SUMMARY OF DATA FOR CHEMICAL SELECTION

Decane
124-18-5

BASIS OF NOMINATION TO THE NTP

Decane is brought to the attention of the Chemical Selection Working Group as an environmental pollutant with widespread human exposure but limited toxicological information.

Decane was selected from a group of hydrocarbons found in fuels, but it is also a ubiquitous pollutant in indoor and outdoor air and in water. The National Institute for Occupational Safety and Health (NIOSH) estimated that approximately 1,667 workers are exposed to decane based on a survey done in the 1980s. However, its main uses as a solvent, as a component of paints, and in the rubber and paper industries do not appear to be reflected in the NIOSH survey.

No adequate 2-year carcinogenicity study of decane was found in the available literature. Chronic toxicity studies described decane as a cocarcinogen and tumor promoter in skin cancer. In *in vitro* studies, decane was comutagenic, but not mutagenic.

The human toxicological impact of decane may be considerable, since it occurs with proven carcinogenic hydrocarbons in many mixtures of environmental concern such as fuel combustion products, cigarette smoke, and certain petroleum distillates.

INPUT FROM GOVERNMENT AGENCIES/INDUSTRY

According to the NTP reviewers of the summary sheets on decane and undecane, a draft report (TR-519) of a 2-year carcinogenicity study of Stoddard solvent is tentatively scheduled for peer review in May 2003. Male Fischer 344 rats inhaled Stoddard solvent at doses of 0, 188, 550, or 1100 mg/m^3 and female Fischer 344 rats and male and female B6C3F$_1$ mice were exposed at 0, 550, 1100, or 2200 mg/m^3. Stoddard solvent is a widely used chemical mixture, with production in 1990 exceeding 38 million pounds. Stoddard solvent contains hydrocarbons ranging from C7 to C12, with the majority in the C9 to C11 range. The hydrocarbons are 30-50% alkanes, 30-

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40% cycloalkanes, and 10-20% aromatics. Both decane and undecane are present in Stoddard Solvent. Although Stoddard solvent was negative in the micronucleus assay, pathologic studies on the mice have been completed. These studies indicate treatment-related effects in the liver in both sexes of mice. The pathologic results in the rats were not available for the CSWG's evaluation.

SELECTION STATUS: Selected
ACTION BY CSWG: 12/17/02
Studies Requested:
Carcinogenicity
Priority: High
Rationale/Remarks:

- Consider nomination with undecane and select one of these chemicals for testing.
- Consider also testing in an initiation/promotion protocol.
- Test pure compound rather than a complex mixture of alkanes.
- Ubiquitous air pollutant with widespread human exposure.
- Some evidence that this class of chemicals act as tumor promoters.
- HPV chemical; industry is sponsoring a mixture of alkanes

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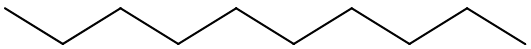
CHEMICAL IDENTIFICATION

CAS Registry No.: 124-18-5

Synonyms: Decyl hydride, *n*-decane, alkane C_{10} (ChemID, 2002; Lewis, 2002; Sigma-Aldrich, 2002)

Structure, Molecular Formula, and Molecular Weight:



$C_{10}H_{22}$ Mol. wt.: 142.29

Structural Class: Aliphatic alkane

Chemical and Physical Properties:

Description: Clear, colorless liquid; gasoline odor (Matheson Tri-Gas, 2001; NTP, 2001)

Melting Point: -32 – -29 °C (Matheson Tri-Gas, 2001)

Boiling Point: 171-174 °C (Matheson Tri-Gas, 2001)

Flash Point: 44 °C (Lewis, 2002)

Solubility: Soluble in ethanol, ether, acetone, organic solvents; slightly sol. in carbon tetrachloride, dimethyl sulfoxide; insol. in water (Matheson Tri-Gas, 2001; NTP, 2001; Lide, 2001)

Density/Specific Gravity: 0.7266 g/cm^3 (25 °C) (Lide, 2001)

Log $P_{O/W}$: 6.25 (Lide, 2001)

Reactivity: Stable at normal temperatures and pressure; combustible (Lewis, 2002; Matheson Tri-Gas, 2001)

Technical Products and Impurities: Decane (≥99.8%, 99+%, or ≥98.0%) is available from Sigma-Aldrich (Sigma-Aldrich, 2002).

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EXPOSURE INFORMATION

Production and Producers:

Manufacturing process: Most decane is prepared from petroleum refining. Other sources of decane include coal liquefaction through the Fischer-Tropsch synthesis and the hydrogenation of 1-decene (Griesbaum *et al*., 1989; HSDB, 2002a).

Production/import level: Decane is listed in the US Environmental Protection Agency's (EPA's) Toxic Substances Control Act (TSCA) Inventory (ChemID, 2002).

Decane is a high production volume (HPV) chemical with production exceeding 1 million pounds annually in the US. It has no sponsor in the HPV Challenge Program (EPA, 2002).

The Port Import/Export Reporting Service (PIERS) reported decane imports with a cargo weight of 392,416 lbs over the 14-month period from August 2001 to October 2002. Exporting countries were Belgium and the United Kingdom. For the 21-month period between January, 2001 and September, 2002, PIERS reported decane exports with a cargo weight of 7,966 lbs (Dialog Information Service, 2002).

Producers and Importers: Thirty-five US suppliers of decane are listed by Chem Sources USA (Chemical Sources International, 2002).

According to recent issues of chemical directories, decane is manufactured and/or distributed by Alfa Aesar/Johnson Matthey; Chevron Phillips Chemical Co. LP; Dow Chemical Co.; J.T. Baker; Mallinckrot Laboratory Chemicals; Phillips Chemical Co.; Roper Thermals; Spectrum Chemical Mfg. Corp.; TCI America; The Humphrey Chemical Co. Inc. (Chemcyclopedia Online, 2002; Hunter, 2001; Tilton, 2001).

Use Pattern: Decane is a component of engine fuels (Cavender, 1994). Other uses include (Lewis, 2002; Verscheuren, 2001; Wolkoff *et al.*, 1998):

- s a solvent

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- in organic synthesis
- as a hydrocarbon standard
- in jet fuel research
- in the manufacturing of paraffin products
- in the rubber industry
- in the paper-processing industry
- in cleaning agents

Decane is also found in several widely used petroleum distillates, such as Stoddard solvent and jet fuel. According to two studies, decane represents 7.6-11% of white spirits, a mixture of saturated aliphatic and alicyclic, and alkyl aromatic C_7-C_{12} hydrocarbons. Stoddard solvent, a form of white spirit, contains 30-50% of linear and branched alkanes (ATSDR, 1995a; World Health Organization, 1996).

The source used to prepare the jet fuel JP-4 apparently affects the amount of decane present. Decane was found at percentages of 11.25 or 2.24 in JP-4 fuel when the source was shale or petroleum, respectively (Irwin, 1997).

In 1985, the US consumption of aliphatic hydrocarbon-based solvents in the paint industry was 433,000 tons. The annual sale of white spirits in the US was 717,000 tons in 1985 (World Health Organization, 1996).

Human Exposure:

Occupational Exposure: The National Occupational Exposure Survey (NOES), which was conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983, estimated that 1,667 workers in 3 industries, including 43 female workers, were potentially exposed to decane in the workplace. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemical listed therein (RTECS, 2000a). Apparently the NOES survey does not address the presence of decane in other solvents since NOES estimates, for example, that 1,922,235 employees in 142,653 facilities are exposed to Stoddard

solvent (RTECS, 2000b).

Measurements of airborne decane have been taken in several industries. In a shoe sole factory, the atmospheric concentration of decane was 1-370 $\mu g/m^3$ in the vulcanization area. In a tire retreading plant, decane concentrations were 0-20 $\mu g/m^3$ in the vulcanization area and 0-2 $\mu g/m^3$ in the extrusion area. In an electrical insulation manufacturing plant, decane levels were 0-20 $\mu g/m^3$ in the extrusion area (HSDB, 2002a).

A 1983/1984 petroleum industry study involving 247 measurements reported that outside journeyman operators at oil refineries, transport drivers, gaugers, and service station attendants were exposed to decane from gasoline vapors. For the journeyman operators, decane was detected in 24 of 56 samples at an average airborne concentration of 144 $\mu g/m^3$. Decane was present in 44 of 49 samples taken in truck cabs; the average concentration was 75 $\mu g/m^3$. Decane had an average concentration of 73 $\mu g/m^3$ in 28 of 49 samples from service station attendants. he highest concentrations of total hydrocarbons were observed among dock and deck personnel from marine operations. In these two settings, decane was present in 13 samples at 448 and 136 $\mu g/m^3$, respectively (American Petroleum Institute, 1986).

In a 1996 US report, office workers were exposed to 1.0-1.1 ppb of decane. This exposure may be linked to the use of carbonless copy paper in offices (NIOSH, 2000).

Painters may also be exposed to decane. An average atmospheric concentration of decane of 6.8 mg/m^3 was found when painters applied an alkyl resin paint diluted with white spirits. According to the World Health Organization, even higher exposures might be expected in spray-painting (HSDB, 2002a; World Health Organization, 1996).

Decane was detected in gas samples emitted during the germination phase in malting and beer manufacture using a pilot-scale brewery (Gibson *et al.*, 1995).

Environmental Exposure: The most probable route of human exposure to decane is by inhalation. Expired air from humans has also been shown to contain decane; in one study of 54 subjects, 8.5% of the 387 samples collected contained measurable amounts of decane. Decane was also detected in 7 of the 12 samples of breast milk from mothers living in four US urban areas (HSDB, 2002a).

Consumer Exposure: Decane was identified in the vapor and liquid phases of unleaded regular gasoline during self-service refueling in a single pump island. The vapor concentration of decane was 1.47 ppm at an emission point of 6 inches from the refueling intake point and at an elevation of 5 feet above ground level (American Petroleum Institute, 1985).

Decane was detected in premiums and coupons from food packages, contributing to an off-flavor effect on foods such as breakfast cereals (Reineccius, 1991). Other consumer products that may contain decane include rubber flooring, wall coverings (cove base), wainscoting, scatter rugs, bathmats and sets, wood office furniture, wood office secretarial chairs, and wood office work surfaces (modular systems) (Scorecard, 2002).

The general population is also exposed to decane through the inhalation of white spirits vapors from paints and lacquers containing white spirits (World Health Organization, 1996).

Environmental Occurrence: Decane is found in the paraffin fraction of both crude oil and natural gas (HSDB, 2002a). Crude oil is the raw material for manufacturing petroleum products. It is a naturally occurring substance found trapped among sedimentary rocks below the earth's crust (BIRTH, 2002; Chevron, 2002; NETLAB, 1997). Natural gas is also found in porous geologic formations beneath the earth's surface, including sandstones, shales, and coal (Woodcock & Gottlieb, 1994).

Several processes or materials release decane to the environment (HSDB, 2002a; Verscheuren, 2001):

- the manufacture, use, and disposal of many products associated with the petroleum and gasoline industries, mainly the combustion of plastics, gasoline, and diesel fuel

- vulcanization and extrusion operations during rubber and synthetic production as with shoes, tires, and electrical insulation

- solvent-based building materials, printing pastes, paints, varnishes, adhesives, and other coatings

- landfills and waste incinerators

- air fresheners

- polyolefin manufacturing wastes

Air Pollution: Decane is an air pollutant and a component of volatile organic compounds (VOCs) (EPA, 2001).

Decane has been detected among VOCs in several studies analyzing indoor air quality.

- Concentrations of decane, elevated in a new building at completion of construction, fell off markedly within six months (EPA, 1988).

- In the winters of 1981-1982 and 1982-1983, the median indoor concentration of decane in Dutch homes ranged between 8-14 $\mu g/m^3$. The concentration in outdoor air was 0.6 $\mu g/m^3$ (median) with a maximum of 5 $\mu g/m^3$ (Verscheuren, 2001).

- In a 1983-1984 Italian study, the indoor and outdoor mean concentration of decane was 92 and 3 $\mu g/m^3$, respectively (Verscheuren, 2001).

- Decane was identified in 6 of 7 samples of household waste headspace at a concentration of 0.1-1 mg/m^3 in a Danish study (Wilkins, 1994).

- In a Finnish study, the concentrations of 48 VOCs, including decane, exceeded normal levels more often in sick houses than in normal houses. Sick houses were defined as dwellings in which inhabitants show symptoms such as headache, nausea, irritation of the eyes, and general malaise, among others (Kostiainen, 1995).

- In the late 1980s and early 1990s, decane was one of the main components detected among VOCs in air samples from 150 concrete office buildings in the Helsinki area. The mean total VOC concentration was 150 $\mu g/m^3$ (Kahkonen & Sunden, 1995).

- Indoor concentrations of *n*-alkanes (C_8-C_{11}) and other organic solvents were

significantly elevated in newly painted Swedish dwellings.. *n*-Alkanes were emitted from both solvent- and water-based paints, the emissions being 100 times higher with solvent-based paints (Wieslander *et al*.,1997).

Several reports have show the presence of decane in the atmosphere of US and European cities (HSDB, 2002a). Atmospheric concentrations of decane have also been measured.

- In polluted urban atmospheres, the concentration of decane was 1-2.7 ppb (Cavender, 1994).
- The ground level concentration in a carpark was 140 $\mu g/m^3$ and on a motorway, 1,060 $\mu g/m^3$ (Verscheuren, 2001).
- Decane has been detected in the gaseous emissions from gasoline powered vehicles, diesel trucks, and motorboats. The average exhaust from 67 gasoline-fueled vehicles contained decane at a concentration of 0.4% by weight of fuel (HSDB, 2002a).

Soil Accumulation: In a 1986 study, hydrocarbon characterization of soils containing spilled crude oil (>3 yr) revealed the presence of *n*-alkanes, including decane, in some soil samples. The abundance of *n*-alkanes decreased in contaminated soils because of biological transformation and volatilization (Saterbak *et al*., 1998).

Water Pollution: Decane has been identified as an industrial wastewater pollutant, as a pollutant of concern (POC) in centralized wastewater treatment facilities with an impact on human and aquatic life, and in the drinking water of several US cities. It has also been found in the water samples from lakes in a British study, and in rain water. Decane was detected in 6 of 8 surface water samples in the Gulf of Mexico with an average concentration of 1.3 ng/l. However, surface waters from unpolluted coastal areas showed only trace amounts of decane (EPA, 1998 & 1999; HSDB, 2002a).

Decane was one of over 300 compounds detected in neutral extracts of 24-hr composite samples from petroleum refinery wastewaters in a 1978 study (Burks, 1982).

Decane was identified in 1 of 63 industrial wastewater effluents at a concentration less than 10μg/l. It was also found at a concentration of 20 ng/l in underwater hydrocarbon

vents and the formation water discharges from offshore oil production platforms (HSDB, 2002a).

In an EPA cost-effectiveness analysis of waste water pollution control options for industrial laundries facilities, decane was calculated to have an industry baseline load of 673,669 lbs/yr with removals of 218,400 lbs/yr after treatment in publicly-owned treatment works (POTW) (EPA, 2000).

Biodegradation and Ecotoxicity: Decane is readily hydroxylated to decanol by *Pseudomonas desmolytica S11* and *P. oleovorans*. It is degraded by *Candida tropicalis* via the 1,2-dehydrogenated and 1-hydroxylated intermediates. lternate pathways proceed via the 1,2-diol and include terminal oxidation (Cavender, 1994). ecane is also a growth substrate for yeasts and *Aspergillus japonicus* (Verscheuren, 2001).

The 24-hr and 48-hr LC_{50} for decane in *Daphnia magna* was 23 and 18 mg/l, respectively (Syracuse Res. Corp., 1978). The 48-hr EC_{50} in *Daphnia magna* was 72 g/l, the IC_{50} in bacteria (aerobic heterotrophs, nitrosomonas, and methanogens) was 0.18 mg/l, and the IC_0 in *Mytilus edulis* (larvae growth) was 10 mg/l with an 80% increase of growth rate between 50-100 mg/l. Larvae growth rate changes appeared at 50 to 100 ppm, although no significant alterations were observed at 10 ppm (Verscheuren, 2001). Most C_2-C_{10} paraffins prevent germination of *Bacillus megaterium* spores (Cavender, 1994).

Regulatory Status: No standards or guidelines have been set by NIOSH or OSHA for occupational exposure to or workplace allowable levels of decane. Decane is not on the American Conference of Governmental Industrial Hygienists (ACGIH) list of compounds for which recommendations for a threshold limit value (TLV) or biological exposure index (BEI) are made.

As a component of VOCs, decane is a recognized air pollutant (EPA, 2001). It is also a pollutant of concern (POC) in centralized wastewater treatment facilities (EPA, 1999).

EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the specific association of exposure to decane and cancer risk in humans were identified in the available literature.

An epidemiological study of chronic workplace exposure to white spirits reported an odds ratio >1 for prostate cancer, Hodgkin's lymphoma, and squamous cell carcinoma of the lung. In addition, several epidemiological studies have shown increased risks of respiratory, pancreatic, kidney, and lung cancer in workers exposed mostly to white spirits. None of the studies mentioned above demonstrated a causal association between cancer and exposure to white spirits (ATSDR, 1995a; World Health Organization, 1996). The role of decane, if any, was not examined.

At very high concentrations involving acute exposure, decane is an asphyxiant and narcotic (NTP, 2001). Human subjects exposed to decane (10, 35, or 100 μl/l) in a chamber for 6 hr/day, 1 day/wk for 4 wk developed decreased tear film stability, increased number of conjunctival polymorphonuclear leukocytes, and irritation of mucous membranes of the eyes (Kjærgaard *et al*., 1989). Decane, in solutions as strong as 30%, produced no skin irritation in human subjects when applied for 24 hr (Criteria Group for Occupational Standards, 1983).

Animal Data:

Acute Studies: Information on the acute toxicity of decane in laboratory animals is presented in Table 1.

Table 1. Acute toxicity of decane.

Species	Route	LC_{50}
rat	inhalation	>1,369 ppm/8 hr
mouse	inhalation	72,300 mg/m^3/2 hr

Source: Matheson Tri-Gas, 2001; RTECS, 2000

Decane (0.05 ml) produced no irritation when left for 24 hr on the skin of rabbits (Criteria Group for Occupational Standards, 1983).

Subacute Studies: Rats exposed to decane by inhalation at 2,000 ppm for 12 hr/day for 14 days exhibited reversible behavioral changes such as impaired motor performance, reduced vigilance and learning abilities, and increased gross motor activity and aggression (Eide, 1990).

Decane (0.2 ml) reduced the biosynthesis of lipids, RNA, and DNA in the epidermis for 3 days when applied to the skin of rabbits for 1 hr. Synthesis subsequently increased to normal (Criteria Group for Occupational Standards, 1983).

Subchronic/Chronic Studies: Inhalation studies in rats exposed to 540 ppm decane, 18 hr/day, 7 days/wk for 123 days, showed an increase in body weight and a reduction of white blood cell count as compared to controls. However, no histopathological changes in bone marrow or other organs were noted (Criteria Group for Occupational Standards, 1983).

Mice exposed dermally to decane (total dose 16.3 g, 3/wk, up to 50 wk) had higher incidences of fibrosis of dermis, pigmentation and ulceration of skin; and hemorrhage, pigmentation, and inflammation of the kidneys and lungs (Nau *et al*., 1966).

Carcinogenicity Studies: No 2-year carcinogenicity studies of decane were identified in the available literature. Decane has been shown to have cocarcinogenic and tumor-promoting activities in several studies.

Decane (25 mg) and benzo[*a*]pyrene (BP) (5 μg) applied to the skin of female ICR/Ha Swiss mice, 3/wk for 440 days, induced papillomas in 38 of 50 animals. BP alone induced tumors in 12 of 50 animals in the same time, while decane alone produced a papilloma in 1 of 50 mice (Van Duuren & Goldschmidt, 1976).

Decane (ca. 4 mg) applied to the skin of female Swiss mice, 3/wk for 60 wk, beginning 1 wk after initiation with 7,12-dimethylbenz[a]anthracene (DMBA), induced tumors in 2 of 30 animals (Sicé, 1966).

Decane (50 μl) was applied to the skin of male C3H/HeJ mice, 3/wk, prior to UV light exposure 5 d/wk at 254 nm, for 3 d/wk at 290-320 nm, or for 7 d/wk at >350 nm. Decane accelerated the tumorigenesis in the 254 and >350 nm UV-radiation treatment. In the latter case, decane induced tumors in 15 of 24 animals. Control animals (only UV light exposure) did not show tumors in this treatment (Bingham & Nord, 1977).

Several studies that examine the potential carcinogenicity of JP-4 jet fuel have been conducted. No increase in the incidence of tumors was found in rats and mice one year after 8 months of inhalation exposure to JP-4 fuel. In a 1993 study, F344 rats exposed to JP-4 at 5,000 mg/m^3 for 12 months had an increase of interstitial cell tumors in the testis 12 months after the termination of the exposure. However, mice exposed to the same regimen did not show an increase in the incidence of neoplastic lesions. Dermal administration of JP-4 jet fuel (25 mg, 3/wk for 105 wk) increased the incidence of squamous cell carcinomas and fibrosarcomas in mice exposed to shale-derived JP-4 (50% incidence), and in animals exposed to petroleum-derived JP-4 (26% incidence) compared to the appropriate controls (2% and 0%, respectively) (ATSDR, 1995b). The relevance of these studies to decane has not been determined.

Short-Term Tests: Decane was not mutagenic when tested in five strains of *Salmonella typhimurium* (TA97, TA98, TA100, TA1535 & TA1537) at concentrations of up to 10 mg/plate. Mutagenicity was not enhanced by rodent liver S-9 (CCRIS, 2002). An NTP study reported results for decane in *Salmonella* as "non-mutagenic" and "inconclusive" with no further details (NTP, 2002).

Decane, at a concentration of 0.12 mM, enhanced by 24% the mutagenic effect of methylazoxymethanol at the ouabain-resistant locus in cultured V79 Chinese hamster

cells (Lankas *et al*., 1978).

Decane, at low concentrations (<10 mM), enhanced the mutagenic and recombinogenic effect of triethylene melamine in the *Saccharomyces cerevisiae* MP1 strain. At higher concentrations (>10 mM), decane was corecombinogenic and antimutagenic. This activity resembled the one found for substances that are both cocarcinogens and tumor promoters (Fahrig, 1984).

Decane did not induce *in vitro* proliferation of murine lymphocytes. However, it increased the mitogenic effect of phytohemagglutinin in lymphocytes by ~16% (Baxter *et al*., 1981).

Decane did not induce *in vitro* transformation of Syrian hamster embryo cells. Neither did it enhance co-transformation when added with BP. Decane also had no effect on the intercellular communication in a monolayer of Syrian hamster embryo cells (Rivedal *et al*., 1992).

Metabolism:

Absorption and Distribution: Inhaled decane is rapidly distributed from the blood to different organs and tissues, especially those with high lipid content. The concentration of decane in the brains of rats exposed to decane at 100 ppm, 12 hr/day for 3 days was 60.2 μmol/kg. Corresponding figures were 6.8 μmol/kg in blood, 45.9 μmol/kg in liver, 77.7 μmol/kg in kidneys, and 1,230 μmol/kg in fat (Zahlsen *et al*., 1992).

Cellular Metabolism: Aliphatic hydrocarbons, such as decane, undergo oxidative conversion to alcohols in liver cells, catalyzed by cytochrome P-450-dependent monooxygenases. For *n*-alkanes with a carbon chain length of 8 or more, only omega oxidation has been observed (oxidation of terminal carbon). After this conversion, conjugation of the hydroxy group to a glucuronic acid or sulfate ester may occur. Further oxidation to aldehyde/ketone or carboxylic acid by other enzyme systems may take place in some substances. The fatty acids formed from the *n*-alkanes can be degraded by ß-oxidation

(World Health Organization, 1996).

Decane is oxidized by microsomes from the livers of mouse, rat, rabbit, and other species. The oxidation of decane by mouse liver microsomes requires NADPH and oxygen. The major metabolites of this biochemical process were identified as decanol, decanoic acid, and decamethylene glycol. Decane hydroxylation took place in the liver, other organs, and microsomes isolated from the kidneys and lungs. Phenobarbital pretreatment in rats markedly increased decane hydroxylase activity in liver microsomes (HSDB, 2002a).

Decane has been shown to directly affect *in vitro* P-450 enzyme activity toward other substrates. Decane caused reduced recovery of products of liver and lung 7-ethoxycoumarin deethylase and of lung benzo[*a*]pyrene hydroxylase activities in microsome preparations from Sprague-Dawley rats. However, it did not reduce NADPH formation and did not affect P-450 reductase activity when the enzyme was assayed with the substrate, cytochrome *c* (Rabovsky *et al.*, 1986).

Other Biological Effects:

Neurological Alterations from Products Containing Decane: Decane may be linked to the development of neurological impairment associated with acute exposure to a high level of JP-4 jet fuel (ATSDR, 1995b). Minor neurological effects (dizziness, changes in simple reaction time, and visual-motor coordination) have also been reported in humans from short-term exposure to Stoddard solvent. Similarly, minor neurobehavioral changes were seen in subjects exposed to other white spirits (World Health Organization, 1996). More severe neurological changes were described from chronic exposure to Stoddard solvent, white spirits, and other similar solvents; although a cause-effect relationship could not be established (ATSDR, 1995a).

Several inhalation studies in rats involving various types of white spirits described minor behavioral changes and some neurochemical effects. Dearomatized white spirits (mostly alkanes) induced alterations in sensory-evoked potentials in rats (ATSDR,

1995a; World Health Organization, 1996).

Kidney Toxicity from Products Containing Decane: Animals exposed to vaporized white spirits and Stoddard solvent did not have kidney pathology (ATSDR, 1995a). In contrast, a C_{10}-C_{11} solvent fraction (mainly aliphatic) and JP-4 jet fuel caused the type of renal damage in male rats generally associated with the binding of xenobiotic compounds to α_{2u}-globulin (ATSDR, 1995a; World Health Organization, 1996).

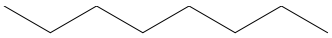
Male Sprague-Dawley rats exposed to a white-spirit-like solvent (99% C_{10}-C_{12} aliphatics) showed a significant decrease in urine osmolality after 9.5 months of exposure. Increased activity of urinary lactate dehydrogenase was further noted as an indication of distal tubular dysfunction (Viau *et al*., 1984).

Several human studies found no association between exposure to Stoddard solvents and kidney dysfunction. However, the studies lacked sufficient exposure data to draw firm conclusions. A man who was exposed to Stoddard solvent by direct dermal contact and inhalation for 1 year developed glomerulonephritis (ATSDR, 1995a).

Hemapoietic System Effects from Stoddard Solvent: Studies of humans with aplastic anemia who were also exposed to Stoddard solvent have been reported, although a causal relationship was not established (ATSDR, 1995a).

Liver and White Spirits: Studies on humans exposed to white spirits and other chemicals in the workplace reported no histopathological changes in liver biopsies, however, some hepatic enzymes had elevated serum levels (ATSDR, 1995a).

Structure-Activity Relationships: *n*-Alkanes are thought to modulate carcinogenesis, especially because of their ubiquitous distribution and their tumor-promoting activity (Baxter *et al*., 1981). Octane [111-65-9] and dodecane [112-40-3], two hydrocarbons structurally related to decane, were selected for review.



Structure of octane

Structure of dodecane

No carcinogenicity bioassays conducted to modern regulatory standards are available for these compounds. Several studies have reported that dodecane is a cocarcinogen and tumor promoter; these activities are stronger than for decane.

- Dodecane (ca. 4 mg) applied to the skin of female Swiss mice, 3/wk for 60 wks, beginning 1 wk after initiation with DMBA, induced tumors in 6 of 30 animals. In this study, dodecane had a stronger tumor- promoting activity than decane while octane did not induce any tumors (Sicé, 1966).

- Dodecane painted on the skin of Swiss mice 2/wk for 63 wk, beginning 1 wk after initiation with DMBA, produced tumors in 6 of 15 mice (2 groups, females and males). However, dodecane did not induce skin tumors when administered alone (Saffiotti & Shubik, 1963).

- BP (0.14%) in dodecane, 40% v/v in decalin (decahydronaphthalene), applied 2/wk for 1 year in the interscapsular area of male C3H mice, induced malignant tumors in 15 of 15 mice (100%). Only 33% of control animals exposed to BP in decalin exhibited malignant tumors (Horton *et al*., 1976).

- Dodecane (50 μl) was applied to the skin of male C3H/HeJ mice, 3/wk, prior to UV light exposure for 5 d/wk at 25 nm, for 3 d/wk at 290-320 nm, or for 7 d/wk at >350 nm. Dodecane significantly increased the UV radiation-induced tumorigenesis in all treatments (Bingham & Nord, 1977).

Octane was described as a tumor promoter in a 1981 study. Octane (60 μl, 75% v/v in cyclohexane, 2/wk for 50 wks) was applied after 2 wk of dermal exposure to DMBA in benzene to C3H mice. Octane treatment produced 6 tumors in 11 animals, while 2 tumors were observed in 32 control animals (Horton *et al*., 1981).

Octane has been described as a CNS depressant, however, it does not cause the type of peripheral neuropathy associated with hexane exposure (HSDB, 2002b). The distribution of octane in rats following inhalation exposure was similar to that found for decane, although the concentrations of octane were lower (Zahlsen *et al*., 1992).

Octane and dodecane did not induce *in vitro* proliferation of murine lymphocytes. However, dodecane increased the mitogenic effect of phytohemagglutinin in lymphocytes by ~38% (Baxter *et al*., 1981).

Octane was not mutagenic in a bioassay using L5178Y mouse lymphoma cells with or without activation (Microbiological Assoc. Inc., 1987). Dodecane enhanced by 18 % the mutagenic effect of methylazoxymethanol at the ouabain-resistant locus in cultured V79 Chinese hamster cells (Lankas *et al*., 1978).

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