SUMMARY OF DATA FOR CHEMICAL SELECTION

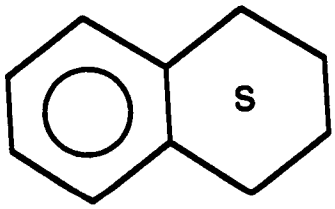
In 1984, the TSCA Interagency Testing Committee (ITC) reviewed the information available on Tetralin (CRCS, Inc., 1984). Since that time, new data have become available and these are included in the summary sheet.

CHEMICAL IDENTIFICATION

CAS Registry Number:	119-64-2
Chemical Abstracts Name:	Naphthalene, 1,2,3,4-tetrahydro- (9 CI)
Synonyms and Trade Names:	Benzocyclohexane; naphthalen-1,2,3,4-tetrahydride; 1,2,3,4-tetrahydronaphthalin; delta(sup 5,7,9)-naphthalene; naphthalene 1,2,3,4-tetrahydride; tetrahydronaphthalene; tetraline; Tetralin

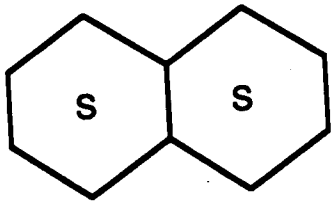
CAS Registry Number:	91-17-8
Chemical Abstracts Name:	Decahydronaphthalene (8 CI, 9 CI)
Synonyms and Trade Names:	Bicyclo[4.4.0] decane; Dec; Dekalin; naphthalane; napthan; naphthane; perhydronaphthalene; UN 1147; Decalin

Structure, Molecular Formula and Molecular Weight:
Tetralin



$C_{10}H_{12}$ Mol. wt.: 132.2

Decalin



$C_{10}H_{18}$ Mol. wt.: 138.2

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Chemical and Physical Properties:

From Budavari (1989) unless otherwise noted.

Tetralin

Description:	Liquid with odor resembling that of a mixture of benzene and menthol
Boiling Point:	207.2° C
Melting Point:	-31° C
Solubility:	Insoluble in water; soluble in methanol at 50.6% wt/wt and aniline; very soluble in ether; miscible with petroleum ether, chloroform, and Decalin, ethanol, butanol, acetone and benzene
Stability:	Prolonged, intimate contact with air may cause the formation of tetralin peroxide which may cause explosion. Peroxide formation is prevented by addition of an antioxidant such as hydroquinone
Vapor Pressure:	1 mm Hg at 38° C (Sax & Lewis, 1989)
Flash Point:	171° F (77°C) open cup 180° F (82°C) closed cup
Specific Gravity:	0.9702 at 20/4° C
Reactivity:	Combustible when exposed to heat or flame; can react with oxidizing materials; emits acrid smoke and irritating fumes when heated to decomposition (Sax & Lewis, 1989)

Log Octanol/Water Partition Coefficient: 3.52 (CRCS, Inc., 1984)

Decalin

Description:	Liquid with slight odor resembling menthol
Boiling Point:	195.7° C (cis isomer) 187.25° C (trans isomer)
Melting Point:	-43.26° C (cis isomer) -30.4° C (trans isomer)

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Solubility:	Insoluble in water; very soluble in alcohol, methanol, ether and chloroform; miscible with propyl and isopropyl alcohol; miscible with most ketones and esters
Stability:	Stable at normal temperatures and conditions of storage. Potentially explosive peroxides can form on long-term storage in contact with air (Du Pont, 1990a)
Density:	0.8963 (at 20°C/4°C) (cis isomer) 0.8700 (at 20°C/4°C) (trans isomer) (Sandmeyer, 1981)
Vapor Pressure:	1 mm @ 22.5°C (cis isomer) (Sandmeyer, 1981) 10 mm @ 47.2°C (trans isomer) (Sandmeyer, 1981)
Flash Point:	136°F (58°C) closed cup

Technical Products and Impurities:

Tetralin. Commercial Tetralin is typically about 97% pure by weight, with decahydronaphthalene and naphthalene comprising the major impurities. Union Carbide's products contain 90 and 98% tetrahydronaphthalene, with naphthalene making up most of the remainder (CRCS, Inc., 1984).

Du Pont's Tetralin^{R} contains 97% tetrahydronaphthalene, 2% decahydronaphthalene, and 1% naphthalene (Du Pont, 1990b). The Aldrich Chemical Co. (1990) offers Tetralin at 99% purity.

Decalin. The commercial Decalin product is a mixture of cis- and trans-isomers. It may be practically all trans-Decalin or a mixture containing up to 60% cis-Decalin (Budavari, 1989). Decalin supplied by Du Pont has a minimum decahydronaphthalene content of 97.0% and a maximum tetrahydronaphthalene (Tetralin) content of 3.0% (Du Pont, 1990a). The Aldrich Chemical Co. (1990) offers the following products: cis-isomer 99%; trans-isomer 99% and mixtures of cis- and trans-isomers 98% and 99%.

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BASIS OF NOMINATION TO THE CSWG

Tetralin and Decalin are both in high demand with annual production/importation amounts in the millions of pounds. Tetralin has been reported to be one of three chemicals which together account for 10% of the 250-350 million pound demand for naphthalene between 1983 and 1987. Tetralin and Decalin are both widely used solvents and substitutes for turpentine in the manufacture of paints, lacquers, waxes and polishes. Each, in addition, has specific secondary uses.

A high potential for human inhalation or dermal exposure to Tetralin or Decalin exists as a result of contact with naturally occurring crude oil, cigarette smoke, or other combustion products; during manufacturing or solvent uses; or because of environmental releases. A data gap exists as far as short term mutagenicity or chronic human health effects testing are concerned. A decision to test these two compounds, along with parent compound naphthalene, in both Ames *Salmonella* and mouse lymphoma assays was made by NCI's Division of Cancer Etiology (DCE) in January 1991. A chronic carcinogenicity bioassay is also needed to fill the gap in knowledge on risk of adverse health effects from exposures to these two chemicals.

[N.B. Subsequent to the nomination, the following *in vitro* test results have been reported by the DCE Short Term Testing Program:

Naphthalene

Ames *Salmonella*: negative (DR:3.3-10,000 μg/plate)
Mouse lymphoma (L5178Y TK+/- cell line):
negative without S-9 (DR: 22-87 μg/ml)
positive with S-9 (DR: 8-30 μg/ml)

Tetralin

Ames *Salmonella*: negative both with and without S-9 in strains TA98, TA100, TA1535, TA1537 and TA1538. (Max. dose tested: 333 μg/plate without S-9; 1000 μg/plate with S-9)
Mouse lymphoma (L5178Y TK+/- cell line):
positive without S-9 (DR: 50-30 μg/ml)
negative with S-9 (DR: 15-1.0 μg/ml)

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Decalin

Ames *Salmonella*: negative with and without S-9 (DR: 100-10,000 μg/plate)
Mouse lymphoma: negative without S-9 (DR: 9-61 μg/ml)
negative with S-9 (DR: 250-450 μg/ml)

SELECTION STATUS

ACTION BY CSWG: 6/07/91

Studies Requested: Chemical disposition studies and carcinogenicity bioassay

Priority: Moderate-to-high

Comments: Nominated because of their structure, the potential for high consumer exposure through their use as solvents in paints, waxes, and polishes, and the lack of adequate testing. Both compounds are products of the hydrogenation of naphthalene. Both are available commercially. It was noted that the ITC looked at both Tetralin (in 1983) and Decalin (in 1977) and scoring seems to indicate little information was available.

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EXPOSURE INFORMATION

Commercial Availability:

Production and Producers: Tetralin and Decalin are the commercially significant hydrogenation products of naphthalene. Tetralin is produced by hydrogenation of naphthalene in the presence of a nickel or modified nickel catalyst. Because these catalysts are sensitive to sulfur, naphthalene with low sulfur levels is used. The major naphthalene sulfur compound, thionaphthene, is removed by sodium treatment and catalytic hydrodesulfurization processes. Decalin is produced by complete catalytic hydrogenation of naphthalene or Tetralin (Gaydos, 1981). Hydrogenation of naphthalene in glacial acetic acid in the presence of a platinum catalyst at 15°C and 130 atm. yields a mixture of 77% cis-Decalin and 23% trans-Decalin. Hydrogenation of Tetralin under the same conditions yields almost entirely cis-Decalin (Budavari, 1989).

Du Pont is the largest U.S. manufacturer of tetrahydronaphthalene and decahydronaphthalene sold under the company trade names Tetralin and Decalin. A Du Pont spokeswoman confirmed that Tetralin and Decalin are produced commercially at Deepwater, N.J., but no production volumes were indicated (Du Pont, 1991a).

Current domestic production volumes for Tetralin and Decalin were not found in the literature [see Research Resource List]. However, the fact that Du Pont supplies both by tank cars, tank trucks and 55 gallon drums indicates a significant market (Kuney, 1990; Du Pont, 1991b). In addition, it has been estimated that from 1983 to 1987, Tetralin, along with 1-naphthol and 1-naphthyl methyl carbamate insecticide, account for 10% of the naphthalene market. Naphthalene demand was 360 million pounds in 1983, 285 million pounds in 1984, 255 million pounds in 1987, and is estimated to reach 270 million pounds in 1991 and 260 million pounds in 1994 (Anon., 1984,1987,1990). The estimated production of Tetralin was probably greater than 1,000 pounds in 1972 and greater than 2,000 pounds in 1975 (National Library of

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Medicine, 1991). According to the public portion of the TSCA inventory, in 1977 from 1.1 to 11 million pounds of Tetralin were produced and/or imported by five companies: Henkel, Inc.; Koppers, Co., Inc.; Union Carbide Corp.; Thorson Chemical Corp.; and Carrell Products, Inc. Of these companies, Koppers reported that they do not manufacture tetrahydronaphthalene *per se*; the compound is present in small amounts in process streams from the manufacture of other chemicals. Koppers does not sell tetrahydronaphthalene commercially in a refined form.

Importation volumes for Tetralin from 1979 to 1983 were reported by the USITC as follows (CRCS, Inc., 1984):

Year	Importation Volume (lbs.)
1979	28,604
1980	8,818
1981	39,683
1982	88,162
1983	69,932

Use Pattern: Tetralin and Decalin are widely used as industrial solvents, primarily for naphthalene, fats, resins, oils, and waxes. Both find use as a substitute for turpentine in lacquers, paints and varnishes; as solvents and stabilizers for shoe polishes and floor waxes; and as a constituent of motor fuels and lubricants. Tetralin is also used as a solvent for pesticides, rubber, asphalt, and aromatic hydrocarbons (naphthalene, anthracene); in alkali resistant lacquers for cleaning printing ink from rollers and type; as a dye solvent carrier in the textile industry; for the removal of naphthalene in gas-distribution systems; as an insecticide for clothes-moths and a larvicide for mosquitoes; in paint thinners and as a paint remover when mixed with Decalin or white spirit; and as an intermediate in the manufacture of certain agricultural chemicals such as carbaryl, napropamide, and 1-naphthoxyacetic acid. Decalin is also used as a patent fuel in stoves; as a high density fuel in submarine-launched cruise missile systems; and in stain removal and cleaning machinery. Mixtures of Tetralin and Decalin are used for certain applications where a synergistic solvency is desired

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(Budavari, 1989; Longacre, 1987; Sax & Lewis, 1987; CRCS, Inc., 1984; Gaydos, 1981; Gaworski *et al.*, 1980).

Human Exposure: The most probable human exposure to Tetralin and Decalin is through dermal contact or inhalation during manufacture or use. Potential occupational exposures are controlled by the use of engineering controls (e.g., the 8-hour TWA PEL/TLV for the reactant naphthalene is 10 ppm) and the routine use of personal protective equipment. Du Pont, the major manufacturer, also recommends that the compound be handled in closed systems where possible, or in work areas with good ventilation (National Library of Medicine, 1991; Du Pont, 1990a,b; CRCS, Inc., 1984; American Conference of Governmental Industrial Hygienists, 1990). Based on data collected during the period 1972 to 1974, the National Occupational Hazard Survey (NOHS) estimated that 2,237 workers were potentially exposed to Tetralin and 935 workers to Decalin. The 1981 to 1983 National Occupational Exposure Survey (NOES) reported 282 workers potentially exposed to Tetralin and 28 to Decalin. Note that the NOES estimate represents actual observations (i.e., the surveyor observed the use of the specific compound) only, whereas the NOHS estimate is made up of actual observations, tradename observations (i.e., the surveyor observed the use of a tradename product known to contain the compound), and generic observations (i.e., the surveyor observed a product in some type of general use which led NIOSH to suspect that the compound might be contained in that product).

Du Pont reported that a total of 15 workers (12 in operations, 3 in maintenance) are potentially exposed to the compound during manufacturing at an estimated concentration of less than 0.03 mg/m^3 of workplace air on an 8-hour TWA basis. Operators are potentially exposed for 9 days/year and maintenance personnel for 3 days/year. A study at a small pilot-scale direct coal liquefaction facility in British Columbia detected Tetralin at a mean concentration of 0.07 mg/m^3 in 11/58 samples of workplace air. Tetralin was not detected, however, in air samples obtained from

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another plant. The limit of detection was 0.05 mg/m^3 (National Library of Medicine, 1991; Leach *et al.*, 1987; CRCS, Inc., 1984).

Submarine personnel may be exposed to Decalin when it is transferred or transported for cruise missile fueling (Gaworski *et al.*, 1980).

Consumers may be exposed to Tetralin and Decalin used as solvents in paints, varnishes, lacquers, waxes, shoe polishes, and in finished petroleum products (gasoline, motor oils). In addition, non-occupational exposure to Tetralin and Decalin may occur via urban atmospheres, contaminated drinking water supplies, and recreational activities at contaminated waterways (National Library of Medicine, 1991; CRCS, Inc., 1984). Krotoszynski & O'Neill (1982) identified Decalin in the expired air of male and female nonsmokers. It was found in all three study populations (control, diabetic, and prediabetic subjects). No levels were reported.

Environmental Occurrence: Tetralin and Decalin are expected to be released to the environment in wastestreams from downstream, non-consumptive (i.e., solvent) use operations, in the disposal of products containing the compounds as solvents (e.g., paints, waxes, etc.), and from releases of crude oil and refined petroleum products

Tetralin. The following summarizes studies on the environmental concentration of Tetralin.

- Tetralin occurs naturally in petroleum and coal (CRCS, Inc., 1984).
- Tetralin was identified as a contaminant in oil refinery wastewater effluent from a dissolved air flotation unit but was not detected in effluents from final clarifier units or a pilot-scale mixed-media filter/activated carbon unit (Burks, 1982).
- Tetralin was not detected in water samples or suspended solid samples collected at Minnesota sites in the Rainy River near pulp and paper mills (Merrimam, 1988).

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- The mean annual loading of Tetralin in urban runoff from the Canadian Great Lakes Basin was estimated to be 36 kg/yr. This value was based on calculated annual runoff volumes and solids loadings and urban stormwater and street sediment samples. The urban samples, however, did not contain detectable levels of Tetralin (Marsalek and Schroeter, 1988).

- Tetralin was detected at 100 ppb in a pond water sample obtained in an uninhabited forested area in central New Brunswick in May 1977 (CRCS, Inc., 1984).

- Tetralin was below the limit of detection (0.05 ug/l) in snowpack samples collected in the Sault Ste. Marie area, a municipal area northwest of Toronto which is characterized by anthropogenic sources of PAHs (Boom and Marsalek, 1988).

- Tetralin was present in the benzene fraction of residential oil burner fuel, but was not detectable following cyclic combustion (Leary *et al.*, 1987).

Decalin. Decalin is a component of crude oil and a product of combustion and is produced and released to the environment during natural fires. Major contributors of Decalin to the environment include: emissions from petroleum refining; coal tar distillation and gasoline and diesel fueled engines; and manufacturing effluents (National Library of Medicine, 1991).

In a 1979 study, Decalin was identified as a component of vehicle exhaust emissions in the Allegheny Mountain Tunnel of the Pennsylvania Turnpike (Hampton *et al.*, 1982). Decalin was also identified in the effluent discharged from the production platforms in the Bucanner Gas and Oil Field located in the Gulf of Mexico (Middleditch, 1982). Decalin was 1 of 53 chemicals detected at all 5 indoor sampling sites during a 1983 air monitoring study at a Washington, D.C. home for the elderly (Ziegenfus, 1987). The preceding studies are indicative of the widespread presence of Decalin in the environment; however, no levels were reported.

Regulatory Status: No standards or guidelines have been set for occupational exposures or environmental levels of Tetralin or Decalin [See Search Resource List].

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EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports associating Decalin with a cancer risk in humans were found in the published literature [See Search Resource List]. Results of an epidemiologic study which indicate that occupational exposure to organic solvents may promote the development of Hodgkin's disease suggest that exposure to Tetralin may be an occupational risk. Hodgkin's disease was diagnosed in a varnish research chemist who worked daily with Tetralin, toluene, xylene, hexane, ethyl acetate, cyclohexane, and white spirit (Olsson & Brandt, 1980).

Tetralin and Decalin are irritating to the eyes, skin and mucous membranes. Tetralin is known to produce nausea, vomiting, intragastric discomfort, transient liver damage, green-gray urine, and some clinical and enzymatic changes. It is also a CNS depressant at high concentration. Both have been reported to cause dermatitis in painters. Several case studies on the acute effects of these solvents have been reported. Tetralin has been associated with restlessness of babies sleeping in a room recently treated with a Tetralin-based varnish (direct action on the CNS), asthenia in persons sleeping in rooms that had been waxed with a Tetralin-containing polish, and temporary liver and kidney damage following ingestion of about 250 ml of Cuprex, an ectoparasiticide containing 31.5% Tetralin, 0.03% copper oleate, 52.7% paraffin oil, and 15.7% acetone. By inhalation the lowest dose of Decalin to indicate an effect in man was 100 ppm. Decalin has been associated with the development of vesicular eczema accompanied by intense pruritus in a man who had used the solvent to clean paving stones. Traces of albumen and urobilin in the urine and a few leucocytes in the sediment suggested possible involvement of the kidneys (Budavari, 1990; CRCS, Inc., 1984; Sandmeyer, 1981; Browning, 1965).

Animal Data: Neither Tetralin or Decalin are currently on test nor scheduled for testing in a standard carcinogenicity bioassay [See Search Resource List].

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Tetralin. No information was found on the carcinogenicity, teratogenicity, embryotoxicity, or fetoxicity of Tetralin [see Search Resource List]. Subchronic and acute toxic effects of Tetralin have been documented. Subchronic effects include:

Oral Administration

- Nephrotoxicity in male Fischer 344 rats administered Tetralin (485 mg/kg bw on alternate days for 2 weeks) intragastrically. The renal lesions, however, were not as severe as the kidney damage observed by Olson *et al.* (1986) following administration of Decalin (Serve *et al.*, 1989).
- Restlessness or apathy, roughening of the skin, anorexia, and intense diarrhea in guinea pigs given 0.25 ml Tetralin daily (240 mg).
- Signs of cataracts in a rabbit study, unspecified dose. Cataracts were not seen in rats fed a diet containing 2% Tetralin for 2 months.

Inhalation Exposure

- Cataracts within 6 days and mild kidney damage in guinea pigs exposed to Tetralin daily for 30 minutes.
- Severe kidney and liver damage in guinea pigs exposed to 275 ppm Tetralin 8 hours a day for approximately 3 weeks.

Dermal Exposure

- Eczema in guinea pigs receiving a daily dermal application.

Unknown Route

- Methemoglobin formation in cats.

Rabbit eye irritation studies demonstrated that undiluted Tetralin caused very mild injury and no corneal damage. Rabbit skin irritation studies showed Tetralin caused severe irritation at 500 mg and erythema with 0.01 ml (CRCS, Inc., 1984). The LC_{10} in guinea pigs for 17 8-hour exposures is 275 ppm. The acute oral LD_{50} in rats is 2.86 g/kg and the dermal LD_{50} in rabbits is 17.3 g/kg (Longacre, 1987).

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Decalin. A slightly greater incidence of pituitary tumors was noted in male F344 rats and female C57BL/6 mice following inhalation of 5 or 50 ppm of Decalin for 90 days. The incidence of pituitary adenomas in male rats was 5/50 (control), 16/49 (low dose) and 16/48 (high dose), $p<0.05$. The incidence of pituitary carcinomas in female mice was 0/77 (control), 3/81 (low dose), and 8/80 (high dose), $p<0.05$ (male mice were not studied). The authors felt that the apparent increase of pituitary tumors was the result of an unusually low control group incidence.

Postexposure changes noted in Decalin-exposed female mice included the increased presence of crystals, macrophages, and lymphoid perivascular cuffing in the lungs; cysts in the mammary and thyroid glands; thyroid hyperplasia; and reversible hepatocellular cytoplasmic vacuolization. The most significant histopathologic changes in rats exposed to Decalin were observed in the kidneys of exposed males. Virtually all of the exposed male rats exhibited a toxic tubular nephrosis characterized by hyaline droplets, necrosis, and intratubular casts as well as accentuated tubular degeneration and medullary mineralization. In addition, no distinct exposure-related lesions were noted in dogs following inhalation of 5 or 50 ppm Decalin for 90 days (Gaworski *et al.*, 1985).

Decalin has been used as a noncarcinogenic vehicle in studies of cutaneous tumorigenesis in mice. Bingham & Falk (1969) reported no skin tumors in C_3H mice below a 0.02% concentration of benzo[a]pyrene when Decalin was used as the solvent. However, when n-dodecane was the diluent, skin tumors were produced at 0.00002% benzo[a]pyrene. Male C_3H mice were given topical applications of chrysene, fluoranthene, pyrene, triphenylene, perylene and benzo[b]triphenylene for 80 weeks. When applied in Decalin, only benzo[b]triphenylene produced malignant tumors. When applied in a 50:50 mixture of Decalin:n-decane, chrysene, triphenylene and pyrene, but not benzo[b]triphenylene, produced malignant tumors (Horton & Christian, 1974).

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In a subchronic inhalation study, MacEwen & Vernon (1978) exposed male rats, male guinea-pigs, and female mice to 0, 50, or 200 ppm Decalin for 6 hr/day, 5 days/week for 22 days. No gross lesions were seen which could be attributed to Decalin exposure. Respiratory tract irritation was evident in all three species and kidney changes in the male rat were similar to those found in the Gaworski study.

Hardin *et al.* (1987) evaluated the developmental toxicity of Decalin in a short-term *in vivo* assay. Pregnant CD-1 mice were given 2700 mg/kg Decalin on days 6-13 of gestation and allowed to deliver litters. Litter size, birth weight, and neonatal growth and survival to postnatal day 3 were recorded as indices of potential developmental toxicity. Decalin had no effect in the offspring for the parameters tested. Decalin produced 10% maternal mortality and was the only chemical of the 60 tested associated with a significant increase in maternal body weight gain.

The oral LD_{50} in the rat for Decalin is 4170 mg/kg and the dermal LD_{50} in the rabbit is 5.9 g/kg (Sandmeyer, 1981).

Short-Term Tests:

Tetralin. Tetralin did not show mutagenic activity at 0.03, 0.3 and 3 umoles/plate in an assay of 239 tobacco smoke components for mutagenicity towards *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537. Tetralin was assayed without metabolic activation and with activation with a liver fraction (S-9) from methylcholanthrene-induced rats. The toxic dose was $\geq$3 umoles/plate (Florin *et al.*, 1980).

A study of the mutagenicity of diesel fuel determined that the addition of Tetralin (10% by volume) did not significantly alter the direct-acting mutagenicity of extracts of particles (Jensen *et al.*, 1988). Tetralin (100 ppm) was highly toxic to Ehrlich-Landschgutz diploid ascites tumor cells during short-term *in vitro* incubations. Tetralin appeared to be more cytotoxic than classic hepatotoxic agents such as carbon

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tetrachloride and carbon disulfide, suggesting that the cytotoxic effect was due to the parent compound and not metabolites (Longacre, 1987).

Decalin. Decalin tested negative in a series of cytogenetic toxicologic tests to assess the ability of several classes of chemicals to induce SCEs and micronuclei in canine peripheral lymphocytes (Benz & Beltz, 1980).

Metabolism:

Tetralin. A case study of a woman who had ingested 250 ml of an ectoparasiticide containing 31.5% Tetralin found the following in the 24-hour urine: nonconjugated 1,2,3,4-tetrahydro-1-naphthol, unchanged Tetralin, and the glucuronides of 1,2,3,4-tetrahydro-1-naphthol and 1,2,3,4-tetrahydro-2-naphthol (Longacre, 1987).

Excretion studies in rats and rabbits have demonstrated that Tetralin undergoes hydroxylation at the nonaromatic portion of the molecules. The following summarizes the studies:

- In male Fischer 344 rats administered 0.5 ml/kg (48.5 mg/kg bw) intragastrically on alternate days for 2 weeks, metabolites recovered in the 24- and 48-hour urine were primarily disubstituted molecules. The six Tetralin metabolites identified were the mono alcohols, 1-tetralol and 2-tetralol; the hydroxyketones, 2-hydroxy-1-tetralone and 4-hydroxy-1-tetralone; and the diols, 1,4-tetralindiol and 1,2-tetralindiol. These metabolites were excreted as glucuronic acid or sulfate conjugates. With the exception of 2-tetralol, oxidation occurred at the carbon of the saturated ring closest to the aromatic ring. Kidney homogenate extracts did not contain Tetralin metabolites (Serve *et al.*, 1989).

- The biliary excretion of Tetralin metabolites in rats dosed intraperitoneally with Tetralin (45 mg/kg) amounted to 13% of the dose, mainly as tetralin-1,2-diol glucuronide.

- A study on the hydroxylation of Tetralin by rat liver homogenates indicated that tetralin hydroperoxide can be an intermediate in the conversion of Tetralin to 1-hydroxytetralin.

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- In rabbits treated with 3.4 mmol/kg ^{14}C-Tetralin via a stomach tube, 87-90% of the dose was excreted in urine within 2 days, 0.6-1.8% in feces, and <0.2% in expired breath. The radioactive residue in tissues amounted to 0.07% of the dose. Analysis of urinary metabolites indicated that biotransformation of Tetralin involved oxidation of the nonaromatic portion of the molecule. The major metabolites were conjugates of 1-hydroxytetralin (52.4%) and 2-hydroxytetralin (25.3%). Minor metabolites were cis-tetralin-1,2-diol (0.4%), trans-tetralin-1,2-diol (0.6%), and 4-hydroxy-1-tetralone (6.1%). Traces of mercapturic acids were found but did not appear to originate from the Tetralin that was administered (Longacre, 1987; CRCS, Inc., 1984).

- Hansen & Andersen (1988) estimated the affinity of Tetralin in several biological materials using solubility parameter techniques. Results were reported as relative energy difference (RED) numbers. Values approaching zero indicate strongest affinity and values less than 1.0 indicate a strong affinity while progressively higher values indicate increasingly lower affinities. The RED was 0.65 in fat (lard) at 37°C, 0.52 in fat (lard) at 23°C, 1.36 in 1% water, 1.73 in blood serum, 1.78 in sucrose, 1.49 in urea, and 0.90 in Psoriasis scales.

Decalin. The metabolism of Decalin has also been investigated. Following the administration of cis- and trans-Decalin to female rabbits, both hydrocarbons were oxidized to racemic secondary alcohols and excreted as ether-linked glucuronides in amounts equal to 60% of the dose administered. The principal glucuronides were isolated as triacetyl methyl esters and as sodium salts. cis-Decalin gave rise to (±)-cis,cis-2-decalol and small amounts of cis,trans-2-decalol. trans-Decalin yielded mainly (±)-trans,cis-2-decalol and small amounts of trans,trans-2-decalol (Elliot *et al.*, 1966).

Olson *et al.* (1986) studied the metabolism in rats gavaged with either the cis- or trans- isomer of Decalin. The urinary metabolites of cis-Decalin were cis,trans-1-decalol and cis,cis-2-decalol in males and females and cis-1-decalol in males. The urinary metabolites of trans-Decalin were trans,cis-2-decalol in both sexes and trans,trans-1-decalol in males. Extracts of kidney homogenates from male rats dosed with cis- and trans-Decalin yielded cis-2-decalone and trans-2-decalone, respectively. The female rats had no detectable Decalin metabolites in their kidney extracts.

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Structure/Activity Relationships:

Tetralin and Decalin both contain ten carbons and are composed of two fused six-membered rings. However, the structural and electronic character of the two differ. Structurally the aromatic ring of Tetralin causes that part of the molecule to be planar while the aliphatic portion of the molecule remains non-planar. Both of the Decalin isomers are composed of two fused cyclohexane rings which exist in non-planar chair configurations. Electronically, the aromatic ring of Tetralin will activate the alpha-carbons toward oxidation. The structural and/or electrical differences may preclude or facilitate the metabolism of Tetralin to potentially toxic intermediates (Serve, 1989).

Findings on the carcinogenicity of compounds structurally related to Decalin include the following:

- The NTP conducted a two-year inhalation study on naphthalene which found no evidence of carcinogenicity in male mice. In female mice there was some evidence based on alveolar/bronchiolar adenomas (5/68, 2/64, 28/134, incidence in control, low dose and high dose respectively). The bioassay is not yet published but has been peer reviewed and approved (NTP Executive Committee, 1991).

- Following review of the available information on anthracene and phenanthracene, the IARC classified both compounds as Group 3 (the agents are not classifiable as to their carcinogenicity in humans) (IARC, 1983,1987).

No information was found in the available literature on the carcinogenicity of compounds structurally related to Tetralin.

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