. Actual volume of test material ingested in diet/group was not calculated. Adherence to GLP was not indicated.
References	Johnston, C.D. and Belilies, R.P. 1979. Three generation reproduction study in rats using dicyclopentadiene. LBI Proj. #10734-07. Litton Bionetics, Inc. Kensington, MD, for U.S. Army Medical Research and Development Command, Washington, DC Contract No. DAMD17-77-C-7003 (1980)
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary – Group 7: Resin Oils

Invertebrate Acute Toxicity

Test Substance	Dicyclopentadiene, CAS# 77-73-6 (95% purity)
Method	
Method/guideline followed	U.S. EPA, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians
Year (guideline)	1975
Type (test type)	Acute toxicity
GLP	Unknown
Year (study performed)	Unknown
Species	Water Flea (*Daphnia magna*)
Analytical Monitoring	Unknown
Exposure Period	48 hours
Statistical Methods	Probit and least squares regression analysis
Test Conditions	
Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, supplier of organisms, age, size, weight, loading	Test organisms were obtained from Bionomics Aquatic Toxicology Laboratory and were they were cultured in static, aerated well water with a hardness of 35 mg/L as CaCO3, pH of 7.1, temperature of 21=/-1C, and dissolved oxygen concentration of greater than 60% saturation. Testing was conducted in 250 ml beakers, which contained 166 ml of treatment solution. Diluent water used was aged for at least 24 hours prior to test initiation. For each treatment level, the appropriate amount of test compound was pipetted into 500 ml of diluent water and mixed with a magnetic stirrer. This solution was then divided into three equal aliquots in triplicate beakers to provide replicate exposure treatments. All beakers were maintained at 20=/-1C and test solutions were not aerated during the test. Five organisms were randomly assigned to each test vessel within 30 minutes after the test compound was added and in control vessels resulting in a total of 15 test organisms per treatment level and control.
Results	
Units/Value: Note: Deviations from protocol or guideline, analytical method, biological observations, control survival	24-hour LL50 = 11.6 mg/L (95% confidence limits = 9.2-14.2 mg/L) based on nominal loadings 48-hour LL50 = 10.5 mg/L (95% confidence limits = 8.4-13.2 mg/L) based on nominal loadings
Conclusions (study author)	
Data Quality	
Reliabilities	**(2)** Reliable with restrictions There is less raw data and information on the testing procedure than is desirable in order to rate this study for reliability at a level higher than 2 (reliable with restrictions). There is sufficient information in the report to suggest that the testing procedure followed an acceptable test guideline (U.S. EPA, 1975).
Reference	Bentley, R.E., G.A. LeBlanc, T.A. Hollister, and B.H. Sleight. 1976. Acute Toxicity of Diisopropylmethyl Phosphonate and Dicyclopentadiene to Aquatic Organisms. Gov. Rep. Announc. NTIS Report #AD-AO 37750. (original report from EG&G Bionomics, Wareham, MS, USA)
Other	
Last changed	Revised December 12, 2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary – Group 7: Resin Oils

Fish Acute Toxicity

Test Substance	Dicyclopentadiene, CAS# 77-73-6
Method	
Method/guideline followed	Japanese Industrial Standard, JIS K 0102-1986-71
Year (guideline)	1986
Type (test type)	Acute toxicity
GLP	Unknown
Year (study performed)	Unknown
Species	Orange-Red Killifish (*Oryzias latipes*)
Analytical Monitoring	Unknown
Exposure Period	48 hours
Statistical Methods	Doudoroff or Probit method
Test Conditions	
Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, supplier of organisms, age, size, weight, loading	Organisms were supplied by Nakashima Fish Farm (Kumamoto, Japan). Fish were acclimated prior to test initiation in flow through systems using lab water at a temperature of 25+/- 2C for approximately 28 days. Test organisms used in the study were from one lot. Ground water from the testing lab, Kurme Research Laboratories, was used in the study. Water temperature, pH, and dissolved oxygen were continuously monitored in the lab. Total hardness, evaporated residue, chemical oxygen demand, chloride ion, ammonia nitrogen, selected organic substances, and selected heavy metals are periodically measured in water samples to ensure water quality standards are met. Test systems were glass vessels containing 4 L of treatment solution at 25+/- 2C with 10 fish per treatment level and the control. The exposure system used either a static or semistatic procedure with renewal of treatment solution every 8 to 16 hours.
Results	
Units/Value:	48-hour LC50 = 3.7 mg/L
Note: Deviations from protocol or guideline, analytical method, biological observations, control survival	
Conclusions	
(study author)	
Data Quality	
Reliabilities	**(2)** Reliable with restrictions There is less raw data and information on the testing procedure than is desirable in order to rate this study for reliability at a level higher than 2 (reliable with restrictions). There is sufficient information in the report to suggest that the testing procedure followed an acceptable test guideline, JIS K 0102-1986-71. It is unknown if the data represent measured values.
Reference	Chemicals Inspection and Testing Institute, Japan. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center. ISBN 4-89074-101-1.
Other	
Last changed	Revised December 12, 2001 (Prepared by a contract to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Methylcyclopentadiene – dimer (MCPD-d). MRD78-91. Analytic characterization, stability and purity refer to Project report #44-521
Method	
Method/guideline followed	None specified.
Type (test type)	Acute
GLP	Not specified
Year	1978
Species/Strain	Rat, Wistar
Sex	Male
No. of animals per sex/dose	5
Vehicle	None
Route of administration	Oral gavage
Test Conditions	Male Wistar rats, at least 8 wks old (255-281g) were individually housed in elevated wire mesh cages in a temperature-controlled room reserved for rats. AAALAC standards were adhered to. Purina rat chow and water were available ad lib, except for the 16-20 hrs prior to dosing. Test material was delivered by gavage to 5 rats, at a dose of 10.0g/kg body wt. as calculated from the specific gravity. Rats were observed for clinical signs 1, 2, 4, and 6 hrs after dosing and once daily thereafter for 14 days. Mortality, toxicity and pharmacological effects were recorded for each rat. These included: piloerection, ptosis, lethargy, chromodacryorrhea, emaciation and diarrhea. Body wt was recorded at initiation and termination. All rats were examined for gross pathology.
Results	
LD_{50} with confidence limits.	The LD_{50} was not reached at 10g/kg. One rat died on day 4. Significant toxic signs were lethargy, ptosis, ataxia and diarrhea, which cleared by day 7. Rats gained weight normally over the 14-day period.
Remarks	
Conclusions (study author)	The LD_{50} was not reached at 10g/kg.
Data Quality	
Reliability	**2.** Reliable with restrictions. Not known whether GLP were applied to this study.
References	Cerven, D.R. 1978. Single oral dose toxicity in rats. Project #MB78-3290. MB Research Laboratories, Inc. Spinnerstown, PA., for Exxon Corp. Dodd, D.E., Fait, D.W. and Eisler, D.L. 1981. Four-hour acute LC50 inhalation study in rats and mice. Proj. Rpt. #44-521. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ.
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Methylcyclopentadiene – dimer (MCPD-d), MRD78-91. Analytic characterization, stability and purity refer to Project report #44-521.
Method	
Method/guideline followed	None specified.
Type (test type)	Acute limit test
GLP	Not specified
Year	1978
Species/Strain	Rabbit, New Zealand White
Sex	Not specified
No. of animals per sex/dose	4
Vehicle	None
Route of administration	Dermal
Test Conditions	New Zealand White rabbits, at least 8 wks old (2.0-2.7kg) were individually housed in elevated wire mesh cages in a temperature controlled room reserved exclusively for rabbits on acute tests. Cages and rooms were kept in accordance with AAALAC standards. Rabbit chow and water were freely available. Immediately prior to dosing, the abdomens of 4 rabbits were clipped (200m^2; approx. 10% of body surface) and abraded deep enough to penetrate the stratum corneum, but not deep enough to produce bleeding. Test material was applied dermally to each site at a dose of 3.16g/kg. The area was covered with gauze and secured by 2mil thick plastic dams. After 24 hr of exposure, dams were removed, and the site was wiped free of test article. Signs of dermal irritation were recorded and evaluated at 24hrs, 3, 7, 10, and 14 days. Rabbits were observed for mortality and toxic effects at 2 and 4 hrs post dose and once daily for 14 days. Body wt was recorded pre-test and at termination. Necropsies were performed on all rabbits.
Results	
LD_{50} with confidence limits.	LD_{50} was not reached at 3.16g/kg
Remarks	No mortality was observed. All rabbits exhibited signs of lethargy and ataxia, 3 rabbits had tachypnea, and 2 rabbits had visible, dilated conjunctival blood vessels during the first 4 hr of exposure, which cleared after the first day. Skin reactions were severe and worsened over time until day 10, with signs of recovery by day 14. All rabbits showed severe erythema and skin flaking with 3 rabbits showing scar formation and skin cracking. Upon removal of the binding, rabbits showed moderate skin edema (raised approx. 1mm) that resolved progressively over time. At day 14, there was barely perceptible edema. Approx. 65-70% of the applied dose remained at the application site. At necropsy, one rabbit showed dark areas on the lungs and mottled kidneys.
Conclusions	
(study author)	LD_{50} was not reached at 3.16g/kg
Data Quality	
Reliability	**2.** Reliable with restrictions. Not known whether GLPs were applied to this study.
References	Cerven, D.R. 1978. Acute dermal toxicity in albino rabbits. Project #MB78-3290. MB Research Laboratories, Inc. Spinnerstown, PA. for Exxon Corp. Dodd, D.E., Fait, D.W. and Eisler, D.L. 1981. Four-hour acute LC50 inhalation study in rats and mice. Proj. Rpt. #44-521. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ.
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Methylcyclopentadiene dimer (MCPD-d), CAS #26472-00-4. 92% dimer. Liquid of pungent odor. Compositionally stable for at least one month
Method	
Method/guideline followed	None specified.
Type (test type)	Acute Limit test
GLP	Yes
Year	1980
Species/Strain	Rats, Fischer 344
Sex	Males and females
No. of animals per sex/dose	6
Vehicle	Filtered air
Route of administration	Whole Body Inhalation (4hr exposure)
Test Conditions	Rats (5wk. old; males 173g; females 127g) were housed in stainless steel wire mesh cages (3/sex/cage) except during exposure (2/sex/cage). Temperatures were between 68-74^{0}F, with relative humidity between 35-57% and a 12 hr light-dark cycle. Powdered food and water were available ad lib except during exposure. Liquid MCPD-d was heated in a glass evaporator at the lowest temperature sufficient to produce a vapor of 495ppm. Chamber concentration of the test article was monitored by gas chromatography flame ionization detection. One group of 6 male and 6 female rats were exposed once for 4 hrs on day 1 and sacrificed on day 15. Rats were examined during exposure and daily for 14 days. Body wt was recorded at initiation and on days 2, 6, 9 and 15. All rats were necropsied for gross lesions. No tissues were saved for microscopic evaluation
Results	
LC_{50} with confidence limits.	LC_{50} was not reached at 495ppm.
Remarks	No adverse effects were observed in any rats during exposure to 495ppm MCPD-d or post-exposure over the 14-day observation period, and no gross lesions were observed. There was no change in body wt attributable to exposure and body wt increases were within normal limits.
Conclusions (study author)	None of the rats died during the exposure period or within the 14-day observation period. No adverse effects attributable to test article were observed.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Zelenak, J.P. 1980. Methylcyclopentadiene dimer: Four-hour acute LC_{50} inhalation study on rats and mice. Proj. Rpt. #43-536. Bushy Run Research Center, Pittsburgh, PA for Exxon Corp. Linden, NJ
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Methylcyclopentadiene dimer (MCPD-d), CAS #26472-00-4. 92% dimer. Liquid of pungent odor. Compositionally stable for at least one month
Method	
Method/guideline followed	None specified.
Type (test type)	Acute Limit test
GLP	Yes
Year	1980
Species/Strain	Mice, B6C3F1
Sex	Males and females
No. of animals per sex/dose	6
Vehicle	Filtered air
Route of administration	Whole Body Inhalation (4hr exposure)
Test Conditions	Mice (5wk. old; males 24g; females 19g) were housed in stainless steel wire mesh cages (3/sex/cage) except during exposure (2/sex/cage). Temperatures were between 68-74^{0}F, with relative humidity between 35-57% and a 12 hr light-dark cycle. Powdered food and water were available ad lib except during exposure. Liquid MCPD-d was heated in a glass evaporator at the lowest temperature sufficient to produce a vapor of 495ppm. Chamber concentration of the test article was monitored by gas chromatography flame ionization detection. One group of 6 male and 6 female mice were exposed once for 4 hrs on day 1 and sacrificed on day 15. Mice were examined during exposure and daily for 14 days. Body wt was recorded at initiation and on days 2, 6, 9 and 15. All mice were necropsied for gross lesions. No tissues were saved for microscopic evaluation
Results	
LC_{50} with confidence limits.	LC_{50} was not reached at 495ppm.
Remarks	No adverse effects were observed in any mice during exposure to 495ppm MCPD-d or post-exposure over the 14-day observation period, and no gross lesions were found. There was no change in body wt attributable to exposure, and body wt increases were within normal limits.
Conclusions (study author)	None of the mice died during the exposure period or within the 14-day observation period. No adverse effects attributable to test article were observed.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Zelenak, J.P. 1980. Methylcyclopentadiene dimer: Four-hour acute LC_{50} inhalation study on rats and mice. Proj. Rpt. #43-536. Bushy Run Research Center, Pittsburgh, PA for Exxon Corp. Linden, NJ
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Methylcyclopentadiene dimer. 92% dimer. Analytical characterization provided; refer to
Remarks	Project report #44-521 for stability and purity and conditions under which aerosol formation occurs.
Method	
Method/guideline followed	Not specified
Test type	Subacute
GLP	Yes
Year	1982
Species	Rat
Strain	F344
Route of administration	Whole Body Inhalation
Duration of test	12 days
Doses/concentration levels	0, 5, 50 and 404ppm (actual)
Sex	Male and female (10/sex/group)
Exposure period	6hrs/day
Frequency of treatment	once a day for 9 days (days 1-5, 8-11)
Control group and treatment	10 mice, filtered air, 6hrs/day for 9 days (days 1-5, 8-11).
Post exposure observation period	None
Statistical methods	Bartlett's test, analysis of variance, Duncan's multiple range test, F-test or Student's t-test to compare group vs. control, Cochran t-test when Students t-test was significant.
Test Conditions	Fischer F-344 rats, approx. 70 days old at study initiation, were housed in stainless steel, wire mesh cages at 66-76^{0}F and 43-78% relative humidity. The exposure chamber was maintained at 72-82^{0}F and 37-66% relative humidity and kept on a 12 hr light-dark cycle. Food and water were available ad lib, except during exposure. During exposure, rats were housed 2 per cage. Rats were assigned to 4 test groups (10/sex). The liquid test article was vaporized in a heated, spiral-grooved Pyrex tube and diluted with air prior to entering the exposure chamber. Chamber samples were taken once/hr. and analyzed by gas chromatography/flame ionization detection. Rats were observed prior to, during and following exposure for clinical signs and toxic effects. Body weight was taken prior to exposures on days 1, 2, 5, 8, 9, and prior to sacrifice on day 12. Food consumption was measured prior to initiation and 2-3 times during the study. Urine was collected after for 17hrs. after the fifth and ninth exposures. Hematologic tests were performed on all surviving rats at sacrifice; blood was taken from the orbital sinus. At sacrifice on day 12, liver, lungs, kidneys, gonads, and any gross lesions were saved for possible histological evaluation. Histologic evaluation was performed on livers and kidneys from all rats. Livers, lungs and kidneys of all rats and testes of all males were weighed.
Results	
NOAEL (NOEL)	NOAEL females = 50ppm; males < 5ppm
LOAEL (LOEL)	LOAEL females = 404ppm (based on dec. wt. gain);
	males = 5ppm (based on histopathologic effects).
Remarks	Female rats in the 404ppm group had urogenital wetness and periocular redness that persisted. In the second week of exposure, male rats showed periocular redness. Also during the second week of exposure, rats of both sexes had lacrimation. Rats of both sexes at the 404ppm exposure level, had significant decreases in body wt. Male and female rats at 404ppm had significantly lower food consumption after 8 exposures; females also had decreased consumption after 4 exposures. Urinalysis indicated that males were more seriously affected than females. After 5 exposures, males at all exposure levels, had epithelial cells and cell casts in the urine; however, the effects were not seen in females. Urine specific gravity and osmolality were significantly depressed in males. The number of cells and cell casts in male urine were dose related. There were no exposure related hematological effects observed. Rats of both sexes had significant increases in absolute and relative wts, and relative kidney wt at 404ppm. Males, but not females from the 50ppm

	group had increased absolute liver and kidney wts and relative kidney wts. Gross pathology showed a significant frequency of kidney color changes at 404ppm and 2 males were affected at 50ppm; these effects were not seen in females. Treated male rats also showed an occasional reticular pattern in the liver. Histopathological lesions were seen in the kidneys of male rats at all doses; these were concentrations-related, involving protein accumulation in proximal tubule epithelial cells, and tubular hyperplasia in the cortex. In males at all doses, there was an increase in liver mitotic index; this effect was not seen in females.
Conclusions (study authors)	Male rats were more sensitive than females to test article vapor, exhibiting decreased wt. gain, food consumption, and urine specific gravity, increased urine epithelial cells, cell casts, relative liver, kidney and testes wt. Histopathological lesions were also noted in males, as well as increased mitotic index in the liver. Several of the findings in males were dose-related through the lowest dose. Females showed decreased food consumption, wt. gain, clinical signs and increased kidney wt at 404ppm.
Quality Reliabilities	**1.** Reliable without restrictions.
References	Dodd, D.E. and Longo, L.C. 1982. Methylcyclopentadiene – dimer vapor: Nine-day subchronic rat and mouse inhalation study. Proj. Rpt. 44-519. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ Dodd, D.E., Fait, D.W. and Eisler, D.L. 1981. Four-hour acute LC50 inhalation study in rats and mice. Proj. Rpt. #44-521. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ.
Other Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Methylcyclopentadiene dimer. 92% dimer. Analytical characterization provided; refer to
Remarks	Project report #44-521 for stability and purity and conditions under which aerosol formation occurs.
Method	
Method/guideline followed	Not specified
Test type	Subacute
GLP	Yes
Year	1982
Species	Mouse
Strain	B6C3F1
Route of administration	Whole Body Inhalation
Duration of test	12 days
Doses/concentration levels	0, 5, 50 and 404ppm (actual)
Sex	Male and female (10/sex/group)
Exposure period	6hrs/day
Frequency of treatment	once a day for 9 days (days 1-5, 8-11)
Control group and treatment	10 mice, filtered air 6hrs/day for 9 days (days 1-5, 8-11).
Post exposure observation period	None
Statistical methods	Bartlett's test, analysis of variance, Duncan's multiple range test, F-test or Student's t-test to compare group vs. control, Cochran t-test when Students t-test was significant.
Test Conditions	B6C3F1 mice, approx. 70 days old at study initiation were housed in stainless steel, wire mesh cages at 66-76^{0}F and 43-78% relative humidity. The exposure chamber was maintained at 72-82^{0}F and 37-66% relative humidity and kept on a 12 hr light-dark cycle. Food and water were available ad lib, except during exposure. During exposure, mice were housed 2 per cage. The liquid test article was vaporized in a heated, spiral-grooved Pyrex tube and diluted with air prior to entering the exposure chamber. Chamber samples were taken once/hr. and analyzed by gas chromatography/flame ionization detection. Mice were observed prior to, during and following exposure for clinical signs and toxic effects. Body weight was taken prior to exposures on days 1, 2, 5, 8, 9, and prior to sacrifice on day 12. Food consumption was measured prior to initiation and 2-3 times during the study. Hematologic tests were performed on all mice surviving to sacrifice; blood was taken from the orbital sinus. At sacrifice on day 12, liver, lungs, kidneys, gonads, and any gross lesions were saved for possible histological evaluation. Histologic evaluation was performed on livers and kidneys from all mice. Livers, lungs and kidneys of all mice and testes of all males were weighed.
Results	
NOAEL (NOEL)	NOAEL females = 50ppm; males = 5ppm
LOAEL (LOEL)	LOAEL females = 404ppm (based on hematology, liver wt, kidney wt); males = 50ppm (based on hematology, liver wt, liver mitotic figures).
Remarks	One male mouse in the 404ppm group died following the first exposure; no other mice died during the study. Test article-related changes in body wt. gain of females were obscured by a drop in control wt. during the first week, but there appeared to be some weight gain thereafter in the exposed groups. In males, there were no test article body wt. effects at sacrifice, but there was an initial decrease. In females there was a significant increase in food consumption after 4 and 9 exposures (values were not obtained for males). In mice of both sexes, there was a statistically significant decrease in erythrocyte count, hemoglobin concentration and hematocrit for the 404ppm group; the decrease was much smaller in the 50 and 5ppm groups, and only significant for hemoglobin concentrations in the 50ppm males. In females, lymphocyte count was decreased at 404ppm. At 404ppm, both sexes had significant increases in absolute and relative liver wt. Male mice did not show kidney or liver perturbations upon microscopic examination. Male mice of the 404 and 50ppm groups had increased mitotic figures in liver, but females did not. No significant histopathological

	effects were seen in kidneys of female or male mice.
Conclusions (study authors)	Most toxic effects were limited to the 404ppm exposure groups, but male mice of the 50ppm group also had an increase in absolute and relative liver wt and increased liver mitotic rate.
Quality Reliabilities	**1**. Reliable without restrictions.
References	Dodd, D.E. and Longo, L.C. 1982. Methylcyclopentadiene – Dimer vapor: Nine-day subchronic rat and mouse inhalation study. Proj. Rpt. 44-519. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ Dodd, D.E., Fait, D.W. and Eisler, D.L. 1981. Four-hour acute LC50 inhalation study in rats and mice. Proj. Rpt. #44-521. Bushy Run Research Center, Export, PA for Exxon Corp., East Millstone, NJ.
Other Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	C9 Resin Oil (L) D-47-94. Yellowish liquid of pungent odor. Composition described; major components: indene 21.2%, vinyl toluene 13.9%, methyl styrene 7.0%, dimethyl styrene 7.9%, methyl indene 3.9%.
Method	
Method/guideline followed	Drugs Directorate Guideline, HPB, Health and Welfare Canada, 1990; OECD Guidelines, Sec. 401 and 420, Paris, France 1981 and 1992
Type (test type)	Acute, Limit test
GLP	Yes
Year	1995
Species/Strain	Rats, Sprague Dawley CD[Crl: CD(SD)BR]
Sex	Males and females
No. of animals per sex/dose	5
Vehicle	None
Route of administration	Oral gavage
Test Conditions	Rats (200-300g) were housed in separate quarters in suspended wire cages, 3-5/cage. The animal room was maintained at 22±2^{0}C and 40-70% relative humidity with 12 hr light-dark cycle. Chow diet and water were available ad lib. Rats were dosed with a single oral dose of 2.0g/kg on day 1 and sacrificed on day 15. Rats were observed daily for 14 days for morbidity, mortality and clinical signs. Rats were weighed at initiation and at sacrifice. Gross necropsies were performed on all rats.
Results	
LD_{50} with confidence limits	LD_{50} was not reached at 2.0g/kg. There were no deaths at the limit dose of 2.0g/kg.
Remarks	Male rats showed signs of apathy, piloerection, dyspnea and passivity that cleared by day 3; female rats showed no abnormal signs. Rats of both sexes gained weight normally over the 14-day study period. There were no organs with gross pathological findings.
Conclusions	
(study author)	The rat oral LD_{50} of C9 resin oil was in excess of 2.0g/kg.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Pucaj, K. 1995. Acute oral toxicity of C9Resin Oil, (L) D-47-94. Project #97383. Nucrotechnics, Scarborough, Ontario, for Novacor Chemicals, Ltd., Calgary Canada
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	C9 Resin Oil (#D-16-95, and #D-17-95). Yellow oily liquid. Composition described; major components: indene 21.2%, vinyl toluene 13.9%, methyl styrene 7.0%, dimethyl styrene 7.9%, methyl indene 3.9%.
Method	
Method/guideline followed	OECD Guidelines, Proc. 403.
Type (test type)	Acute
GLP	Yes
Year	1995
Species/Strain	Rats, Sprague-Dawley
Sex	Males and females
No. of animals per sex/dose	5; 3 dose levels: 1.03±0.2; 2.07±0.31; 5.01±0.34mg/l (actual)
Vehicle	None
Route of administration	Whole Body Inhalation
Test Conditions	Rats (males 236-300g; females 220-257g) were individually housed in suspended stainless steel cages with mesh bottoms. The facility was maintained at 69-72^{0}F and relative humidity of 45-60% with a 12 hour light-dark cycle. Rats were fed chow diet and received water ad lib. Rats were exposed to aerosols generated by a 0.25" atomizer. Gravimetric samples were collected on a 25mm glass fiber filter (GF/B Whatman), weighed and divided by air flow volume to determine chamber concentration. Particle mass median aerodynamic diameters for the 3 dose levels were 1.9-3.4µm. The exposure period lasted slightly longer than 4 hrs to provide for chamber equilibrium. At the end of the exposure period, rats were removed from the chamber, and returned to holding cages. Body wt. was recorded at initiation day 0, day 7 and day 14. Rats were observed for toxic signs, including mortality and morbidity, every 30 min. during exposure, at removal from chambers and once daily thereafter. Gross necropsies were performed on all rats. LC_{50} ± 95% confidence limits were determined by Probit analysis.
Results	
LC_{50} with confidence limits.	LC_{50}: Males 1.40mg/l (no confidence limits calculated); Females 1.90 (± 0.96-3.75) mg/l: combined sexes 1.65 (±1.18-2.32) mg/l.
Remarks	Following exposure, rats from all dose levels exhibited one or more of the following signs: facial staining, abnormal respiration, abnormal posture, loss of balance, piloerection, hunched posture and/or hypoactivity. All rats at the 5.01mg/l dose died within 3 days following exposure, with 4 rats dying during exposure; these rats showed irregular and shallow breathing, dyspnea and prostration. Gross necropsy showed discoloration of the lungs, liver and gastrointestinal tract. At the 2.07mg/l dose, all males and 2 females died within 3 days of exposure. The 3 surviving females developed loss of balance but all symptoms cleared by day 7, and animals showed normal body wt gain for the duration of the study. Gross necropsy of the rats dying during study showed discoloration of the lungs, but no remarkable findings were seen in rats sacrificed on day 14. At the 1.03mg/l dose, one female rat died within 3 days of exposure. Surviving rats developed loss of balance, gasping, and prostration. The surviving rats recovered by day 5, and gained body wt. normally for the remainder of the study. Gross necropsies done at terminal sacrifice were unremarkable.
Conclusions (study author)	LC_{50}: Males 1.40mg/l (no confidence limits calculated); Females 1.90 (± 0.96-3.75) mg/l: combined sexes 1.65 (±1.18-2.32) mg/l.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Wnorowski, G. 1995. Acute inhalation toxicity defined LC50, OECD Guideline #403, Study #3718. Product Safety Labs, East Brunswick, NJ, for Novacor Chemicals Ltd., Calgary, Canada
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	C9 Resin Oil (#D-16-95, and #D-17-95). Yellowish liquid of pungent odor. Composition described; major components: indene 21.2%, vinyl toluene 13.9%, methyl styrene 7.0%, dimethyl styrene 7.9%, methyl indene 3.9%.
Method	
Method/guideline followed	Modified Draize method- OECD Guidelines, Sec. 404, Paris 1981 (revised 1992)
Type (test type)	Acute Irritation
GLP	Yes
Year	1995
Species/Strain	Rabbit, New Zealand albino
Sex	Females
No. of animals per sex/dose	3
Vehicle	None
Route of administration	Dermal
Test Conditions	Rabbits were housed in individual stainless steel cages and received rabbit chow and water ad lib. The facility was maintained at 22^0C and 40-70% relative humidity with a 12 hr light-dark cycle. About 24 hrs before dosing, the back of each of three rabbits was closely clipped free of hair and divided into two 3cmx3cm sites with a marker. One site was designated the control and the other, the test site. Each test site was covered with a sterile gauze patch to which 0.5ml of test article was applied and affixed to the rabbit with adhesive tape. The control site was patched but untreated. The entire trunk was wrapped In a rubber dam for a 4 hr exposure period. Control and test article-exposed sites were examined at 1, 24, 48,72, and 96hrs and on days 5, 7, 10, and 14 following exposure period, and scored by the Draize method.
Results	The readings for the first 7 days indicated slight erythema and edema of test article-exposed skin (score 1-2). From days 10-14, there was no irritation, however, there was slight skin desquamation. The primary irritation score was 2.6±0.2.
Remarks	
Conclusions	
(study author)	The test article was concluded to be a mild irritant to the skin.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Pucaj, K., 1995. Dermal irritation/corrosion test of resin oil, (L) D-47-94, in rabbits. Proj. #97811. Nucrotechnics, Scarborough, Ontario, for Novacor Chemicals, LTD, Calgary, Canada.
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	C9 Resin Oil (L) D-47-94. Yellowish liquid of pungent odor. Composition described; major components: indene 21.2%, vinyl toluene 13.9%, methyl styrene 7.0%, dimethyl styrene 7.9%, methyl indene 3.9%.
Method	
Method/guideline followed	Modified Draize method- OECD Guidelines, Sec. 405, Paris 1992
Type (test type)	Acute Eye Irritation
GLP	Yes
Year	1995
Species/Strain	Rabbit, New Zealand albino
Sex	Not specified
No. of animals per sex/dose	3
Vehicle	None
Route of administration	Lower conjunctival sac of one eye/rabbit
Test Conditions	Rabbits were housed in individual stainless steel cages and received rabbit chow and water ad lib. The facility was maintained at 22^0C and 40-70% relative humidity with a 12hr light-dark cycle. A 0.1ml volume of C9Resin oil was instilled into the lower conjunctival sac of one eye of each of 3 rabbits. The test article stayed in contact with the eye for a 24 hr exposure period. The opposite eye of each rabbit served as a control. Evaluation for irritancy was made at 24, 25, 48, 72, and 96 hrs and on day 5 following exposure. Scoring was by the Draize method.
Results	The cornea and iris were not affected by the test material, but there were conjunctival redness and discharge in treated eye of each of the 3 rabbits. Effects were maximal after 72 hrs and gradually cleared by post-dose day 5. At 72 hr, total scores for redness, chemosis and discharge in the 3 rabbits were 8, 12, and 2 with 2 of the 3 rabbits having individual scores of 2 or higher.
Remarks	
Conclusions (study author)	Because 2 rabbits showed individual Draize scores for redness of 2 and 3, at 72 hr post-dose, C9 Resin oil, (L) D-47-94 was considered to be a strong eye irritant.
Data Quality	
Reliability	**1.** Reliable without restrictions.
References	Pucaj, K., 1995. Acute eye irritation/corrosion test of C9 resin oil, (L) D-47-94, in rabbits. Proj. #97811. Nucrotechnics, Scarborough, Ontario, for Novacor Chemicals, LTD, Calgary, Canada.
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Genetic Toxicity - in Vitro

Test Substance	C9 Resin Oil, CAS # 68477-54-2. Steam cracked C8-C12 fraction naphtha; Lyndell Resin Oil 90. Clear, pale yellow to yellow colored liquid with gasoline-like naphtha odor
Test substance	
Method	
Method/guideline followed	Standard method based on Ames et al, 1975, Maron & Ames, 1983, and Green & Muriel, 1976.
Type	Reverse mutation bacterial assay
System of testing	Salmonella typhimurium and Escherichia coli with and without metabolic activation
GLP	Yes
Year	1994
Species/Strain	S. typhimurium TA97, TA98, TA100, TA102, TA1535, and E. coli WP2 uvrA (pKM101)
Metabolic activation	Yes
Species and cell type	Sprague Dawley male rat liver (S9 fraction) from Molecular Toxicology, Inc. College Park, MD
Quantity	20µl S9 fraction in 0.5ml S9 mix/plate
Induced or not induced	Aroclor 1254-induced, rats were given a single ip 500mg/kg dose, 5 days prior to sacrifice.
Concentrations tested	0, 39, 78, 156, 313, and 625µg/plate –S9, and 0, 78, 156, 313, 625, and 1250µg/plate + S9; samples diluted in dimethyl sulfoxide (DMSO). Negative control 100µl DMSO
Statistical Method	None. Criteria for a positive response were dose related increase in mutant frequency and more than one dose level exhibited a mutant frequency at least 2-fold greater than solvent control. Equivocal response was defined as a 2-fold increase above control level at one or more doses with no evidence of a dose response.
Remarks for Test Conditions	C9 resin oil test solutions were prepared in DMSO immediately prior to use. Salmonella strains and E. coli WP2 (approx. 10^9cells/ml) were exposed to either test solution or DMSO ±S9 in 3 plates/dose/strain by the plate incorporation method. A preliminary toxicity assay using TA97 and TA100 -S9 was performed over 9 doses from 78-20,000µg/plate to establish optimal doses for the mutagenicity assay. In the mutagenicity assay, dose concentrations were 37-625µg/plate –S9, and 78-1250µg/plate +S9. All plates were incubated at 37^0C for 48 hrs, then revertant colonies were counted. Positive control compounds were: -S9, ICR191 (1µg/plate) for TA97, 2-nitroflourene (2-NF, 5µg/plate) for TA98, sodium azide (NaA, 1.5µg/plate) for TA100 and TA1535, mitomycin C (0.5µg/plate) for TA102 and methyl methanesulfonate (MMS, 1000µg/plate) for E. coli WP2; +S9 2-aminofluorene (2-AF, 10µg/plate) for all Salmonella strains and 2-aminoanthacene (2-AA, 5µg/plate) for E. coli WP2. Two independent assays were performed.
Results	
Genotoxic effects	In the preliminary toxicity assay, precipitate was visible at all dose levels (78-2000µg/plate). Number of revertants relative to solvent control was reduced for all doses, with a dose-related decline from =625µg/plate. Background lawn for both TA100 and TA97 showed a marked clearing beginning at 625µg/plate. In the first mutagenicity test without activation, all tester strains showed a progressive decline in revertant colony count with increasing dose (e.g. TA100: 142, 88, 124, 77, 63, and 70 revertants/plate, and E. coli: 246, 256, 262, 247, 218, and 200 at 0 [DMSO], 39, 78, 156, 313, and 625µg/plate, respectively). Clearing of background lawn was observed at 625µg/plate. In the S-9 activated cultures, all strains except TA100, TA1535 and E. coli WP2, showed a dose-related reduction in revertant frequency at all dose levels (e.g. TA97: 287, 290, 269, 247, 219, and 155 at 0, 78, 156, 313, 625, and 1250µg/plate. In TA100, TA1535 and E. coli WP2, the revertant frequency was similar to vehicle controls. No increase in revertant colonies was observed. Clearing of background lawns was observed at 625 and 1250µg/plate for all tester strains. In the independent repeat assay, although little discussion is provided in the text, the data tables demonstrate that toxicity did not appear to be as severe as in the initial assay. No significant reduction in revertants occurred over the range of doses, and there was no increase in revertant frequency above the solvent control in any strain at any dose level ±S9 (e.g. TA100 –S9: 161, 173, 196, 190, 169, 153 at 0, 37, 78, 156, 313, and 625µg/plate;

	+S9: 174, 161, 154, 161, 150, and 119 at 0, 78, 156, 313, 625, and 1250µg/plate, respectively. Positive control compounds performed appropriately: in -S9 cultures: ICR191- 483; 2-NF- 1200; NaA- 1378 for TA100, 867 for TA1535; mitomycin C 800; MMS- 4277 for E. coli; in +S9: cultures: 2-AF 953-3167 for Salmonella strains; 2-AA-2083 for E.coli. C9 resin oil was considered non-mutagenic in this test system. (Reviewer's note: This Salmonella/ E. coli assay is an acceptable, negative mutagenicity test based on the results of the independent repeat assay. Although both assays were performed at the same dose levels ± S9, the toxicity in the first assay, evidenced by a dose-related reduction in revertant colonies and inhibition of background lawn at most doses made it a less reliable predictor of mutagenicity. The second assay had less toxicity at the same dose levels and did not demonstrate any increase in revertants above vehicle control for any dose in any strain tested.)
Conclusions (contractor)	C9 Resin Oil did not induce a significant increase in Salmonella strains or E. coli with or without metabolic activation at any dose level and is not considered a mutagen in this test system.
Data Quality *Reliabilities*	**2.** Reliable with restrictions. Given toxicity seen in the preliminary test, some doses lower than 39 or 78ug/plate should have been employed to provide a better profile of effect.
Reference	Mehta, R.D. 1995. Mutagenicity of C9 Resin Oil in the Salmonella/E. coli assay. Study No. 950315/2. Prairie Biological Research Ltd., Edmonton, Alberta, Canada, for Novacor Chemicals, Ltd., Calgary, Alberta, Canada Ames, B.N. et al. 1975. Mutat. Res. 31: 347-364. Green, M.H.L., and Muriel, W.J. 1976. Mutat. Res. 38: 3-32. Maron, D.M., and Ames, B.N. 1983. Mutat. Res. 113: 173-215.
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Composition analysis, purity and stability referred to sponsor. T-119
Method	
Method/guideline followed	None specified, comparable to standard study
Type (test type)	Acute
GLP	Yes
Year	1983
Species/Strain	Rat, Fischer 344
Sex	Males and females
No. of animals per sex per dose	5
Vehicle	Corn oil
Route of administration	Oral gavage
Test Conditions	Rats (64 days old, 131-222g) were individually housed in metal, screen-bottomed cages and received food and water ad lib. Animal rooms were maintained at 75^0F with relative humidity of 61% and a 12-hour light/dark cycle. Test article was administered, as a suspension in corn oil, to 24 hr fasted animals, at levels of 0.32, 0.56, 1.0, and 1.8 g/kg. Rats were evaluated daily for 14 days following dosing. Observations for morbidity/mortality were performed daily for 14 days. Body wts were taken at initiation, day 8 and day 15. Each rat was observed at 1 and 4 hr post-dosing, and at least once daily thereafter for clinical signs for 14 days. Gross necropsies were performed on all rats. Acute oral LD_{50}s for each sex and combined sexes were determined by Probit analysis. A precise oral LD_{50} could not be obtained in male rats because there was only one data point between 0 and 100% deaths.
Results	
LD_{50} with 95% confidence limits.	Female: 0.97 (0.57-1.96)g/kg; Male: >0.56<1.8g/kg; Combined: 0.96 (0.73-1.26)g/kg. Normal body wt. increases were observed in surviving animals at 7 and 14 days. Clinical signs (other than death) occurred sporadically in all groups. Signs included arching of the back, bloody discharge from nose/mouth, hypersensitivity, backward-moving motor activity, and tremors. All deaths occurred within 48 hrs of dosing. Deaths occurred as follows: 1) Males; 0.32g/kg, 0/5; 0.56g/kg, 0/5; 1.0g/kg, 3/5; 1.8g/kg, 5/5; 2) Females; 0.32g/kg, 0/5; 0.56g/kg, 1/5; 1.0g/kg, 3/5; 1.8g/kg, 4/5. Necropsies of rats dying during the study showed dose-related congestion in abdominal, cranial, and thoracic cavities. At terminal sacrifice, only 2 rats showed congestion (sex and dose group not reported).
Remarks	
Conclusions	
(study author)	LD50 for combined sexes was 0.96 (0.73-1.26)g/kg.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Rausina, G.A. 1983. Acute oral toxicity study in albino rats using Resin-Former Feedstock. Proj. #2016. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co. Houston, TX
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Composition analysis, purity and stability referred to sponsor.
Method	
Method/guideline followed	None specified, comparable to standard study
Type (test type)	Acute limit test
GLP	Yes
Year	1983
Species/Strain	Rats, Fischer 344
Sex	Males and females
No. of animals per sex per dose	5
Vehicle	Filtered air
Route of administration	Inhalation (whole body)
Test Conditions	Rats (16 wks old, 157-276g) were maintained at 24.6^{0}C with 48% relative humidity and a 12-hour light/dark cycle. One group of 10 rats was exposed to the test article at an actual concentration of 5.4g/m^3, for 4 hrs in a stainless steel, dynamic exposure chamber. A test article aerosol was generated with a ball-jet nebulizer, and chamber concentration was controlled by varying both dilution air and inlet pressure of filtered air. Chambers were sampled with a gas-tight syringe and samples were directly injected directly into a gas chromatograph. Concentrations were determined by comparing peak area of sample with that of standards. Test article was volatile and gravimetric samples could not be taken, so particle size was determined during exposure by laser velocity measurement (MMAD 5.0µm±1.4 SD; 89% of particles <10µm). Body wt. was taken after exposure and on day 7 and 14. Mortality checks were made during exposure and daily thereafter. Clinical signs were noted at 1 and 4 hrs post-exposure, and daily thereafter. Non-fasted rats were sacrificed and necropsied for gross lesions.
Results	
LC_{50} with confidence limits.	Not reached at 5.4g/m^3.
Remarks	There were no deaths during the study. Rats were hyper-excitable/hyperactive for the first 2 days of the study, and had dry red material around nose/mouth; clinical signs abated by day 5. Rat body wt did not change for the first 7 days, but increased normally thereafter. No gross necropsy findings were attributable to test article exposure.
Conclusions	
(study author)	No deaths occurred after exposure to 5.4g/m^3 for 4 hrs.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Gordon, T. 1983. LD_{50} Resin-Former Feedstock inhalation toxicity study in rats. Proj. #82-083. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co. Houston, TX
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Acute Toxicity

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Composition analysis, purity and stability referred to sponsor.
Method	
Method/guideline followed	None specified, comparable to standard study
Type (test type)	Acute- limit test
GLP	Yes
Year	1983
Species/Strain	Rabbit, New Zealand White
Sex	Males and females
No. of animals per sex per dose	5
Vehicle	none
Route of administration	dermal
Test Conditions	Rabbits (11-19 wks old, 2.04-3.10 kg) were individually housed in metal, screen-bottomed cages and received chow diet and water ad lib. Rooms were maintained at 72-85^{0}F with relative humidity of 30-80% and a 12-hour light/dark cycle. Before test article application, backs of the rabbits were shaved, and 4 parallel epidermal abrasions were made lengthwise on the shaved test site that penetrated the stratum corneum but not the dermal layer. Neat test article was applied over the site at 2000mg/kg and covered with a gauze patch and occlusive dressing that was taped in place, covered with a cotton sock and wrapped in an elastic bandage. Each animal was fitted with an Elizabethan collar to prevent ingestion. Test article remained on the skin for 24hrs after which wrappings were removed and residual test article wiped off. Observations for mortality, moribundity, clinical signs, and skin reactions were made immediately after removal of test article and then daily for 14 days, after which the rabbits were sacrificed and gross necropsies performed. Irritation was scored by the Draize method (scores 2-4).
Results	
LD_{50} with confidence limits.	Not reached at 2000mg/kg.
Remarks	No mortality occurred during the study, and body weight increased normally. Immediately after test article removal, rabbits showed slight to severe edema and slight to well-defined erythema (scores 1-4), which partially resolved over the 14-day observation period. Most of the rabbits had moderate to severe skin desquamation during the study, and by the end of the observation period, sloughing of dry patches revealed red skin, indicative of a persistent irritation. Gross necropsy did not reveal any adverse findings other than skin desquamation.
Conclusions (study author)	The median lethal dose is greater than 2000mg/kg. A persistent skin irritation was observed at the application site.
Data Quality	
Reliability	**1.** Reliable without restrictions
References	Rausina, G.A. 1983. Acute dermal toxicity study in albino rabbits, Resin-Former Feedstock. Proj. #82-075. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co. Houston, TX
Other	
Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Genetic Toxicity - in Vitro

Test Substance	
Test substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Amber colored, clear aromatic liquid with hydrocarbon odor. Composition analysis, purity and stability referred to sponsor.
Method	
Method/guideline followed	Standard method based on Hsie et al. (1981), O'Neill & Hsie (1979)
Type	In vitro mammalian cell forward mutation
System of testing	Chinese hamster ovary (CHO) cell culture
GLP	Yes
Year	1984
Species/Strain	CHO-K-1 heterozygous for hypoxanthine-guanine phosphoribosyl transferase (HGPRT+/-) from Oak Ridge National Laboratory, TN.
Metabolic activation	Yes
Species and cell type	Rat liver (S9) fraction purchased from Litton Bionetics, Kensington, MD
Quantity	1.0mg S9 fraction/ml treatment medium/flask
Induced or not induced	Aroclor 1254 induced (treatment not specified)
Concentrations tested	Cytotoxicity: 4, 8, 64, 128, 256, 512, 1024, 2048µg/ml ± S9; Mutagenicity: 64, 128, 256, 300µg/ml (350, 400µg/ml, cytotoxicity only) ±S9; all diluted in 10% Pluronic® polyol F68 (prepared in deionized water, mol. wt. 8350).
Statistical Methods	Frequency of mutant colonies per million clonable cells, corrected for absolute survival by viability plates, was calculated and comparisons of treated cultures with vehicle controls made on transformed data using a two-tailed t-test (Irr & Snee, 1979) using the MUTANT computer program (Snee et al., 1981). Criteria for positive results were significant ($p<0.05$) increase in mutant colonies (HGPRT+/-? HGPRT-/-) at any dose level and a dose related response. If only one criterion was met, results were considered equivocal.
Remarks for Test Conditions	Sufficient Resin-Former Feedstock was weighed separately for each dose level into 10ml volumetric flasks; 6.9ml of 10% F68 was added along with sufficient medium (Ham's F-12 without hypoxanthine) to achieve final 10ml volume for testing. All dosing preparations were vortexed just after addition of medium and just prior to addition of 20µl to each 3ml medium culture flask. All cultures were incubated at 37^0C in 5% CO_2 enriched, humidified atmosphere. Positive control mutagens were ethyl methanesulfonate (100µg/ml) for –S9 cultures, and benzo(a)pyrene (4µg/ml) for +S9 cultures. For cytotoxicity, each dose group was composed of 2 flasks, one –S9, one+S9, negative controls ± S9, seeded with $5x10^5$ cells on day 1. Cultures were exposed to test compound for 5 hours on day 2. On day 3, cells were trypsinized and counted with a Coulter Model ZB, then 200 cells were transferred into each of 3 60mm culture dishes. These viability plates were incubated until day 10, fixed in methanol and stained with Giemsa. Colonies were counted visually or with an Artek Model 981 colony counter. Absolute survival = total colony count ÷ number of cells seeded/flask. Relative survival = absolute survival in treated cultures ÷ vehicle control survival. Acceptable survival level is at least 10%. For mutagenicity, cells were seeded on day 1 into 6 flasks/dose group, 3-S9, 3+S9; on day 2 approximately 10^6 cells were exposed to Resin-former feedstock for 5 hours. Vehicle control had 12 flasks, 6-S9, 6+S9. On day 3, cultures with excessive cytotoxicity were discarded. From remaining cultures, 200 cells were seeded to each of 4 viability plates/dose level; incubated to day 10, fixed with methanol, stained with Giemsa, and colonies counted for survival. Expression cultures (10^5-10^6 cells/one dish/dose) were seeded on day 3; subcultured three times until day 10 when 200 cells were seeded on each of 4 viability plates/dose and $2x10^5$ cells seeded on each of 5 mutagenicity plates/dose with selective medium containing 10^{-5}M 6-thioguanine to allow expression of HGPRT mutation. Cultures were incubated undisturbed until day 17 when they were fixed and stained. For mutagenicity, a ratio of total colony counts in mutagenicity plates over absolute survival in viability plates was calculated for each treatment group. Frequency of mutant colonies/million clonable cells was calculated

	and statistical comparisons with negative control data were made.
Results Genotoxic effects	In the cytotoxicity test, Resin-Former Feedstock induced post treatment cell toxicity (greater than 10%) at dose levels of 128µg/ml and higher –S9 and at all dose levels+S9. Cloning of these cells showed toxicity compared to vehicle controls in -S9 cultures beginning at 8µg/ml (86%relative survival); survival decreased to 54.1% at 256µg/ml and 0% at higher doses with the exception of outlier value of 94.5% relative survival at 128µg/ml; in +S9 cultures, relative survival was equal or greater than vehicle controls up to 256µg/ml, above which dose no cells survived. In the mutagenicity test, post-treatment cell counts showed cytotoxicity at all levels -S9 (64-400µg/ml) and at 128µg/ml and higher +S9. Decreased cloning efficiency was evident at 256µg/ml and higher –S9, and at 350µg/ml and higher +S9. Cell viability after expression passage, at the time of mutant selection for dose levels 64-300µg/ml, was slightly decreased at 300µg/ml –S9 (90.3% relative survival) only. For all Resin-former feedstock exposed cultures ±S9, there were no significant dose-related responses nor any significant increase in mutation frequency compared to vehicle controls. Negative and positive controls responded appropriately: EMS –S9 induced 175.7 mutants/10^6cells; B(a)P +S9 induced 63.9mutants/10^6cells.
Conclusions (contractor)	Resin-Former Feedstock did not induce a mutagenic response with or without metabolic activation in CHO/HGPRT cells at any dose level. Resin-Former Feedstock does not cause gene point mutations in mammalian cells under the conditions of this assay.
Data Quality *Reliabilities*	**1**. Reliable without restrictions. Study conforms to standard design. GLPs have been followed
Reference	Papciak, R.J., and Goode, J.W. 1984. CHO/HGPRT test using Resin Former Feedstock Proj. #2065. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX Hsie, A.W. et al. 1981. Mut. Res. 86: 193-214 O'Neill, J.P. and Hsie, A.W. 1979. Banbury Report 2: 55-63 Irr, J.D. and Snee, R.D. 1979. Banbury Report 2: 263-275. Snee, R.D., Smith, R.L., and Irr, J.D. 1981. MUTANT. A computer program for the evaluation of short-term mutation test results. E.I. Dupont de Nemours Co.
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Genetic Toxicity - in Vitro

Test Substance	
Test substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Amber colored, clear aromatic liquid with hydrocarbon odor. Composition analysis, purity and stability referred to sponsor.
Method	
Method/guideline followed	Standard method based on Williams (1977) and Williams et al. (1977,1982)
Type	In vitro mammalian cell DNA repair assay
System of testing	Unscheduled DNA Synthesis (UDS) in primary hepatocyte cultures.
GLP	Yes
Year	1984
Species/Strain	Fischer 344 male rat (13-14 wks old) – 1 rat per test
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	Range-finding: 4, 8, 16, 32, 64, 128, 256, 512, 1024, 2048µg/ml: UDS assay: 10, 20, 40 100µg/ml; all diluted in 10% Pluronic® polyol F68 (prepared in deionized water, mol. wt 8350, 80% hydrophilic)
Exposure period	18-20 hours
Statistical Methods	None employed. Criteria for positive response are incorporation of radioactive precursor (^{3}H-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. A positive response need not be dose related.
Remarks for Test Conditions	Sufficient Resin-Former Feedstock was weighed separately for each dose level, 0.70ml 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 stored at 37^{0}C until dosing and mixed just prior to addition at 30µl to each 3ml culture. The conc. of ^{3}H-thymidine (½ life 12.5 yrs.) used in these assays was 1mCi/ml. All cultures were incubated at 37^{0}C in 5% CO_2 enriched humidified atmosphere. For range-finding, primary hepatocytes derived from freshly perfused rat liver were seeded (approx. 1x10^5 cells/ml) into treatment vessels, exposed to test material for 19 hours (2 cultures/ dose level; 2 untreated cultures, and two vehicle F68 control cultures), then fixed in formalin and stained with trypan blue for viability determination. At least 50% viability needed for the assay. In the UDS assay, 1x10^5 cells/ml were seeded into coverslip cultures, exposed to ^{3}H-thymidine and test substance for 18-20 hours (3 cultures/dose level). Positive control was 2-acetyl aminofluorene (0.2µg/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^{0}C. Autoradiographs were developed, stained and coverslipped on day 14. Number of grains overlying 50 randomly selected nuclei/slide were counted. The highest of 3 cytoplasmic grain counts/cell were subtracted 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. Slides with negative average net nuclear grain count were scored as zero.
Results	
Genotoxic effects	Resin-Former Feedstock induced toxicity in primary rat hepatocytes beginning at 32µg/ml (67.8% relative viability) following 19 hours exposure. Viability continued to decrease in a dose related manner (i.e. relative viabilities of 60.6% at 64, 34.7% at 128, and 29.1% at 256µg/ml) to the maximum dose of 2048µg/ml (2.5% relative viability). Resin-former feedstock did not induce UDS at any treatment level in this assay. Negative and positive controls responded appropriately (vehicle control mean net count of 0.80 and 2-acetyl aminofluorine mean net count of 122.61 net nuclear grains).

Conclusions (contractor)	Resin-Former Feedstock did not induce unscheduled DNA synthesis at any dose level administered to cultured rat hepatocytes. Resin-former feedstock does not cause DNA damage and repair in this assay.
Data Quality *Reliabilities*	**1**. Reliable without restrictions. Study conforms to standard design. GLPs have been followed.
Reference	Brecher, S., and Goode, J.W. 1984. Hepatocyte primary culture/DNA repair test of resin-former feedstock. Proj. #2067. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX Williams, G.M. 1977. Cancer Res. 37: 1845-1851 Williams et al. 1977. In Vitro 13: 809-817 Williams et al. 1982. Mut. Res. 97:359-370
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Genetic Toxicity - in Vitro

Test Substance	
Test substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Amber colored, clear aromatic liquid with hydrocarbon odor. Composition analysis, purity and stability referred to sponsor.
Method	
Method/guideline followed	Standard method based on Cortesi et al (1983), Dunkel et al (1981), Reznikoff et al (1973)
Type	In vitro cell transformation
System of testing	Mouse embryo cells
GLP	Yes
Year	1983
Species/Strain	BALB/3T3-A31-1-1 from T. Kakunaga, National Cancer Inst., 1982
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	Cytotoxicity: 4, 8, 16, 32, 64, 128, 256, 512, 1024 and 2048µg/ml; Transformation: 16, 32, 64, 200µg/ml, all diluted in 10% Pluronic® polyol F68 (prepared in deionized water, mol. wt. 8350, 80% hydrophilic).
Exposure period	2 days
Statistical Methods	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 dose.
Remarks for Test Conditions	Sufficient Resin-Former Feedstock was weighed separately for each dose level; 0.7ml of 10% F68 added per ml of final volume and medium (Eagle's MEM with 10% heat-inactivated fetal calf serum + antibiotics) was added as required to achieve final volume for testing. Preparations were mixed and added at 50µl to each 5 ml culture. All cultures were incubated at 37^0C in 5% CO_2 enriched humidified atmosphere. For cytotoxicity, 2 flask cultures/dose group, 2 cultures for vehicle F68 or medium negative control were seeded with $1x10^4$ cells/culture 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 flask cultures ($1x10^4$ cells/culture/dose group) and two colony formation flask cultures (100 cells/culture/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 formation cultures were fixed, stained, and counted visually on day 8 to determine cloning efficiency (avg. number colonies/flask ÷ 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.
Results	
Genotoxic effects	Resin-former feedstock induced toxicity in BALB/3T3 cells after two days exposure beginning at 32µg/ml (63% viability) with increasing toxicity to highest dose level, 2048µg/ml (7% viability); 80% cytotoxicity occurred between 128-256µg/ml. In the transformation assay, inhibition of cloning efficiency (C.E.) became evident at 64µg/ml (30.9% relative CE) and no colonies were detected at 200µg/ml. All treated cultures induced type III foci compared to negative controls. The 16µg (6 type III foci) and 200µg (8 type III foci) dose cultures had at least twice the type III foci seen in untreated medium controls (3 type III foci), and the 32µg and 64µg cultures had 4 and 5 type III foci, respectively. The positive control, 3- methylcholanthrene induced the expected response for transformation: 17 type III foci. Transformation frequencies were 0.43, 0.29, 0.38, and 0.62 for 16, 32, 64, and 200µg/ml groups, respectively, compared to 0.20 for medium control and 2.43 for positive control.

Conclusions (contractor)	Resin-Former Feedstock induced transformation at all dose levels in BALB/3T3 cells under conditions of this assay, with a significant 2.7 fold increase at the highest dose. Cytotoxicity and impairment of cloning efficiency were also observed.
Data Quality *Reliabilities*	**1.** Reliable without restriction. Study conforms to standard design. GLPs have been followed.
Reference	Brecher, S, and Goode, J.W. 1983. BALB/3t3 transformation test: Resin-Former Feedstock. Proj. #2068. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co, Houston, TX Cortesi, E. et al. 1983. Teratogenesis, Carcinogenesis, Mutagenesis 3: 101-110. Dunkel, V.A. et al. 1981. J. Nat'l Cancer Inst. 67: 1303-1315. Reznikoff, C.A. et al. 1973. Cancer Res. 33: 3239-3249.
Other *Last changed*	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel).

Genetic Toxicity - in Vivo

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Amber colored, clear organic liquid with hydrocarbon odor. Composition analysis, purity and stability referred to sponsor.
Remarks	
Method	
Method/guideline followed	Comparable to standard assay
Type	Mammalian bone marrow erythrocyte micronucleus
GLP	Yes
Year	1984
Species	Mouse
Strain	Crl:CD®–1 (ICR) BR Swiss
Sex	Male and female: 10M, 10F/group; 15M, 15 F in 1 group (11 wks old, 24-39g at start)
Route of administration	Oral gavage
Doses/concentration levels	0, 0.125, 0.25, 0.5g/kg in corn oil
Exposure period	1 dose/day for 2 days; 1 group- 1 dose, 1 day only
Statistical methods	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.
Remarks for Test Conditions.	Resin-Former Feedstock dosing solutions were prepared fresh for each day of dosing – 1.25 g was weighed into a 50 ml volumetric flask, corn oil was added to make up 50ml volume and contents blended by shaking. No range finding study was performed. Four groups of mice were given 0.0 (20ml/kg corn oil), 0.125-0.5g/kg test material in a single oral dose by gavage for 2 days. All mice were weighed on day 1 and on day of sacrifice. One half of each treated group and vehicle control (5M, 5F) was killed on day 3 and the remainder on day 4. One group (15M, 15F), given 0.5g/kg by gavage in a single dose for 1 day only, was killed on days 2, 3, 4 (5/sex/day). Positive control mice given cyclophosphamide (75 mg/kg) ip daily for 2 days were killed on day 3. 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 evaluated for presence of micronuclei. Data collected included group mean body weights for each day, total PCEs, total NORMs, PCEs with MN, and NORMs with MN.
Results	
Genotoxic effects NOAEL (NOEL) LOAEL (LOEL)	NOEL (genetic) = 0.5g/kg; NOAEL (systemic) = 0.25g/kg (levels assigned by reviewer). Mortality occurred in 1/10 males, 6/10 females in the 0.5g/kg for 2 days dose group, on or before day 2; in the 0.5g/kg for 1 day dose group, 2/15 males and 9/15 females died. Gross necropsy revealed yellow oily or red material in small intestines and/or stomach; 1 female had bilateral hydrometra. Perianal staining was observed. No significant wt loss occurred in surviving animals; 50% or more total treated animals survived to sacrifice, although mortality at 0.5g/kg single dose and 2 doses was 73% and 10% respectively among males, and 60% females in both dose regimens. Surviving animals treated with Resin-former feedstock did not show any significant change in frequency of micronucleus formation in polychromatic erythrocytes. In the 2 surviving females given 0.5g/kg test material for 2 days and sacrificed on day 4, a statistically significant decrease in PCE/NORM ratio was seen – 0.7 compared to 0.8 in solvent controls; all females in other dose groups and all males had PCE/NORM ratios comparable to controls. Positive and negative controls produced expected results; cyclophosphamide induced 4.5% and 3.30% micronucleated PCEs in male and female mice, respectively, sacrificed on day3.

Conclusions (study authors)	Oral treatment of Resin-Former Feedstock for 1-2 days at doses up to 0.5g/kg/day had no effect on frequency of micronucleated PCE in bone marrow. Resin-former feedstock did induce mortality at 0.5g/kg and some inhibition of PCE/NORM ratio in 2 high dose females treated for 2 days and killed on day 4. Under conditions of this study, Resin-Former Feedstock is not a clastogen.
Data Quality *Reliabilities*	**2.** Reliable with restrictions. Significant mortality at the highest dose.
References	Khan, S.H., and Goode, J.W. 1984. Micronucleus test in mouse bone marrow: Resin-Former Feedstock administered orally for 2 days. Proj. #2066. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX
Other *Last changed*	Revised 11/21/2001 (Prepared by a consultant to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Composition analysis, purity and stability referred to sponsor
Remarks	
Method	
Method/guideline followed	None specified, comparable to standard study
Test type	Subacute
GLP	Yes
Year	1984
Species	Rat
Strain	Fischer 344
Route of administration	Dermal
Duration of test	14 days
Doses/concentration levels	0, 1.0, 2.0g/kg
Sex	5 Males, 5 Females/dosing group
Exposure period	6hr/day for 9 days (days 1-5, 8-11)
Frequency of treatment	Once/day
Control group and treatment	5 Males, 5 Females; corn oil (1g/kg)
Post exposure observation period	None
Statistical methods	Standard deviation, Bartlett's test, analysis of variance, Dunnett's test, Modified t-test, two-tailed Kolmogorov-Smirnov test.
Test Conditions	Rats (49 days old, 112-199g at initiation) were housed individually in suspended, stainless steel cages, with wire mesh fronts and bottoms, and equipped with automatic watering. Chow diet and water were provided ad lib. Room temperature and relative humidity were maintained at 75^0F and 51%, respectively, with a 12-hour light/dark cycle. Rats received a fixed volume of 2g/kg/day of dosing solution (including corn oil vehicle); test article doses were 0, 1.0, 2.0g/kg applied to the shaved area on the back, representing approx. 10% of body surface area. Test site was uncovered during exposure. After 6 hrs exposure, residual test article was wiped off. During exposure, rats wore Elizabethan collars to retard ingestion. Rats were observed for mortality and moribundity twice daily on dosing days and once daily on non-dosing days. Body wt was recorded at initiation, day 6 and at necropsy on day 12. Rats were observed for clinical signs once daily on dosing days. Dermal reactions were observed/scored immediately before dosing and after test article removal. Blood was taken from the orbital sinus before initiation and at sacrifice for measurement of total/differential white blood cells, red blood cells, platelets, hemoglobin, hematocrit, mean cell vol., mean corpuscular hemoglobin, mean corpuscular hemaglobin concentration, BUN, creatinine, alkaline phosphatase, Na, K, glucose, SGPT, protein, albumin and albumin/globulin ratio. All rats were sacrificed on day 12 and gross necropsies were performed. The following organs were weighed and processed for histopathology: liver, brain, heart, spleen, kidneys, testes. Skin sections, thymus, uterus, lungs, and ovaries were processed for histopathology.
Results	
NOAEL (NOEL)	NOEL systemic: Male not established (hydrocarbon nephropathy); Female 2.0g/kg. NOEL dermal: Male 1.0g/kg; Female 1.0g/kg (based on skin irritation).
LOAEL (LOEL)	LOEL systemic: Male 1.0g/kg (hydrocarbon nephropathy); Female not established. LOEL dermal: Male 2.0g/kg; Female 2.0g/kg (based on skin irritation). Values assigned by reviewer.
Remarks	No deaths occurred during the study and no moribund animals were found. There were no statistically or biologically significant changes in body wt. Mild to moderate erythema and edema were present in most rats at the 2.0g/kg dose (undiluted) but no rats were affected at 1.0g/kg (diluted 50:50 in corn oil). There were slight increases in total WBC counts and segmented neutrophils, in both males and females at 2.0g/kg. There were no biologically significant changes in organ wt at necropsy, but the skin of all high dose rats displayed variable degrees of visible pathological changes including erythema, and edema and

	desquamation. Histopathological examination of skin showed acanthosis, hyperkeratosis, and ballooning degeneration of keratinocytes with vesicle formation in all high dose rats. There was an excessive, statistically significant accumulation of hyaline droplets in the epithelial cytoplasm in kidneys from all male rats at the 1.0 and 2.0g/kg doses. There were no other test article related effects observed.
Conclusions (study authors)	The test article caused no overt signs of systemic toxicity at 2.0g/kg. Barely perceptible to well-defined erythema, edema, and desquamation were seen on the application sites of males and females. Kidneys of all test article treated male rats showed excessive levels of hyaline droplets.
Quality Reliabilities	**2.** Reliable with restrictions. In the absence of occlusion, some test material might have been lost through volatilization.
References	Rausina, G.A. 1984. Two-week repeated dose toxicity study in rats using Resin-former feedstock. Proj. # 82-085. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX
Other Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Repeated Dose Toxicity

Test Substance	Resin-Former Feedstock; 50-60% DCPD. 15-20% CPD/methyl CPD dimer, <2% BD/CPD dimer, 10-12% styrene, <2%xylene, <2%CPD. Composition analysis, purity and stability referred to sponsor.
Remarks	
Method	
Method/guideline followed	None specified
Test type	Subacute
GLP	Yes
Year	1983
Species	Rat
Strain	Fischer 344
Route of administration	Whole body Inhalation
Duration of test	12 days
Doses/concentration levels	0, 0.6, 2.5g/m^3 (actual)
Sex	5 Males, 5 Females/exposure group
Exposure period	9 days
Frequency of treatment	6hr/day for 9 days (days 1-5, 8-11)
Control group and treatment	5 Males, 5 Females; filtered air
Post exposure observation period	None
Statistical methods	Bartlett's test for organ wt followed by Dunnett's test, or modified t-test and analysis of variance. Microscopic findings were evaluated using Kolmogorov-Smirnov analysis.
Test Conditions	Rats (14 wks old, 152-297g) were housed individually in stainless steel, screen bottomed cages in a room maintained at 76.1^{0}F and relative humidity 42%, with a 12-hour light/dark cycle. Animals were provided with water and chow ad lib, except during exposure. Three groups of 10 rats were exposed to aerosolized test article for 6 hr/day for 9 days. Test article was aerosolized with a ball jet nebulizer. Chambers were sampled with a gas-tight syringe and samples were injected directly into a gas chromatograph. Chamber concentrations were determined by GC; comparing sample peak area with that of standards. High volatility of the test article prevented collection of gravimetric samples, so particle size was determined during exposure by lazer velocity measurement (MMAD= 4.8 at 0.6g/m^3 and 6.9 at 2.5g/m^3; 60-65% of particles <10µm). Rats were observed twice daily on dosing days and once daily on weekends for mortality, and once daily after exposure on dosing days for clinical signs. Body wt was taken prior to exposure on day 1 and 5, and prior to sacrifice on day 12. Blood was collected via orbital sinus on days 5 and 12 for measurement of total/differential white blood cells, red blood cells, platelets, hemoglobin, hematocrit, mean cell vol., mean corpuscular hemoglobin, mean corpuscular hemoglobin conc., blood urea nitrogen, creatinine, alkaline phosphatase, Na, K, glucose, SGPT, protein, albumin, and albumin/globulin ratio. Rats were sacrificed on day 15 and gross necropsies were performed. Organs were weighed and tissues collected for histological examination of tissues from high dose and control rats, and kidneys from low dose males and females. The following organs were weighed: liver, brain, heart, spleen, lungs, kidneys, and testes. The following organs/tissues were prepared for histopathology: brain, heart, lungs, liver, spleen, kidneys, testes, nasal turbinates, thymus, and ovaries; tissues from control and 2.5g/m^3 groups were examined microscopically.
Results	
NOAEL (NOEL)	NOEL was not established in this study.
LOAEL (LOEL)	LOEL: Male 0.6g/m^3 (based on walking with arched back, exclusive of hydrocarbon nephropathy which occurred at 0.6 and 2.5g/m^3); Female 0.6g/m^3 (based on walking with arched back, muscular tension, twitching) (All values assigned by reviewer.)
Remarks	There were no deaths during the study. Statistically non-significant decrease in body wt was seen in both sexes in all groups, including controls (males 1-6%, females 1-7%); it was suggested that nauseating test article vapors were present in the animal holding room, indicating some exposure to controls. The control group showed no remarkable clinical findings during the study and there was no indication of test article deposition on the body

	surface. At 0.6g/m^3, by the second week, several rats walked with arched back and had body rigidity and twitching. At 2.5g/m^3, arched back and rigidity were seen throughout the study, twitching was common by day 4 and lasted until termination; 8/10 rats convulsed at least once. The duration and severity of convulsions varied, but incidence increased by the second wk; males and females were equally affected. Frequency and severity of neurological symptoms were related to level and duration of exposure. There were infrequent occurrences of hyper-excitability, pupil dilation, ocular darkening, and swaying. There were no biologically significant differences in clinical pathology values between treated and untreated rats, but low glucose values were seen at 2.5g/m^3 in both sexes. Liver wt was significantly increased in females at 2.5g/m^3 (18%). Male rats showed microscopic and dose responsive changes in tubular epithelium of kidneys with excessive accumulation of hyaline droplets. No brain abnormalities were observed.
Conclusions (study authors)	Resin-Former Feedstock exposure caused no mortality. Important clinical signs were seen, including convulsions, muscular tension, arched back, ocular and respiratory discharges that were dose related. Gross and microscopic tissue changes were seen including increased liver wt in females at 2.5g/m^3, and excessive hyaline droplets in proximal convoluted tubular epithelium of 0.6 and 2.5g/m^3 exposed males.
Quality Reliabilities	**1.** Reliable without restrictions
References	Gordon, T. 1983. Nine-day repeated dose inhalation toxicity study in rats, Resin-former feedstock. Proj. # 2025. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX
Other Last changed	Revised 11/21/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: Resin Oils and Cyclodiene Dimer Concentrates Category

Fish Acute Toxicity

Test Substance	Resin-Former Feedstock (50-60% dicyclopentadiene, 15-20% methylcyclopentadiene/cyclopentadiene dimer, <2% butadiene dimer, 10-12% styrene, <2% xylene, <2% cyclopentadiene)
Method	
Method/guideline followed	None specified, comparable to standard method
Year (guideline)	Unknown
Type (test type)	Acute toxicity, static renewal
GLP	Yes
Year (study performed)	1983
Species	Rainbow trout (*Salmo gairdneri* now refered to as Oncorhynchus mykiss) and Bluegill sunfish (*Lepomis macrochirus*)
Analytical Monitoring	Yes
Exposure Period	96 hours ± 1hr
Statistical Methods	24, 48, and 96-hour LL50 values were calculated using Probit analysis (SAS system). Chi square performed on each dose response curve to ensure non-heterogeneity and goodness of fit.
Test Conditions Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, supplier of organisms, age, size, weight, loading	Treatment solutions of resin-former feedstock were prepared 1 day before test initiation to achieve maximum saturated test material loadings. Test substance was added to 25L charcoal-filtered, municipal water in each of the 100 mg/l, test vessels and stirred vigorously throughout the day. Test concentrations were assigned by a random numbers table (2 vessels/dose group). 10 fish/species/vessel were added. Starting at one end of the bioassay table, 2 fish were placed in each vessel in consecutive order to the opposite end of the table, then proceeding in reverse direction, 2 more fish were added per vessel until all vessels had 10 fish. Sexes were not determined; at least 120 fish of each species were tested. A preliminary limit test of 100 mg/l resulted in 100% mortality in both species. Dose levels for this assay were 3.2, 5.6, 10, 14, 18, 32 mg/L nominal concentrations to rainbow trout and 10, 14, 18, 32, 56, 100 mg/L to bluegill sunfish. A glass lid was placed on top of each vessel to minimize volatile losses. Solutions were not aerated. Dissolved O_2 concentrations were within acceptable ranges (8.6-10.2mg/l for rainbow trout, 7.4-9.1 for bluegill sunfish). Experimental conditions were: water temp. 10.6-11.6^{0}C and pH 6.8-7.8 for rainbow trout; water temp. 18.2-19.4^{0}C and pH 7.5-8.0 for bluegill sunfish; photoperiod of 12-hr light/dark cycle for both species. Animals were not fed during the 96-hour exposure period. Positive control compound was benzene at concentrations of 5.6, 7.5, 10, 14, 18 mg/l, prepared as an aqueous solution immediately prior to administration to rainbow trout only. There was an insufficient supply of bluegill sunfish for positive control exposure. Mortality and pharmacotoxic signs were recorded daily at intervals of 1, 6, 24,48, 72, and 96 hours, as number fish affected/total fish exposed. Water temp., dissolved O_2 conc., and pH were measured daily for each bioassay vessel in old and freshly prepared test solutions. Total alkalinity (39-41 mg/l as $CaCO_3$), total hardness (97-106 mg/l as $CaCO_3$), and specific conductance (336-421 µmhos/cm) were measured in each vessel during the first 6 hours, and at 48 and 96 hours. A water sample was taken at mid depth from each test solution daily for a total of 8 samples: 1 before test initiation when introduced into vessels, 2 for each of next 3 days (1 from old solution, 1 from fresh solution), and 1 at test termination, to analyze for actual conc. of test material by gas chromatography/FID. Rainbow trout: 36-48 mm length, 0.56-1.86 g supplied from Castalia/Millsite Farms, Castalia, OH, USA. Bluegill sunfish: 30-50 mm length, 0.57-2.99 g supplied from Sea

Results Units/Value: Note: Deviations from protocol or guideline, analytical method, biological observations, control survival	Plantations, Inc., Salem MA, USA. LL50 values (with 95% feducial limits) are based on nominal concentrations: Rainbow Trout (mg/L) — Bluegill Sunfish (mg/L) 24-hr LL50: 14.34 (12.5-16.27) — 21.95 (19.71-25.80) 48-hr LL50: 10.92 (not determined) — 17.91 (16.28-20.69) 96-hr LL50: 10.60 (3.60-63.88) — 13.54 (12.28-14.66) For rainbow trout, % mortality at 96 hours was 5, 10, 25, 95, 100% at nominal concentrations of 3.2, 5.6, 10, 18, 32 mg/l respectively, with pharmacotoxic signs of surfacing, rapid respiration, dark discoloration, bloated abdomens, gyratory swimming, and lying on bottom of vessels. For bluegill sunfish, % mortality at 96 hrs was 0, 75, 85, 100, 100, 100% at nominal concentrations of 10, 14,18, 32, 56, 100 mg/l, respectively, with pharmacotoxic signs of surfacing, rapid respiration, swimming on side, excreting mucus, and lying on bottom of vessel. The benzene 96-hour LC50 in rainbow trout = 7.64 mg/l. Results of chemical analysis of water samples were inconsistent and highly variable, and analyses were discontinued. Test material was observed on water surface and adhering to sides of vessels in treatment solutions.
Conclusions (study author)	
Data Quality *Reliabilities*	**(2)** Reliable with restrictions Analytical characterization of test material in aqueous test solution was inaccurate and unreliable. Quality Assurance final report statement had not been signed by a reviewer. Test material was observed on water surface and adhering to sides of vessels in treatment solutions.
Reference	Glenn, L.S. and Rausina, G.A. 1983. 96-Hour Aquatic Toxicity Study in Rainbow Trout and Bluegill Sunfish with Resin-Former Feedstock. Project #2021. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX, USA.
Source	American Chemistry Council, Olefins Panel