n-Alkane Category:
decane, undecane, dodecane
(CAS Nos. 124-18-5, 1120-21-4, 112-40-3)

Voluntary Children's Chemical Evaluation Program (VCCEP) Tier 1 Pilot Submission

Docket Number OPPTS – 00274D

American Chemistry Council
n-Alkane VCCEP Consortium

Sponsors:
Chevron Phillips Chemical Company LP
Sasol North America Inc.
Shell Chemical LP

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GLOSSARY OF TERMS

μg	Microgram
ACGIH	American Conference of Governmental Industrial Hygienists
alkyd paint	A hydrocarbon solvent (typically mineral spirits) based paint.
Alkylate Bottoms	A mixture of unreacted n-alkanes and benzene that remain after the production of Linear Alkyl Benzene (LAB).
ATSDR	Agency for Toxic Substances and Disease Registry
CAA	Clean Air Act
CNS	Central Nervous System
Cycloalkane	Synonymous with cycloparaffin. A saturated hydrocarbon with a ring - typically a 6-carbon single ring or a 10-carbon double ring – with unspecified branching off of the ring.
EHC	Environmental Health Criteria
EPA Research House	A model house in Cary, NC where EPA conducted indoor air studies to validate the Wall Paint Exposure Model (WPEM).
IPCS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System
Isoalkane	Synonymous with isoparaffin. A saturated hydrocarbon with carbon branching.
Kg	Kilogram
LAB	Linear Alkyl Benzene
LAS	Linear Alkyl Sulfonate
LOAEL	Lowest Observed Adverse Effect Level
mg	Milligram
NCEA	National Center for Environmental Assessment
NOAEL	No Observed Adverse Effect Level
n-Alkane (Normal Alkane)	Synonymous with n-paraffin. A straight-chained, saturated hydrocarbon, with no branching or cyclic components.
NTP	National Toxicology Program
OECD	Organization of Economic Cooperation and Development
OSHA	Occupational Safety and Health Administration
Paraffin	Equivalent term to alkane
ppb	Parts Per Billion
RfC	Inhalation Reference Concentration
RfD	Oral Reference Dose
SD	Standard Deviation
SEM	Standard Error of the Mean
SIAM	SIDS Initial Assessment Meeting
SIAR	Screening Information Assessment Report
SIDS	Screening Information Data Set
STEL	Short-Term Exposure Limit
TEAM	Total Exposure Assessment Method
TLV	Threshold Limit Value
TPHCWG	Total Petroleum Hydrocarbon Criteria Working Group
TSCA	Toxic Substances Control Act
TWA	Time-Weighted Average
VOC	Volatile Organic Compound
VCCEP	Voluntary Children's Chemical Evaluation Program
WAGM	Weighted Average Geometric Mean
WHO	World Health Organization

1. Executive Summary

This submission covers n-decane (C_{10}), CAS No. 124-18-5, n-undecane (C_{11}), CAS No. 1120-21-4, and n-dodecane (C_{12}), CAS 112-40-3, the three n-alkanes sponsored under the Tier 1 of the VCCEP Pilot Program by the American Chemistry Council n-Alkane VCCEP Consortium (the "Consortium"). As these three chemicals are very similar in chemical structure, physical and chemical properties, hazard properties, potential health effects, and exposure sources, the Consortium is considering them together as a category.

These three n-alkanes were included in the VCCEP pilot program because the Total Exposure Assessment Methodology (TEAM) project detected them in indoor air and exhaled breath. They are also sponsored under the Organization for Economic Cooperation and Development (OECD) High Production Volume (HPV) Screening Information Data Set (SIDS) Program.

Production and Use

These three chemicals present an interesting VCCEP case because the production and use of these chemicals as pure chemicals and high-purity n-alkane process streams is quite small relative to the petroleum substances (i.e., kerosene, jet fuel, home heating oil, hydrocarbon solvents) that contain these n-alkanes as constituents. In addition, almost all (99+%) of the purified n-alkane production is not as single chemicals but as process streams that contain a range of n-alkanes, typically C_{10}-C_{13}, C_{12}-C_{14}, C_{12}-C_{16}, and C_{14}-C_{16}. These n-alkane process streams are consumed as closed-system chemical intermediates in the manufacture of linear alkylbenzenes (LABs), which are a chemical building block for the manufacture of detergents. A very small volume (estimated at less than 20,000 pounds) is produced in pure form for use as laboratory reagents. There are no known consumer product applications for pure n-decane, n-undecane, and n-dodecane. There are several different types of petroleum substances that may contain these n-alkanes, including aliphatic hydrocarbon solvents (e.g. mineral spirits) and middle-distillate fuels such as kerosene, jet fuel, diesel fuel and home heating oil. Generally these substances contain approximately 25% n-alkanes, but given their large production volumes and wide usage they were the primary source of exposure identified in the exposure assessment.

Exposure

The Consortium conducted an exposure assessment of n-decane, n-undecane, and n-dodecane, with emphasis on exposure to children, potential parents and the fetus. The Consortium also reviewed the TEAM and indoor air studies discussed in the VCCEP Federal Register notice (65 FR 81700, December 26, 2000). Four routes of exposure - inhalation, oral, dermal, and human milk - were considered in the exposure assessment. Of these, only inhalation was determined to be sufficiently significant to undergo detailed risk characterization. The most common exposure sources identified were fuels (particularly jet fuel, kerosene and diesel), paints, and other products containing solvents. Due to the low volatility of these compounds and the limited CNS effects, even at saturated

concentrations, solvent abuse involving decane, undecane, or dodecane is improbable and was not considered in this assessment.

Based on the analyses of the available exposure data, the following scenarios were identified as being the most representative of situations where children and prospective parents are likely to have the highest potential exposure to decane, undecane, and dodecane. These scenarios are:

1. Chronic exposure of infants and children to indoor air.
2. Chronic exposure of prospective parents to indoor air.
3. Short term exposure of infants and children in a newly renovated (painted) home.
4. Short term exposure of prospective parents in a newly renovated (painted) home.
5. Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

Relevant exposure concentration data for these scenarios were abstracted from the studies summarized in Appendix A and are summarized below in Table 1. These exposure concentrations are the combined exposure to decane, undecane, and dodecane since the chemicals are being considered together as a category.

Table 1: Exposure Concentrations for Selected Scenarios

Type of Measurement	Representative Concentration[1]	Upper Bound Concentration[2]	Applicable Scenario[3]	References
Average daily household indoor air concentrations	42 μg/m3	129 μg/m3	1,2	Brown et al, 1994; BRE, 1996;
Interior painting average ambient air concentrations and personal samplers	122 μg/m3	910 μg/m3	3,4,5	Brown & Crump, 1998 Wallace, 1989
Highest exposed Air force fuel workers: 1 hour average ambient exposures (personal monitors)	5,061 μg/m3	16,800 μg/m3	5	Pleil et al, 2000

1. Representative concentration is defined as the average of a set of exposure data.
2. Upper bound concentration is generally defined as the upper 95th percentile of the exposure data when adequate data were available to develop a log-normal distribution or the maximum reported level when no distribution was available.
3. 1) Chronic exposure of infants and children to indoor air.
   2) Chronic exposure of prospective parents to indoor air.
   3) Short term exposure of infants and children in a newly renovated (painted) home.
   4) Short term exposure of prospective parents in a newly renovated (painted) home.
   5) Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

Hazard

Hazard information from animal studies or human experience of these individual n-alkanes and n-alkane process streams is provided in this submission. Additional hazard information on aliphatic hydrocarbon solvents that contain these n-alkanes has also been provided as supporting information. Acute toxicity information is available for all Tier 1 endpoints for all materials, either directly or by read-across to other materials (see Table 2). The major acute hazards from human experience and animal studies appear to be lung damage secondary to ingestion and aspiration, and irritation effects from repeated dermal or inhalation exposure. These materials have a low potential for toxicity by the inhalation route. No-observed-adverse-effect-levels (NOAELs) are reported from several animal studies on which point-of-departures can be based for risk assessment purposes.

Table 2: Tier 1 Hazard Identification Studies Available

TIER 1 HAZARD		DECANE	UNDECANE	DODECANE	OTHER n-ALKANES
Acute Toxicity	Oral	✓	✓	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Dermal	RA	RA	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Inhalation	✓	✓	✓	✓ (n-nonane, n-tridecane)
In Vitro Gene Tox	Bacterial	✓	✓	RA	✓ (n-nonane, n-tetradecane; C_{10}-C_{13} n-alkane product)
	Cytogenetics	✓	✓	✓	✓ (n-tetradecane, C_{11}-C_{14} aliphatic hydrocarbon solvent)
In vivo Genetic Toxicity	Micronucleus	RA	RA	RA	✓ (C_{10}-C_{13} n-alkane product)
Repeat Dose Toxicity		✓	✓	RA	✓ (n-nonane, C_9-C_{13}, C_{10}-C_{13}, C_{11}-C_{14}, aliphatic hydrocarbon solvents)
Reproductive Toxicity Screen		✓	✓	RA	✓ (C_9-C_{13} aliphatic hydrocarbon solvent)

✓ = one or more studies available
RA = Read Across

Health Benchmarks/Exposure Limits

No U.S. regulatory agency has established a chronic reference concentration (RfC), chronic reference dose (RfD), an acute exposure limit or an occupational exposure limit (OEL) for decane, undecane or dodecane. Considering that these chemicals are not commercial products (such as kerosene, jet fuel, solvents) this is probably not unexpected. However, this did require the Consortium to identify or develop health benchmarks and exposure limits for the risk assessment. A subchronic NOAEL of 1.0 g/m^3 (adjusted for continuous exposure to 0.25 g/m^3) was developed based on the analysis of several inhalation studies on n-alkanes and aliphatic hydrocarbon solvents and used for the non-occupational chronic margin of exposure analyses. The RfC derived by the Total Petroleum Hydrocarbon Criteria Working Group (TPHCWG) for C_{10}-C_{12} aliphatic hydrocarbons of 1.0 mg/m^3 was selected for the non-occupational chronic margin of safety analyses. An acute NOAEL of 5,000 mg/m^3 based on an 8-hr acute rat study of decane, undecane, and dodecane was selected for the short-term margin of exposure analyses. The proposed occupational exposure limit (OEL) of 1,200 mg/m^3 developed by the European Chemical Industry Council (CEFIC) Hydrocarbon Solvent Producers Associations for C_9-C_{15} aliphatic and cyclo-aliphatic hydrocarbons was identified as an occupational exposure limit for decane, undecane, and dodecane. The values are summarized in the following table (Table 3). Reproductive/developmental NOAELs of 5 g/m^3, 300 mg/kg/day and 1,000 mg/kg/day (equivalent to approximately 2 g/m^3 and 7 g/m^3, respectively) were identified. Since all of these values were larger than the subchronic NOAEL, no further risk assessment was conducted for reproductive or developmental effects.

Table 3: Health Benchmarks and Exposure Limits for Risk Assessment

Benchmark	Value	References
Subchronic NOAEL (adjusted to continuous exposure)	250 mg/m^3	Several. See Section 7.3
Chronic Reference Concentration (RfC)	1.0 mg/m^3	Total Petroleum Hydrocarbon Criteria Working Group, 1997
Acute Toxicity NOAEL (Short Term Exposure)	5,000 mg/m^3	Nilsen, 1988.
Inhalation Reproductive/ Developmental NOAEL (adjusted to continuous exposure)	1,250 mg/m^3	ExxonMobil Biomedical Sciences, Inc., 1978
Occupational Exposure Limit (8 hour- TWA)	1,200 mg/m^3	CEFIC Hydrocarbon Solvent Producers Associations, 2001

Risk

Primary exposure of infants and children was in the home. In every domestic scenario relevant to infants, children and parents, including home renovation activities, Margins of Exposure (MOE) based on the subchronic NOAEL were comfortably in excess of 1,000 for both representative and upper bound exposures. Worst case short term exposure based on modeling a home painting scenario was comfortably in excess of 100 for a short term (days), increasing rapidly to greater than 1,000 despite very conservative exposure assumptions. This suggests a low risk of harm to infants, children or parents.

Margins of Safety (comparison with the TPHCWG derived RfC) were similarly protective, with values much greater than 1. Highest occupational exposure (fuel workers) also indicated a high margin of safety with high-end exposures almost two orders of magnitude less than the (8 hour) Occupational Exposure Limit (OEL).

Margins of Exposure and Margins of Safety are presented in Section 8 and summarized in Appendix H for each scenario considered.

VCCEP Data Needs

The generally low level of human exposure, when considered with the results of repeat dose and reproductive screening studies, and the lack of genotoxicity, indicates a low need to conduct higher tier repeat dose, reproductive and chronic studies.

2. Basis for Inclusion of Decane, Undecane, and Dodecane in VCCEP Pilot Program

In selecting compounds for the VCCEP Pilot Program, EPA relied on biomonitoring and environmental monitoring databases that it considered relevant to assessing the potential for children's exposure. *See* VCCEP Federal Register Notice (Dec. 26, 2000), at III.Q. Availability of hazard data was an additional factor that influenced chemical selection decisions; EPA stated that it wanted to select chemicals for which Tier I hazard data was available. Decane, undecane, and dodecane were selected for the following reasons: (1) they are currently being evaluated under the Organization for Economic Cooperation and Development (OECD) SIDS Program; (2) they were reported in human exhaled air in the TEAM study; and (3) they have been detected in indoor air. The following is a summary of the EPA review of the available biomonitoring and environmental monitoring databases for decane, undecane, and dodecane. The ongoing OECD SIDS program activities for these n-alkanes are discussed in Section 3.

Table 2.1 The results of EPA's VCCEP candidate chemical selection process for Decane, Undecane and Dodecane

Working List of Candidate Chemicals to be Addressed by the Voluntary Children's Chemical Evaluation Program									
CAS No.	CHEMICAL NAME	Chemicals found in Human Tissues					Chemicals Found in Drinking Water, Food and/or Indoor Air		
		NHANES	NHAT	NHEXAS	TEAMS	Human Milk	NCOD	EAFUS	INDOOR AIR
124-18-5	decane				Y				Y
1120-21-4	undecane				Y				Y
112-40-3	n-dodecane				Y				Y

Reference: EPA VCCEP Website (http://www.epa.gov/chemrtk/vccep/vccepmth.htm).

2.1 Total Exposure Assessment Methodology Data

The Total Exposure Assessment Methodology (TEAM) study was designed to develop methods to measure individual total exposure (exposure through air, food, and water) to chemicals and to apply these methods within a probability-based sampling framework to estimate the exposures of urban populations in several U.S. cities. The TEAM Study reports the results of eight monitoring studies performed in five communities during different seasons of the year. Phase III of the TEAM study, conducted in California during the first half of 1984, includes breath data and air monitoring data for decane, undecane and dodecane. The Consortium has reviewed these data closely as they represent the primary basis for section of these three n-alkanes into the VCCEP Pilot program.

Phase III of the TEAM study included study populations from the Los Angeles, California area and Contra Costa County California (towns of Antioch and Pittsburg) in the Northern California Bay area. In Los Angeles, studies were conducted during the winter

(January/February) of 1984 on 117 people and then a second follow-up study during the summer (May/June) of 1984 on 51 of the original 117 participants. In Contra Costa, one study was conducted on 71 people during the summer (May/June) of 1984. Each study collected breath, personal air samples (day/night), and area (fixed-site) air samples from outdoor locations. There were no indoor fixed-site samples collect, but personal nighttime samples were used as a surrogate for ambient indoor air concentrations, the assumption being that the participants were indoors during the night. The air sampling results of the TEAM study appear to be very consistent with other air monitoring studies in that decane, undecane, dodecane are frequently observed, but at very low concentrations. These air monitoring data are discussed in Section 6, the Exposure Assessment. EPA's particular interest in Phase III of the TEAM study for the VCCEP Pilot Program is that these chemicals were also detected in human breath. Finding these n-alkanes in breath is not unexpected since the personal air samples showed exposure had occurred. The concentrations in breath, shown in Table 2.2, are consistent with the indoor air concentration and personal air samples from the TEAM and other exposure studies. Even when the three alkanes are combined, the reported breath concentrations are below 1 $\mu g/m^3$ or ~0.15 ppb.

Table 2.2 Breath Concentrations for Decane, Undecane and Dodecane from TEAM Study reported on EPA's VCCEP website

Frequency of Detection and Tissue Concentration of Select VCCEP Pilot Chemicals in Human Monitoring Studies				
CAS No.	**CHEMICAL NAME**	**MEDIUM**	**DETECTION FREQUENCY**	**CONCENTRATION**
124-18-5	Decane	breath	53% of 110	GM= 0.27 $\mu g/m^3$
1120-21-4	Undecane	breath	56% of 110	GM= 0.28 $\mu g/ m^3$
112-40-3	n-Dodecane	breath	30% of 110	GM = 0.19 $\mu g/m^3$

Reference: EPA VCCEP Website (http://www.epa.gov/chemrtk/vccep/vccepmth.htm).

2.2 Air Monitoring Data

Several of the air monitoring references cited by EPA for the VCCEP program provide data on indoor and/or outdoor air concentrations of these n-alkanes. The air data samples reported in these studies were generally collected between the mid -1980's and 1991. The most recent study was conducted by Shields, *et. al*. (1996) in March and April 1991 at telecommunication centers, data centers, and administrative offices. Daisey, *et. al.* (1994) collected indoor and outdoor air samples at 12 office buildings in the San Francisco Bay area between June and September 1990, including several buildings with indoor air quality complaints. Brown, *et. al.* (1994) compiled the results of several previous indoor air studies on established and new buildings and reported n-alkane air concentrations for dwellings, offices and a hospital. Samfield (1992) and Shah and Singh (1988) also compiled the results of numerous indoor and outdoor air monitoring studies. These studies generally reported average air concentrations in the low part per billion (ppb) range. Brown (1994)

showed that indoor air concentration of decane, undecane, and dodecane can be considerably higher in new buildings than in established buildings, although the authors noted that the sample size for new buildings was limited. These elevated levels are likely the result of recent use of solvent containing products such as paints, adhesives, etc. The results of these and other exposure studies, from the Consortium's exposure literature review, are presented in Section 6.

Most of these studies also focused on the ratio of indoor air concentrations to outdoor air concentrations (I/O), generally finding that indoor air concentrations tend to be higher than outdoor concentrations by a factor of 2 or more.

2.3 How Sponsors Were Identified for the n-Alkane VCCEP Effort

EPA identified potential VCCEP sponsors based on those company names shown in the 1998 TSCA Inventory Update Rule (IUR) that reported the specific n-alkane CAS numbers on pilot list. This list was subsequently updated by the 2002 TSCA IUR, which is shown in Table 2.3. In the case of the n-Alkane VCCEP Consortium, Sasol North America, Inc reported decane, undecane, and dodecane, Shell Chemical LP reported undecane and dodecane, and Chevron Phillips Chemical Company LP reported decane and dodecane. Although these companies reported production under the individual chemical CAS numbers, most (99+%) of this n-alkane production was (and is today) in the form of process streams that contain a range of n-alkanes, typically C_{10}-C_{13}, C_{12}-C_{14}, C_{12}-C_{16}, and C_{14}-C_{16}. These n-alkane process streams are produced in closed systems and consumed primarily as chemical intermediates in the manufacture of linear alkylbenzenes (LABs). The production by the Consortium members of pure n-alkane products compared to petroleum substances that contain these n-alkanes as constituents (e.g. kerosene, jet fuel, diesel fuel, hydrocarbon solvents) is very small. Petroleum substances are typically reported under complex petroleum CAS numbers rather than individual chemical CAS numbers, as it would be technically and practically infeasible to report complex petroleum substances under individual chemical CAS numbers. The VCCEP sponsors of decane, undecane, and dodecane represent a small group of specialty chemical manufacturers. While an attempt has been made to address sources of exposure including fuels, solvents, combustion sources, etc., these sources are outside the chain-of-commerce of these chemicals.

Table 2.3 Manufacturers and Importers of VCCEP Pilot Chemicals (Decane, Undecane and Dodecane) listed on EPA's website

Manufacturers and Importers of VCCEP Pilot Chemicals as reported to the 2002 TSCA Inventory Update Rule on a Non-Confidential Basis		
CAS Number	**CHEMICAL NAME**	**COMPANY NAME**
124-18-5	Decane	CHEVRON PHILLIPS CHEMICAL COMPANY LP
		SASOL CHEMICALS NORTH AMERICA LLC
		STERLING CHEMICALS, INC.
		ZEELAND CHEMICALS, INC
1120-21-4	Undecane	SASOL CHEMICALS NORTH AMERICA LLC
		SHELL CHEMICAL LP
112-40-3	n-Dodecane	CHEVRON PHILLIPS CHEMICAL COMPANY LP
		SASOL CHEMICALS NORTH AMERICA LLC
		SHELL CHEMICAL LP
		SOLUTIA INC

Reference: EPA VCCEP and 2002 IUR Websites (http://www.epa.gov/chemrtk/vccep/vccepmth.htm and http://www.epa.gov/oppt/iur/iur02/search.htm).

3. Previous and On-Going Health Assessments

This section reviews the previous and on-going assessments for decane, undecane, and dodecane.

3.1 OECD SIDS Program/ICCA HPV Initiative

Decane, undecane, and dodecane have all been sponsored under the Organization for Economic Cooperation and Development's (OECD) "Screening Information Data Set" (SIDS) process. As was discussed in Section 2, one of the criteria for selecting chemicals for the VCCEP Pilot program was that they had gone through or are currently in the HPV Challenge or OECD SIDS program. The SIDS process is part of an international program for collecting and sharing information on high production volume chemicals. Once a chemical has been selected for SIDS, a sponsor country collects available data and determines if additional testing is needed to complete the SIDS data set. The SIDS data set includes information on chemical identity, physical characteristics, sources and levels of exposure, environmental fate and pathways, and ecotoxicological and toxicological data. Once a SIDS data set is completed, a SIDS Initial Assessment Report (SIAR) is prepared and discussed at an OECD meeting. The SIAR includes a detailed assessment of all relevant hazard and exposure information, not just the base SIDS data set. Based on the information in the SIAR, OECD makes a determination regarding the need for additional work. EPA represents the United States in the SIDS program. The International Council of Chemical Associations' (ICCA) High Product Volume (HPV) Initiative is a program in which chemical manufacturers sponsor chemicals through the OECD SIDS program. Through the ICCA HPV Initiative chemical sponsors will develop the SIDS data set (e.g., dossier) and SIAR. ICCA sponsors then work with an OECD sponsor country to have these documents reviewed and ultimately presented to OECD at a SIDS Initial Assessment Meeting (SIAM).

These three alkanes currently have three separate OECD SIDS sponsors:

n-Decane – Italy
n-Undecane – Japan
n-Dodecane – U.S./ICCA (ACC IHSC)

Both decane and undecane were sponsored many years ago by Italy and Japan, respectively, although final dossiers or SIARs have not been developed. Dodecane was recently sponsored by the U.S. as an ICCA sponsored chemical. The ICCA sponsor of dodecane is the American Chemistry Council International Hydrocarbon Solvents Consortium (IHSC), in which members of the n-Alkanes VCCEP Consortium also participate. The IHSC has been working with industry participants from Italy and Japan and hopes to coordinate the sponsorship of these chemicals into one effort. Many of the toxicity data/summaries used in the VCCEP hazard assessment for these chemicals were developed through the SIDS/ICCA activities of IHSC and the OECD sponsor countries. A final OECD SIDS dossier and SIAR for the category that contains these n-alkanes is expected in 2005.

3.2 Total Petroleum Hydrocarbon Criteria Working Group

The Total Petroleum Hydrocarbon Criteria Working Group (TPHCWG) was formed in 1993 to address the problem of widely varying cleanup standards being used by the states at sites which were contaminated by hydrocarbon materials such as fuels, lubricating oils, and crude oils.

The Working Group was guided by a steering committee consisting of representatives from government, academia, and industry including the EPA and a number of state governments. The derived health benchmarks have been adopted and implemented by a number of government agencies since 1997 (TPHCWG, 1997).

The TPHCWG developed reference concentrations (RfCs) and reference doses (RfDs) for a number of hydrocarbon ranges. The TPHCWG derived a C_{10}-C_{12} aliphatic fraction RfC of 1.0 mg/m^3 and RfD of 0.1 mg/kg/day. The studies considered by TPHCWG in deriving the RfC for the C_{10} – C_{12} aliphatic fraction are reviewed in the hazard assessment (Section 7). EPA methodologies were used in the derivation of these benchmarks and provide a valuable independent comparison to the conclusions of this report.

The relevant TPHCWG chronic benchmarks are detailed in Section 8.2.

3.3 Hydrocarbon Solvent Guidance Group Values (GGVs) for Setting Occupational Exposure Limits (OELs) for Hydrocarbon Solvents

The European Chemical Industry Council (CEFIC) Hydrocarbon Solvent Producers Associations recently reviewed the existing OELs and toxicology data for a broad range of aliphatic and aromatic hydrocarbon solvents and established a recommended occupational exposure guidance value of 1,200 mg/m^3 for C_9-C_{15} aliphatic and cycloaliphatic hydrocarbons (CEFIC, 2001). This guidance value was based on a review of the toxicology data and set to protect against irritation and possible CNS effects. The documentation for this group guidance value is provided in Appendix C.

4. Regulatory Overview

The regulations impacting n-alkanes are generally on hydrocarbon or petroleum products that may contain n-alkanes.

4.1 CPSC Child-Resistant Packing for Hydrocarbons

The Consumer Product Safety Commission's (CPSC) established standards for child-resistant packaging of products that contain 10% or more hydrocarbons with a viscosity less than 100 SUS at 100^{o} F. The standard was implemented in 2002 to avoid accidental ingestion of hydrocarbons by children, which can result in chemical pneumonitis if the ingested material is aspirated into the lungs. The examples from the CPSC of household products and cosmetics covered by the packaging regulation include some baby oils; sunscreens; nail enamel dryers; hair oils; bath, body and massage oils; makeup removers; some automotive chemicals (gasoline additives, fuel injection cleaners, carburetor cleaners); cleaning solvents (wood oil cleaners, metal cleaners, spot removers, adhesive removers); some water repellents containing mineral spirits used for decks, shoes, and sports equipment; and general-use household oil. Some of these hydrocarbon-containing products may contain decane, undecane, and dodecane.

Hydrocarbons that have a viscosity level higher than the standard were determined to be unlikely to be aspirated and therefore not subject to the regulation.

In establishing the rationale for the regulation, CPSC noted five fatalities of children under 5 years old from 1993 through 2001 involving aspiration of hydrocarbon products. CPSC data for 1997 through 1999 revealed an estimated 6,400 emergency room visits involving children under 5 years of age who ingested household chemical products that frequently contain hydrocarbons that can pose an aspiration hazard. In addition, data from the American Association of Poison Control Centers for 1993 through 1999 revealed 11,115 potential aspiration exposures to cosmetic and household products containing hydrocarbons (CPSC, 2001).

4.2 Occupational Exposure Limits

While there are no regulatory occupational exposure limits for decane, undecane, or dodecane, both NIOSH and ACGIH have recommended exposure limit for nonane of 200 ppm (1050 mg/m^3) on an 8-hour time-weighted average (TWA) basis. The primary basis for the limit is to protect against irritation and CNS effects (ACGIH, 2003; NIOSH, 1994).

4.3 VOC Regulations

There are numerous regulations to control volatile organic compounds (VOCs) in regions of the country where ozone formation is a concern. While these regulations are not specific to decane, undecane or dodecane, products that contain these chemicals (fuels, solvents, etc.) are generally subject to VOC regulations. A notable impact of these regulations is that they have created a downward trend in VOC levels in ambient air, around highways, etc. due to the reduced emissions from automobiles, trucks, stationary sources, consumer products, etc. See Appendix E which details one category of VOC regulations (mobile source emissions) and the declines in ambient air levels for decane and undecane. As this analysis shows, the ambient air levels of decane and undecane have dropped by approximately four-fold between 1993 and 2001. This reduction likely means that much of the exposure literature reviewed in this assessment, where samples were collected during the 1980's and 1990's, is over-reporting current exposures.

5. Product Overview

This section presents an overview of the physical, chemical, and environmental fate properties of decane, undecane, and dodecane; the production and uses of n-alkanes, and a brief overview of complex petroleum substances which contain n-alkanes as constituents.

5.1 Physical, Chemical, and Environmental Fate Properties

The physical, chemical and environmental fate properties of decane, undecane and dodecane are very similar. These chemicals have a moderate to low vapor pressure, which decreases with increasing carbon-chain length. These chemicals are not likely to persist in the environment, as they will largely partition to the air where they will degrade via photo-oxidation. Half-lives in air (during daytime) are calculated to be 9.2 hours for n-decane, 10.2 for n-undecane, and 11.5 hours for n-dodecane. As these chemicals have shown an ability to biodegrade, the small portion that partitions to soil or sediment should not persist. Being insoluble in water and less dense than water, any releases to water of these n-alkanes should separate and volatilize to the air.

An important physical property of these chemicals for considering hazard, exposure and risk is the vapor saturation point in air. Nilsen, *et. al.* (1988) measured the saturation point of n-alkanes from C_9 (nonane) through C_{13} (tridecane) and found a dramatic reduction in saturation point across this series – approximately a 3-fold reduction in saturation point for each carbon number increase. For decane, undecane, and dodecane, the saturation points were found to be 1369 ppm, 442 ppm, and 142 ppm respectively. This reduction in saturation point becomes critical when assessing the inhalation hazards of these chemicals. In Nilsen's short-term inhalation study, only nonane produced an atmospheric concentration sufficiently high to result in any acute toxicity effects in rats.

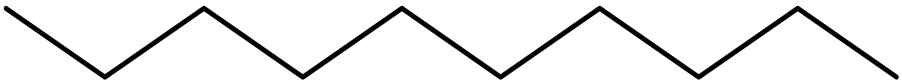
Table 5.1 Physical, Chemical, and Environmental Fate Properties of n-Decane, n-Undecane, and n-Dodecane

Chemical:	**Decane**	**Undecane**	**Dodecane**
CAS Number:	142-18-5	1120-21-4	112-40-3
Empirical Formula:	$C_{10}H_{22}$	$C_{11}H_{24}$	$C_{12}H_{26}$
Molecular Weight:[1]	142.29	156.32	170.34
Density:[1]	0.7300 g/cm^3 at 20° C	0.7402 g/cm^3 at 20° C	0.7487 g/cm^3 at 20° C

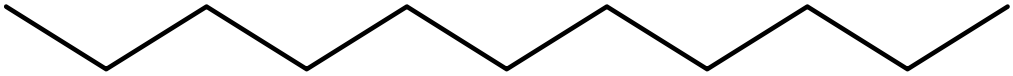
Chemical:	**Decane**	**Undecane**	**Dodecane**
Boiling Point: (at 760 mmHg)[1]	174.1° C	196° C	216.3° C
Saturation Point in Air (@21.6oC)[4]	1369 ± 19 ppm (7968 ± 111 mg/m^3)	442 ± 32 ppm (2826 ± 205 mg/m^3)	142±13 ppm (990 ± 91 mg/m^3)
Vapor Pressure (@ 38° C):	1.298 mmHg	0.502 mmHg	0.205 mmHg
Water Solubility:[1]	Negligible	Negligible	Negligible
Hydrolysis	Not Applicable	Not Applicable	Not Applicable
Fugacity/ Partitioning in the Environment[3]			
Air	98.1%	97.1%	93.3%
Water	0.01%	0.01%	<0.01%
Soil	1.89%	2.83%	6.56%
Sediment/ Suspended Sed.	0.04% <0.01%	0.06% <0.01%	0.14% <0.01%
Biota	<0.01%	<0.01%	<0.01%
Half-Life in the Atmosphere[2]	9.2 hrs	10.2 hrs	11.5 hrs
Biodegradation	Readily Biodegraded	Readily Biodegraded	Readily Biodegraded

1. CRC (1986). Handbook of Chemistry and Physics, 66th Edition.
2. EPIWIN (1999). Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Mackay D (1998). Level I Fugacity-Based Environmental Equilibrium Partitioning Model, Version 2.1 (16-bit). Environmental Modelling Centre, Trent University, Ontario, Canada.
4. Nilsen, O; *et. al.* 1988. Toxicity of n-C9 to n-C13 Alkanes in the Rat on Short Term Inhalation. Pharmacology & Toxicology. 62: 259-266.

STRUCTURES OF N-ALKANE CATEGORY MEMBERS



N-DECANE



N-UNDECANE

N-DODECANE

5.2 Production of n-Alkanes

The vast majority of n-alkane production is as n-alkane process streams and not as individual n-alkanes. N-alkanes in the C_{10} to C_{16} range are generally produced from petroleum distillates through a two-step process: 1) close-cut distillation to produce the desired carbon range and then, 2) isolation of the n-alkanes from the close-cut distillation stream by molecular sieves. Further distillation of the n-alkanes streams may be done to manufacture products with an even narrower carbon number range (SRI-CEH, 1998). The carbon number ranges of the finished n-alkanes process streams will vary depending on the desired length for a given application, but typical ranges include: C_{10}-C_{13}, C_{12}-C_{14}, C_{12}-C_{16}, and C_{14}-C_{16} (Sasol, 2003). A small amount of n-alkane streams are produced through a different process which involves the hydrogenation of olefin oligimerization by-products. Petrochemicals produced in this manner are commonly referred to as synthetics because they are synthesized from smaller molecules rather than being derived from petroleum streams. In both case, the resulting n-alkane products have a high purity – generally 97-99% n-alkanes. In 1996, the estimated U.S. production for n-alkanes was approximately 762 million pounds (SRI-CEH, 1998).

5.3 Uses of n-Alkanes

The predominant use of pure n-alkanes in the C_{10}-C_{12} carbon range is as chemical intermediates in the production of linear alkylbenzenes (LABs), an intermediate in the production of linear alkyl sulfonates (LASs) which are used as surfactants and detergents. There are four primary processes by which LABs can be manufactured; all use n-alkanes or n-alkanes as a primary feedstock. All of these processes are run in completely closed-systems.

1. **Chloroalkane/$AlCl_3$**: n-Alkanes are converted to a mixture of n-chloroalkanes and n-alkanes by thermal chlorination using chlorine gas. This chloroalkane/alkane mixture is fed along with excess benzene and a small amount of $AlCl_3$ catalyst to the alkylation reactor. The reaction mixture is then separated from the catalyst layer and distilled to isolate the LAB and alkylate bottoms products. The benzene and n-alkane fractions from distillation, as well as the separated catalyst phase, are recycled back into the process.

2. **Olefin/$AlCl_3$**: n-Alkanes are converted to a mixture of n-olefins and n-alkanes by catalytic dehydrogenation. This olefin/alkane mixture is fed along with excess benzene and a small amount of $AlCl_3$ catalyst to the alkylation reactor. The resulting organic phase is then separated from the catalyst layer and distilled to isolate the LAB and alkylate bottoms products. The benzene and n-alkane fractions from distillation, along with the separated catalyst layer, are recycled back into the process.

3. **Olefin/HF**: n-Alkanes are converted to a mixture of n-olefins and n-alkanes by catalytic dehydrogenation. This olefin/alkane mixture is fed along with an excess of benzene and HF catalyst to the alkylation reactor. The organic reaction phase is then separated from the catalyst and distilled to isolate the LAB and alkylate bottoms products. The benzene and n-alkane fractions from distillation, along with the separated catalyst layer, are recycled back into the process.

4. **DETAL**: n-Alkanes are converted to a mixture of n-olefins and n-alkanes by catalytic dehydrogenation. This olefin/alkane mixture is fed along with excess benzene to a fixed bed reactor containing a solid supported acidic alkylation catalyst (DETAL). The resulting reaction mixture is then distilled to isolate the LAB and alkylate bottoms products. The benzene and n-alkane fractions from distillation are recycled back into the process.

None of the processes described above are 100% efficient so the LAB process streams will contain unreacted n-alkanes and benzene (alkylate bottoms). As a final stage for all LAB production processes, the LAB is separated from the alkylate bottoms by distillation at various temperatures influenced by the alkyl chain length composition of the starting materials.

A very small volume (estimated at less than 20,000 pounds) of pure n-alkanes are used as laboratory reagents.

5.4 Petroleum Products which Contain Decane, Undecane, and Dodecane

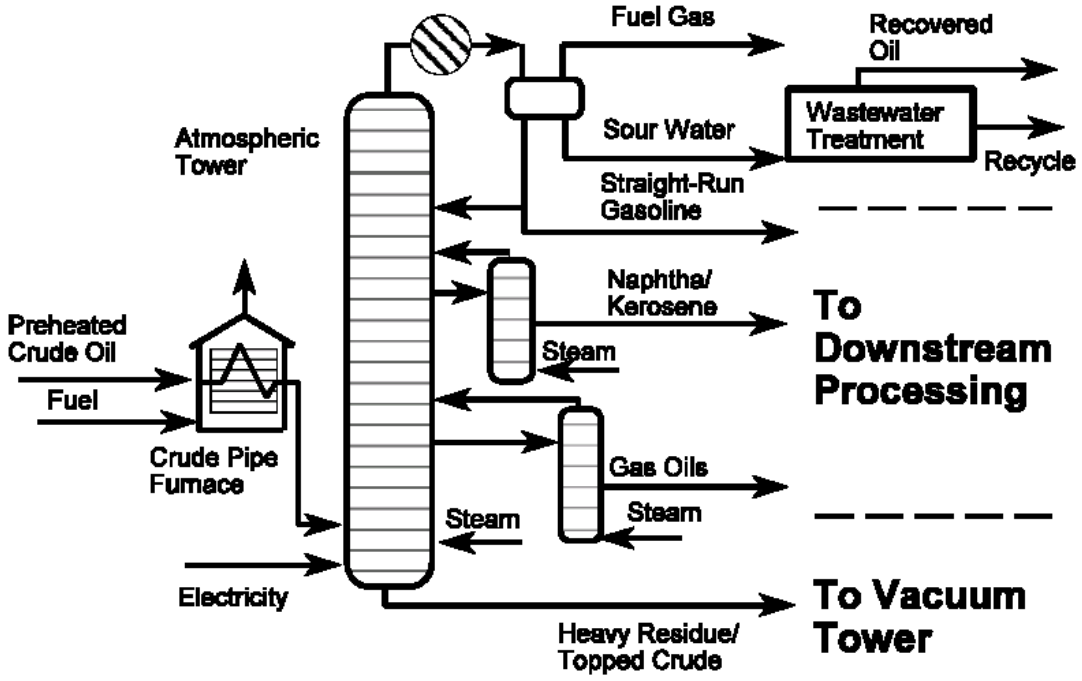
The production and use of these three n-alkanes as individual chemicals or n-alkane process streams is quite small and limited relative to the production and use of petroleum substances that contain them as constituents. As the Consortium members represent manufacturers of pure n-alkane substances, this assessment is not intended to address the petroleum substances which may contain one or more of these n-alkanes. Nonetheless, the Consortium recognizes that these substances play an important role in the exposure

and risk assessments of decane, undecane, and dodecane, so it is providing a brief overview of these substances.

There are several different types of petroleum substances that may contain these n-alkanes, including middle-distillate fuels such as kerosene, jet fuel, diesel fuel, and home heating oil and medium to low volatility aliphatic hydrocarbon solvents (e.g. mineral spirits, white spirits). These substances will vary in carbon number range and composition, but generally they are in the carbon number range of C_9-C_{16}+ and contain approximately 25% n-alkanes. Figure 5.1 provides a simple diagram of petroleum refining from a U.S. Department of Energy (DOE) profile of the refining industry. The process streams in Figure 5.1 that mostly contain n-alkanes in the C_{10}-C_{12} range are Naphtha/Kerosene and Gas Oils. These intermediate process streams undergo additional processing to make the fuels and hydrocarbon solvents mentioned above.

The U.S. DOE reports the U.S. refining capacity is 16.5 million barrels per day (or approximately 729.3 million gallons per day); of this capacity approximately 21% goes toward the production of diesel fuel, 10% for kerosene/jet fuel, and 0.2% towards hydrocarbon solvents (U.S. DOE, 2004, www.oit.doe.gov/petroleum/profile.shtml).

Figure 5.1 Simplified Petroleum Refining Diagram



Source: US DOE, 1998.

5.4.1 Aliphatic Hydrocarbon Solvents

Aliphatic hydrocarbon solvents consist of carbon and hydrogen molecules arranged as straight chain (n-alkanes), branched chain (isoparaffins), or cyclic hydrocarbons (naphthenes). Hydrocarbon solvents are primarily defined by distillation range and flash point. In addition, aliphatic hydrocarbon solvents may also be defined by the amount of aromatic compounds they contain. The petroleum feedstocks used to make many aliphatic hydrocarbon solvents contain some aromatic hydrocarbons (normally less than 23%). For some aliphatic hydrocarbon solvents, such as regular mineral spirits or white spirits, these aromatic hydrocarbons are purposely retained in the final product to achieve or enhance certain solvency properties. The term "dearomatized" refers to those products that have undergone an additional step to remove or hydrogenate the aromatic compounds contained in the feedstock (e.g., dearomatized mineral spirits), resulting in an aliphatic hydrocarbon solvent with no or little aromatic content ($\leq$ 2%).

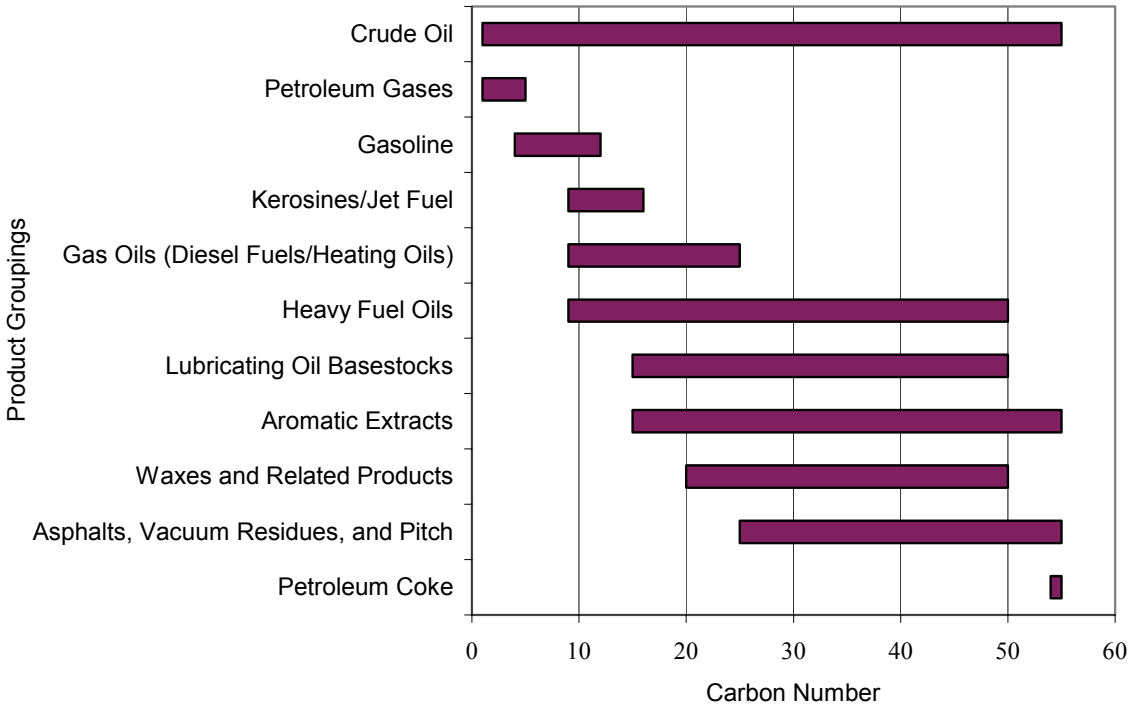
Aliphatic hydrocarbon solvents of the mineral spirits or Stoddard solvent variety are the hydrocarbon solvents most likely to contain n-decane, n-undecane, or n-dodecane. Aliphatic hydrocarbon solvents in this class typically have boiling ranges between 150-200° C (300-400° F) and a carbon number range between C_9-C_{13}. Composition of mineral spirits and Stoddard solvent type hydrocarbon solvents will vary depending on manufacturing processes and composition of crude oil feedstocks, but generally they contain approximately 25% n-alkanes. These solvents have a wide variety of applications including paints, coatings, adhesives, automotive polishes/waxes, etc.

Hydrocarbon solvents are further refined than fuels to produce products with narrower distillation ranges, defined aromatic content, removal of benzene, polyaromatic hydrocarbons (PAHs), sulfur- and nitrogen-containing compounds, and low color.

5.4.2 Kerosene, Jet Fuel, and Diesel Fuel

There are several types of petroleum fuels that may contain n-decane, n-undecane, n-dodecane including kerosene, jet fuel, and gas oils (e.g. diesel fuel, home heating oil). Figure 5.2 provides an approximate overview of petroleum product classes by carbon number range. Kerosene is a generic name for the lighter end of petroleum substances known as middle distillates. Kerosenes generally contain C_9 to C_{16} hydrocarbons; the composition varies somewhat depending on the crude source and manufacturing process. The typical distillation range is 145 to 300° C. The major components are branched and straight chain alkanes, naphthenes (cycloalkanes), and aromatic hydrocarbons, mainly alkylbenzenes and alkylnaphthalenes (CONCAWE, 1995). Jet fuel is a major use for kerosene streams; generally, it's blended from several kerosene streams. Gas Oils are the heavier end of middle distillates. They contain a complex combination of hydrocarbons in the carbon number range of C_{11} to C_{25}, with distillation ranges between 150 and 450° C. Gas oils are primarily used as automotive fuels (e.g. diesel fuel) and home heating oil (CONCAWE, 1996).

Figure 5.2 Petroleum Products by Carbon Number Range



6. Exposure Assessment

6.1 Summary

This section describes and quantifies potential sources of exposure to the n-decane, n-undecane, and n-dodecane, and the situations in which exposure may occur. Of the routes of exposure considered, inhalation was determined to be the main exposure pathway. In accordance with the aims of VCCEP, the focus of this assessment is on children's exposure and exposure of potential parents and the fetus.

The first step in the exposure assessment was a literature search, the results of which are presented in Appendix A. Table A.1, found on page A-1, provides a summary of the principal exposure studies identified in the literature search. Table A.2, found on page A-9, provides the n-alkane exposure data reported in the studies considered by EPA in identifying chemicals for the VCCEP program. In evaluating the results from the available exposure literature, the Consortium found that adequate exposure information was available on decane, undecane, and dodecane in order to characterize the exposure to children and prospective parents. All of the data summarized in the exposure assessment and carried forward to the risk assessment are measured air samples, so they consider all possible sources of exposure in a particular environment (e.g. indoor air). Based on those environments where n-alkanes have been detected it would appear that the major sources of exposure are attributable to complex petroleum products including diesel fuel, kerosene, heating oils, and solvent containing products such as paints, toners and adhesives. The key studies used to quantify potential exposure in the analysis are summarized in Table 6.1.

Exposure Pathways

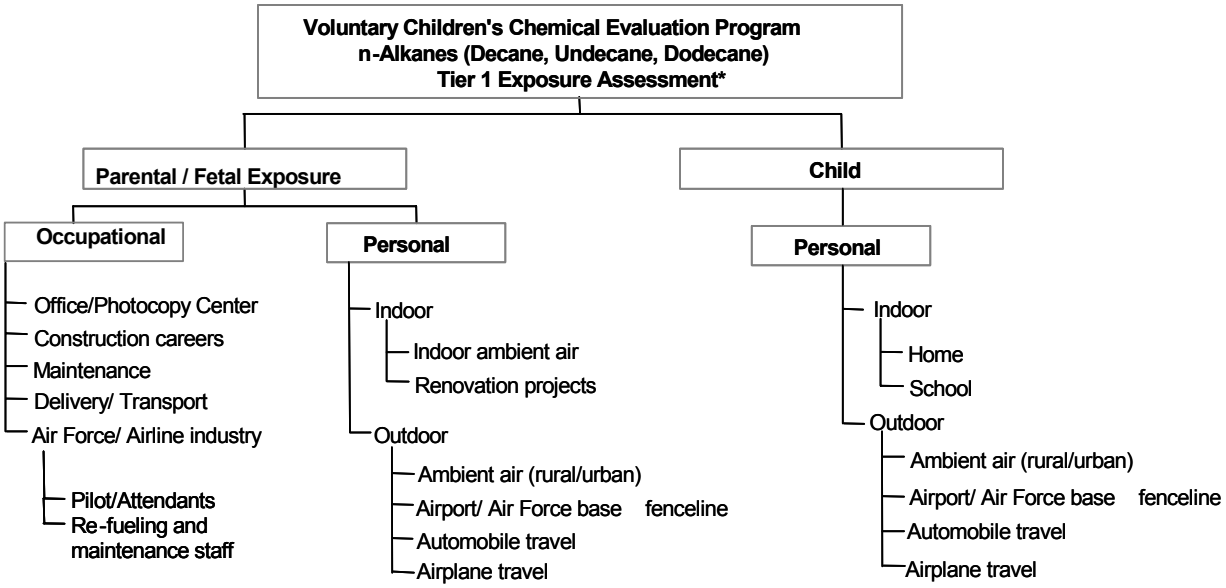
Four routes of exposure, namely inhalation, oral, dermal, and human milk, were considered. Of these, only inhalation was determined to be of sufficient significance to undergo detailed risk characterization. This conclusion was based on several considerations including the physicochemical characteristics of the chemicals, the use and release patterns of the major sources of exposure, the results from the literature review, and the comparative estimations of oral, dermal, and human milk routes. As discussed in Section 5.1, decane, undecane, and dodecane are hydrophobic chemicals that partition almost entirely into the air. In addition, emissions from many of the major exposure sources such as fuels, paints, and solvents, are generally to the air. These facts together suggest that inhalation is likely to be the main route of exposure. This assumption is further supported by the fact that all of the exposure data available in the literature is inhalation exposure. To evaluate the potential importance of the oral, dermal and human milk routes of exposure, screening exercises were conducted on these routes. In these exercises, bounding estimates were calculated for the maximum amount of the n-alkanes which could be ingested or absorbed assuming very conservative exposure conditions. The results, presented in Sections 6.2.3 and 6.5, indicate that exposures from these routes are likely to be significantly lower than inhalation exposures, further supporting the conclusion that inhalation is the only significant route of exposure.

Children's and parental exposure to decane, undecane, or dodecane is likely to occur on a regular basis, generally at extremely low levels, due to the ubiquitous presence of these chemicals in the environment. Non-occupational exposure concentrations are similar for adults and children as both are exposed to the same air levels in homes, schools, office buildings, and during automotive and air travel. Indoor air exposure, particularly in-home, was the focus of the non-occupational exposure assessment as the majority of time for both children and prospective parents is spent indoors. Indoor air levels vary somewhat from study to study and can be higher during home renovation, particularly during interior painting. As these exposure levels to indoor air are the same for adults and children, there is no need to discriminate by age in estimating non-occupational exposure. Occupational exposure was considered separately for prospective parents. Several occupations have the potential for exposure to decane, undecane, and dodecane, including persons employed in aircraft refueling and maintenance work in the Air Force or airline industry, indoor painters, construction workers, persons working in photocopy centers, and delivery or freight hauling careers.

Due to the low volatility of these compounds and the limited CNS effects even at saturated concentrations (Section 7.2), solvent abuse involving C_{10}-C_{12} n-alkanes is improbable.

For non-occupational exposure, literature published post-1990 was considered of more relevance given the increased EPA regulations under the Clean Air Act affecting mobile sources and the VOC content of consumer products, such as paints. As shown in Appendix E, the ambient air levels of decane and undecane have dropped approximately fourfold from 1993 to 2001.

Based on the literature review, the following diagram summarizes the pathways of exposure identified for analysis.



* Does not include smoking and exposure through product misuse

Based on the analyses of the pathways described in this Section, the following scenarios were identified as being the most representative of situations where children and prospective parents are likely to have the highest potential exposure to decane, undecane, and dodecane. These are the scenarios that will be considered in the risk assessment:

1. Chronic exposure of infants and children to indoor air.
2. Chronic exposure of prospective parents to indoor air.
3. Short term exposure of infants and children in a newly renovated (painted) home.
4. Short term exposure of prospective parents in a newly renovated (painted) home.
5. Prospective parents exposed occupationally in the painting trade, and refueling operations at an airport.

Relevant exposure concentration data for these scenarios were abstracted from the studies summarized in Appendix A, distributions estimated, and representative and upper bound exposure (95^{th} percentile) concentrations calculated (see section 6.6.2). The exposure concentrations reported are the combined exposure to decane, undecane, and dodecane since the chemicals are being considered together as a category. The data are summarized in Table 6.1.

Table 6.1 Exposure Concentrations for Selected Scenarios

Type of Measurement	Representative Concentration[1]	Upper Bound Concentration[2]	Applicable Scenario[3]	References
Average daily household indoor air concentrations	42 μg/m3	129 μg/m3	1,2	Brown et al, 1994; BRE, 1996;
Interior painting average ambient air concentrations and personal samplers	122 μg/m3	910 μg/m3	3,4,5	Brown & Crump, 1998 Wallace, 1989
Highest exposed Air force fuel workers: 1 hour average ambient exposures (personal monitors)	5,061 μg/m3	16,800 μg/m3	5	Pleil et al, 2000

1. Representative concentration is defined as the average of a set of exposure data.
2. Upper bound concentration is generally defined as the upper 95^{th} percentile of the exposure data when adequate data were available to develop a log-normal distribution or the maximum reported level when no distribution was available.
3. 1) Chronic exposure of infants and children to indoor air.
   2) Chronic exposure of prospective parents to indoor air.
   3) Short term exposure of infants and children in a newly renovated (painted) home.
   4) Short term exposure of prospective parents in a newly renovated (painted) home.
   5) Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

Analytical Limitations

In evaluating the n-alkane exposure literature, it is worth noting that many studies report the data as decane, undecane, and dodecane exposure without indicating whether the value is for just the normal isomer or a combination of isomers. In addition, some analytical techniques used to characterize organic vapor samples may not be sufficiently specific to distinguish between the n-alkanes, and branched (iso) or cyclic isomers. So what is reported as an n-alkane exposure value may include exposure to other alkane isomers. As most exposure is due to complex fuels and hydrocarbon solvents and not to individual n-alkanes or n-alkane process streams, it's possible that some of the exposure data used in this assessment is on multiple isomers of decane, undecane, and dodecane and not just the normal isomers. This analytical limitation would only have the effect of over-predicting exposure, so it was not considered an impediment to the exposure assessment rather just an unquantifiable source of conservatism in the exposure estimation.

6.2 Non-Occupational Exposure

Numerous studies were identified which quantify the exposure levels to decane, undecane, and dodecane in non-occupational settings, including indoor and outdoor environments, where children and prospective parents are likely to be. No personal exposure samples for children were found in the literature, though this was not felt to be problematic as children spend a substantial portion of their day indoors at home, daycare facilities, or school and data are available on these environments. Preschool children and newborns spend an average of 85 to 95 percent of the day inside (USEPA, 2001). Therefore, indoor sources of decane, undecane, and dodecane are major points of exposure for young individuals. Chronic exposure levels in the home are anticipated to be the same for infants, children, and adults.

No specific information was identified regarding decane, undecane, and dodecane exposure to children from the use of consumer products. Further, decane, undecane, and dodecane were not reported as ingredients in any of the thousands of consumer products reviewed in the National Library of Medicine's Household Products Database (http://householdproducts.nlm.nih.gov/) or in any of the literature or product MSDSs reviewed by the Consortium. This made it infeasible to conduct exposure modeling of consumer products that may contain decane, undecane or dodecane. However, measured indoor air data from recently renovated homes and from a painting scenario at an EPA test house provide information to characterize the potential exposures from consumer products (e.g. paints, adhesives) that are likely to be used in indoor environments where children may be present. Given the nature of consumer products that may contain decane, undecane, and dodecane (e.g., solvent-based paints, construction adhesives, degreasers, etc.), it is not anticipated that children will be the primary users of these products. Information on adult exposure from the direct use of these types of consumer products is provided in the occupational exposure section (see Section 6.4).

6.2.1 Indoor Sources of Exposure

6.2.1.1 Household Exposures

Non-occupational indoor VOC exposures predominately occur within the exposed individual's home during day-to-day activities. Potential sources of non-occupational decane, dodecane, or undecane exposure are household emissions from furniture, carpet, wallpaper, paint, painted sheetrock, adhesives, glued wallpaper, and glued carpet (Wallace, 1987). Such contributors were not quantified specifically but it can be expected that air measurements integrate all such potential sources.

Average daily household indoor air concentrations of decane, dodecane, and undecane range from 3.5 to 118 µg/m^3, 2.2 to 104 µg/m^3, and 1 to 57 µg/m^3 respectively (BRE, 1996 as reported in MRC, 2000; Brown and Crump, 1995, 1998; Kostiainen, 1995; Phillips et al, 1997; Wallace et al., 1991, Heavner, 1996, Samfield, 1992, Brown et al, 1994). In contrast, Brown, 1994, in a compilation of U.S. and European data, concluded a geometric mean of 5 µg/m^3, a 95th percentile of 20 µg/m^3, and a 98th percentile of 47 µg/m^3 for decane in established dwellings. In another study of 173 homes, undecane concentrations averaged 14 µg/m^3 with a standard deviation of 17 µg/m^3 (Brown and Crump, 1995, BRE, 1996). Median and 90th percentile concentrations of decane in a "typical" home were reported by the World Health Organization as 10 µg/m^3 and 50 µg/m^3, respectively, and 5 and 25 µg/m^3, respectively for undecane (WHO, 1989). Therefore, maternal domestic exposures are not expected to exceed these levels under normal conditions.

Concentrations detected in the home for the chemicals of interest are reported on a website (Aerias.org, 2003). This site was considered as a resource for exposure data, but it could not be used because it is not in a form that allows the reported concentrations to be put into scientific perspective. There is no description of study design, measurement methodology, or QA/QC procedures. The study is not peer reviewed. Aerias is a private company in the indoor air quality field. The data on this site were acquired by a commercial analytical lab, Air Quality Sciences, which funds the Aerias organization. Much of the labs' activity relates to conducting studies of buildings where problems have been reported (sick buildings, remediation sites etc.) and the highest levels reported are associated with such sites. Aerias is considering refining their data presentation in this light. (Personal Communication with B. Epstein of Aerias, 3/12/04). Accordingly, the maximum concentrations reported on the Aerias website are of little use in understanding upper bound on exposures in the general community. The maximum values reported were: 5.96 mg/m^3, 24.1 mg/m^3, and 50.8 mg/m^3 for n-decane, n-undecane, and n-dodecane respectively. However, the average values reported by Aerias for decane, undecane and dodecane of 66, 54, and 62 µg/m^3, respectively, are within the range of the peer-reviewed studies described in this report. This database may be capable of providing valuable data but much more analysis would be required.

For non-occupational exposure, indoor exposure has likely declined since 1990 given the increased EPA regulations under the Clean Air Act affecting mobile sources and specific VOC initiatives that lead to net decreases in VOC content of paints used indoors post-1990.

6.2.1.2 New and Renovated Homes

New and renovated homes represent a potential opportunity for VOC exposures due to emissions from building compounds or consumer products used during the renovation or construction process. New homes may have higher VOC concentrations in the ambient air immediately after construction. For example, Brown (1994) surveyed new dwellings in Europe and the USA and reported mean concentrations up to 75 $\mu g/m^3$ for n-decane with an upper 90th percentile of 310 $\mu g/m^3$. However, VOC concentrations drop significantly in the first six months following construction (Crump et al., 1997). In a study of newly constructed test homes, undecane concentrations decreased from a highest average of 82 $\mu g/m^3$ in the first year post-construction to an average of 16 $\mu g/m^3$ in the second year post-construction (Crump et al., 1997). Total VOC concentrations dropped by a factor of 20 over the first 6 months and by 50 fold after 16 months. These homes were unoccupied and windows remained sealed. Potential exposures to decane, undecane, and dodecane are likely to decrease even more rapidly in an occupied home where the opening of windows and doors greatly increase air exchange rate. Rothweiler (1992) reported on concentrations of decane measured in new and renovated homes of 11 $\mu g/m^3$ (10th percentile), 141 $\mu g/m^3$ (50 th percentile), 669 $\mu g/m^3$ (90 th percentile), with a maximum recorded concentration of 916 $\mu g/m^3$. Again, these homes were unoccupied and rooms were sealed for 8 hours prior to sampling. These concentrations would likely be reduced if the homes were occupied and doors and windows were opened.

6.2.1.3 Household Maintenance or Renovation

Renovation projects within the home can cause temporarily elevated decane, dodecane, and undecane ambient air concentrations and potentially increased exposure for the mother and child. Home renovation (*i.e.*, redecoration or remodeling) is quite frequent at or around the time of childbirth. Forty-two to 61 percent of homes are renovated within three months prior and six months after childbirth, resulting in an increased opportunity for exposure (Herbath et al., 1998).

Diez (2000) conducted a clinical study of 475 children in the first year of life, together with parental surveys. This study was designed to investigate potential associations of smoking and home renovation with atopy risk to children. The study determined that approximately 48% lived in homes that were freshly painted, 52% contained new furniture, and new carpet was installed in 37% of the homes. Upper confidence limits on the concentrations of decane, undecane and dodecane were reported as 25.6 $\mu g/m^3$, 23.5 $\mu g/m^3$, and 17.6 $\mu g/m^3$, respectively, in the first 4 weeks of life.

Individuals painting the home interior have an increased potential for exposure to VOCs, because interior painting projects have resulted in mean decane and undecane ambient air concentrations of 60 (SD= 150) and 31 (SD= 37) $\mu g/m^3$, respectively measured as a 4 week average (Brown and Crump, 1998). In another study of volunteers painting in the home, individuals had reported personal air samples of decane and undecane as high as 350 and 280 $\mu g/m^3$, respectively (Wallace et al., 1989). Median personal air levels reported in this study were significantly lower at 48 $\mu g/m^3$ and 30 $\mu g/m^3$ respectively. Measured

breath concentration of decane in one of the subjects increased from 2.9 μg/m^3 to 290 μg/m^3 following painting and use of solvents.

More data is available from an EPA sponsored study on exposure levels resulting from application of an alkyd (oil) based primer and paint to gypsum walls of a bedroom (USEPA, 2001). A primer coat (AP-F) was applied followed 2 days later by a coat of alkyd paint (ASG-G). Concentrations of "decane", "undecane", and "dodecane" (isomer not specified as discussed in Appendix G) were measured over a period of up to 23 days. The house was unoccupied and sealed. The Air Exchange Rate was measured as 0.48 air changes per hour. Concentrations of three alkanes combined peaked at about 500 mg/m^3 during priming and 620 mg/m^3 during painting in the bedroom with corresponding values in the den (at the other corner of the house) of 80 mg/m^3 and 140 mg/m^3. The 24-hour time weighted average (TWA) concentration (calculated from the EPA report and detailed in Appendix G) reached about 50 mg/m^3 in the 24-hour periods during priming or painting. These levels rapidly dropped in a matter of hours by over two orders of magnitude and, after three weeks the combined concentrations of decane, undecane, and dodecane had dropped another order of magnitude to 40 μg/m^3 in the painted bedroom. The levels in this study were probably significantly higher than would be expected if normal ventilation precautions had been followed (opening windows, use of fans, and other ventilation). As noted, without specification of the isomers detected, the exact concentrations of the normal isomers cannot be determined.

6.2.2 Outdoor Sources of Exposure

6.2.2.1 Ambient Air

Non-occupational outdoor VOC exposure to decane, dodecane, or undecane occurs by various sources and activities. Typical ambient air concentrations in residential and urban areas tend to be lower than indoor concentrations, with mean concentrations ranging from 0.47 to 3.7 μg/m^3, 0.20 to 4.0 μg/m^3, and 0.10 to 6.7 μg/m^3, for decane, dodecane, and undecane, respectively (Bertorelli and Derwent, 1995 in CONCAWE, 1999; Brown and Crump, 1995, 1998; Hartwell et al., 1992; Michael et al., 1990; Phillips et al., 1997).

National air emissions for most pollutants peaked around 1970 (EPA, 2000). The decrease in VOC emissions is largely attributable to the Clean Air Act of 1970 (CAA), Clean Air Act Amendments of 1990 (CAAA) and voluntary emissions reductions. Programs created to implement the CAAA, including inspection and maintenance programs, reformulated gasoline (RFG) programs, tail pipe emission standards and new car technology. These ongoing programs will continue to decrease the amount of VOC released. Because of these programs EPA has projected that VOCs will decline an additional 20% between 1999 and 2010 (EPA, 2001). The decline in n-alkane emissions over the years from 1993-2001 is detailed in Appendix E.

6.2.2.2 Living by an Airport / Air Force Base

Ambient air concentrations of decane, dodecane, and undecane are potentially elevated along the perimeter of airports and Air Force bases due to airplane exhaust and volatilized jet fuel but there are no data reported. However, receptors off-site would not expected to be exposed to higher concentrations than non-aircraft related jobs on site who were exposed to levels of only 1 – 2 $\mu g/m^3$ of each of the n-alkanes (Pleil et al, 2000)

6.2.2.3 Airplane Travel

Passenger exposure to VOCs including decane, dodecane, and undecane may occur on-board commercial airliners at low levels. Total VOC (TVOC) concentrations aboard commercial airliners have been evaluated at levels of 3 ppb. (this would correspond to about 17 $\mu g/m^3$ if all VOC was decane). However, TVOC concentrations drop to 0.001 ppb (~0.006 $\mu g/m^3$) within three hours of flight onset, and alkane levels become non-detectable during this time-period. No difference in VOC concentrations occur between coach, business class, and first class cabins (Brady et al., 1999).

6.2.2.4 Automotive Travel

Average air concentrations of 17.4 $\mu g/m^3$ decane, 5.9 $\mu g/m^3$ dodecane, and 16.4 $\mu g/m^3$ undecane were reported inside vehicles during travel. Personal air samples have resulted in median and maximum decane concentrations of 10 $\mu g/m^3$ and 53 $\mu g/m^3$ respectively, and median and maximum undecane concentrations of 7.8 $\mu g/m^3$ and 43 $\mu g/m^3$, respectively (Wallace et al., 1991; Wallace et al., 1989). It was assumed that exposure during automotive travel would be representative of these levels.

6.2.3 Unique Children's Exposure

Unique children's exposure to decane, undecane, and dodecane, was considered by the Consortium. Most exposures, such as indoor air, are not unique to children. The following sources of exposure were considered for their potential to contribute uniquely to children's exposure: school related exposures and human milk.

School-Related Exposures

School indoor air is a potential source of decane, undecane, and dodecane exposure in children. Average decane, undecane and dodecane concentrations in a kindergarten school were reported as 6.6, 12.8, and 15.6 $\mu g/m^3$, respectively (Herbath et al., 1998). Similarly, maximum decane concentration in a Canadian elementary school was 7.5 $\mu g/m^3$ (Probert et al., 2000). Samfield (1992) has also reported mean concentrations of 6 $\mu g/m^3$ for decane and 6.8 $\mu g/m3$ for undecane in school. Outdoor air at a kindergarten school contained VOC concentrations of 2.0 $\mu g/m^3$ decane, 0.8 $\mu g/m^3$ undecane, and 1.1 $\mu g/m^3$ dodecane (Herbarth, 1998). These exposure levels appear to be similar or even lower than

indoor air levels in homes, so this source does not appear to present unique exposures for children.

Infant Ingestion of Human Milk

Erickson (1980), and Pellizzari (1982) have reported the detection of the n-alkanes of interest in human milk, and are based on the same study. The report of Erickson et al is the more comprehensive and includes chromatograms. This study collected 42 samples of human milk in women living in 4 urban areas containing chemical manufacturing plants: Bridgeville, PA; Bayonne, NJ; Jersey City, NJ; and Baton Rouge, LA. All 42 samples were analyzed, then of these the 8 samples with the greatest number of peaks or very intense unique peaks, were selected for qualitative identification. Isomers of decane, undecane and dodecane were identified but not quantified in 7 of the 8 samples. Identification was by professional judgment rather than by comparison with standards. Over 100 compounds were manually identified but not quantified and background contamination was not fully characterized. From this analysis, 9 compounds (none of them alkanes) were selected for quantitation.

The Consortium performed an evaluation of the data to estimate possible levels of the n-alkanes actually detected. This analysis is presented fully in Appendix F and was used to estimate an upper bound on potential infant exposure through mother's milk as described below.

Estimated Quantitation

There was no attempt in Erickson (1980) to quantify most of the peaks in the samples. Only four chlorinated compounds were quantified. The report does, however, provide information on the estimated limit of detection for compounds and based on that information, the following conclusions were made:

Volatile Organics in Milk:
30ng is required for identification by GC/MS. If 50g milk was used, then about 0.6 ng/g could be detected.

Decane, undecane, and dodecane potential concentrations were estimated by comparison of peak heights with the peak heights of PCE (perchloroethylene) and dichlorobenzene and using the geometric mean for the particular cities for calculations. All were either ND (not detected) or <1 or up to <10ppb.

Using the geometric mean calculated for perchloroethylene and dichlorobenzene (Table 19 in the report) and assuming a similar response factor for the n-alkanes, a rough estimate was made of the potential concentration of n-alkanes in these eight samples. This estimate is summarized in the table below. It must be noted that nearly all of these peaks were confounded by other peaks, making it likely that additional chemicals beyond decane, undecane, and dodecane were considered in the estimate.

Table 6.2 Estimated Potential Concentration of Selected n-Alkanes

Compound/ Sample #	1081	1040	1107	1115	2048	2071	3053	3111
n-Decane	<1	<1	<10	<10	<1	<1	<5	<1
n-Undecane	<1	<1	<10	<10	<1	<1	~10	<1
n-Dodecane	<1	<1	~5	~5	<1	<1	~10	<1

Units are ng/mL (ppb)

Semivolatile Organics in Milk:
These were almost always siloxane hits (column bleeding). Decane, undecane, and undecane were not detected in any sample, so the detection limit must have been <20ppb. The semivolatile analysis starts with toluene and the n-alkanes of interest would have been picked up by this analysis if present above detection.

Estimation of dose based on 60 µg/kg C_{10}-C_{12} n-alkanes in milk:
It was conservatively assume that all three target chemicals were present at the higher detection level in the semi-volatile analysis level (where no detections were reported) for a total milk concentration of 60 ppb (60 µg/kg).

A bounding estimate on infant exposure via human milk can be calculated as:

$$Dext = \frac{C \times IR \times EF \times ED \times UCF}{BW \times AT}$$

Where
D = External Dose (mg/kg/day)
C = Concentration (mg/kg)
IR = Ingestion Rate of human milk (g/day)
EF = Exposure Frequency (365days/year)
ED = Exposure Duration (1 year)
AT = Averaging Time (365 days)
UCF = Unit Conversion Factor, here 1 kg/1000 g
BW = Body Weight (infant) (kg)

From the USEPA Child Specific Exposure Factors Handbook, average human milk intake for ages birth to 12 months is 688 mL/day (709 g/day), with an upper 95th percentile of 980 mL/day (1009 g/day). The same report indicates a mean weight for infants 6-11 months of 9.1 kg. Conversion from mL/day to g/day is made using a density of 1.03 g/mL (USEPA 2002b)

Assuming a human milk concentration for C_{10}-C_{12} normal alkanes equal to 60 ppb yields a potential exposure of 0.0047 mg/day (mean intake) or 0.0067 mg/day (upper bound intake) for infants. These compare with a subchronic NOAEL of 1,000 mg/kg/day (see 7.3. Repeat Dose Toxicity: Health Benchmark) indicating Margin of Exposure in excess of 150,000. It should be emphasized that this Margin of Exposure is based on detection limits and not on

actual detections which, when they occurred, were estimated to be less than 1-10 ppb. Therefore, it would be expected that Margins of Exposure would be significantly higher.

Results are summarized in Table 6.3:

Table 6.3
Calculation of Infant Dose from Human Milk based on the Erickson et al (1980) Study

Human Milk Intake

1. Representative Intake:

Dext= Conc*IR*EF*ED*UCF/(BW*AT)

Conc	Concentration	0.06 mg/kg
IR	Ingestion rate	709 g/day
EF	Exposure Frequency	365 days/year
ED	Exposure Duration	1 year
AT	Averaging Time	365 days
UCF	Unit Conversion Factor	0.001 kg/1000g
BW	Infant Bodyweight	9.1 Kg
Dext	Dose	0.0047 mg/kg/d
MOE*	Margin of Exposure	213,000

2. Upper Bound intake (95%)

Dext= Conc*IR*EF*ED*UCF/(BW*AT)

Conc	Concentration	0.06 mg/kg
IR	Ingestion rate	1009 g/day
EF	Exposure Frequency	365 days/year
ED	Exposure Duration	1 year
AT	Averaging Time	365 days
UCF	Unit Conversion Factor	0.001 kg/1000g
BW	Infant Bodyweight	9.1 kg
Dext	Dose	0.0067 mg/kg/d
MOE*	Margin of Exposure	150,000

*MOE based on subchronic NOAEL of 1,000 mg/kg/d (section 7.10.2)

Based on this study, infants do not appear to be significantly exposed to decane, undecane, or dodecane from human milk of mothers' residing in heavily industrialized areas. There are no data on occupationally exposed mothers. The complete analysis is presented in Appendix F.

6.3 Integrated 24 hour Exposure

Personal air measurements (using personal monitors) evaluate VOC concentrations over the entire day encompassing both non-occupational and occupational exposures. Personal air measurements are useful in establishing a general daily exposure potential for maternal /fetal exposures. The reported ranges of mean personal air concentrations for an adult are 9.4 to 54 µg/m^3 decane, 7.4 to 73 µg/m^3 undecane, and 3.4 to 8.0 µg/m^3 dodecane (Hoffman et al., 2000; Wallace et al., 1991, Wallace et al., 1989). The Hoffman study of 113 randomly selected adults over a 7 day period reported upper 95% levels of 41, 29, and 21 µg/m^3 for decane, dodecane, and undecane, respectively. The Wallace (1989) study involved subjects performing specific activities that increased personal VOC exposure (such as painting). Therefore, average maternal exposure is not expected to exceed these levels under normal conditions.

6.4 Occupational Exposure

Individuals exposed to these compounds occupationally are expected to have higher exposures than that of the general population. In the literature reviewed, individuals employed in home construction or renovation, maintenance, delivery or freight transport, office buildings, photocopy centers, and the Air Force or airline industry may have an increased opportunity for exposure compared to the general population.

6.4.1 Office Buildings/ Photocopy Centers

VOC concentrations in ambient air may be increased in office buildings due to work-related activities (*e.g.*, photocopying) or from emissions from furniture and carpeting. Maximum ambient air concentrations in the vicinity of an employee's office area of decane, undecane, and dodecane were reported as 23, 77, and 153 µg/m^3 when evaluated at the breathing level of a seated employee. Mean concentrations of decane, undecane, and dodecane in general office air were reported in the range 0.40 to 0.60 µg/m^3, 0.76 to 56.2 µg/m^3 and 13.3 µg/m^3, respectively (Daisey et al., 1994; Hodgson and Daisey, 1991; Hodgson et al., 1988). New office buildings may have temporarily elevated levels. For example, Brown (1994) reports a geometric mean concentration for decane of 75 µg/m^3 in new office buildings with a 90th percentile of 310 µg/m^3 and a 98th percentile of 710 µg/m^3.

Office furniture may contribute to VOC concentrations in office building ambient air. For example, new office chairs emit undecane at a rate of 0.31 mg/chair/ hour on the day of manufacture; however, this rate drops to ≤0.04 mg/ chair/ hour within 168 hours after manufacturing (RTI, 1999). Other contributors to indoor air levels of decane, undecane, and dodecane include cleaning agents, pesticides, paint, painted sheetrock or drywall, adhesives, glued wallpaper, and glued carpet (Wallace et al., 1987). Such contributors were not quantified specifically but it can be expected that air measurements integrate all such potential sources.

Use of photocopiers may increase office area concentrations of decane, dodecane, and undecane due to VOC emissions created during the reproduction process. VOC emissions from dry-process photocopiers vary between machines with emission rates ranging from 62 to 450 µg decane /hr, 62 to 2,000 µg undecane /hr, and 70 to 960 µg dodecane /hr (Leovic et al., 1998; Leovic et al., 1996). Employees of commercial photocopy or reproduction centers may have exposures due to the amount of VOCs emitted from the various photocopy machines utilized. Employees' personal breathing-zone air measurements taken over a full shift indicated concentrations ranging from 1.7 – 530 $\mu g/m^3$ decane and 3.8 – 65 $\mu g/m^3$ undecane in three large volume photocopy centers (Stefaniak et al., 2000). In the same study, air concentrations recorded in the establishments indicated average concentrations for decane in the range 1.7 – 620 $\mu g/m^3$. Undecane concentrations ranged from 3.2 – 96 $\mu g/m^3$. It is not known how much of this exposure may in fact be due to branched isomers of the C_{10}-C_{12} alkanes. Mixtures of branched C_{10} and C_{11} alkanes have been identified as a solvent for clear dispersants and toner premixes used in certain copiers and printers (Hodgson et al, 1991 cited by Shields et al, 1996). Most of the publications give no details on how effectively branched alkanes are discriminated in sampling. It is likely that n-alkanes concentrations are consequently overestimated.

These emissions were not incorporated in any model to predict air concentrations in this assessment as there are adequate air monitoring data in both newly constructed/renovated buildings and other buildings which address the cumulative emissions from construction materials and furnishings.

6.4.2 Construction Occupations

Employment in construction or renovation careers may lead to an increased exposure to decane, undecane, or dodecane depending upon the building compounds or consumer products utilized in the workplace. For example, professional painters have an increased potential for exposure to VOCs. Interior painting projects have resulted in mean decane concentrations of 60 $\mu g/m^3$ (SD=150 $\mu g/m^3$) and mean undecane concentrations of 31 $\mu g/m^3$ (SD=37 $\mu g/m^3$) measured over a 4-week period in 44 homes. (Brown and Crump, 1998). In volunteers painting home interiors, personal air samples of decane and undecane up to 350 and 280 $\mu g/m^3$, respectively were reported (Wallace et al., 1989). Median levels reported in this study were significantly lower at 48 $\mu g/m^3$ and 30 $\mu g/m^3$ respectively. Breath samples up to 290 $\mu g/m^3$ were recorded.

More data is available from an EPA sponsored study on exposure levels resulting from application of an alkyd based primer and paint to gypsum walls of a bedroom (USEPA, 2001). A primer coat (AP-F) was applied followed 2 days later by a coat of alkyd paint (ASG-G). Concentrations of "decane", "undecane", and "dodecane" (isomer not specified as discussed in Appendix G) were measured over a period of up to 23 days. The house was unoccupied and sealed. The Air Exchange Rate was measured as 0.48 air changes per hour. Concentrations of three alkanes combined peaked at about 500 mg/m^3 during priming and 620 mg/m^3 during painting in the bedroom with corresponding values in the den (at the other corner of the house) of 80 mg/m^3 and 140 mg/m^3. The 24-hour time

weighted average (TWA) concentration (calculated from the EPA report and detailed in Appendix G) reached about 50 mg/m^3 in the 24-hour periods during priming or painting. These levels rapidly dropped in a matter of hours by over two orders of magnitude and, after three weeks, the combined concentrations of decane, undecane, and dodecane had dropped another order of magnitude to 40 μg/m^3 in the painted bedroom. The levels in this study were probably significantly higher than would be expected if normal ventilation precautions had been followed (opening windows, use of fans, and other ventilation). As noted, without specification of the isomers detected, the contribution of the normal isomers cannot be estimated.

6.4.3 Maintenance

Maintenance workers may have an increased potential for exposure due to the nature of job duties such as painting (similar to those described previously), working in ventilation ducts and other mechanical areas, and duties requiring the employee to be on the building roof. Mean ambient air concentrations of undecane and dodecane in return-air ventilation shaft air were reported as high as 831.3 and 280.8 μg/m^3 respectively in a new office building. On days prior to and after this sample was taken, levels were considerably lower, ranging from 11 to 116 μg/m^3. Mean undecane and dodecane concentrations in the ventilation shafts were reported as 48.3 and 10.9 μg/m^3, respectively (Hodgson and Daisey, 1991). Obviously, due to dilution and air exchange, such concentrations do not reflect exposures to occupants of the building. Direct measurements of interior building concentrations are the appropriate measure for residents and workers. It is reasonable to assume that occupational exposure to maintenance workers in ducts is restricted to short irregular periods of an acute nature. Exposures to other maintenance workers, such as airline workers, are higher on a more continuous basis and are addressed below.

Mean ambient air concentrations encountered on the roofs of buildings tend to be higher than general outdoor air samples, but substantially lower than indoor air samples with undecane concentrations of 5.3 μg/m^3 and dodecane concentrations of 2.0 μg/m^3 (Hodgson and Daisey, 1991).

6.4.4 Delivery / Transport

Individuals employed in product or retail delivery and freight-hauling may have unique exposures due to the number of hours spent per day in a vehicle. Auto travelers may be exposed to average air concentrations of 17.4 μg/m^3 decane, 5.9 μg/m^3 dodecane, and 16.4 μg/m^3 undecane during travel; while personal air samples resulted in median and maximum decane concentrations of 10 μg/m^3 and 53 μg/m^3 respectively, and median and maximum undecane concentrations of 7.8 μg/m^3 and 43 μg/m^3 respectively (Wallace et al., 1991; Wallace et al., 1989). Therefore, it is reasonable to assume that the occupational exposure of pregnant delivery persons and freight-haulers would be representative of these levels.

6.4.5 Pilots / Flight Attendants

Aircraft pilots and flight attendants may have low level occupational exposures to decane, undecane, and dodecane onboard commercial airliners. Total VOC (TVOC) concentrations aboard commercial airliners have been evaluated at levels of 3 ppb. However, TVOC concentrations drop to 0.001ppb (~0.006 μg/m^3) within three hours of flight onset, and alkane levels become non-detectable during this time-period. No difference in VOC concentrations occurs between coach, business class, and first class cabins (Brady et al., 1999).

6.4.6 Air Force / Airline Industry / Re-Fueling

Employees with job duties requiring direct or indirect exposure to airplane fuels and exhaust have an increased opportunity for exposure to n-alkanes in the fuels. Refueling attendants at Air Force bases (the most highly exposed) exposed to JP-8 jet fuel and exhaust had reported 1 hour average ambient exposures (personal monitors) of approximately 3,500, 1,000, and 500 μg/m^3 for n-decane, n-undecane, and n-dodecane respectively (Pleil et al., 2000). Breath samples of these workers also showed an increased exposure to decane, dodecane, and undecane in those working directly with jet fuel. Corresponding post-shift breath concentrations were reported as 491 μg/m^3, 270 μg/m^3, and 208 μg/m^3 for decane, undecane, and dodecane respectively. The air measurements were 1-hour average values and no details were provided as to sampling schedules versus working practices throughout the day. Consequently, the significantly lower post shift breath measurements reflecting integrated exposure may be more representative of average exposure. All fuel related personnel, including refuelers, foam handlers, fireguards, and runners, had mean post-work breath measurements of 240 μg/m^3 decane, 100 μg/m^3 undecane, and 63 μg/m^3 dodecane. Although tank entry employees work in an environment with significantly higher ambient air concentrations of VOCs than attendants, tank entry workers have reduced occupational exposure to decane, dodecane, and undecane due to safety equipment required for tank entry, particularly forced-air respirators, not required for other employees. Such workers indicated lower breath concentrations than attendants which is consistent with their increased protection (Pleil et al., 2000).

Lower exposures occur in personnel without direct aircraft fuel contact. Aircraft exhaust workers were exposed to air levels of 54 μg/m^3 decane, 43 μg/m^3 undecane and 26 μg/m^3 dodecane. Workers with non-aircraft related job duties on the Air Force base (*e.g.*, workshops/hospital/ clinic staff) were exposed to air levels of 16 μg/m^3 decane, 16 μg/m^3 undecane, and 18 μg/m^3 dodecane, representative of the ambient air concentrations of their work environment (Pleil et al., 2000).

6.5 Potential for Dermal and Oral Exposure

This section provides the justification for eliminating dermal and oral routes of exposure by focusing on the most highly exposed receptors.

Dermal Route:
Dermal exposure is possible for people working directly with products containing n-alkanes, particularly fuel handlers and, to a lesser extent, painters. In both situations, dermal exposure would be expected to be unintentional and either infrequent, of short duration, or both. Chronic dermal exposure to these materials is not considered a realistic human scenario, because potential skin irritation is likely to preclude repeated exposures (Section 7.9).

In either case, the percentage of the C_{10}-C_{12} n-alkanes under consideration in the actual product is generally 25% or less (Section 5.4).

The permeability of skin and consequent absorption of the C_{10}-C_{12} n- alkanes are relatively low compared to the lower molecular weight and aromatic hydrocarbons (see Section 7: Disposition/Metabolism). These factors would suggest a low potential for dermal exposure being significant as an exposure route. Data is available on the skin permeability of the n-alkanes and it is relatively simple to estimate the relative contribution of dermal exposure to total exposure with some reasonable assumptions. The dermal penetration of the skin has been shown to be negligible (Section 7). Measured permeabilities for dodecane were reported as (mean $\pm$ SE) 0.000011 cm/h $\pm$ 0.000001 cm/h. This would correspond to an upper 95% bound of 1.27×10^{-5} cm/h assuming a log-normal distribution.

The chronic absorbed dose may be estimated from the following equation:

$$\text{Absorbed Dose} = \frac{Concentration * Kp * SA * ED * EF * CF}{BW * AT}$$

Concentration = g/cm^3 (= 0.75 g/cm^3) for dodecane
Kp = skin permeability (c/min)
SA = exposed skin surface area (cm^2)
ED = exposure Duration (minutes)
EF = Exposure frequency (days/year)
BW = Bodyweight (kg)
AT=Averaging time (days)
CF = Conversion Factor = 16.67 mg*hr/g*min

In this screening analysis, the highest exposed workers were considered, namely Air Force fuel attendants. The analysis assumes an 18-35 year-old woman fuel attendant occupationally exposed and accidentally getting hands wet with fuel. Due to potential dermal irritation from such exposure, frequent incidences of this nature are unlikely.

Assuming both hands are wet with the fuel, the total skin area exposed (SA) would be 862 cm^2 (EPA Exposure Factors Handbook, 1997). The exposure duration (ED) is not expected to be long due to discomfort and odor, it was assumed to be 15 minutes. It was assumed that this event happens one day per week (EF= 50 days/year). A body weight of 62.4 kg was used (EPA Exposure Factors Handbook, 1997) in the analysis.

Assuming even an unrealistic 25% n-dodecane content in the fuel, the dose per accidental exposure amounts to only $8.2x10^{-3}$ mg/kg and a chronic exposure of $1.1x10^{-3}$ mg/kg/day assuming 50 days per year of such incidents. These are essentially negligible doses compared with repeat dose subchronic oral NOAELs of 1,000 mg/kg/day and only 1% of the chronic RfD of 0.1 mg/kg/day. Margins of Exposure were in excess of 88,000 on a chronic basis for a fuel containing up to 25% of decane, undecane, and dodecane.

Applying an even more conservative scenario by assuming 1 hour exposure per day to both hands on a daily basis (250 days per year), chronic margins of exposure still exceeded 4,000 as shown in Table 6.4 below.

It might be expected in such a case that irritation as a result of the defatting action would lead to protective measures being taken even if no systemic effects would be expected.

Table 6.4 Dermal Exposure Modeling Results

1. Exposure Duration 15 minutes/day; 50 days/year

Chronic Dose = C X Kp X SA X ED X EF X UCF/(BW X AT)

	neat undecane	percent undecane			
		5%	25%		
Conc	0.75	0.0375	0.1875	g/cm3	
Kp	1.27E-05			cm/hour	upper bound
SA	862			cm2	both hands
ED	15			minutes	
EF	50			days/year	
BW	62.4			kg	
AT	365			days	
UCF	16.7			mg*hr/g*min	
Dose per Event	3.3E-02	1.6E-03	8.2E-03	mg/kg	
Chronic Dose	4.5E-03	2.3E-04	1.1E-03	mg/kg/day	
Sub-chronic NOAEL	100			mg/kg/d	
MOE Per Event	3040	60800	12160		
MOE Chronic	22192	443839	88768		

2. Exposure Duration 60 minutes/day; 250 days/year

Chronic Dose = C X Kp X SA X ED X EF X UCF/(BW X AT)

	neat undecane	percent undecane			
		5%	25%		
Conc	0.75	0.0375	0.1875	g/cm3	
Kp	1.27E-05			cm/hour	upper bound
SA	862			cm2	both hands
ED	60			minutes	
EF	250			days/year	
BW	62.4			kg	
AT	365			days	
UCF	16.7			mg*hr/g*min	
Dose per Event	1.3E-01	6.6E-03	3.3E-02	mg/kg	
Chronic Dose	9.0E-02	4.5E-03	2.3E-02	mg/kg/day	
Sub-chronic NOAEL	100			mg/kg/d	
MOE Per Event	760	15200	3040		
MOE Chronic	1110	22192	4438		

Oral Route:
The oral route of exposure was quickly eliminated because other than accidental ingestion of fuel, paints or solvents, there is no opportunity to ingest normal decane, undecane, or dodecane from other sources, such as drinking water, as alkanes are essentially insoluble in water. The EPA Estimations Program Interface for Windows (EPAWIN) cited solubilities of 0.052, 0.0044 and 0.0037 mg/l for n-decane, n-undecane, and n-dodecane respectively (http://www.epa.gov/oppt/p2framework/docs/epiwin.htm :accessed 3/16/04). Not surprisingly, the literature did not report these compounds being detected in drinking water.

A bounding estimate of potential exposure from a saturated drinking water supply may be obtained by assuming an upper 95% limit on direct and indirect intake from all sources for an infant up to 1 year old of 1,182 mL/day as reported in the EPA Children's Exposure Factors Handbook (USEPA, 2002). This age group was selected as this age group has the highest intake per unit of body weight. The same report indicates a mean weight for infants 6-11 months of 9.1 kg.

The daily dose of such a contaminated water supply would result in dose of 6.8×10^{-3} mg/kg/day of n-decane and 4.8×10^{-4} mg/kg/day n-dodecane. Such intakes, unrealistic as they are, provide Margin of Exposure of about 150,000 based on the subchronic NOAEL of 1,000 mg/kg/day.

There were no reports found of the target chemicals being detected in food.

Decane, undecane, and dodecane can cause chemical pneumonitis if aspired into the lungs. This could result in serious or fatal lung damage (pulmonary edema). Appropriate

warning labels are attached to consumer products with this potential for misuse. This effect can occur after accidental ingestion and is not quantifiable for this exposure assessment.

6.6 Selection of Exposure Scenarios and Exposure Concentrations

From all the scenarios considered above, only those with the highest exposure were selected to go forward to the risk assessment. For example, transport, maintenance, construction, and office workers were not considered further because refueling workers were exposed to much higher concentrations. For non-occupational exposure, automobile travel and outdoor concentrations were dropped from further consideration as integrated 24 hour exposure data and other studies indicated indoor concentrations contributed significantly more to exposure than outdoor concentrations. Highest exposure for children was in the home during painting or renovation activities and therefore carried through the analysis.

6.6.1 Exposure Scenarios

The following scenarios involving the highest potential exposure were selected:

1. Chronic exposure of infants and children to indoor air.
2. Chronic exposure of prospective parents to indoor air.
3. Short term exposure of infants and children in a newly renovated (painted) home.
4. Short term exposure of prospective parents in a newly renovated (painted) home.
5. Prospective parents exposed occupationally in the painting trade, and refueling operations at an airport.

6.6.2 Selection of Exposure Concentrations

6.6.2.1 Chronic Domestic Exposure

As noted above, exposure is the same for all age categories. Exposure in the home has been measured to range between 3.5 – 118 $\mu g/m^3$ for decane; 2.2 – 104 $\mu g/m^3$ for undecane and 1.5 – 57 $\mu g/m^3$ for dodecane. The highest values reported are clearly exceptional. For example, in the study reporting a maximum of 118 $\mu g/m^3$ decane (Heavner et al, 1996) in 61 homes monitored the median value was only 2.5 $\mu g/m^3$ with a mean of 6 $\mu g/m^3$ and standard deviation of 16 $\mu g/m^3$. Brown et al (1994) reported a geometric mean of 5 $\mu g/m^3$ and a 98th percentile of 47 $\mu g/m^3$ for decane. The largest value for undecane of 104 $\mu g/m^3$ was measured in a study of 173 homes where the living room and bedroom were both sampled (BRE, 1996). The mean level of undecane in both the living room and bedroom was 14 $\mu g/m^3$ with a standard deviation of 17 $\mu g/m^3$ indicating this to be an extreme value.

Selection of Representative and Upper Bound Concentrations

Assuming a log-normal distribution in the latter study, it would suggest an upper 95% bound of 43 μg/m^3, the value actually reported by the authors. This value is also consistent with the data from Brown et al (1994). The highest value reported for dodecane is 57 μg/m^3 and was reported as a 95th percentile in a study of homes indicating a median level of 2.7 μg/m^3 (Phillips et al, 1997). Therefore, we will conservatively assume an average for **each** of the alkanes of 14 μg/m^3 with a high-end estimate of 43 μg/m^3 for **each** chemical. As these chemicals all have similar toxicities, these exposure concentrations for the individual alkanes were simply summed to estimate total exposure.

The use of a lognormal distribution for exposure data is consistent with theoretical considerations (Ott, 1990) and the results of previous studies (Lebret et al, 1986; Krause et al, 1991; Wallace (1987), and Shields et al (1996) who reported that within a given building type, both the total VOC concentration as well as individual VOCs tended to be lognormally distributed.

6.6.2.2 Short Term Exposure in a Newly Renovated Home

For new homes, it is reported that average initial levels of undecane of 82 μg/m^3 declined to 16μg/m^3 in the second year post construction (Crump et al, 1997). In home renovation, interior painting projects have resulted in mean decane concentrations of 60 μg/m^3 (SD=150 μg/m^3) and mean undecane concentrations of 31 μg/m^3 (SD=37 μg/m^3) measured over a 4-week period in 44 homes (Brown and Crump, 1998).

A high-end short-term exposure estimate may also be estimated from the volunteers painting indoors wearing personal samplers: Decane and undecane levels of up to 350 and 280 μg/m^3, respectively, were recorded. These levels are consistent with the average and Standard Deviations reported in the Brown and Crump (1988) study. In the latter study, for decane, a normal distribution results in an upper 95% level of 307 μg/m^3 (log-normal 226 μg/m^3). For undecane, the corresponding upper bound is 94 μg/m^3.

Selection of Representative and Upper Bound Concentrations

For short-term exposure (days to weeks), representative concentrations were taken to be 60 μg/m^3 and 31 μg/m^3 for decane and undecane, respectively. With no data for dodecane, and as monitoring data consistently shows dodecane to be significantly lower in concentration, an average concentration equal to that of undecane was adopted. A high end estimate for decane of 350 μg/m^3 and 280 μg/m^3 for undecane and dodecane based on the Wallace et al study (1989) was assumed. Total exposure was estimated by summing concentrations for each chemical.

6.6.2.3 Occupational Exposure of Parents

The highest occupational exposure to parents and prospective parents was to workers dealing directly in fuel operations. Employees with job duties requiring direct or indirect

exposure to airplane fuels and exhaust have an increased opportunity for exposure to n-alkanes in the fuels. Refueling attendants at Air Force bases (the most highly exposed) exposed to JP-8 jet fuel and exhaust had reported 1-hour average ambient exposures (personal monitors) of approximately 3,500, 1,000, and 500 $\mu g/m^3$ for n-decane, n-undecane, and n-dodecane respectively (Pleil et al., 2000). Breath samples of these workers also showed an increased exposure to decane, dodecane, and undecane in those working directly with jet fuel. Corresponding post shift breath concentrations were reported as 491 $\mu g/m^3$, 270 $\mu g/m^3$, and 208 $\mu g/m^3$ for decane, undecane, and dodecane respectively. The air measurements were 1-hour average values and no details were provided as to sampling schedules versus working practices throughout the day. Consequently, the significantly lower post-shift breath measurements reflecting integrated exposure may be more representative of average exposure. This assertion is supported by the study by Wallace (1989) who took both breath and personal air samples for painters. He reported decane breath concentrations of 290 $\mu g/m^3$ were associated with personal air concentrations of 350 $\mu g/m^3$ suggesting that breath concentrations may be a reasonable surrogate for exposure concentration. Nevertheless, in the absence of more data, the reported air concentrations were used.

Selection of Representative and Upper Bound Concentrations

Standard errors for the highest ambient air measurements were reported as 2,147, 405, and 137 $\mu g/m^3$ respectively for 9 measurements (Pleil et al, 2000). These data were used to calculate upper bounds assuming log-normal distributions for the data. Specifically, 8 hour average exposures to decane, undecane, and dodecane were assumed to be 3,552 $\mu g/m^3$, 1,020 $\mu g/m^3$, and 489 $\mu g/m^3$ respectively. Similarly, upper bounds were 12,480 $\mu g/m^3$, 3,077 $\mu g/m^3$ and 1245 $\mu g/m^3$ respectively. The exposure concentrations for each alkane were simply summed to estimate total exposure

6.6.2.4 Peak (Acute) Exposures

Very short-term peak concentrations may be expected during painting activities. In the EPA Research House Study, peak combined levels of decane, undecane, and dodecane (isomers not specified) of 620 mg/m^3 were recorded. The data also indicates levels dropped rapidly (to 260 mg/m^3 in 1 hour, 89 mg/m^3 in 2 hours, 40 mg/m^3 after 6 hours, and 40 $\mu g/m^3$ after 3 weeks.

The selected representative and upper bound exposure concentrations are summarized in Table 6.1, page 27 in Section 6.1. A copy of this table is provided below for convenience.

Table 6.1 Exposure Concentrations for Selected Scenarios

Type of Measurement	Representative Concentration[1]	Upper Bound Concentration[2]	Applicable Scenario[3]	References
Average daily household indoor air concentrations	42 μg/m3	129 μg/m3	1,2	Brown et al, 1994; BRE, 1996;
Interior painting average ambient air concentrations and personal samplers	122 μg/m3	910 μg/m3	3,4,5	Brown & Crump, 1998 Wallace, 1989
Highest exposed Air force fuel workers: 1 hour average ambient exposures (personal monitors)	5,061 μg/m3	16,800 μg/m3	5	Pleil et al, 2000

1. Representative concentration is defined as the average of a set of exposure data.
2. Upper bound concentration is generally defined as the upper 95th percentile of the exposure data when adequate data were available to develop a log-normal distribution or the maximum reported level when no distribution was available.
3. 1) Chronic exposure of infants and children to indoor air.
   2) Chronic exposure of prospective parents to indoor air.
   3) Short term exposure of infants and children in a newly renovated (painted) home.
   4) Short term exposure of prospective parents in a newly renovated (painted) home.
   5) Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

7. Hazard Assessment

7.1 Category Justification

The C_{10}-C_{12} n-alkanes are a short homologous series of hydrocarbons that are physically and chemically similar (Table 7.1, taken from Low LK, 1987). Nonane is shown for comparison. As summarized below, and in more detail elsewhere, their toxicological effects are primarily a function of their physical properties, and are similar for all three materials. This supports their consideration as a category.

Table 7.1 Properties of C_{10}-C_{12} n-Alkanes

n-Alkane	Mol. Wt.	Specific Gravity At 25° C	Melting Pt° C	Boiling Pt° C	Solubility in Water	Vapor Pressure (mmHg at 38° C)	Saturated Vapor Concentration
Nonane	128.3	0.714	-53.5	150	Insoluble	10	5280 ppm (28,000 mg/m^3)
Decane	142.3	0.734	-29.6	174	Insoluble	1.298	1369 ppm (7,968 mg/m^3)
Undecane	156.3	0.744	-25.6	196	Insoluble	0.502	442 ppm (2,824 mg/m^3)
Dodecane	170.3	0.753	-9.6	216	Insoluble	0.205	142 ppm (990 mg/m^3)

These alkanes are liquids at ambient temperature with low vapor pressures, and are essentially insoluble (nonane ~ 70 ng/mL; decane-dodecane ~ <10 ng/mL) in water, but soluble in ethanol. The maximum vapor concentration able to be generated limited the ability to conduct toxicology testing by the inhalation route (Nilsen et al, 1988). In the Nilsen study, the acute inhalation toxicity of n-alkanes from C_9-C_{13} was assessed. Only C_9 (n-nonane) showed effects at high concentrations (above 3,500 ppm) in rats exposed for 8 hours, but no such effects at a concentration of 2414 ppm. Decane, undecane, and dodecane did not show any effects, including no central nervous system depression, when rats were similarly exposed at their saturated vapor concentrations. Repeat dose inhalation studies of mixed products caused respiratory tract irritation (MacFarland and Holdsworth, 1987).

Aliphatic hydrocarbons in this C_{10}-C_{12} category also do not cause systemic toxicity by the dermal route. Dermal absorption of alkanes with more than eight carbon atoms (octane) is reported to occur very slowly (Low, 1987; McDougal *et. al.* , 2000). However, C_{10}-C_{12} n-alkanes are similar in that they can cause dermal irritation on repeated exposure in both

animals and humans, depending on time and if exposures are occluded. One repeat dose dermal study in rabbits reported severe skin irritation.

Aliphatic hydrocarbons in this C_{10}-C_{12} category also do not cause significant toxicity by the oral route. Acute oral LD50 values exceeded the limit dose tested. However, n-decane and presumably the other materials in this category can cause chemical pneumonitis if ingested material is aspirated into the lung (MacFarland and Holdsworth, 1987).

Some systemic effects have been reported in repeat dose animal studies, but are similar for all three materials in this C_{10}-C_{12} category. There may be increased liver weights with little apparent histopathology, suggestive of an adaptive response to a metabolic load. Both n-decane and n-undecane, and complex aliphatic mixtures, cause a characteristic change in male rat kidneys in common with many other hydrocarbon materials, but which has been deemed irrelevant to human risk assessment.

Higher tier hazard information on a limited number of other materials, complex mixtures of linear, branched and cyclo-alkanes in the same carbon range, is also presented to supplement that for the materials in this category. The toxicological effects of all materials in this C_{10}-C_{12} category, where tested, are very similar and appear to be more reflective of the physical solvent properties of the materials than their chemical structure. This supports the consideration of these materials as a single category for potential adverse health effects in adults and children.

Robust summaries for the hazard studies are provided in Appendix B.

7.2 Acute Toxicity

Acute toxicity studies have been conducted for n-decane (C_{10}), n-undecane (C_{11}) and n-dodecane (C_{12}), members of this category, and for the structural homologues, n-nonane (C_9) and n-tetradecane (C_{14}), which are not part of this category but are included for comparative information. Studies have also been conducted on complex mixtures containing various members of the category and related linear homologues. Table 7.2 summarizes these studies which have been conducted by the oral, dermal and inhalation routes of exposure. Review of these data indicates a low order of acute toxicity for these substances, supporting the treatment of these chemicals as a single category.

Table 7.2 Acute Toxicity Data

Predominant Hydrocarbon Structure	Rat Oral LD_{50} (g/kg)	Rabbit Dermal LD_{50} (g/kg)	Inhalation LC_{50} (Rat; 4 or 6 hours unless specified)
n-Nonane	No data	No data	16,753 mg/m^3 (8 hr)
n-Decane	>5.0	No data	>7,951 mg/m^3 (8 hr)*
n-Undecane	>2.0	No data	>2,693 mg/m^3 (8 hr)*
n-dodecane	No data	No data	>987 mg/m^3 (8 hr)*
n-tridecane	No data	No data	>309 mg/m^3 (8 hr)*
C10-13 normal alkanes	>5.0	>3.2	No data
C12-14 normal alkanes	>5.0	>5.0	No data
C14-17 normal alkanes	>5.0	>3.2	No data
n-tetradecane	>5.0	>2.0	No data

*At or near saturation concentration

Oral:
With one exception in which a single death occurred in animals treated with C_{10}-C_{13} alkanes (EMBSI, 1983a), no mortality was observed in any of the studies at the highest dose tested. Clinical signs reported in some studies following treatment included soft stool, ano-genital staining, piloerection, alopecia, and unthrifty coat. The acute oral LD_{50} values for decane and undecane were reported to be >5g/kg (Petresa, 1984) and >2g/kg (Yoshimura et al., 1996), respectively. No acute oral data were available on dodecane. However, considering that the oral LD_{50} values for the other members of the category and tetradecane (Petresa, 1984), as well as the complex C_{10}-C_{13}, C_{12}-C_{14}, and C_{14}-C_{17} alkane mixtures (EMBSI, 1983a, b, c) range from >2 g/kg to > 5 g/kg, suggests it is reasonable to anticipate that the oral LD_{50} of dodecane would not vary significantly from that of the other members of the category.

Dermal:
Dermal acute toxicity data were not available for decane, undecane or dodecane. Results of studies with tetradecane (Petresa, 1984) and mixed-alkanes of C_{10}-C_{13}, C_{12}-C_{14}, and C_{14}-C_{17} tested in rabbits, demonstrate minimal toxicity with LD_{50} >2 g/kg (EMBSI, 1983a, b and EMBSI, 1994). A single death was reported following treatment with a C10-13 alkane mixture (EMBSI, 1983a). No other deaths were reported following treatment with any of the other test materials, although one animal treated with a C_{12}-C_{14} alkane mixture at 5,000 mg/kg was sacrificed in moribund condition (EMBSI, 1994). All materials within the series produced irritation ranging in severity from slight to severe. Clinical signs included decreased food consumption, emaciation, alopecia, nasal discharge and fecal staining. One test material, the C_{12}-C_{14} alkane mixture, was reported to have possibly produced effects of neurological origin, although microscopic examination did not reveal any neurohistopathologic changes (EMBSI, 1994). Since these n-alkanes encompass the C_{10}-C_{12} range of interest, a read-across dermal acute toxicity value of > 2 g/kg can be estimated for decane, undecane and dodecane.

Inhalation:
The 4-hour acute LC_{50} for nonane (C_9) was reported to be 16,753 mg/m^3 with a response pattern progressing from salivation, lacrimation, to tremors, convulsions and death. No effects were observed at 4,600 mg/m^3 (Carpenter, et al., 1978). Nilsen et al. (1988) exposed rats to nonane at four concentrations up to near saturation (27,642 mg/m^3), and to decane, undecane, dodecane and tridecane at near saturation concentrations of 7,951, and 2,693, 987, and 309 mg/m^3. The LC_{50} for nonane was 23,386 mg/m^3 and no deaths or toxic effects occurred at 12,638 mg/m^3. Decane, undecane, dodecane and tridecane did not produce any signs of toxicity. All studies were conducted at the highest vapor concentration practically attainable due to vapor pressure limitations. Only one substance (n-nonane) was sufficiently volatile to create a vapor concentration at which some deaths occurred (LC_{50} = 16,753 mg/m^3). For all other substances tested, the LC_{50}'s are all greater than the highest vapor concentration tested, in the range of greater than 3,600 to greater than 12,400 mg/m^3.

Acute toxicity Health Benchmark

Observed and estimated acute LC_{50}'s of >2 g/kg for both oral and dermal toxicity, and the lack of mortality following inhalation exposure at high air saturation concentrations (except for nonane which is not a member of the category), demonstrate that these materials are of low acute toxicity potential. The acute health benchmark for this category is proposed as 5 g/m^3 for purposes of risk assessment, a concentration at which no lethality would be expected. This is above the saturation air concentration for C_{11} and C_{12} alkanes, but there were no deaths even at the air saturation concentration of 8g/m^3 for n-decane. The only significant acute effect directly demonstrated for the members of this category is dermal irritation.

7.3 Repeat Dose Toxicity

Repeat dose toxicity studies have been conducted for n-decane (C_{10}) and n-undecane (C_{11}), members of this category, and for a lower structural homolog, n-nonane (C_9), which is not part of this category but which is included for comparative information. There are no data for n-dodecane (C_{12}), but studies have also been conducted on complex mixtures containing all three category members as well as other related mixed linear, branched and cyclic alkanes. Studies have been conducted by the oral, dermal and inhalation routes, and are summarized in Table 7.3. Most of these studies were performed in rats or mice. The available data indicate that the subchronic toxicity of these substances is primarily due to the physical solvent properties and route of administration (gastrointestinal, respiratory or dermal irritation, CNS depression), and male rat kidney effects, and do not appear to be dependent on the chemical structure or the carbon number of the components, supporting the treatment of these chemicals as a single category.

Table 7.3 Summary of the Repeat Dose Toxicity of n-alkanes and Related Materials

Test Material	Test System	NOAEL	LOAEL (Effects)	REFERENCE (Robust Summary)
C9 n-Nonane	90 day rat oral gavage	100 mg/kg/day	aspiration	Dodd et al., 2000
	Rats, male; inhalation 6 hr/d, 7 days/wk, 62-65 days	3.1g/m^3	8.4g/m^3 mortality, salivation, tremors, lacrimation, decreased body wt	Carpenter et al, 1978 (RS# RPDT-1)
C10 n-Decane	OECD 422 Rat, oral	1000 mg/kg/day	None	Maraschin et al., 1995 (RS# RPDT-2)
C10 n-Decane	Rat 90 day inhalation 18 hr/day, 7 day/wk, 91 dys.	3.14 g/m^3 (540 ppm)	None	Nau et al., 1966 (RS# RPDT-3)
C11 n-Undecane	OECD 422 Rat, oral	100 mg/kg/day	300 mg/kg/day: salivation and decreased food consumption; 1000 mg/kg/day; males - decreased Hb, albumen, increased white cells; increased liver and thymus wts. 1000: females - increased liver weights. No histopathological effects	Yoshimura et al., 1996 (RS# RPDT-5)
C9-C13 n-, Iso-, and Cyclo-alkanes	Rats, inhalation; 12 wks; 6 hr/d, 5d/wk,	300 ppm (~ 2 g/m^3)	890 ppm (~5 g/m^3); decreased weight gain. Male rat nephropathy observed.	Phillips and Egan. 1984. (RS# RPDT-8)
C10-C13 n-, Iso-, and Cyclo-alkanes	Rat, oral daily 13 wk	>5000 mg/kg	None except gastrointestinal irritation, male rat nephropathy	ExxonMobil Biomedical Sciences, Inc. 1991 (RS# RPDT-7)
C11-C14 n-, Iso-, and Cyclo-alkanes	Rat, oral daily for 90 days	>1000 mg/kg	None except male rat nephropathy	ExxonMobil Biomedical Sciences, Inc. 1991 (RS# RPDT-9)

Conversion factor for decane (mwt 142): 1 mg/L = 172 ppm; 1 ppm = 0.00581 g/m^3

After oral administration, substances in this category have a low potential for subchronic toxicity. In some oral studies, high doses caused gastrointestinal irritation. Effects also included increased liver weights in males and females, and increased kidney weights in males. There was histological evidence of hepatic centrilobular hypertrophy with some reversibility in the recovery phase; this was interpreted as an adaptive change to increased metabolic load, and not an adverse effect. The increase in male rat kidney weights was associated with accumulation of hyaline droplets in the cytoplasm of the proximal tubules of the cortex, and degenerative and regenerative changes of the tubular epithelium. In studies where this was examined, these changes were reported to be typical of those associated with production of a male rat specific protein $\alpha_2\mu$-globulin. The US EPA has determined that changes in the male rat kidney as a consequence of an $\alpha_2\mu$-globulin-mediated process are not relevant for assessing human risk (U.S. EPA, 1991).

A dermal exposure study in rabbits with C_{10}-C_{12} n-alkanes found that severe skin irritation occurred on repeated dermal exposure under occlusion (see 7.7 Neurotoxicity).

The inhalation exposure concentrations were limited by the volatility of these test materials (See 7.1 Category Justification). All studies report high No-Observed-Adverse-Effect-Levels (NOAEL) by oral and dermal routes; only the values obtained by the inhalation route, considered the most relevant for human exposure, are considered for risk assessment. Because of the potential for objectionable skin irritation, repeated dermal exposure is not likely to be a significant exposure scenario for risk assessment.

Results for specific category members and related materials

N-Nonane

Oral:
N-nonane was administered via gavage to female rats and male mice at doses of 0, 100, 1000 and 5000 mg/kg/day, 7 days/wk for 90 days (Dodd et al., 2000). Clinical signs indicated gastro-intestinal irritation. There were no body weight changes, and slight organ weight changes with no histopathological lesions, except both species had hyperplasia of the forestomach at all doses, similar to that reported orally for n-decane. There was also nasal inflammation and pulmonary lesions, indicative of aspiration of the oral dose in the rat. Excluding the forestomach irritation, the NOAEL was 100 mg/kg. The forestomach irritation was not considered of clinical significance for human risk assessment.

Inhalation:
A 13 week inhalation study was performed in male rats at exposure concentrations of 0, 1.9, 3.1, and 8.4g/m^3, 6 hrs/day, 5 days/wk for 13 weeks (Carpenter et al., 1978). At 8.4g/m^3, there was significant depression of weight gain, and salivation and lacrimation were observed throughout the study indicative of sensory irritation. There were a few early and late mortalities, but no dose-related changes in hematology or clinical chemistry

parameters, or treatment-related gross or microscopic pathological effects. The NOAEL was reported to be 3.1 g/m^3.

n-Decane

Oral:
Commercial decane, containing 97% n-decane, was administered via gavage to male rats for 28 days (14 days prior to mating and for 2 weeks during mating), and to female rats from 14 days prior to mating, through mating and gestation to day 4 of lactation at doses of 0, 25, 150, or 1000 mg/kg/day, according to OECD protocol 422 (Maraschin et al., 1995). N- Decane did not induce clinical, behavioral or histopathological effects with the exception of a dose-responsive hyperplasia of the non-glandular stomach and subacute submucosal inflammation. Neurological tests of startle reflex, open field behavior and forelimb grip strength also revealed no effects. The systemic NOAEL was 1000 mg/kg (without consideration of forestomach inflammation at the gavage site).

Inhalation:
Nau et al (1966) exposed rats to 3.1 g/m^3 (540 ppm) n-decane by inhalation for 18hr/day, 7 days/wk for 91 days with 32 days recovery. There was a reported increase in weight gain and in white blood cell count, but no gross or microscopic organ effects, and no significant effects on bone marrow or polymorphonuclear leukocytes were observed. The adequacy of reporting of this study lowers confidence in the NOAEL of 540 ppm (3.1g/m^3).

Dermal:
Approximately 0.1 to 0.15 g of n-decane was applied dermally three times per week for a year to the back of C3H mice (Nau et al. 1966). There was gross and microscopic evidence of chronic skin irritation and of kidney and lung hemorrhage, but no hematological changes nor skin tumors were reported.

n-Undecane

Oral:
N-Undecane was administered via gavage to male rats for 46 days, and to female rats from 14 days prior to mating, through mating and gestation to day 3 of lactation, at doses of 0, 100, 300 or 1000 mg/kg/day (Yoshimura et al. 1996) following a similar OECD protocol 422 to that used for n-decane. Changes in liver and thymus weights were noted for males and females, respectively, at the 1000 mg/kg dose level only. Some changed hematological and blood chemistry parameters were noted in males at the 1000 dose level. No gross or histopathological effects were noted at the 100 mg/kg dose level. The systemic LOAEL was 300 mg/kg, based on salivation and decreased food intake, and the NOAEL was 100 mg/kg.

Other Alkanes

Multiconstituent Alkanes (C_9-C_{13}, C_{10}-C_{13} and C_{11}-C_{14} alkanes; n-, iso- and cycloalkanes)

Inhalation:

Male and female rats were exposed by inhalation for 6 hrs/day, 5 days/wk for 12 weeks to 300 or 890 ppm of a C_9-C_{13} multiconstituent alkane (Dearomatized White Spirit (DAWS), containing 58% normal and iso-alkanes and 42% cyclo-alkanes, Philips and Egan, 1984, RPTD-8). The main purpose of the study was to determine susceptibility to kidney toxicity. There were slight decreased body weights at the top dose, but no hematological or clinical signs. There were increased liver/body weight ratios especially in females with no associated histopathology, indicative of an adaptive effect. Kidney weights were increased only in males, and histological effects are consistent with chronic progressive nephritis and/or $\alpha_2\mu$-globulin induced nephropathy, effects in male rats that have been determined to have no relevance to humans. Under the conditions of this test, the NOAEL is 300 ppm (approximately 2 g/m^3), excluding the kidney effects.

Oral:

Two 90-day rat oral gavage studies have been conducted with C_{10}-C_{13} and C_{11}-C_{14} multiconstituent alkanes at doses up to 500 and 1000 mg/kg/day, respectively (EMBSI, 1991a; EMBSI, 1991b). Some mortality occurred suggestive of aspiration of the test materials or dosing trauma. Primary findings in both sexes were gastrointestinal irritation, and increased liver weights. The primary effect in males was consistent with $\alpha_2\mu$-globulin induced nephropathy, effects in male rats that have been determined to have no relevance to humans. The NOAEL for systemic toxicity was considered to be >1000 mg/kg/day.

Other Studies

The National Toxicology Program has conducted subchronic and carcinogenicity studies by inhalation in rats and mice of Stoddard Solvent IIC (NTP TR 519), a low aromatic (< 1%) hydrocarbon solvent containing C_{10}-C_{14} n-, iso-, and cycloalkanes. Animals were exposed for 6 hr/day, 5 days/wk for 13 weeks to concentrations of 0.138, 0.275, 0.550, 1.1 or 2.2 g/m^3. In mice, only at the highest dose, liver weights of males were increased, which may have been an adaptive effect, and sperm motility was reported decreased. In rats, the relative weights of kidney, liver and testis were reported increased at all dose levels. Male rats exhibited renal tubule hyaline droplet accumulation and other signs of nephropathy with increasing incidence at higher concentrations. NTP considered this as evidence of an $\alpha_2\mu$-globulin mechanism. There were no reported histological effects on the liver or testes, or on sperm counts, but sperm motility was reported to be decreased about 10% at all concentrations of 0.55 g/m^3 and above. However, there was no increased severity with increasing dose, and no similar effect was reported in mice, suggesting that the small decreased sperm motility may be an artifactual result. These data are not used in deriving the health benchmark because the report is not yet finalized. However, they indicate low toxicity for C_{10}-C_{12} alkanes and are consistent with the proposed 1 g/m^3 NOAEL for C_{10}-C_{12} n-alkanes.

A subchronic (12 wk) inhalation study has been conducted in rats with 100% isoparaffins in the C_{10}-C_{11} range (Phillips and Egan, 1984, RPTD-10) at concentrations of 1.97 and 5.61 g/m3 (approx 300 and 900 ppm, respectively). Decreased body weight gain occurred at both doses in male but not female rats. The most significant findings were increased male rat kidney weights and nephropathy, although the authors indicate this may be related to Chronic Progressive Nephritis, a phenomenon in aged untreated rats, and may be irrelevant for human risk assessment. There was an apparent approximately 5% decrease in erythrocytes in male rats at both the middle and high doses for both materials. Although this effect is small and not dose-related, it was used by California EPA as the basis to develop an Interim Reference Exposure Level of 1.2 mg/m^3 (See 8.0 Risk Assessment).

Health Benchmark

Male rat nephropathy associated with hyaline droplets and $\alpha_2\mu$-globulin formation, is not considered by EPA to be a relevant finding for human risk assessment (U.S. EPA, 1991). Several studies, including the Yoshimura study of undecane and the NTP study of Stoddard Solvent Type IIC, definitively measured the formation of $\alpha_2\mu$-globulin in exposed male rats. Although the mechanism of male rat nephropathy in some of these alkane studies cannot be definitively associated with an $\alpha_2\mu$-globulin mechanism because $\alpha_2\mu$-globulin levels were not measured, this seems the most likely mechanism. When this effect is excluded from consideration, there are few other toxic effects reported in animal studies.

No relevant adverse effects were noted in repeat dose inhalation studies for n-decane at a concentration of 3.1 g/m^3 (540 ppm) for 18 hrs/day (Nau, 1966), approaching the theoretical maximum vapor concentration of 1369 ppm. In a 12-week study of a C_9-C_{13} multiconstituent alkanes (Dearomatized White Spirit (DAWS), there was a decrease in body weight gain at approximately 5.0 g/m^3 and a NOAEL of approximately 2.0 g/m3 for 6 hr/day, 5 days/wk (Phillips and Egan, 1984). No effects were reported for n-nonane at 3.1 mg/m^3, for 6 hr/day, 5 dy/wk, but because n-nonane has a significantly higher vapor pressure it could be tested up to 8.4 g/m^3, when some lethality and other effects were reported (Carpenter, 1975). Based on the studies on individual n- alkanes, and on mixed products, an inhalation concentration of 1 g/m^3 for 6 hrs/day for 7 days/week for 13 weeks is proposed as a NOAEL for repeated dose toxicity to be used as a point of departure for risk assessment. This value is supported by the other studies on Stoddard Solvent and C_{10}-C_{11} alkanes. The 1000 mg/kg/day NOAEL dose for oral subchronic studies of decane is calculated to be theoretically equivalent to a 6 hr/day inhalation concentration of approximately 7 g/m^3, (see Appendix D), also supporting the conservatism of the 1 g/m^3 NOAEL value based on inhalation studies.

7.4 Reproductive and Developmental Toxicology

OECD guideline oral reproductive toxicity screening studies have been conducted with n-decane (C_{10}) and n-undecane (C_{11}), and a Segment II developmental toxicity study by inhalation with a C_9-C_{13} mixed aliphatic hydrocarbon solvent. There are no data for n-dodecane (C_{12}). These data are summarized in Table 7.4, and discussed individually

below, and indicate a low potential for reproductive and/or developmental toxicity. In support of this, substances in this category have been tested in subchronic studies in which testicular, ovarian and uterine histopathology have been evaluated (see Repeat Dose Toxicity). In no case was there an effect on testis histopathology that would indicate a male reproductive toxic effect, or on ovarian or uterine histopathology that would have suggested an effect on female fertility. The weight of evidence indicates that n-decane, n-undecane and n-dodecane have a low potential to cause reproductive or developmental toxicity.

Results for Specific Category Members and Related Materials

Decane:
Commercial decane (> 97% n-decane) was administered to male rats for 28 days (14 days prior to mating and 2 weeks during mating), and to female rats from 14 days prior to mating, through mating and gestation to day 4 of lactation at doses of 0, 25, 150, or 1000 mg/kg/day (Maraschin et al., 1995). n-Decane did not induce effects in offspring at a dose as high as 1000 mg/kg. There were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The mean mating time of the 1000 mg/kg/day groups was slightly longer than of the control; however, the increase was not statistically significant and was within the normal range of variability for this strain of rats. There was a non-dose-related decreased fertility index in all treated groups (not statistically significant) compared to controls. However, this effect took place in the absence of any adverse effects on reproductive organs and may have resulted from changes in mating behavior related to stomach irritation experienced by the treated animals. The NOAEL for parental reproductive effects was 1000 mg/kg/day and the NOAEL for effects on the offspring was also 1000 mg/kg/day, which was calculated to be equivalent to about 7 g/m^3 for 6 hr/day (see Appendix D).

Undecane:
n-Undecane was administered to male rats for 46 days, and to female rats from 14 days prior to mating, through mating and gestation to day 3 of lactation, at doses of 0, 100, 300 or 1000 mg/kg/day (Yoshimura et al., 1996). There were some clinical effects in parental animals (see Repeat Dose Toxicity). However, no effects on reproductive ability or on reproductive organ weights were observed. There were no gross or histopathological findings in reproductive organs of either sex. There was no apparent effect on deliveries or maternal behavior dams. Body weight gain was slightly decreased in male and female offspring at the 1000 mg/kg/day dose level. No effects were noted in terms of viability, general condition or gross observation of offspring. The NOAEL for parental reproductive effects was 1000 mg/kg/day, and the NOAEL for effects on the offspring was 300 mg/kg/day based on decreased body weight gain. The inhalation equivalent of 300 mg/kg/day was calculated to be approximately 2 g/m^3 6 hr/day; derived in the same manner as that for decane (see Appendix D).

Multiconstituent Complex Alkane Mixture:
A solvent consisting of C_9-C_{13} mixed alkanes has been tested in a rat segment II developmental toxicity study, and no treatment-related embryotoxic nor teratogenic effects were reported (EMBSI, 1978). Pregnant rats were exposed to two nominal concentrations of 300 or 900 ppm for 6 hrs/day during days 6-15 of gestation. At the top concentration in each study there were signs of maternal respiratory irritation indicating that a maximal inhalation concentration had been used. The NOAEL for developmental effects was greater than the highest concentration tested, 866 ppm (actual - approx 5 g/m^3).

Table 7.4 Summary of Reproductive and Developmental Toxicity

Material Class	Test Material	Test System	NOAEL	LOAEL (Effects)	Reference (Robust Summary No.)
Pure n-alkane	C10 n-Decane	OECD 422 Rat, oral	1000 mg/kg/day	None	Maraschin 1995 (RPRO-1; DEVL-1)
		F1 offspring	1000 mg/kg/day	None	
	C11 n-Undecane	OECD 422 Rat, oral	1000 mg/kg/day	None	Yoshimura et al., 1996 (RPRO-2; DEVL-2)
		F1 offspring	300 mg/kg/day	1000 mg/kg/day Decreased body wt gain	
Multi-constituent Complex	C9-C13 n-, Iso-, and Cyclo-alkanes	Rat inhalation Segment II developmental toxicity	>866 ppm (~ 5 g/m^3, 6 hr/day)	None	ExxonMobil Biological Sciences, Inc. 1978. (DEVL-3)

Conversion factor for decane (mwt 142): 1 mg/L = 172 ppm; 1 ppm = 0.00581 g/m^3

Reproductive and Developmental Health Benchmark Assessment

The available studies indicate no primary reproductive or developmental toxicity in rodents from oral exposure to n-decane at 1000 mg/kg/day, the highest dose administered, (Maraschin, 1995) or to n-undecane at 300 mg/kg/day (Yoshimura, 1996); equivalent to an inhalation concentration of 7 and 2 g/m^3 for 6 hrs/day, respectively. The only effect noted in the Yoshimura n-undecane study was slight decrease in fetal body weight gain in the offspring of the 1000 mg/kg/day dose group. Inhalation exposure to a complex mixture of C_9-C_{13} mixed alkanes consisting of n-, iso- and cycloparaffins also showed no evidence of

developmental toxicity at approximately 5 g/m^3, the highest vapor concentration tested and close to the vapor limit. This lack of toxicity supports the consideration of these three materials as a category. The inhalation health benchmark for reproductive and developmental toxicity is 5 g/m^3 and the oral health benchmark is 300 mg/kg/day, equivalent to approximately 2 g/m^3 for 6 hrs/day. The health benchmark for reproductive and developmental toxicity is in the range 2 - 7 g/m^3. Since this range is greater than for the subchronic toxicity health benchmark of 1 g/m3, no specific reproductive or developmental risk assessment was conducted.

7.5 Genetic Toxicity

Introduction

Genetic toxicity studies have been conducted for n-decane, n-undecane and n-dodecane, members of this category, and for a lower and higher structural homologues, n-nonane and n-tetradecane, which are not part of this category but are included for comparative information. Genetoxicity data on a C_{10}-C_{13} n-alkane product and on an aliphatic hydrocarbon solvent are also provided for comparative and supporting information. The available data indicate that, decane, undecane and dodecane, possess a low potential for any significant cytogenetic activity. The results of this endpoint support the treatment of these chemicals as a single category.

Mutagenicity (bacterial and mammalian):
Table 7.5 shows that nonane (Zeiger, 1992), decane (Petresa, 1985, Zeiger, 1992), undecane (Shibuya et al., 1996), tetradecane (Petresa, 1985) and a C_{10}-C_{13} n-alkane product (EMBSI, 1991) did not exhibit mutagenic activity in the *Salmonella typhimurium bacterium* assay both in the presence and absence of metabolic activation. Undecane has also shown a lack of mutagenic potential in the *Escherichia Coli* assay (Shibuya et al., 1996). While there is no bacterial genetic toxicity data for dodecane, dodecane, decane, and tetradecane showed no mutagenic activity in Chinese hamster lung V79 cells (Lankas, 1978). These studies support the conclusion that this category of substances does not possess significant mutagenic potential.

Cytogenicity:
As shown in Table 7.5, bone marrow cells of mice treated orally with high doses (>5g/kg) of a C_{10}-C_{13} alkane product failed to induce micronuclei formation (EMBSI, 1991). Furthermore, n-decane or n-dodecane did not induce DNA adducts in the skin of treated mice (Shell, 1998d). These observations suggest that decane, undecane and dodecane possess a low potential for any significant cytogenetic activity.

Table 7.5 Summary of Genetic Toxicity Data

Assay Type	Test System	Compound	Results	Reference (Robust Summary)
In vitro: bacterial				
Ames test (OECD 471)	S. typhimurium TA1535, 1537, 1538, 98, 100 ±S9 (rat)	1-decane (97% pure)	Negative ±S9	Petresa, (Petroquimia Espanola, S.A.), 1985 (RS# GTVT-7)
Ames test (OECD 471)	S. typhimurium TA1535, 1537, 1538, 98, 100 ±S9 (rat)	Tetradecane	Negative ±S9	Petresa (Petroquimia Espanola, S.A)., 1985 (RS# GTVT-3)
Ames test (OECD 471)	S. typhimurium TA1535, 1537, 97, 98, 100 ±S9 (rat, hamster)	nonane n-decane	Negative ±S9 Negative ±S9	Zeiger et al., 1992 RS# GTVT-2)
Ames test (OECD 471)	S. typhimurium TA1535, 1537, 98, 100 ±S9 (rat)	n-undecane	Negative ±S9	Shibuya et al., 1996
OECD 472	*E. coli* WP2uvrA ±S9 (rat)	n-undecane	Negative ±S9	Shibuya et al, 1996
Ames test (OECD 471)	S. typhimurium TA1535, 1537, 1538, 98, 100 ±S9 (rat)	C10-C13 n-alkane product	Negative ±S9	ExxonMobil Biomedical Sciences Labs, Inc., 1991 (RS# GTVT-1)
In vitro: Mammalian				
Cytogenetics:	Chinese hamster lung V79 cells ±S9 (rat)	1-decane (97% pure)	Negative ±S9	Sasol, Italy, 1994 (RS# GTVT-4)
Cytogenetics	CHL/IU cells ±S9 (rat)	n-undecane	Negative ±S9	Tanaka et al., 1996
Gene mutation	Chinese hamster lung V79 cells –S9	n-decane n-dodecane n- tetradecane	Negative –S9, enhanced mutant frequency of methylazoxy-methanol	Lankas et al., 1978
Cytogenetics	Human lymphocytes ±S9 (rat)	Shellsol D70	Negative ±S9	Shell, 1998c
In Vivo: Mouse				
DNA adducts	32P-postlabeling in skin of C3H mice; 25µl/day once or daily for 3 days	n- decane n-dodecane	No adducts No adducts Did not enhance b(a)p activity	Shell, 1998d

Assay Type	Test System	Compound	Results	Reference (Robust Summary)
Micronucleus (OECD 474)	CD-1 mice – both sexes/ oral gavage 0, 1.0, 2.5, & 5.0g in corn oil/kg; exposure period of 24, 48, 72 hrs	C10-C13 n-alkane product	NOEL>5.0g/kg No increase in micronuclei/PCE in bone marrow	ExxonMobil Biomedical Sciences Labs, Inc., 1991 (RS# GTVI-1)

7.6 Neurotoxicity

Potential behavioral effects of hydrocarbon and other organic solvents have been discussed extensively in the literature, but no definite conclusion has been drawn for complex hydrocarbon solvents (reviewed in ECETOC, 1996) or the three specific members of this category. Two short-term studies are available which specifically address potential neurotoxicity of n-decane and a C_{10}-C_{12} linear alkane, and several repeat dose studies with n-nonane, n-decane, n-undecane and multiconstituent aliphatic solvents (see 7.3 Repeat Dose Toxicity). There is some evidence of neurobehavioral changes after short-term high inhalation (>1.5 g/ m^3) or dermal (>1.5 g/kg/day) exposure to alkanes in this category, but no evidence that these are due to a neuropathological effect on the peripheral or central nervous system.

n-Decane:
Rats were exposed 8 hours daily for three successive days to n-decane at concentrations of 0.5, 1.5 and 5 g/m3 (85, 260, 860 ppm, respectively; Lammers et al, 2000; RS# Other-2). Rats were evaluated for neurobehavioral changes including functional observational battery (gait, arousal and convulsive behavior, sensory reactivity, grip strength and landing foot splay) immediately prior to exposure, and 30 minutes after exposure on each of the three days and 24 hours after the last exposure. In a separate study, response speed and accuracy were evaluated in separate groups of rats using a discrete trial operant visual discrimination task (water-deprived rats were trained to depress the lever to obtain a reward). N-Decane treatment produced a small reduction in forelimb, but not hind limb, grip strength at the top concentration, only after the third day of exposure. Peripheral neurotoxins such as n-hexane affect long axons of the hind limbs before the forelimbs, suggesting that n-decane was not acting by a similar mechanism to n-hexane. The effect was not apparent 24 hrs after the last exposure. There was also a temporal, but not dose-related, decrease in the visual discrimination test. All effects were normal on the day following exposure, suggesting that there was no cumulative neurotoxic effect. The NOAEL for behavioral effects was reported to be 1.5 g/m^3. In the Marachin et al (1995) rat subchronic oral study of commercial decane, startle reflex, an open field test, and forelimb grip strength were examined, and no effects were reported at any concentrations up to 1000 mg/kg/day (calculated to be 7 g/m3 for 6 hr/day). The slight and reversible nature of the findings in the Lammers et al. 2000 study, and the fact that no evidence of any behavioral or neurotoxic effects including forelimb grip strength were observed in the rat oral study at doses up to 1000 mg/kg/day of n-decane, suggest that these effects are questionable.

C_{12}-C_{14} N-Alkanes:
Rabbits were treated dermally for 6 hours per day for 28 days with material at 100, 500 or 2000 mg/kg (O'Conner et al., 1995, 1997; RS# RPTD-6). Neuropathological examination was conducted from tissue samples from 20 sites in the peripheral and central nervous system. At the top dose, all animals were euthanized for humane reasons due to severe dermal irritation, between Day 7 and 14. This study did produce minor effects (i.e., decreased righting reflex, staggered gait) seen in previous acute studies. However, these effects may have been caused by the severe dermal irritation, thus hindering animal movement. There were no neuropathological lesions, suggesting that there was no true neurotoxicological effect. Under the conditions of this study, a NOEL of 100 mg/kg (dermal irritation) and a NOAEL of 500 mg/kg (behavioral changes) were identified for this test material.

7.7 Carcinogenicity

C_{10}-C_{14} N-Alkanes:
Decane, undecane and tetradecane did not produce skin tumors when tested alone in initiation/promotion studies conducted in mice (Van Duuren and GoldSchmitt, 1976). These findings are consistent with those of a prior initiation/promotion study in which dodecane administered alone failed to produce skin tumors in mice (Horton, 1957). This conflicts with other reports indicating that dodecane alone did induce skin tumors in mice (C. Weil, 1961,1967). However, the dodecane used in the latter studies was found to contain impurities, including unspecified aromatics, which confounds their interpretation. Decane, undecane, and dodecane have been shown to not promote morphological transformation or inhibit intercellular communication in primary Syrian hamster embryo cells in culture (Rivedal, 1992).

n-Alkanes have been shown to exhibit skin tumor promoting activity in the mouse (Horton et al., 1957, 1966; Saffioti and Shubik, 1963). This promotional activity appears to be related to carbon chain length, with maximal activity occurring within the range of C_{12} to C_{14} (Sice, 1966). n-Dodecane was shown to be more than one order of magnitude less potent in promotional activity than phorbol ester (TPA) (Baxter and Miller, 1987). Consequently, the promotional potency of each of the members of the C_{10}-C_{12} n-alkane category is likely to be less than that of TPA.

A recent study provided evidence that the skin tumor promoting effects of C_{10}-C_{14} normal alkanes is secondary to skin irritation (Nessel et al., 1999) by showing that undiluted, C_{10}-C_{14} alkanes produced irritation and significant increases in tumor incidence in DMBA pretreated mice. When applied in mineral oil diluent, skin irritation was ameliorated and tumor incidence dropped to an insignificant level. An underlying relationship between irritation and promotional activity is a likely explanation for the cocarcinogenic activity reported for n-dodecane. (Horton et.al., 1957; Bingham and Falk, 1969).

Multiconstituent Complex Alkane Mixture:
As mentioned previously, the National Toxicology Program has conducted 2-year inhalation carcinogenicity studies in rats and mice of Stoddard Solvent IIC (NTP TR 519). The test material was low in aromatics (<1%) but contained C_{10}-C_{14} n-, iso-, and cycloalkanes (30 components over 1%). NTP reported some evidence of carcinogenic activity of Stoddard solvent IIC in male F344/N rats based on increased incidences of adrenal medulla neoplasms; a slightly increased incidences of renal tubule adenoma may have been related to Stoddard solvent IIC exposure. There was no evidence of carcinogenic activity of Stoddard solvent IIC in female F344/Nrats exposed to 550, 1,100, or 2,200 mg/m^3. There was no evidence of carcinogenic activity of Stoddard solvent IIC in male B6C3F1 mice exposed to 550, 1,100, or 2,200 mg/m^3. There was equivocal evidence of carcinogenic activity of Stoddard solvent IIC in female B6C3F1 mice based on increased incidences of hepatocellular adenoma; this slight increase was associated with increased body weight in exposed females. Exposure of male rats to Stoddard solvent IIC resulted in nonneoplastic lesions of the kidney characteristic of α2µ-globulin accumulation, which have been determined to have no relevance to humans. This study is referenced for the sake of completeness; however, these data are not used in consideration of the health benchmark because the report is not yet finalized.

7.8 Disposition and Metabolism

Overview

Disposition of n-alkanes of different chain lengths have been investigated (Ichihara *et al*., 1969; Lu *et al*., 1979; Buhrer and Widgren, 1963; Servé *et al*., 1995; McDougal, *et al*., 2000; McDougal and Robinson, 2002; BIBRA, 1992; Tulliez and Bories, 1975a,b, 1978). Absorption of n-alkanes with greater than 9 carbons has been demonstrated to occur via the respiratory and to a limited degree via intragrastric and dermal routes of exposure. Once n-alkanes enter systemic circulation, they demonstrate a greater affinity to distribute in adipose tissue, brain, kidney, and liver. Limited metabolism studies have shown that n-alkanes undergo phase I oxidation/biotransformation and can be excreted into urine. In addition, n-alkanes can also be further metabolized endogenously through gluconeogenesis and/or exhaled via the lungs.

Absorption and Distribution

Inhalation:
The major route by which hydrocarbons enter systemic circulation is via the inhalation route of exposure (Snyder, 1987). Absorption of C_9-C_{14} n-alkane vapors and aerosols can occur by respiration where vapor pressure determines whether, at a given temperature, exposure is to vapor or aerosol. Compared to other hydrocarbons, the uptake of aliphatic hydrocarbons after inhalation is in general less efficient than the uptake of the aromatic hydrocarbons due to their lower vapor pressure and lower blood : air partition coefficients (Astrand et al., 1975;). Compared to unsaturated hydrocarbons, saturated hydrocarbons

are absorbed to a lesser extent by inhalation in rats (Dahl et al., 1988). Based on the studies described herein, C_{10}-C_{12} are likely to have the following distribution ratios: fat (180-260): brain (3-9): blood (1).

Zahlsen and coworkers (1992) studied the inhalation kinetics of hydrocarbons of different carbon chain lengths (C_6-C_{10}) by exposing rats to an average of 100 ppm of each test substance for three consecutive days and measuring the concentration of hydrocarbons in blood, brain, liver, kidney, and adipose tissue. Distribution of decane by day 3 was as follows (µgmol/ kg, mean $\pm$ SD): blood (6.8 $\pm$ 0.5), liver (45.9 $\pm$ 3.9), brain (60.2 $\pm$ 12.7), kidney (77.7 $\pm$ 27.3) and fat (1230 $\pm$ 63). The n-alkanes showed lower concentrations in the liver when compared to other organs investigated and may be attributed to different rates of metabolic elimination in the rat liver or differences in liver partitioning between other hydrocarbons which included napthenes and aromates. The overall study concluded that n-alkanes show very low concentrations in the blood, relatively elevated concentrations in brain and a potential for accumulation in fat with repeated exposures.

Another study exposed rats to 0.5 (~85), 1.5 (~260), or 5 (~860) g n-decane/m3 (ppm) and found that the concentration of n-decane in the brain was approximately 12-23 fold higher than the concentration in blood. n-Decane concentration in the blood after a single 8 hour exposure with air, 0.5, 1.5, or 5 g/m3 was < 30 (detection limit), 567, 1173, and 73333 ng/mL, respectively. The peak brain/blood ratio after a single 8 hour exposure reached its maximum at 2 hours and begins to decline through 8 hours post-exposure with both brain and blood concentrations decreasing (TNO, 1999).

Lof *et al*. (1999) studied the distribution of nonane, decane, undecane, and other hydrocarbons after repeated exposure of dearomatised white spirit in brain, blood, and fat tissue of rats. Nonane, decane, and undecane comprise 3.6, 16.6, and 9.9%, respectively, of dearomatised white spirit (DAWS) used for this study. Rats were exposed whole-body in inhalation chambers to air, 400 ppm, and 800 ppm DAWS vapors for 6 hrs/day, 5 days/week for 1, 2, or 3 weeks. The concentration of the n-nonane, n-decane, and n-undecane in blood as well as in brain was nearly the same after 1, 2, and 3 weeks of exposure. Two hours after the end of exposure, the concentration of n-decane decreased to about 25% of the highest concentration in blood and 50% in the brain. However, in fat tissue the concentration of n-nonane, n-decane, and n-undecane increased during the 3 weeks of exposure and decreased very slowly after the end of exposure. The half-lives in blood, brain, and fat tissue were roughly estimated for the n-alkanes. Post exposure decay in blood could be separated into two phases with half-lives of approximately 1 and 8 hours. In brain tissue two slopes with half-lives of 2 and 15 hours were identified. In fat tissue only one slope with half-life of about 30 hours was identified. These findings suggest similar and independent toxicokinetics of these three n-alkanes. In conclusion, 3 week exposure to decane and undecane resulted in fat:brain:blood tissue concentration coefficients of 260:3:1. After 3 week exposures, concentrations in blood and brain decrease rapidly compared with the decrease in fat tissues. The possibility of redistribution from fat to brain may exist, but was not addressed in this study.

Skin:
Absorption through the skin is negligible; studies have shown that alkanes having 8 or more carbons penetrate the skin with difficulty (Tsuruta, 1982). In a study by McDougal *et al*. (2000), dodecane was used as a marker to measure the dermal penetration and absorption of JP-8. Static diffusion cells were used to measure penetration across skin and the kinetics of absorption into the skin. Results from this study suggest that dodecane (~4.5% w/w of JP-8) will not cause systemic toxicity because of low penetration across skin as determined by low measured fluxes (% dose/min mean $\pm$ SEM): naphthalene (0.015 $\pm$ 0.003) > dodecane (0.0036 $\pm$ 0.0004) > hexadecane (0.0011 + 0.0002). The rank order of marker absorption (% dose mean $\pm$ SEM) is naphthalene (1.17 $\pm$ 0.07) > dodecane (0.63 $\pm$ 0.04) > hexadecane (0.18 $\pm$ 0.08). In addition, higher amounts of aliphatic markers remain deposited in the skin surface and stratum corneum, compared to naphthalene. The absorption of aliphatic components into the skin may be the cause of skin irritation as demonstrated by penetration profiles in the outermost layers of skin: hexadecane (8.63 % dose) > dodecane (5.13 % dose) > naphthalene (0.71% dose).

Baynes *et al*. (2001) studied the effects of JP-8 additives on the dermal disposition of (^{3}H)-n-dodecane in isolated perfused porcine skin flaps. This study along with other studies (Mumtaz and Hertzberg, 1993; Clewell, 2000) concluded that the presence of other chemicals can have synergistic or antagonistic effects on dermal disposition of chemicals. In the case of n-dodecane, JP-8 additives were associated with synergistic interactions. Despite these interactions, this study demonstrated that after a 5 hour exposure, n-dodecane has a flux (mean $\pm$ SE) of ~0.001 $\pm$ 0.0001 μg/cm^2/h and a permeability (mean + SE) of ~0.000011 + 0.000001 cm/h. Permeability is determined from the ratio of individual fluxes to the concentration (μg/cm^3) of the initial topical dose. The applied surface concentration was 180 μg/cm^2 (^{3}H)-n-dodecane. Dodecane deposition in stratum corneum was 1.28-5.13% of initial dose; further supporting that decane and similar n-alkanes are not readily absorbed via the dermal route.

Less volatile components such as dodecane remained on the skin surface after a 5-hour exposure. This is important for risk assessment because, with repeated occupational exposure, the cumulative levels of dodecane in skin will persist more than the more volatile aromatic components (e.g., naphthalene) and may cause dermatological effects in unprotected workers or those exposed dermally.

Ingestion and Intravenous:
The less likely routes of exposure include ingestion and intravenous exposure. The mechanism of GI absorption is not understood, but it is likely that the alkanes pass predominantly into the lymphatic system prior to entering the blood stream. However, direct entry into the portal system cannot be ruled out especially for n-alkanes of shorter chain lengths.

n-Alkanes of C_9 and above can be absorbed to some degree by the intestinal tract of rodents. Albro *et. al.* (1970) showed that the major site of absorption of rats fed intragastically with a mixture of hydrocarbons of varying chain lengths was the small intestine and that the rate of absorption is inversely related to carbon chain length.

Intravenous experiments have demonstrated that, after entering the blood, there is rapid transport into the liver followed by redistribution and temporary deposition in fatty tissues, such as adipose tissue. Once in fat, release is slow and, depending on dose, levels can be detected after one month. Based on studies performed by Lof *et al.* (1999), the half-life for n-decane and n-undecane is approximately 30 hours.

Metabolism and Excretion:
The metabolism of C_{10}-C_{12} n-alkanes has not been extensively characterized. In general, the identification of specific metabolites and the monitoring of enzyme activities indicate that the biotransformation is mediated by hepatic microsomal cytochrome P-450 system. Metabolism of n-alkanes is rapid and proceeds via the P_{450} enzyme system to either 1- or 2-hydroxydecane, which are further oxidized to carboxylic acids, which are, in turn, oxidized to CO_2. In an alternative pathway detected with n-decane, n-decanoic acid can be further oxidized to 10-hydroxydecanoic acid prior to further oxidation. It is also likely that amounts of partially oxidized conjugated metabolites appear in the urine but overall it is likely that little excretion occurs via the urine. Servé *et al*. (1995) identified several cyclized derivatives (lactones) in urine derived from unlabelled n-nonane but were unable to quantify the amounts. The rate limiting metabolic step is probably an initial omega hydroxylation as no significant accumulation of metabolites in tissues has been reported with n-alkanes of various chain lengths. The hydroxylated metabolites are also products of normal body metabolism, and, therefore, are likely to be used in various bodily biosynthetic routes and for generating ATP. The CO_2 produced from n-alkane metabolism can also be reincorporated in the process of gluconeogenesis, as well as eliminated through the lungs during exhalation.

Conclusion

The major route by which n-alkanes can be absorbed and enter the system circulation is via inhalation. Inhalation absorption tends to be low in comparison with other aliphatic and aromatic hydrocarbons due to the n-alkanes lower vapor pressure and blood-air partition coefficients. Less than 1% of the dermal exposure dose may be absorbed while 1-5% can be deposited in the stratum corneum. This deposition in the skin, in conjunction with low vapor pressures (increased residence time), can cause dermatological effects (skin irritation) in those exposed via the dermal route. Once absorbed via the inhalation route, C_{10}-C_{12} n-alkanes are likely to be deposited in the following tissues by ratio: fat (180-260): kidney (~11): liver (~7): brain (3-9): blood (1). The half-life of C_{10}-C_{12} n-alkanes is expected to be ~ 8 hours in blood, ~15 hours in brain, and ~30 hours in fat. Furthermore, n-alkanes such as n-nonane and n-decane can be metabolized at relatively high rates to hydroxyl derivatives, which are converted to the corresponding ketone. Undecane and dodecane are likely to be metabolized similarly, but their metabolism is not well characterized.

7.9 Human Experience

N-decane, n-undecane and n-dodecane are components of many multiconstituent hydrocarbon solvents such as mineral spirits, and fuel streams such as diesel and kerosene. These n-alkanes are usually minor components along with isoparaffins, cycloalkanes and aromatics. The carbon range for solvents is usually much narrower than for fuels. Although there are no reports of human exposures to the individual n-alkanes, the potential human toxicity can be understood from the toxicity of the multiconstituent products.

Acute Toxicity:
The human acute health hazards of hydrocarbons depend on their volatility and viscosity, and to the route by which humans are exposed to them (Seymour and Henry, 2001). An important acute human hazard, especially for children, of hydrocarbons in the C_{10}-C_{12} range is chemical aspiration pneumonia. This effect only occurs when chemicals of sufficient volatility and lower viscosity are ingested in fairly large quantities. The threshold for determining when a chemical poses this hazard is somewhat difficult to predict precisely because individual physiology plays a large role. The Consumer Product Safety Commission (CPSC) established a viscosity cut-off of 100 SUS at 100°F for this hazard. Children are likely to be more susceptible to this hazard because of their shorter esophagi. The CPSC requires consumer products that contain 10% or more hydrocarbons, meeting their viscosity definition, to be packaged in child-resistant packaging (see Section 4). CNS depression by inhalation of vapors is not an issue with these materials because they are not sufficiently volatile, and gastrointestinal absorption is not considered significant.

Local effects:
Cutaneous injury appears to be due to local irritant effects and fat solvency properties, hence the term “defatting.” The extent of the injury is related to duration of exposure, resulting usually in superficial damage. Clinical significance of cutaneous absorption is considered insignificant. Ocular exposure usually causes little or no injury, though there may be stinging and discomfort. Aspirated hydrocarbons disrupt surfactant and bronchial epithelial cell barrier, leading to alveolar instability, early distal airway closure and eventually hypoxemia. Gastrointestinal effects, although unpleasant, are usually transient and result from direct, local irritation of the pharynx, esophagus, stomach and small intestine.

Vapors of some multiconstituent hydrocarbon solvents such as White Spirit may also cause sensory irritation, depending on the concentration (reviewed in IPCS, 1996). However, White Spirits contains linear, branched and cyclic hydrocarbons in the C_7-C_{12} range, and also including 15- 20% of aromatics. It is not clear if these effects can be attributed to the more volatile aromatic components.

Systemic Effects:
CNS depression following exposure to mixed hydrocarbon products with a wide range of components, e.g. white spirits, appears to be indirect and secondary to hypoxia after pulmonary involvement (aspiration pneumonitis) (IPCS, 1996). Acute inhalation exposure to

the three n-alkanes at their saturated vapor concentration does not cause CNS depression in animal studies. Cardiac sensitization has only been reported for more volatile lower carbon range hydrocarbons, notably the aromatics.

Repeated Exposure Toxicity:
There are no specific human studies of the effects of repeated exposures to decane, undecane or dodecane. In human epidemiological studies it is often impossible to know the extent of hydrocarbon exposure, either qualitatively or quantitatively. There are many effects anecdotally attributed to multiconstituent products containing these alkanes, such as hydrocarbon solvents and fuels. These effects are reviewed in IPCS 1996, and include hematological effects, glomerulonephritis, reproductive effects, cytogenetic damage and cancer. However, these solvents and fuels contain many more chemical constituents than the C10-12 alkanes; for example, White Spirits is a multiconstituent product containing linear, branched and cyclic hydrocarbons in the C_7-C_{12} range, and also including 15-20% of aromatics (IPCS, 1996). None of these anecdotal effects of fuels and solvents can be specifically attributed to the C10-12 Alkanes, based on animal or human data.

The predominant systemic toxic effects attributed to chronic exposure to certain hydrocarbon solvents, such as White Spirits, are the ill-defined behavioral effects collectively known as "painter's syndrome" or OPS (Organopsycho Syndrome). Certain hydrocarbon solvent components are known from animal studies to have neurotoxic potential, such as n-hexane and 1,2-diethylbenzene. However, recent reviews have examined the human epidemiological literature regarding hydrocarbon induced neurotoxic effects and have concluded:

> "*The weight of evidence suggests that exposure to hydrocarbon solvents at current (occupational exposure) limits does not appear to cause adverse neurobehavioral effects*" Gamble, (2000).
>
> and
>
> "*It is not possible to draw reliable conclusions with respect to the presence of absence of nervous system damage related to the common properties of organic solvents*" Ridgeway et al. (2003).

There is currently an extensive program underway to investigate the toxicity of Jet Fuels, a product containing members of the n-alkane category. (National Academy of Sciences, 2003; Ritchie et al., 2001; Ritchie et al, 2003).

7.10 Hazard Assessment Summary and Proposed Health Benchmarks.

7.10.1 Hazard Assessment Summary

The three n-alkanes that comprise this category are specialty chemical products whose toxicity has been evaluated in various animal studies. Because they are structurally very

similar to each other, data on one material is applicable to all members of the category, and can be used in a “read-across” approach for both qualitative and quantitative purposes. Also, some commercial hydrocarbon solvents contain all three alkanes, together with some higher or lower structural homologs, or with branched and/or cyclic alkanes, and data on these similar materials are also considered. Certain fuels such as diesel and kerosene also contain these n-alkanes together with a broader range of many other linear and branched aliphatic, cyclic and aromatic constituents; these fuels were considered to be sufficiently different from the category members that toxicology data on them were not considered in this evaluation.

When all the available relevant data is considered, there is sufficient data on one, two, or all three materials to satisfy all the Tier 1 endpoints for this category, as described in the preceding sections.

Table 7.10 Tier 1 Hazard Identification Studies Available

TIER 1 HAZARD		**DECANE**	**UNDECANE**	**DODECANE**	**OTHER n-ALKANES**
Acute Toxicity	Oral	✓	✓	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Dermal	RA	RA	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Inhalation	✓	✓	✓	✓ (n-nonane, n-tridecane)
In Vitro Gene Tox	Bacterial	✓	✓	RA	✓ (n-nonane, n-tetradecane; C_{10}-C_{13} n-alkane product)
	Cytogenetics	✓	✓	✓	✓ (n-tetradecane, C_{11}-C_{14} aliphatic hydrocarbon solvent)
In vivo Genetic Toxicity	Micronucleus	RA	RA	RA	✓ (C_{10}-C_{13} n-alkane product)
Repeat Dose Toxicity		✓	✓	RA	✓ (n-nonane, C_9-C_{13}, C_{10}-C_{13}, C_{11}-C_{14}, aliphatic hydrocarbon solvents)
Reproductive Toxicity Screen		✓	✓	RA	✓ (C_9-C_{13} aliphatic hydrocarbon solvent)

✓ = one or more studies available
RA = Read Across

The animal acute data confirm the human experience that members of this category may be irritating to the skin, and may present an aspiration hazard if ingested. These materials

(other than n-nonane, which is not a member of the category) do not appear to be sufficiently volatile to cause overt CNS depression or lethality if inhaled, even at their saturation vapor concentrations, but they may cause respiratory irritation. These materials do not cause significant systemic toxicity, and are not primary reproductive or developmental toxicants. The major effect observed in subchronic studies is nephropathy in males rats. Although alpha-2-microglobulin has not specifically been detected, the weight of the evidence for a range of materials suggests that this is the mechanism of toxicity, which is not considered relevant for risk assessment. Data from animal studies on higher tier endpoints indicate that members of this n-alkane category are not genotoxic; are not likely to be neurotoxic; and are not skin carcinogens.

7.10.2 Health Benchmarks

A health benchmark is the point-of-departure from which health risks can be assessed against realistic exposure scenario estimates. This is usually based on No-Observed-Adverse-Effect-Levels (NOAELs) from animal studies for a relevant human health effect.

Acute toxicity:
The acute oral and dermal LD50s, and acute inhalation LC_{50}s, show no lethality or clinical signs at the high limit doses tested. Acute toxic effects in animals confirm human experience: ingestion may pose an aspiration hazard, and acute dermal exposure may cause irritation. The inhalation route is considered the relevant route for quantitative human risk assessment. No signs of CNS depression were reported in acute lethality studies at the maximum vapor concentration, and in an acute behavioral study of n-decane no effects were seen after a single 8 hour acute exposure to 5 g/m^3. A NOAEL for acute toxic effects, including behavioral effects, of 5 g/m^3 is proposed for members of this category, recognizing this is close to the saturated vapor concentration for n-decane, and above it for n-undecane and n-dodecane.

The acute health benchmark for this category is proposed as 5 g/m^3 for purposes of risk assessment, a concentration at which no lethality would be expected. This is above the saturation air concentration for C_{11} and C_{12} alkanes, but there were no deaths even at the air saturation concentration of 8g/m^3 for n-decane.

Repeat Dose:
There are five repeat oral dosing studies in animals with members of this category, or with complex mixtures. For most of the studies, the most sensitive effects are indicative of gastrointestinal irritation, with some indication of nasal or pulmonary lesions suggesting aspiration or gavage errors. Repeat ingestion is not considered a relevant human exposure scenario, and these effects in oral studies are not used as the basis for risk assessment. There are no repeat dermal studies to assess systemic toxicity, but one study in rabbits indicated severe skin irritation. Repeated dermal exposure to these materials is not considered a realistic human scenario, because potential skin irritation is likely to preclude repeated exposures.

The inhalation route is considered the most relevant exposure route for human risk assessment from repeated exposures, and this is borne out by the Exposure Assessment.

There are three repeat dose inhalation studies relevant for human risk assessment summarized in the following table:

Table 7.11 Repeat Dose Inhalation Studies Relevant for Human Risk Assessment

Test Material	Test System	NOAEL	LOAEL (Effects)	REFERENCE
C9 n-Nonane	Rats, male; inhalation 6 hrs/day, 7 days/wk, 62-65 days	3.1g/m^3	8.4g/m^3 mortality, salivation, tremors, lacrimation, decreased body wt	Carpenter et al, 1978 RPTD-1
C10 n-Decane	Rat 90 day inhalation 18 hrs/day, 7 day/wk, 91 days.	3.14 g/m^3 (540 ppm)	None at highest conc. tested.	Nau et al., 1966 RPTD-3
C9-C13 n-, Iso-, and Cyclo- alkanes	Rats, inhalation; 12 wks; 6 hrs/day, 5d/wk	300 ppm (approx 2 g/m^3)	890 ppm (5 g/m^3); decreased weight gain. Male rat nephropathy observed.	Phillips and Egan, 1984 RPTD-8

Conversion factor for decane (mwt 142): 1 mg/L = 172 ppm; 1 ppm = 0.00581 g/m^3

No relevant adverse effects were noted in rat repeat dose studies for n-decane at a concentration of 3.1 g/m^3 (540 ppm); 18 hrs/day for 7 days/week or for a mixed product at the highest vapor concentration that could be tested - 5 g/m^3; 6 hrs/day for 5 days/week. No effects were reported for n-nonane at 3.1 mg/m^3, but this has a higher vapor pressure and could be tested at up to 8.4 g/m^3, when some lethality and other effects were reported. There was a decrease in some neurological endpoints after repeated exposure to n-decane at 5 g/m^3, but not after exposure to 1.5 g/m^3. Based on these studies, and supported by the additional studies on Stoddard Solvent and C_{10}-C_{11} isoparaffins, an inhalation concentration of 1.0 g/m^3 for 6 hrs/day, 7 days/week, for 13 weeks is considered a conservative value for the n-nonane, n-decane and multiconstituent product data, to be used as a NOAEL for repeated dose toxicity from rat studies.

Reproductive/Developmental Toxicity Screening Studies:
The available studies indicate no primary reproductive or developmental toxicity from oral exposure to n-decane at 1000 mg/kg/day, the highest dose administered, (Maraschin, 1995) or to n-undecane at 300 mg/kg/day (Yoshimura, 1996); equivalent to an inhalation concentrations of 7 and 2 g/m^3 for 6 hrs/day, respectively. The only effect noted in the Yoshimura n-undecane study was a slight decrease in fetal body weight gain in the offspring of the 1000 mg/kg/day dose group. Inhalation exposure to a complex mixture of C_9-C_{13} mixed alkanes consisting of n-, iso- and cycloparaffins also showed no evidence of developmental toxicity at approximately 5 g/m^3, the highest vapor concentration tested and close to the vapor limit. This lack of toxicity supports the consideration of these three materials as a category. The inhalation health benchmark for reproductive and

developmental toxicity is 5 g/m^3 and the oral health benchmark is 300 mg/kg/day, equivalent to approximately 2 g/m^3 for 6 hrs/day.

Metabolism:
n-Alkane vapors are readily absorbed by the lung, and alkanes can accumulate in adipose tissue and some organs; however, they may be exhaled unchanged, or readily metabolized by oxidative enzymes to acids which can be incorporated into intermediary metabolism, or degraded completely to carbon dioxide which is exhaled. As such, n-alkanes are not expected to accumulate in tissues from intermittent inhalation exposures to low concentrations.

Overall Health Benchmark:
The proposed subchronic inhalation NOAEL of 1.0 g/m^3 6 hr/day, 7 days/week, based on the rat repeat dose studies of n-nonane, of n-decane, and of mixed C_9-C_{13} alkanes product is consistent, yet more conservative, than the NOAELs from rat reproductive and developmental toxicity studies, which range from 2-7 g/m^3 (inhalation equivalents). Since this range is greater than for the subchronic toxicity health benchmark of 1 g/m3, no further reproductive/developmental toxicity risk assessment was conducted. No consistent adverse systemic effects of relevance to humans were reported in the subchronic studies, usually at the highest vapor concentrations tested, from about 2-5 g/m^3. This value of 1 g/m^3 for 6 hrs/day is considered an appropriate NOAEL for animal studies to be used as a health benchmark for all subsequent human risk assessment.

8. Risk Characterization

8.1 Summary

Risk assessment combines the information on the possible toxic health effects (Hazard Assessment) of a substance and the potential for exposure to the substance (Exposure Assessment) to calculate the likelihood of harm.

Potential risks from exposures to the n-alkanes were evaluated based on the receptors and exposure scenarios identified in the Exposure Assessment (Section 6) and the health benchmarks identified in the Hazard Assessment (Section 7).

In Section 6, primary receptors were identified as infants and children at home, and prospective parents both at home and work. The only significant exposure to children and adults is by inhalation, although there may be limited dermal exposure from fuels and paints. Dermal absorption through the skin is very low for normal alkanes with 8 or more carbon atoms. The screening assessment described in Section 6 confirmed that dermal (and oral) doses are indeed negligible. Human milk consumption, addressed in Section 6 and Appendix F suggests this route is not significant for infants, even those living in highly industrialized areas. The possibility of infant exposure from mothers who are occupationally exposed to n-alkanes (e.g. air line refueling maintenance or painting occupations) could not be addressed due to a lack of data.

The toxicity assessment presented in Section 7 summarized all of the available toxicity data for decane, undecane, and dodecane and selected mixtures containing these compounds. These C_{10}-C_{12} n-alkanes are physically and chemically similar so their toxicological properties are very similar to each other as well as other structurally related alkanes. Studies demonstrate that the aliphatic hydrocarbons in this molecular weight range have low acute toxicity and that CNS depression is not observed even at saturated vapor conditions. These materials are not sufficiently volatile to cause specific toxic effects from repeated inhalation exposures and there are no specific identified target organs from repeated exposure by any route. Carcinogenicity is not expected to be a relevant end-point since none of the alkanes are genotoxic or produce DNA adducts either *in vitro* or *in vivo* by any route of administration. Reproductive screening studies and developmental toxicity studies indicate that materials in this category are not primary reproductive or developmental toxicants. In subchronic inhalation studies there was no evidence of testicular, ovarian or uterine histopathologic effects. No two-generation reproductive toxicity studies are currently available, but this endpoint is addressed by the lack of effects on reproductive organs in the subchronic studies, and lack of developmental toxicity.

Accidental Oral exposure poses an aspiration rather than any systemic hazard. The Consumer Product Safety Commission (CPSC) established a viscosity cut-off of 100 SUS at 100° F for this hazard. Children are likely to be more susceptible to this hazard because of their shorter esophagi. The CPSC requires consumer products that contain 10% or more hydrocarbons, meeting their viscosity definition, to be packaged in child-resistant packaging (see Section 4).

Margins of Exposure (MOE) and Margins of Safety (MOS) were calculated for non-occupational exposure scenarios. Occupational exposures were compared with the proposed Occupational Exposure Limit (OEL). Considering both representative and elevated concentrations of the three n-alkanes measured in monitoring studies the following situations were analyzed.

1. Chronic exposure of infants and children to indoor air.
2. Chronic exposure of prospective parents to indoor air.
3. Short term exposure of infants and children in a newly renovated (painted) home.
4. Short term exposure of prospective parents in a newly renovated (painted) home.
5. Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

Results are presented in the relevant sections below and summarized in Appendix H.

In every domestic scenario relevant to infants, children and parents, MOEs based on the subchronic NOAEL were comfortably in excess of 100, and almost 2,000 for chronic domestic exposures suggesting a very low risk of harm to infants, children or parents. Margins of Safety (comparison with the TPHCWG derived RfC) were similarly reassuring. As described in IRIS, the EPA considers an RfC to be an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime (USEPA, 1988).

Highest occupational exposure (fuel workers) also indicated a high margin of safety with high-end exposures almost two orders of magnitude less than the (8 hour) OEL. When adjusted for continuous exposure, the MOEs ranged from approximately 65 to 200.

8.2. Health Benchmarks

No U.S. regulatory agency has established a chronic reference concentration (RfC), chronic reference dose (RfD), an acute exposure limit or an occupational exposure limit (OEL) for decane, undecane or dodecane. Therefore, the Consortium identified health benchmarks from the toxicology data for use in the risk assessment and considered RfCs and occupational exposure limits on related substances.

The existing mammalian and environmental toxicology information show these C_{10}-C_{12} normal hydrocarbons have similar toxicity profiles which suggest they may be treated as a class. The same Health Benchmarks were therefore assigned to each of the chemicals. Based on a number of repeat dose inhalation studies in rats, a NOAEL of 1.0 g/m^3 (6 hours/day, 7 days/week, for 13 weeks) was derived in Section 7. An acute Benchmark of 5g/m^3 was also derived. The reader is referred to Section 7 for a detailed analysis of the criteria applied and specifically to Section 7.10.2 for a concise summary.

An RfC of 1,000 µg/m^3 for C_{10}-C_{12} aliphatic hydrocarbons was derived by the TPHCWG and this was used for the non-occupational chronic margin of safety analyses. This value is similar to the value of 1,200 µg/m^3, as an interim chronic recommended exposure limit (REL) for C_{10}-C_{11} isoparaffinic hydrocarbon solvents, derived by California Office of Environmental Health Hazard Assessment (OEHHA) (Collins, 2004).

Health Benchmarks selected are summarized in the following table and discussed below.

Table 8.1 Health Benchmarks

Benchmark	Value
Inhalation Subchronic NOAEL (adjusted to continuous exposure)	$2.5x10^5$ µg/m^3
Chronic Reference Concentration (RfC) (Total Petroleum Hydrocarbon Working Group	1,000 µg/m^3
Acute Toxicity (Short Term Exposure)	$5.0x10^6$ µg/m^3
Inhalation Reproductive/ Developmental NOAEL (adjusted to continuous exposure)	1.25 $x10^6$ µg/m^3
Occupational Exposure Limit (8 hour)	1.20 $x10^6$ µg/m^3

Subchronic NOAEL

Inhalation was considered the only significant exposure route and a subchronic health benchmark based on the inhalation NOAEL adjusted for continuous subchronic exposure was derived thus:

Continuous Exposure Subchronic NOAEL = 1.0 g/m^3 x 6/24 = 0.25g/m^3 = $2.5x10^5$ µg/m^3

As this is a tier 1 screening exercise, and as will be seen, the results indicate very low risk, it was not considered necessary to develop formal chronic benchmark doses. The Health Benchmarks are based on subchronic exposures. The calculated Margins of Exposure (MOEs) are of such magnitude that it is clear a more detailed analysis is not necessary.

However, chronic health benchmarks (RfC and RfD) have been developed in an independent analysis of aliphatic hydrocarbons and Margins of Safety (MOS) were also calculated based on these criteria as described below.

Chronic Reference Concentration (RfC) and Chronic Reference Dose (RfD)

The Total Petroleum Hydrocarbon Criteria Working Group (TPHCWG, 1997) was formed in 1993 to address the problem of widely varying cleanup standards being used by the states

at sites which were contaminated by hydrocarbon materials such as fuels, lubricating oils, and crude oils

The Working Group was guided by a steering committee consisting of representatives from government, academia, and industry including the EPA and a number of state governments. The derived benchmarks have been adopted and implemented by several State agencies since 1997.

The TPHCWG considered some of the same studies cited in this report, identified NOAELs, and derived both a Chronic Reference Doses (RfD) and Reference Concentrations (RfC) for various fractions including the C_{10}-C_{12} aliphatic fraction which are the subject of this report. EPA methodologies were used in the derivation of these benchmarks and provide a valuable independent comparison to the conclusions of this report (See Appendix I).

A chronic RfC of 1,000 $\mu g/m^3$ and a chronic RfD of 0.1 mg/kg/day were derived.

In addition, the California Office of Environmental Health Hazard Assessment (OEHHA) recently developed an interim chronic recommended exposure limit (REL) for C_{10}-C_{11} isoparaffinic hydrocarbon solvents of 1,200 $\mu g/m^3$ (Collins, 2004). As this REL is specific to branched (isoparaffinic) aliphatic hydrocarbons it was not used, though the level is consistent with that developed by the TPHCWG. OEHHA derived this REL using a LOAEL of 2000 mg/m^3 for decreased red cell counts in a rat subchronic inhalation study. The exposure level was adjusted to 360 mg/m^3 for continuous exposure and a total uncertainty factor of 300 (3x for use of a LOAEL, 3x for subchronic to chronic, 3x interspecies, and 10x intraspecies) was applied to result in an REL of 1,200 $\mu g/m^3$.

Acute Toxicity Health Benchmarks

There are no established acute exposure limits or acute toxicity health benchmarks for decane, undecane or dodecane. In order to assess the risk from short-term exposures, the Consortium derived an acute toxicity health benchmark based on the toxicology data. From the hazard assessment, the acute health benchmark for this category is proposed as 5 g/m^3, a concentration at which no lethality would be expected. This is above the saturation air concentration for C_{11} and C_{12} alkanes, but there were no deaths even at the air saturation concentration of $8g/m^3$ for n-decane. The only significant acute effect directly demonstrated for the members of this category is dermal irritation.

Occupational Health Benchmarks

The European Chemical Industry Council (CEFIC) Hydrocarbon Solvent Producers Associations recently reviewed the existing Occupational Exposure Limits (OELs) and toxicology data for a broad range of aliphatic and aromatic hydrocarbon solvents and established a recommended occupational exposure guidance value of 1,200 mg/m^3 for C_9-C_{15} aliphatic and cycloaliphatic hydrocarbons. This guidance value was based on a review

of the toxicology data and set to protect against irritation and possible CNS effects. The documentation for this guidance value is provided in Appendix C. This is similar to the ACGIH TLV (ACGIH 2003) and the NIOSH Recommended Exposure Level (NIOSH, 1994) of 1,050 mg/m^3 for nonane (Section 4.3).

8.3. Exposure Assessment

There is a great deal of monitoring data in the peer reviewed literature on measurements of decane, undecane, and dodecane in the air of homes, schools, workplaces, automobiles, and outdoors. These studies are described in Section 6.

Infants and preschool children spend the majority of their time spent indoors at home and day care facilities. Such children are the highest exposed of any children and are therefore a primary focus of this assessment. It was conservatively assumed that such children were exposed 24 hours per day. Normal indoor exposures are higher than outdoors and children may also be more highly exposed during home renovation. School exposures appear to be unremarkable in comparison with home exposure. Similarly, automobile passengers appear to have similar exposure to that in the home.

The highest occupational parental exposure identified in the Exposure Assessment was among aviation fuel related occupations followed by painters.

Additional perspective was obtained from an EPA study. Although not a human exposure study, an EPA sponsored study of a test house (The EPA Research House) has provided data under controlled conditions on possible exposure levels resulting from application of an alkyd based primer and paint to gypsum walls of a bedroom in a sealed uninhabited house (USEPA, 2001). From the paint analysis provided in Appendix G, the authors did not speciate the normal alkane isomers from the other alkane isomers and measurements are presumed to be a combination of normal and branched isomers. Nevertheless, it was considered valuable as a bounding exercise. The results of the study are detailed in Section 6 and Appendix G. It is against manufacturers' recommendations and warnings to apply such products without adequate ventilation as done in this study which was performed to validate a model. Nevertheless, the peak values recorded may be considered to be a real worst case scenario for acute exposure to alkyd paints. Similarly, twenty-four hour TWA concentrations in the days after painting may be compared with sub-chronic benchmarks.

Exposure Scenarios Analyzed

The following receptors and scenarios were identified from the exposure assessment as being most exposed.

1. Chronic exposure of infants and children to indoor air.
2. Chronic exposure of prospective parents to indoor air.
3. Short term exposure of infants and children in a newly renovated (painted) home.

4. Short term exposure of prospective parents in a newly renovated (painted) home.
5. Prospective parents exposed occupationally in the painting trade, and refueling operations at an airport.

The relevant exposure studies applicable to each of these scenarios developed in Section 6 are summarized in Table 8.2 below.

Table 8.2 Exposure Concentrations for Selected Scenarios

Type of Measurement	Representative Concentration[1]	Upper Bound Concentration[2]	Applicable Scenario[3]	References
Average daily household indoor air concentrations	42 μg/m3	129 μg/m3	1,2	Brown et al, 1994; BRE, 1996;
Interior painting average ambient air concentrations and personal samplers	122 μg/m3	910 μg/m3	3,4,5	Brown & Crump, 1998 Wallace, 1989
Highest exposed Air force fuel workers: 1 hour average ambient exposures (personal monitors)	5,061 μg/m3	16,800 μg/m3	5	Pleil et al, 2000

1. Representative concentration is defined as the average of a set of exposure data.
2. Upper bound concentration is generally defined as the upper 95th percentile of the exposure data when adequate data were available to develop a log-normal distribution or the maximum reported level when no distribution was available.
3. 1) Chronic exposure of infants and children to indoor air.
   2) Chronic exposure of prospective parents to indoor air.
   3) Short term exposure of infants and children in a newly renovated (painted) home.
   4) Short term exposure of prospective parents in a newly renovated (painted) home.
   5) Prospective parents exposed occupationally in the painting trade and refueling operations at an airport.

8.4. Risk Assessment

A Margin of Exposure and Margin of Safety approach was taken in this assessment. EPA's definition of Margin of Exposure is the NOAEL for the critical effect divided by the Exposure Concentration (Barnes and Dourson, 1988). The Margin of Safety (MOS) may be used if there is an RfD or RfC and is defined as the RfC divided by the exposure concentration.

Thus:
Margin of Exposure

$$MOE = \frac{NOAEL}{Dose}$$ if the NOAEL is expressed as a dose.

or

$$MOE = \frac{NOAEL}{ExposureConcentration}$$ if the NOAEL is an exposure concentration.

Depending on the type of exposure scenario and animal study (acute/short term/chronic), values of MOE in excess of a 100 or 1,000 generally provide a high level of assurance that there is unlikely to be risk of harm. In this report, as the NOAEL is based on a variety of sub-chronic studies, a factor of 1,000 was considered to signify chronic risk as insignificant.

Margin of Safety:

$$MOS = \frac{RfD}{Dose} \qquad \text{or} \qquad MOS = \frac{RfC}{ExposureConcentration}$$

It might be noted that the margin of Safety is simply the reciprocal of the Hazard Quotient (HQ). An HQ of less than 1 is conventionally considered to be protective of all exposed including potentially sensitive sub-populations. Accordingly, an MOS of greater than 1, is protective.

Occupational Margin of Safety:

An occupational MOS was calculated by dividing the Occupational Exposure Limit by the exposure concentration:

Occupational $$MOS = \frac{OEL}{ExposureConcentration}$$

An Occupational MOS of greater than one is considered protective.

Exposure Assessment (Section 6) indicated that oral or dermal exposure to these volatile compounds was unlikely to be significant in comparison to inhalation.

The similarity in structure and toxicity of the three alkanes (Section 7) results in the same health benchmark for each chemical. It is therefore appropriate to sum the exposures to each chemical before calculating the Margin of Exposure and this was done in all cases.

8.4.1 Chronic Exposure at Home

Exposure in the home has been measured to range between 3.5 – 118 $\mu g/m^3$ for decane; 2.2 – 104 $\mu g/m^3$ for undecane and 1.5 – 57 $\mu g/m^3$ for dodecane (Section 6). As noted in Section 6, the highest values reported are clearly exceptional. For example, in the study reporting a maximum of 118 $\mu g/m^3$ decane (Heavner et al, 1996) in 61 homes monitored the median value was only 2.5 $\mu g/m^3$ with a mean of 6 $\mu g/m^3$ and standard deviation of 16 $\mu g/m^3$. Brown et al (1994) reported a geometric mean of 5 $\mu g/m^3$ and a 98th percentile of 47 $\mu g/m^3$ for decane. The largest value for undecane of 104 $\mu g/m^3$ was measured in a study

of 173 homes where the living room and bedroom were both sampled (BRE, 1996). The mean level of undecane in both the living room and bedroom was 14 μg/m^3 with a standard deviation of 17 μg/m^3 indicating this to be an extreme value.

Margins of Exposure (MOE) and Margins of Safety (MOS) were calculated based on the exposure concentrations derived in Section 6 and detailed in Table 8.2.

Results are summarized below. As the Health Benchmark is based on inhalation, the MOE is the same for all receptors.

Table 8.3 MARGIN OF EXPOSURE FOR CHRONIC IN HOME EXPOSURE

Receptor	Representative Exposure Concentration (μg/m^3)	MOE	Upper Bound Exposure Concentration (μg/m^3)	MOE
Infant	42	6,000	129	1,900
Children	42	6,000	129	1,900
Adults	42	6,000	129	1,900

Table 8.4 MARGIN OF SAFETY BASED ON RfC FOR CHRONIC IN HOME EXPOSURE

Receptor	Representative Exposure Concentration (μg/m^3)	MOS	Upper Bound Exposure Concentration (μg/m^3)	MOS
Infant	42	24	129	8
Children	42	24	129	8
Adults	42	24	129	8

8.4.2 Short Term Domestic Exposure during Renovation

Temporary elevated levels of the n-alkanes are associated with renovation and new construction connected with the use of paints and adhesives. For new homes, it is reported that average initial levels of undecane of 82 μg/m^3 declined to 16μg/m^3 in the second year post construction (Crump et al, 1997). In home renovation, interior painting projects have resulted in mean decane concentrations of 60 μg/m^3 (SD=150 μg/m^3) and mean undecane concentrations of 31 μg/m^3 (SD=37 μg/m^3) measured over a 4-week period in 44 homes. (Brown and Crump, 1998). A high-end exposure estimate may also be estimated from the volunteers painting indoors wearing personal samplers: Decane and undecane levels of up to 350 and 280 μg/m^3, respectively, were recorded.

Margins of Exposure (MOE) and Margins of Safety (MOS) were calculated based on the combined exposure concentrations derived in Section 6 and detailed in Table 8.2.

MOEs are tabulated below.

Table 8.5 MARGIN OF EXPOSURE FOR SHORT TERM DOMESTIC EXPOSURE DURING RENOVATION

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOE	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOE
Infant	122	2,000	910	275
Children	122	2,000	910	275
Adults	122	2,000	910	275

These MOEs are very large, especially considering the short term nature of such exposures.

Table 8.6 MARGIN OF SAFETY BASED ON RfC* FOR SHORT TERM DOMESTIC EXPOSURE DURING RENOVATION

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOS	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOS
Infant	122	8	910	1.1
Children	122	8	910	1.1
Adults	122	8	910	1.1

* The RfC addresses chronic exposure therefore exceedance in a short tern or sub-chronic scenario does not necessarily imply a risk. An acute or sub-chronic benchmark is more appropriate in such cases if available.

As can be seen, even for upper bound short-term exposure the chronic RfC is not exceeded indicating no health effects would be expected. Application of a more appropriate short-term health benchmark would provide even more assurance that health effects are unlikely.

The EPA Research House Study described in Section 6, because of its purpose (model validation), and design (uninhabited, sealed, fixed low exchange rate) does not reflect normal or recommended behavior when painting (opening windows, doors, increasing ventilation). However, short-term concentrations of the combined alkanes (probably including isomers which are not the subject of this submission) over the days following the painting still reflect a comfortable MOE which increases rapidly with time since painting as can be seen in the following table.

Table 8.7 MARGIN OF EXPOSURE (EPA Research House)

Time After painting	Representative Exposure Concentration ($\mu g/m^3$)	MOE
1 day	8,400	30
2 days	2,460	100
4 days	827	300
15 days	109	2,300
23 days	43	5,800

Peak (Acute) Exposures

Very short-term peak concentrations may be expected during painting activities. In the EPA Research House Study, peak combined levels of decane, undecane, and dodecane of 620 mg/m^3 were recorded. This level is only about $1/10^{th}$ the acute benchmark of 5,000 mg/m^3 presented in Section 7.10.2 and half the OEL of 1,200 mg/m^3. The data also indicates levels dropped rapidly (to 260 mg/m^3 in 1 hour, 89 mg/m^3 in 2 hours, 40 mg/m^3 after 6 hours, and 40 $\mu g/m^3$ after 3 weeks. Toxicity data indicates no CNS effects were observed even at near saturated concentrations. Accordingly, no acute exposure effects would be expected in children or adults at the levels of potential exposure.

8.4.3 Occupational Exposure of Parents

Parents are exposed occupationally in offices and photocopier centers, HVAC maintenance, delivery and transport occupations, construction industry and the airline industry. The highest consistent occupational exposure appears to be in aviation fuel related operations and this scenario was therefore selected to assess potential risks to the prospective parent.

The highest exposure was to workers dealing directly in fuel operations. Employees with job duties requiring direct or indirect exposure to airplane fuels and exhaust have an increased opportunity for exposure to n-alkanes in the fuels. Refueling attendants at Air Force bases (the most highly exposed) exposed to JP-8 jet fuel and exhaust had reported 1-hour average ambient exposures (personal monitors) of approximately 3,500, 1,000, and 500 $\mu g/m^3$ for n-decane, n-undecane, and n-dodecane respectively (Pleil et al., 2000). Breath samples of these workers also showed an increased exposure to decane, dodecane, and undecane in those working directly with jet fuel. Corresponding post shift breath concentrations were reported as 491 $\mu g/m^3$, 270 $\mu g/m^3$, and 208 $\mu g/m^3$ for decane, undecane, and dodecane respectively. The air measurements were 1-hour average values and no details were provided as to sampling schedules versus working practices throughout the day. Consequently, the significantly lower post shift breath measurements reflecting integrated exposure may be more representative of average exposure. This assertion is supported by the study by Wallace (1989) who took both breath and personal air samples for painters. He reported decane breath concentrations of 290 $\mu g/m^3$ were associated with personal air concentrations of 350 $\mu g/m^3$ suggesting that breath concentrations may be a reasonable surrogate for exposure concentration. Nevertheless, in the absence of more data, the reported air concentrations were used in deriving the exposure concentrations in Table 8.2.

The exposure concentrations were simply summed to estimate total exposure and adjusted to continuous exposure in the following way:

Occupational Exposure Concentration x (8hr/24hr) x (5days/7days) x 50wks/52 wks

These values were then compared against the Subchronic NOAEL to derive the following MOEs shown below.

Table 8.8 MARGIN OF EXPOSURE FOR OCCUPATONAL EXPOSURE

Prospective Parent Occupationally Exposed in Fuel Related Operations	Representative Exposure Concentration ($\mu g/m^3$)*	MOE	Upper Bound Exposure Concentration ($\mu g/m^3$)*	MOE
8 hour exposure (adjusted for continuous exposure)	1,160	200	3,850	65

*Total concentrations of the three alkanes adjusted to continuous exposure through the relation: Exposure Concentration x (8hr/24hr) x (5days/7days) x50wks/52 wks

A Margin of Safety calculation based on the 8 hour OEL of 1,200 mg/m^3 resulted in the following:

Table 8.9 MARGIN OF SAFETY BASED ON OEL FOR OCCUPATONAL EXPOSURE

Prospective Parent Occupationally Exposed in Fuel Related Operations	Representative Exposure Concentration ($\mu g/m^3$)*	MOS	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOS
8 hour exposure	5,060	237	16,800	71

*Total concentrations of the three alkanes 8-hour exposures (unadjusted)

The MOS based on the Occupational Exposure Limit (OEL), taken together with the MOE, indicate a high degree of protection for the parents in an occupational setting and indicate potential exposures are below a level of concern.

8.5 Uncertainties

There were few assumptions needed in the determination of exposure concentrations, as there is a great deal of monitoring data available. However, some judgment was necessary. In general, upper bound estimates were selected based on studies reporting the highest levels and therefore probably significantly overestimate the general population exposure. In addition, a number of studies may not have discriminated between normal and branched alkanes (or co-elutors) leading to a possible overestimation of exposure.

Extrapolating subchronic health benchmarks from animals to chronic criteria (RfCs) in humans is discussed and detailed in the IRIS draft documents. As described in IRIS, “In general, the Inhalation Reference Concentration (RfC) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human

population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime". The RfCs and RfDs derived by the TPHCWG were derived according to these guidelines and are therefore believed to be conservative (health protective). Swartout et al (1998) demonstrated that the approach used to set most RfDs and RfCs results in estimates that are probably overly conservative for the vast majority of chemicals and that this benchmark is best viewed as the lower bound of the true but unknown threshold.

For short-term exposures, such as in home renovation, the use of a chronic benchmark like the RfC may not be appropriate. However, as health benchmarks were not exceeded in any exposure scenarios, there is no need to refine any of the assumptions employed.

The addition of upper bounds on exposure to estimate combined exposure is generally considered to exceed the actual upper bound unless they are highly correlated. However, some degree of correlation is to be expected for the chemicals of interest, as petroleum streams appear to be the primary source rather than the individual pure sponsor's products.

It is recognized that using an inhalation benchmark dose does not take into account the higher dose to a child based on inhalation rate and bodyweight although EPA and others assert that RfCs are protective of children as well as adults. Calculating inhaled dose is relatively simple and the difference between an adult and a child may be calculated from data provided in the EPA Child-Specific Exposure Factors Handbook (USEPA, 2002). The greatest difference is between an infant (1 year old) and an 18 year old. The infant may receive an external dose approximately three times that of the adult. According to Tables 7-14 and 11-2 of the Handbook, the maximum inhalation dose was calculated to be 0.63 m^3/kg/day at age 1year (6.8m^3/day/10.8kg), decreasing to 0.20 m^3/kg/day (12m^3/day/59kg) by age 18 for females. Such factors are already accounted for by the intraspecies sensitivity factor in the derivation of the RfD. In any case, as can be seen from the above tables, even with a three fold increase in external dose, the adjusted MOEs would remain protective.

The reasonable question of how to aggregate doses across all exposure scenarios often arises. An obvious aggregation in this study would be an occupationally exposed parent returning home to a freshly painted house (or painting her home after work) and breastfeeding an infant. Although unlikely in total, this situation may arise. Assuming representative exposure concentrations for an airline refueler of 1,160 µg/m^3 and 122 µg/m^3 for painting, an MOE of over 200 still results. Even for upper bound exposures of 3,850 µg/m^3 and 910 µg/m^3 respectively, the MOE is over 50. The fact that this would not be a chronic scenario indicates a wider margin of exposure would be expected in the longer term. The potential exposure of the infant from human milk from such an occupational exposed mother cannot be quantified.

The potential for other aggregate exposures from multiple sources was discounted as a scenario requiring separate analysis. There is sufficient data on integrated 24-hour (multi-source) exposure indicating extremely high MOEs and MOSs. Elevated exposures to

children appear to be restricted to home renovation, are of short duration and do not appear to pose an acute or chronic health risk.

In the case of the C_{10}-C_{12} n-alkanes, as inhalation is the predominant route of exposure, no further analysis is considered necessary with the possible exception of an occupationally exposed mother exposing her infant through human milk. There is no data to quantify this scenario. However, it was shown that mothers exposed non-occupationally to urban air do not deliver a significant exposure to infants through human milk.

9. VCCEP Data Needs Assessment for n-Alkane Category

9.1 Hazard Characterization

Tier 1 VCCEP toxicity studies including those on acute toxicity, repeated-dose toxicity, reproductive and developmental toxicity and genetic toxicity are generally available for the three individual n-alkanes that are the subject of this assessment. As these three n-alkanes have similar structure, physical-chemical and fate properties, and are almost always found together in commercial products, they are being treated as a category. As the n-alkanes are not typically traded in commerce as individual chemicals, but rather as commercial n-alkane streams and as minor components of complex hydrocarbon fuel and solvent substances, data on representative commercial substances are included to further support the hazard characterization of the C_{10}-C_{12} n-alkane category. Where data do not exist for an individual n-alkane, data from other individual n-alkanes and commercial products are being used as read-across to support the hazard characterization of the chemical.

Table 9.1 Tier 1 Hazard Identification Studies Available

TIER 1 HAZARD		DECANE	UNDECANE	DODECANE	OTHER n-ALKANES
Acute Toxicity	Oral	✓	✓	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Dermal	RA	RA	RA	✓ (n-tetradecane, C_{10}-C_{13}, C_{12}-C_{14}, C_{14}-C_{17} n-alkane products)
	Inhalation	✓	✓	✓	✓ (n-nonane, n-tridecane)
In Vitro Gene Tox	Bacterial	✓	✓	RA	✓ (n-nonane, n-tetradecane; C_{10}-C_{13} n-alkane product)
	Cytogenetics	✓	✓	✓	✓ (n-tetradecane, C_{11}-C_{14} aliphatic hydrocarbon solvent)
In vivo Genetic Toxicity	Micronucleus	RA	RA	RA	✓ (C_{10}-C_{13} n-alkane product)
Repeat Dose Toxicity		✓	✓	RA	✓ (n-nonane, C_9-C_{13}, C_{10}-C_{13}, C_{11}-C_{14}, aliphatic hydrocarbon solvents)
Reproductive Toxicity Screen		✓	✓	RA	✓ (C_9-C_{13} aliphatic hydrocarbon solvent)

✓ = one or more studies available
RA = Read Across

The sponsors have concluded that there are sufficient data on one or more of the subject alkanes, or on commercial products containing substantial amounts of them, to complete a Tier 1 data set. Beyond Tier 1, there is some information on Tier 2 and Tier 3 endpoints, including metabolism, in vivo genotoxicity, neurotoxicity and carcinogenicity. All of the available animal data indicates a low potential for systemic toxicity, and no indicators of concern for specific endpoint toxicity. Human experience indicates that skin irritation from repeated dermal exposure, and lung damage from ingestion and aspiration are the primary concerns from acute exposure. There are no direct human studies that indicate systemic toxicity from repeated exposure to C_{10}-C_{12} n-alkanes, and no suggestion that children are more sensitive to any effects than adults.

Although there are not studies for all of the Tier 2 and 3 VCCEP endpoints for decane, undecane, and dodecane, these are not considered to be *data needs* which should be satisfied by the sponsors of this category. Human exposure to these n-alkanes does not occur in isolation, but rather together with the other components of hydrocarbon solvents and fuels. There are already programs in place to examine the toxicity of complex hydrocarbon mixtures, including an evaluation of jet and diesel fuel under the U.S. HPV Challenge program, a testing program by the U.S. Air Force and others to investigate the toxicity of jet fuels, and an evaluation of hydrocarbon solvents under the OECD SIDS program.

9.2 Exposure Characterization

There is a great deal of monitoring data in the peer reviewed literature on measurements of decane, undecane, and dodecane in the air of homes, schools, workplaces, automobiles, and outdoors. These studies are described in Section 6. Infants and preschool children are most likely to be exposed at home because most of their time is spent indoors at home. Exposure in the home has been measured to range between 3.5 – 66 $\mu g/m^3$ for decane; 2.2 – 104 $\mu g/m^3$ for undecane and 1.5 – 62 $\mu g/m^3$ for dodecane. The largest value of 104 $\mu g/m^3$ was measured in a study of 173 homes where the living room and bedroom were both sampled. The mean level of undecane in both the living room and bedroom was 14 $\mu g/m^3$ in this assessment. The highest parental exposure identified in the Exposure Assessment was among aviation fuel related occupations. Outdoor air concentrations are low, ranging from undetectable to about 7 $\mu g/m^3$. School exposure also appears unremarkable in relation to home exposure. Automobile passengers' exposure is similar to that in homes. There appears to be no exposure scenario resulting in higher exposures to children than to adults.

In the case of the C_{10}-C_{12} n-alkanes, as inhalation is the predominant route of exposure, no further exposure data are considered necessary with the possible exception of an occupationally exposed mother exposing her infant through human milk. There is no data to quantify this scenario. However, it was shown that mothers exposed non-occupationally to urban air do not deliver a significant exposure to infants through human milk. Additional exposure data can always be collected, so it is difficult to determine where precise data

gaps exist on exposure. The sponsors believe that the existing exposure data are adequate to characterize the exposures that children and parents are likely to experience for these alkanes. When the low toxicity of the n-alkanes is compared to the exposure data, there are large margins of exposure . There appears to be no justification for further quantitative exposure assessment on these n-alkanes.

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APPENDIX A

Table A.1 Summary of n-Alkane Concentration[1] Data Identified in the Literature

Type of Measurement	Decane	Undecane	Dodecane	Reference
1. Parental (24 hour average exposure measurements)				
Personal Air Conc. (work/leisure /travel/home) (personal monitors)	Min 9.4 – Max 54 μg/m3 Average: 9.4 – 11 μg/m3 95% 41 μg/m3	Min 7.4 – Max 73 μg/m3 Average:7.4-9.9 μg/m3 95% 29 μg/m3	Min 3.4 – Max 8.0 μg/m3 Average: 3.4-8.0 μg/m3 95% 21 μg/m3	Hoffman, 2000; Wallace, 1991; Wallace 1989
1.1. Parental/ Occupational				
1.1.1. Office/Photocopy Centers				
Max ambient conc in vicinity of office area - at breathing level of a seated employee	23 μg/m3	70 μg/m3	167 μg/m3	Daisey, 1994; Hodgson & Daisey, 1991; Hodgson, 1988
Average air concentrations in large copy centers	1.7 – 620 μg/m3	3.2 – 96 μg/m3	No Data	Stefaniak, 2000
General Offices (N=12)	GM[3]=2.9 μg/m3 GSD[4]=18 μg/m3	GM=7 μg/m3 GSD=17 μg/m3	GM=10.5 μg/m3 GSD=20 μg/m3	Daisey, 1994
General office air in new to 14 month old buildings	2.3-3.5 μg/m3	0.76 - 56.2 μg/m3	13.3 μg/m3	Hodgson & Daisey, 1991; Hodgson, 1988
New Office Buildings (Summary of data)	WAGM=75 μg/m3 90%=310 μg/m3 98%=710 μg/m3	WAGM=62 μg/m3 90%=250 μg/m3 98%=590 μg/m3	WAGM=30 μg/m3 90%=120 μg/m3 98%=280 μg/m3	Brown,1994

Type of Measurement	Decane	Undecane	Dodecane	Reference
General office air in admin, telephone company and data centers	Geo. Mean of .1-9.8 μg/m^3 with geo mean I/O ratios of 2.4-4.8.	Geo. Mean of 2.7-16.4 μg/m^3 with geo mean I/O ratios of 2.2-5.0.	Geo. Mean of 1.7-9.3 μg/m^3 with geo mean I/O ratios of 2.5-4.7.	Shields 1996
EPA Literature Summary of data on office buildings	Means: 2.3-420 μg/m^3	Means: 2.8-220 μg/m^3	No Data Reported	Samfield, 1992
Dry process photocopiers (emission rate)	62 - 450 μg/hr	62 - 2,000 μg/hr	70 - 960 μg/hr	Leovic, 1998; Leovic, 1996
New office chairs	No Data	0.31 mg/chair/hour @ manuf. Reduce to <0.04 mg/chair/hr 168 hours after manuf.	No Data	RTI, 1999
Personal breathing zones in photocopy centers	1.8 – 530 μg/m3	3.8 – 65 μg/m3	No Data	Stefaniak, 2000

1.1.2. Construction Occupations

Painters - interior painting ambient air concs	60 (150 SD) μg/m3	31 (37 SD) μg/m3	No Data	Brown & Crump, 1998
Interior painters personal air samples	Median: 48 μg/m3 Max: 350 μg/m3	Median:30 μg/m3 Max: 280 μg/m3	No Data	Wallace, 1989
Interior Painters (Oil-based paint. Sealed empty house, 0.48 air changes per hour)	**Total C10 - C12 n-alkanes:** Peak: 4,780 μg/m3 Highest 24 hour TWA: 510 μg/m3 TWA after 15 days: 109 μg/m3 TWA after 23 days: 43 μg/m3			EPA Research House. USEPA, 2001
Interior painters breath samples	290 μg/m3 (one sample)	No Data	No Data	Wallace et al, 1989

1.1.3. Maintenance

Ventilation ducts - ambient air conc	No Data	831.3 μg/m3 (max)	280.8 μg/m3 (max)	Hodgson & Daisey, 1991

Type of Measurement	Decane	Undecane	Dodecane	Reference
Mean conc in ventilation shafts	No Data	48.3 μg/m3	10.9 μg/m3	Hodgson & Daisey, 1991
Mean conc on roofs	No Data	5.3 μg/m3	2.0 μg/m3	Hodgson & Daisey, 1991

1.1.4. Delivery / Transport

Auto travelers average air concs during travel	17.4 μg/m3	16.4 μg/m3	5.9 μg/m3	Wallace, 1991;
Personal air samples for auto travelers	Median 10 μg/m3 Max: 53 μg/m3	Median: 7.8 μg/m3 Max: 43 μg/m3	No Data	Wallace 1989

1.1.5. Air Force / Airline Industry

Pilots/Attendants	(TVOC = 3 ppb)	(TVOC = 3 ppb)	(TVOC = 3 ppb)	Brady, 1999
All Fuel related staff. Average breath concs.	240 μg/m3 (SEM=33 μg/m3) n=85	100 μg/m3 (SEM= 16 μg/m3) n=85	63 μg/m3 (SEM=14 μg/m3) n=85	Pleil, 2000
Fuel tank entry average breath concs. (respiratory protection worn)	243 μg/m3 (SEM=74 μg/m3) n=15	270 μg/m3 (SEM=68 μg/m3) n=15	208 μg/m3 (SEM=67 μg/m3) n=15	Pleil, 2000
Highest exposed Air Force fuel attendants: average post shift breath concentrations	491 μg/m3 (SEM = 57 μg/m3) n=30	270 μg/m3 (SEM = 9 μg/m3) n=30	208 μg/m3 (SEM=9 μg/m3) n=30	Pleil, 2000
Highest exposed Air Force fuel workers: 1 hour average ambient exposures (personal monitors)	3,552 μg/m3 (SEM=2,147 μg/m3) n=9	1,020 μg/m3 (SEM=405 μg/m3) n=9	489 μg/m3 (SEM=95 μg/m3) n=9	Pleil, 2000
Aircraft exhaust workers breath concs	3.8 μg/m3	5.9 μg/m3	6.4 μg/m3	Pleil, 2000
Non-aircraft related job duties on Air Force base breath concs	1.1 μg/m3	1.5 μg/m3	2.1 μg/m3	Pleil, 2000

Type of Measurement	Decane	Undecane	Dodecane	Reference
1.2. Parental Non-Occupational Exposure				
1.2.1. Indoor Sources of Exposure				
Average daily household indoor air concs	3.5 – 118 μg/m3 WAGM[2] = 5 μg/m3 90% = 20 μg/m3 98% = 47 μg/m3	2.2 - 104 μg/m3 mean: 14 μg/m3 SD= 17 μg/m3 95% = 50 μg/m3 (n=173)	1.5 - 57 μg/m3	Brown et al,1994; BRE, 1996; Brown & Crump, 1995; Kostiainen, 1995; Phillips et al, 1997;Wallace, 1991, Heavner,1996
EPA Survey of Literature on concentrations reported in homes	Med: <3-21 μg/m^3 Means: 0.7-92 μg/m^3 Max: 8-1100 μg/m^3	Med: <3-30μg/m^3 Means: 1.1-80 μg/m^3 Max: 9-950 μg/m^3	Med: 1-4 μg/m^3 Means: 1.1-20 μg/m^3 Max: 4-675 μg/m^3	Samfield, 1992
EPA National VOC Data Base	Median: 1.6 μg/m3 Average 4.5 μg/m3 Upper Quartile: 4.1 μg/m3	Median: 1.8 μg/m3 Average 4.8 μg/m3 Upper Quartile: 3.8 μg/m3	No Data Reported	Shah and Singh 1988
Mobile Home	No Data	Max: 41 μg/m^3 SD=4.3 μg/m3	No Data	Samfield, 1992
Hospitals	WAGM – 37 μg/m^3 90%ile – 150 μg/m^3 98%ile – 350 μg/m^3	WAGM – 37 μg/m^3 90%ile – 150 μg/m^3 98%ile – 350 μg/m^3	WAGM – 17 μg/m^3 90%ile – 69 μg/m^3 98%ile – 150 μg/m^3	Brown, 1994
1.2.1.1. New and Renovated Homes				

Type of Measurement	Decane	Undecane	Dodecane	Reference
New homes	WAGM= 390 μg/m3 90% = 1600 μg/m3 98%=3700 μg/m3			Brown, 1994
No humans present. Poor or no ventilation.	Median 141 μg/m3 90th percentile: 669 μg/m3 max: 916 μg/m3	Mean 82 μg/m3 1st year to 16 μg/m3 2nd year max 276 μg/m3	No Data	Crump, 1997; Rothweiler, 1992

1.2.1.2 Household Maintenance or Renovation

Painters - interior painting average ambient air concs	60 (150 SD) μg/m3	31 (37 SD) μg/m3	No Data	Brown & Crump, 1998
Interior painters breath samples	290 μg/m3 (one sample)		No Data	Wallace et al., 1989
Interior Painters (Oil-based paint. Sealed empty house, 0.48 air changes per hour)	**Total C10 - C12 n-alkanes:** Peak: 4,780 μg/m3 Highest 24 hour TWA: 510 μg/m3 TWA after 15 days: 109 μg/m3 TWA after 23 days: 43 μg/m3			EPA Research House. USEPA, 2001
Interior painters personal air samples	Median: 48 μg/m3 Max: 350 μg/m3	Median:30 μg/m3 Max: 280 μg/m3	No Data	Wallace, 1989

1.2.2. Outdoor Sources of Exposure

Ambient air concs. In residential and urban areas	0.47 - 3.7 μg/m3	0.10 - 6.7 μg/m3	0.20 - 4.0 μg/m3	CONCAWE, 1999 (Bertorelli and Derwent, 1995); Brown & Crump, 1995, 1998; Hartwell, 1992; Michael, 1990; Phillips, 1997

1.2.2.3. Automobile Travel

Type of Measurement	Decane	Undecane	Dodecane	Reference
Auto travelers average air concs during travel	17.4 μg/m3	16.4 μg/m3	5.9 μg/m3	Wallace, 1991;
Personal air samples for auto travelers	Median 10 μg/m3 Max: 53 μg/m3	Median: 7.8 μg/m3 Max: 43 μg/m3	No Data	Wallace 1989

2. Childhood

2.1. Indoor Sources of Exposure

2.1.1. Household Exposure

Average daily household indoor air concs	3.5 – 118 μg/m3 WAGM[2] = 5 μg/m3 90% = 20 μg/m3 98% = 47 μg/m3	2.2 - 104 μg/m3 mean: 14 μg/m3 SD= 17 μg/m3 (n=173)	1.5 - 57 μg/m3	Brown et al,1994; BRE, 1996; Brown & Crump, 1995; Kostiainen, 1995; Phillips et al, 1997;Wallace, 1991, Heavner,1996
EPA Survey of Literature on concentrations reported in homes	Med: <3-21 μg/m^3 Means: 0.7-92 μg/m^3 Max: 8-1100 μg/m^3	Med: <3-30μg/m^3 Means: 1.1-80 μg/m^3 Max: 9-950 μg/m^3	Med: 1-4 μg/m^3 Means: 1.1-20 μg/m^3 Max: 4-675 μg/m^3	Samfield, 1992
EPA National VOC Data Base	Median: 1.6 μg/m3 Average 4.5 μg/m3 Upper Quartile: 4.1 μg/m3	Median: 1.8 μg/m3 Average 4.8 μg/m3 Upper Quartile: 3.8 μg/m3	No Data Reported	Shah and Singh 1988
Mean VOC concs in homes of newborn and preschool aged children respectively	20.2 and 19.9 μg/m3	19.7 and 18.9 μg/m3	16.4 and 12.2 μg/m3	Herbath, 1998

Type of Measurement	Decane	Undecane	Dodecane	Reference
Mobile Home	No Data	Max: 41 μg/m^3 SD=4.3 μg/m3	No Data	Samfield, 1992

2.1.1.1. New and Renovated Homes

No humans present. Windows closed Poor or no ventilation.	Median 141 μg/m3 90th percentile: 669 μg/m3 max: 916 μg/m3	Mean 82 μg/m3 1st year to 16 μg/m3 2nd year max 276 μg/m3	No Data	Crump, 1997; Rothweiler, 1992

2.1.1.2.Household Maintenance or Renovation

Painters - interior painting average ambient air concs	60 (150 SD) μg/m3	31 (37 SD) μg/m3	No Data	Brown & Crump, 1998
Interior painters personal air samples	Median: 48 μg/m3 Max: 350 μg/m3	Median:30 μg/m3 Max: 280 μg/m3	No Data	Wallace, 1989
Interior Painters (Oil-based paint. Sealed empty house, 0.48 air changes per hour)	**Total C10 - C12 n-alkanes:** Peak: 4,780 μg/m3 Highest 24 hour TWA: 510 μg/m3 TWA after 15 days: 109 μg/m3 TWA after 23 days: 43 μg/m3			EPA Research House. USEPA, 2001
Home concentrations in 1st 4 weeks after birth Upper confidence limits (n=401)	25.6 μg/m3	23.5 μg/m3	17.6 μg/m3	Diez, 2000
Interior painters breath samples	290 μg/m3 (one sample)	No Data	No Data	Wallace et al., 1989

2.1.2. School-related

Avg. concs in kindergarten school	6.6 μg/m3	12.8 μg/m3	15.6 μg/m3	Herbarth, 1998

Type of Measurement	Decane	Undecane	Dodecane	Reference
School	Mean: 5.98 μg/m3	Mean: 6.77 $\mu g/m^3$	No Data Reported	Samfield, 1992
Concentration in Canadian elementary school	Mean 1.4 μg/m3 Max: 7.5 μg/m3	No Data	No Data	Probert, 2000

2.2. Outdoor Exposures

2.2.1. Ambient Air

Ambient air concs. In residential and urban areas	0.47 - 3.7 μg/m3	0.10 - 6.7ug/m3	0.20 - 4.0 μg/m3	CONCAWE, 1999 (Bertorelli and Derwent, 1995); Brown & Crump, 1995, 1998; Hartwell, 1992; Michael, 1990; Phillips, 1997
Outdoor air at a kindergarten school	2.0 μg/m3	0.8 μg/m3	1.1 μg/m3	Herbarth, 1998

2.2.1.2. Automobile Travel

Auto travelers average air concs during travel	17.4 μg/m3	16.4 μg/m3	5.9 μg/m3	Wallace, 1991;
Personal air samples for auto travelers	Median 10 μg/m3 Max: 53 μg/m3	Median: 7.8 μg/m3 Max: 43 μg/m3	No Data	Wallace 1989

1. All concentration data expressed in μg/m3 through the following conversion factors:
   decane: 1 ppb = 5.8 μg/m3
   undecane: 1 ppb = 6.4 μg/m3
   dodecane: 1 ppb = 7.0 μg/m3
2. WAGM= Weighted Average Geometric Mean
3. GM = Geometric Mean
4. GSD= Geometric Standard Deviation
5. SD=Standard Deviation
6. %=Percentile

Table A.2 EPA Air Monitoring Data for Decane, Undecane and Dodecane

Study	Decane Results	Undecane Results	Dodecane Results
Shields 1996	Geo. Mean of 4.1-9.8 μg/m^3 (0.7-1.6 ppb), with geo mean I/O ratios of 2.4-4.8.	Geo. Mean of 2.7-16.4 μg/m^3 (0.4-2.6 ppb), with geo mean I/O ratios of 2.2-5.0.	Geo. Mean of 1.7-9.3 μg/m^3 (0.2-1.3 ppb), with geo mean I/O ratios of 2.5-4.7.
Daisey 1994	Geo. Mean of 0.49±3.1 ppb (2.85±18.0μg/m^3), and range of <0.1-3.9 ppb (<0.6-22.7μg/m^3), Range I/O ratios of 0.07-4.0.	Geo. Mean of 1.1±2.7 ppb (2.85±18.0μg/m^3), and range of <0.1-11 ppb (<0.6-70 μg/m^3), Range I/O ratios of <0.1-5.9.	Geo. Mean of 1.5±2.8 ppb (10.5±19.5μg/m^3), and range of 0.44-24 ppb (3.1-167μg/m^3), Range I/O ratios of 0.27-110.
Brown 1994	Established Buildings Dwelling: WAGM – 5 μg/m^3 (0.86 ppb) 90%ile – 20 μg/m^3 (3.4 ppb) 98%ile – 47 μg/m^3 (8.1 ppb) New Buildings Office WAGM – 75 μg/m^3 (13 ppb) 90%ile – 310 μg/m^3 (53 ppb) 98%ile – 710 μg/m^3 (122 ppb) Hospital WAGM – 37 μg/m^3 (6.4 ppb) 90%ile – 150 μg/m^3 (26 ppb) 98%ile – 350 μg/m^3 (60 ppb) Dwelling WAGM – 390 μg/m^3 (67ppb) 90%ile – 1600 μg/m^3 (275ppb) 98%ile – 3700 μg/m^3 (636ppb)	New Buildings Office WAGM –62 μg/m^3 (9.7ppb) 90%ile – 250 μg/m^3 (39 ppb) 98%ile – 590 μg/m^3 (92 ppb) Hospital WAGM – 37 μg/m^3 (5.8 ppb) 90%ile – 150 μg/m^3 (23 ppb) 98%ile – 350 μg/m^3 (55 ppb)	New Buildings Office WAGM – 30 μg/m^3 (4.3 ppb) 90%ile – 120 μg/m^3 (17 ppb) 98%ile – 280 μg/m^3 (40 ppb) Hospital WAGM – 17 μg/m^3 (2.4 ppb) 90%ile – 69 μg/m^3 (9.9 ppb) 98%ile – 150 μg/m^3 (22 ppb)
Samfield 1992	Results Reported in Residences: Med: <3-21 μg/m^3 (0.5- 3.6ppb) Means: 0.7-92 μg/m^3 (0.1- 16ppb) Max: 8-1100 μg/m^3 (1.4- 189ppb) Results Reported in Office Buildings: Means: 2.3-420 μg/m^3 (0.4- 72ppb) Result Reported in a School: Mean: 5.98 μg/m^3 (1 ppb) Results Reported in a Nursing Home: Mean: 1.87 μg/m^3 (0.3 ppb)	Results Reported in Residences: Med: <3-30 μg/m^3 (<0.47- 4.7ppb) Means: 1.1-80 μg/m^3 (0.17- 13 ppb) Max: 9-950 μg/m^3 (1.4- 149ppb) Results Reported in Office Buildings: Means: 2.8-220 μg/m^3 (0.44- 34 ppb) Result Reported in a School: Mean: 6.77 μg/m^3 (1.1 ppb) Results Reported in a Mobile Home: Max: 41 μg/m^3 (6.4 ppb)	Results Reported in Residences: Med: 1-4 μg/m^3 (0.14- 0.57ppb) Means: 1.1-20 μg/m^3 (0.16- 2.9 ppb) Max: 4-675 μg/m^3 (0.57- 97ppb)

Table A.2 (cont'd)

Study	Decane Results	Undecane Results	Dodecane Results
Shah and Singh 1988	Indoor Air Median: 0.280 ppb Average 0.775 ppb Upper Quartile: 0.700 ppb	Indoor Air Median: 0.282 ppb Average 0.746 ppb Upper Quartile: 0.600 ppb Outdoor Air Median: 0.188 ppb Average 0.745 ppb Upper Quartile: 0.618 ppb	Not Reported
Conversion	1ppb= 5.82 $\mu g/m^3$	1ppb= 6.39 $\mu g/m^3$	1ppb= 6.97 $\mu g/m^3$
Notes: I/O = indoor/ outdoor ratio; WAGM= weighted average geometric mean; 90%ile = 90th Percentile; 98%ile = 98th Percentile			

Appendix B

Toxicity Studies Robust Summaries

1.0 Acute Toxicity

1.1 Acute Oral Toxicity

Robust Summary No.: ACTO-1

Acute Toxicity

Test Substance:	CAS No. 64741-72-8, C10-C13 normal paraffins
Vehicle:	N/A
Type of Study:	Oral LD_{50}
Species/strain:	Rat / Sprague Dawley
No. of animals/sex/dose:	5/sex
Route of administration:	Oral Gavage
Frequency of treatment:	Single dose
Dose/Conc. Levels:	5000 mg/kg
Doses per time period:	Single
Control group and treatment:	N/A
Remarks on Test Conditions:	
Method/Guideline:	OECD Guideline 401
GLP:	GLP equivalent
Date (Year):	1983
Results (LD_{50} or LC_{50}):	Oral LD_{50} > 5000 mg/kg
Remarks:	There were no mortalities throughout the study. Body weights of all animals increased over the 14 day test period. Ano-genital staining was observed in most of the animals at the 6 hour interval. There were no treatment-related abnormalities on postmortem examination.
Conclusions:	Under the conditions of this study, the oral LD_{50} for this test material is greater than 5000 mg/kg.
Remarks:	

Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1983. Acute Oral Toxicity Study in the Rabbit. Study no. 320501. Unpublished Study**.**

Robust Summary No.: ACTO-2

Acute Toxicity

Test Substance:	PETREPAR® n-C10 (97% 1-decane)
Vehicle:	Test material administered as is without dilution
Type of Study:	Acute Oral Toxicity (limit test)
Species/strain:	Rat/Sprague- Dawley
No. of animals/sex/dose:	5
Route of administration:	Oral (gavage)
Frequency of treatment:	single application
Dose/Conc. Levels:	5.0 g/Kg body weight
Doses per time period:	1
Control group and treatment:	none
Remarks on Test Conditions:	No protocol deviations
Method/Guideline:	OECD 401
GLP:	No
Date (Year):	1984
Results (LD_{50} or LC_{50}):	LD_{50} > 5.0 g/Kg body weight
Remarks:	No deaths occurred during the course of the study. Piloerection was observed shortly after dosing in all animals. Recovery, as judged by external appearance and behavior, was apparently complete by day 3. Terminal necropsy findings were normal.
Conclusions:	The acute lethal oral dose to rats of the test material was found to be > 5.0 g/Kg bodyweight
Remarks:	none
Data Quality:	1

References:	PETRESA (Petroquimia Espanola S.A.) (1984). Acute Oral Toxicity to Rats of PETREPAR® n-C10 (C10).

Robust Summary No.: C9-13ALL ACTO-3

Acute Toxicity

Test Substance:	CAS No. 1120-21-4, undecane (= or > 99%)
Vehicle:	Olive oil
Type of Study:	Acute Oral LD_{50}
Species/strain:	Rat / Crj:CD® (SD)
No. of animals/sex/dose:	5/sex
Route of administration:	Oral Gavage
Frequency of treatment:	Single dose
Dose/Conc. Levels:	0, 500, 1000, 2000 mg/kg
Doses per time period:	One
Control group and treatment:	olive oil- Vehicle control
Remarks on Test Conditions:	none
Method/Guideline:	OECD Guideline 401
GLP:	GLP
Date (Year):	1996
Results (LD_{50} or LC_{50}):	Oral LD_{50} > 2000 mg/kg, for both males and females
Remarks:	All treated and control groups exhibited loose stools, diarrhea was observed in one male. Body weight changes for the treated animals were comparable to controls. No deaths occurred in either males or females of any of the treated groups. No effects were detected in terms of general condition, body weights changes, autopsy, or histopathology findings.
Conclusions:	Oral LD_{50} > 2000 mg/kg
Remarks:	none
Data Quality:	1, no restrictions
References:	Yoshimura et al., 1996. Ministry of Health and Welfare, Japan,

1996. Single Dose Oral Toxicity Test of Undecane in Rats. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

Robust Summary No.: ACTO-4

Acute Toxicity

Test Substance:	CAS No. 64771-72-8, C14-C17 normal paraffins
Vehicle:	N/A
Type of Study:	Acute Oral LD_{50}
Species/strain:	Rat / Sprague Dawley
No. of animals/sex/dose:	5/sex
Route of administration:	Oral Gavage
Frequency of treatment:	Single dose
Dose/Conc. Levels:	5000 mg/kg
Doses per time period:	1
Control group and treatment:	N/A
Remarks on Test Conditions:	-
Method/Guideline:	OECD Guideline 401
GLP:	In the spirit of GLP
Date (Year):	1983
Results (LD_{50} or LC_{50}):	Oral LD_{50} > 5000 mg/kg
Remarks:	There were no mortalities and all animals displayed increases in body weight over their initial Day 0 weights. There were few clinical in-life observations during the test period. Ano-genitial staining was noted in most animals at the 4 and 6 hours observation. Other in-life observations included alopecia and unthrifty coat. The only gross postmortem observation was lung discoloration in 7 of the 10 test animals.
Conclusions:	Based on the results of this study, the acute oral LD_{50} in rats is greater than 5000 mg/kg.
Remarks:	

Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1983. Acute Oral Toxicity Study in the Rat. Study No. 320701. Unpublished Study.

Robust Summary No.: ACTO-5

Acute Toxicity

Test Substance:	CAS No. 64771-72-8, C12-C14 normal paraffins
Vehicle:	N/A
Type of Study:	Acute Oral LD_{50}
Species/strain:	Rat / Sprague Dawley
No. of animals/sex/dose:	5/sex
Route of administration:	Oral Gavage
Frequency of treatment:	Single dose
Dose/Conc. Levels:	5000 mg/kg
Doses per time period:	One
Control group and treatment:	N/A
Remarks on Test Conditions:.	
Method/Guideline:	OECD Guideline 401
GLP:	In the spirit of GLP
Date (Year):	1983
Results (LD_{50} or LC_{50}):	Oral LD_{50} > 5000 mg/kg
Remarks:	All animals survived to study termination. All animals showed body weight increases over their initial Day 0 values. The only inlife finding was ano-genital staining, observed in 6 animals at 4 hours and in 9 animals at the 6-hour observation period. Other toxicological signs noted at a low incidence were dry rales, urinary staining, unthrifty coat and soft stool. No observable abnormalities were noted in the animals after Day 1. Postmortem examination showed a 1 animal with a dilated renal pelvis, 2 animals with mottling of the kidneys, 1 animal with both scattered dark red foci and mottled surfaces and 2 animals with scattered red foci on the lungs.

Conclusions:	Oral LD_{50} > 5000 mg/kg
Remarks:	
Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1983. Acute Oral Toxicity Study in the Rat. Study No. 320601A. Unpublished Study.

Robust Summary No.: ACTO-6

Acute Toxicity

Test Substance:	PETREPAR® n-C14 (95% 1-tetradecane)
Vehicle:	Test material administered as is without dilution
Type of Study:	Acute Oral Toxicity (limit test)
Species/strain:	Rat/Sprague- Dawley
No. of animals/sex/dose:	5
Route of administration:	Oral (gavage)
Frequency of treatment:	single application
Dose/Conc. Levels:	5.0 g/Kg body weight
Doses per time period:	1
Control group and treatment:	none
Remarks on Test Conditions:	No protocol deviations
Method/Guideline:	OECD 401
GLP:	Not reported
Date (Year):	1984
Results (LD_{50} or LC_{50}):	LD_{50} > 5.0 g/Kg body weight
Remarks:	No deaths occurred during the course of the study. Piloerection was observed shortly after dosing in all animals. Recovery, as judged by external appearance and behavior, was apparently complete by day 3. Terminal necropsy findings were normal.
Conclusions:	The acute lethal oral dose to rats of the test material was found to be > 5.0 g/Kg bodyweight
Remarks:	none

Data Quality:	1
References:	Petroquimia Espanola S.A. (1984). Acute Oral Toxicity to Rats of PETREPAR® n-C14 (C14).

1.2 Acute Inhalation Toxicity

Robust Summary No.: ACTI-1

Acute Toxicity

Test Substance:	Technical grade n-nonane (98.4% n-nonane)
Vehicle:	N/A
Type of Study:	Acute Inhalation LC_{50}
Species/strain:	Rats / Harlan-Wistar
No. of animals/sex/dose:	10 males
Route of administration:	Inhalation
Frequency of treatment:	Single
Dose/Conc. Levels:	1.33, 4.6, 11, 23 mg/L
Doses per time period:	4-hour
Control group and treatment:	
Remarks on Test Conditions:	Six of the ten animals were designated for gross necropsy and histopathological evaluation, three immediately after completion of the 4-hr inhalation period and three after 2 days.
Method/Guideline:	Similar to OECD Guideline 403
GLP:	No
Date (Year):	1977
Results (LD_{50} or LC_{50}):	LC_{50} = 17 mg/L or 3200 ppm
Remarks:	Mortality: No deaths in the 1.33 and 4.6 mg/L dose groups. 11 mg/L - 1 out of 10 rats died 23 mg/L - 8 out of 10 rats died The response pattern during inhalation of the highest level progressed from early lacrimation, salivation, and coordination loss to clonic and tonic convulsions, tremors and death.

	Micropathological evaluation of tissues taken at necropsy, 14 days following each of the single 4-hr inhalation periods, revealed no lesion attributable to vapor inhalation.
Conclusions:	Under the condition of this study, the 4-hour inhalation LC_{50} in rats is 17 mg/L (3200 ppm)
Remarks:	
Data Quality:	2, with restrictions
• **Data reliability assessment:**	Only male animals used
References:	Carpenter, C.P. *et al*. 1978. Petroleum Hydrocarbon Toxicity Studies XVII. Animal Response to n-Nonane Vapor. Tox and Appl. Pharmacology. 44:53-61.

Robust Summary No.: ACTI-2

Acute Toxicity

Test Substance:	n-alkanes from C9 to C13 with > 99% purity
Vehicle:	N/A
Type of Study:	Acute Inhalation LC_{50}
Species/strain:	Rat / Sprague Dawley
No. of animals/sex/dose:	10 animals/dose; male only
Route of administration:	Inhalation
Frequency of treatment:	Single 8-hour exposure
Dose/Conc. Levels:	Nonane: 5280±77*, 4438±319**, 3560±17, 2414±7 ppm Decane: 1369±19 ppm** Undecane: 442±32 ppm** Dodecane: 142±13 ppm** Tridecane: 41±8 ppm** * Saturation concentration in air at 22.5° C and at 760 mm Hg. **Saturation concentration in air at 21.6° C and at 760 mm Hg.
Doses per time period:	Nonane: 4 Decane, Undecane, Dodecane, Trideance: 1
Control group and treatment:	Control groups of 4 animals treated to air.
Remarks on Test Conditions:	Air concentrations measured at 15-min intervals. Only nonane had sufficient volatility to test at multiple dose levels, other n-alkanes

	were tested at the maximum achievable vapor (saturation concentration).
Method/Guideline:	Similar to OECD Guideline 403
GLP:	No data
Date (Year):	1988
Results (LD_{50} or LC_{50}):	Nonane: LC_{50} = 4467±189 ppm Decane: LC_{50} >1369 ppm (saturation level) Undecane: LC_{50} > 442 ppm (saturation level) Dodecane: LC_{50} > 142 ppm (saturation level) Tridecane: LC_{50} > 41 ppm (saturation level)
Remarks:	Only Nonane was found to be volatile enough to develop lethal air concentrations. The authors found good dose-response to the 4 nonane air concentrations for mortality; mortality rates by dose: 9/10 at 5280 ppm, 4/10 at 4438 ppm, 1/10 at 3560 ppm, and 0/10 at 2414 ppm. Other clinical effects for nonane included tremor, spasms and limb paralysis at highest dose. All surviving animals made an apparent full recovery within 7 days post-exposure. No additional deaths or symptoms were observed during a 14-day observation period. For nonane, postmortem examination showed dilation of the sinusoids and marked pulmonary edema in the animals that died during treatment. Decane, undecane, dodecane, and tridecane produced no deaths or adverse behavioral effects at the maximum achievable air concentration (saturation level). No deaths or symptoms were observed during a 14-day observation period. No pathological changes in the large brain or other organs were noted in the postmortem examination.
Conclusions:	Based on the results of this study, the inhalation LC_{50} is: 4467 ppm for n-nonane, greater than 1369 ppm for n-decane, greater than 442 ppm for n-undecane, greater than 142 ppm for n-dodecane, and greater than 41 ppm for n-tridecane.
Remarks:	
Data Quality:	2, with restrictions
Data reliability assessment:	8-hour exposure duration, male only
References:	Nilsen, O. G. et al. 1988. Toxicity of n-alkanes in the rat on short term inhalation. Pharmacol. & Toxicol. 62:259-266.

1.3 Acute Dermal Toxicity

Robust Summary No.: ACTD-1

Acute Toxicity

Test Substance:	CAS No. 64771-72-8, C10-C13 normal paraffins
Vehicle:	N/A
Type of Study:	Dermal LD_{50}
Species/strain:	Rabbit / New Zealand White
No. of animals/sex/dose:	3/sex
Route of administration:	Dermal application
Frequency of treatment:	
Dose/Conc. Levels:	3160 mg/kg
Doses per time period:	Single 24 hour topical occlusive application
Control group and treatment:	N/A
Remarks on Test Conditions:	
Method/Guideline:	Similar to OECD Guideline 402
GLP:	GLP equivalent
Date (Year):	1983
Results (LD_{50} or LC_{50}):	Dermal LD_{50} > 3160 mg/kg
Remarks:	One animal was found dead on Day 5 of the study. All but one of the surviving animals gained weight during the test period. Clinical inlife observations included decreased food consumption, emaciation, alopecia, nasal discharge and fecal staining. The test material elicited moderate to severe dermal irritation in all animals at the 24 hours observation period. The severity of the irritation decreased throughout the study and by Day 14 only 4 of the animals exhibited slight irritation. Desquamation was noted in 3 of the animals. Postmortem examination of the animal that died prior to study termination were unremarkable. The only postmortem finding was noted in one animal, an irregular shaped and penetrating white area on the medial lobe surface of the liver.
Conclusions:	Topical occlusive application of this test material produced moderate to severe dermal irritation in all animals. Under the conditions of this study, the dermal LD_{50} for this test material is greater than 3160 mg/kg.

Remarks:

Data Quality: 1

References: ExxonMobil Biomedical Sciences, Inc. 1983. Acute Dermal Toxicity Study in the Rabbit. Study No. 320506. Unpublished Study.

Robust Summary No.: ACTD-2

Acute Toxicity

Test Substance: CAS No. 64771-72-8, C14-C17 normal paraffins

Vehicle: N/A

Type of Study: Acute Dermal LD_{50}

Species/strain: Rabbit / New Zealand White

No. of animals/sex/dose: 3/sex

Route of administration: Dermal

Frequency of treatment: Single occluded exposure (24 hours)

Dose/Conc. Levels: 3.16 g/kg

Doses per time period: 1

Control group and treatment: None

Remarks on Test Conditions: None

Method/Guideline: OECD Guideline 402

GLP: In the spirit of GLP

Date (Year): 1983

Results (LD_{50} or LC_{50}): LD_{50} > 3.16 g/kg

Remarks: There were no animal deaths during the course of the study. Topical 24 hour occlusive application produced moderate to severe dermal irritation in all animals. However, by the Day 14 observations, 4 of the 6 test animals were clear of all signs of irritation, and 2 animals showed very slight erythema. Desquamation was noted in several animals during the test period.

Clinical in-life observations were minimal and there were no lesions noted on the gross postmortem examinations that were considered to be treatment-related.

Conclusions:	Dermal LD_{50} > 3.2 g/kg
Remarks:	
Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1983. Acute Dermal Toxicity Study in the Rabbit. Study No. 320706. Unpublished Study.

Robust Summary No.: ACTD-3

Acute Toxicity

Test Substance:	CAS No. 64771-72-8, C12-C14 normal paraffins
Vehicle:	N/A
Type of Study:	Acute Dermal LD_{50}
Species/strain:	Rabbit / New Zealand White
No. of animals/sex/dose:	5/sex/dose group
Route of administration:	Dermal occlusive application
Frequency of treatment:	Single 24 hour exposure
Dose/Conc. Levels:	5000 mg/kg
Doses per time period:	1
Control group and treatment:	n-hexane was used as a positive control
Remarks on Test Conditions:	This study was conducted to evaluate the acute dermal toxicity of the test material and to duplicate the effects reported in a previous study at another laboratory. A single dose of 5000 mg/kg of the test material (or n-hexane, used as positive control) was applied under occlusive conditions to the skin of 3 groups of 5 rabbits/sex/group. The test material was applied to intact skin (Group 1 animals) and abraded skin (Group 2 animals). In addition to clinical observations, gait and righting reflex were noted and videotaped on selected days. After the 14 day observation, gross necropsies were performed on all animals and peripheral nerve tissues from one animal in Group 2 (abraded skin) and one untreated animal were processed, stained and examined.
Method/Guideline:	Other, Similar to OECD Guideline 402
GLP:	In the spirit of GLP

Date (Year):	1994
Results (LD_{50} or LC_{50}):	Dermal LD_{50} > 5000 mg/kg
Remarks:	Mortality was limited to 1 animal which was euthanized on Day 2 in moribund condition. This animal was noted with impaired use of both hind limbs and the right forelimb, soft stool, poor food consumption, and absence of righting reflex prior to its sacrifice. Clinical signs of toxicity were observed in all treatment groups primarily during the early part of the study, and included decreased food consumption, staggered gait, decreased righting reflex, ataxia, and dermal irritation. All surviving animals displayed increases in body weight over their Day 0 values. There appeared to be suppression of body weight gain and body weight loss in 2 animals during the first week of the study. Treatment-related dermal irritation was comparable in both the abraded and unabraded groups. At postmortem examination, all animals in all groups displayed desquamation. There were also single incidences of scabs, eschar, necrosis and cracking of the test site. No definitive histopathologic changes were observed in the peripheral nerve (brachial plexus) of the 2 animals examined microscopically.
Conclusions:	Topical application of 5000 mg/kg of test material elicited slight to moderate dermal effects in the majority of the animals. The acute dermal LD_{50} is greater than 5000 mg/kg. Several effects (decreased righting reflex, ataxia and staggered gait) may have been neurological in origin. These effects were observed primarily during the early part of the study. Microscopic evaluation did not reveal any neurohistopathologic changes.
Remarks:	
Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1994. Acute Dermal Toxicity Study in the Rabbit. Study No. 140506C. Unpublished Study.

Robust Summary No.: ACTD-4

Acute Toxicity

Test Substance:	PETREPAR® n-C14 (95% 1-tetradecane)
Vehicle:	Test material administered as is without dilution

Type of Study:	Acute Dermal Toxicity (limit test)
Species/strain:	Rat/Sprague- Dawley
No. of animals/sex/dose:	5
Route of administration:	Dermal
Frequency of treatment:	single application
Dose/Conc. Levels:	2.0 g/Kg body weight
Doses per time period:	1
Control group and treatment:	none
Remarks on Test Conditions:	No protocol deviations
Method/Guideline:	OECD 402
GLP:	Not reported
Date (Year):	1984
Results (LD_{50} or LC_{50}):	LD_{50} >2.0 g/Kg body weight
Remarks:	No deaths occurred during the study. Slight to well-defined erythema with or without slight to well-defined edema was observed at the treatment site of the majority of rats. Recovery was generally complete by day 7 except for one female showing signs of erythema until day 9. On day 4, eight rats developed small, slightly raised erythematous areas at the dose site. Signs of recovery from this were indicated on day 10, when small focal scab formation was observed in all ten rats. Four female rats showed complete recovery by day 14. Scab formation was still present in the remaining animals on day 15 (the last day of observations). There were no signs of systemic toxicity. Terminal necropsy findings were normal.
Conclusions:	The acute lethal dermal dose to rats of the test material was found to be > 2.0 g/Kg bodyweight
Remarks:	none
Data Quality:	1
References:	Petroquimia Espanola S.A. (1984). Acute Dermal Toxicity to Rats of PETREPAR® n-C14 (C14).

2.0 Repeated Dose Toxicity

Robust Summary No.: RPTD-1

Repeated Dose Toxicity

Test Substance:	n-nonane (CAS No. 111-84-2)
Vehicle:	None
Type of Study:	13-Week Inhalation
Species/strain:	Rats / Albino Harlan-Wistar
Age at study initiation:	
Route of administration:	Inhalation
Duration of test:	13 weeks
Dose/Conc. Levels:	1.9, 3.1, 8.4 mg/L (360, 590, 1600 ppm)
Sex:	25 males / dose group
Exposure period:	13 weeks
Frequency of treatment:	6 hours/day, 5 days/week
Control group and treatment:	Yes
Post exposure observation period:	No
Statistical methods:	Not provided in reference
Remarks on Test Conditions:	No recovery group.
Method/Guideline:	Similar to OECD Guideline 413
GLP:	No
Date (Year):	1978
Results (NOAEL, LOAEL):	NOAEL = 3.1 mg/L
Actual dose received by dose level by sex:	
Toxic response/effects by dose level:	1.9 mg/L: 2 animals died during the 13 week exposure period, one during the 46th exposure and the other after 52nd exposure. Both showed weight gains during the previous week. Gross and micropathological examination of the lung tissue revealed suppurative bronchopneumonia. These deaths were determined to be not dose or

	treatment related. 3.1 mg/L: All animals survived through study termination. There were no signs of distress throughout the 13-week study. 8.4 mg/L: Two rats died during the first day of exposure. Lung congestion and hemorrhage were noted at necropsy and no other significant lesions were found upon histopathological examination. Rats in this dose group exhibited salivation, mild loss of coordination and fine tremors throughout the first 4 days of exposure. Throughout the remaining 59 days, salivation and lacrimation were observed during the 6-hr exposure period. The mean body weights or mean body weight changes of rats were statistically significantly lower than controls when compared at 3, 17, 32, 46 and 61 exposure days. Serum glutamic pyruvic transaminase value for blood taken from rats after 4 weeks was statistically significantly greater than that of controls. However, the increases were not observed after 8 or 13 weeks suggesting a transient effect. Micropathological evaluation of tissues after 4, 8, and 13 weeks revealed only common sporadic lesions that were not considered to be treatment related.
Statistical results:	
Remarks:	
Conclusions:	Under the conditions of this inhalation study in rats, the NOAEL was 3.1 mg/L (590 ppm) based on the weight gain changes and clinical signs observed in the high dose group animals (8.4 mg/L).
Data Quality:	2, with restrictions (Only male mice were used, no recovery period)
References:	Carpenter, C.P. et al. 1978. Petroleum Hydrocarbon Toxicity Studies. XVII. Animal Response to n-Nonane Vapor. Tox and Appl. Pharm. 44:53-61.

Robust Summary No.: RPTD-2

Repeated Dose Toxicity

Test Substance	CAS No.: 124-18-5
Remarks	LINPAR 10 (commercial Decane) approx. composition: 97% n-decane
Method	
Method/guideline followed	OECD 422
Test type	A Combined Repeated Dose Toxicity Study With The Reproduction/Developmental Toxicity Screening Test In

	Sprague Dawley Rats By The Oral Route
GLP	Yes
Year	1995
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) BR
Route of administration	Oral (gavage)
Duration of test	Males were treated from day 14 prior to the mating phase until the end of the mating phase and then killed. Females were treated from day 14 prior to mating, through day 4 of lactation and then killed.
Doses/concentration levels	0, 25, 150, or 1,000 mg/kg/day (10 ml/kg dosing volume)
Sex	10 male, 10 female per group
Exposure period	Single daily injection
Frequency of treatment	7 days/week
Control group and treatment	10 male, 10 female, 0.5% methylcellulose
Post exposure observation period	None: all surviving animals were sacrificed following dosing
Statistical methods	Adult body and organ weight, food consumption, clinical chemistry, open field activity and hematologic data (raw or transformed) were compared using either parametric or nonparametric (Kruskal-Wallis) ANOVA depending on whether the data were found to be homogeneous or nonhomogeneous using Bartlett's homogeneity of variance procedure. If ANOVA analysis indicated significant differences, Dunnett's test and Mann Whitney's U test, for parametric and nonparemetric data, respectively, were used to analyze for differences between the various dose groups.
Test Conditions	Groups of 10 male and 10 female CD rats were dosed via gavage with test material daily by gavage at exposure levels of 0, 25, 150, or mg/kg/day. Males were dosed from the 14th day prior to mating, during mating until the end of the mating period. Females were dosed from the 14th day prior to the start of the mating phase to day 4 of lactation. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. Gross necropsies and histopathologic examination of tissues were conducted with emphasis on the male reproductive tract.

Results

NOAEL (NOEL)	NOEL = 1,000 mg/kg/day (for systemic toxicity) NOEL = 25 mg/kg/day (for effects on stomach mucosa)
LOAEL (LOEL)	Not applicable.
Remarks	No deaths or clinical signs of toxicity or behavioral changes were noted. No significant differences in body weights or feed consumption were observed. Startle reflex, open field test, and forelimb grip reflex performance data also revealed no treatment-related findings. There were also no treatment-related changes in hematology or blood chemistry parameters, organ weights or gross pathology. An apparent treatment-related, slight to moderate hyperplasia of the non-glandular mucosa of the stomach, associated with degeneration, hyperkeratosis and submucosal subacute inflammation and, in a few cases, with erosion, was seen in animals of all treated groups. This effect was considered an artifact of the dosing method and not directly related to the toxicity of the test material. No other treatment related histological changes were observed.
Conclusions	Oral dosing of Linpar 10 to male and female Sprague Dawley rats at levels of 0, 25, 150, or 1,000 mg/kg/day produced no evidence of any adverse effects on clinical observations, organ weights, gross pathology, neurobehavioral activity, clinical chemistry or hematology endpoints. Evidence of irritation of the nonglandular mucosa of the stomach was observed, but was considered an artifact of the dosing method and not attributed to the inherent toxicity of the test material. Based on these data, the no-observable- effect level (NOEL) for repeated dose toxicity was 1,000 mg/kg/day, the highest dose tested. The no-observable- effect level (NOEL) for effects on stomach mucosa was 25 mg/kg/day.
Data Quality	
Reliabilities	1
References	Maraschin, R., Comotto, L., R., Conz, A. (1995) LINPAR 10: Combined repeated dose toxicity study with the reproduction/developmental screening test in Crl:CD (SD) BR male and female rats Sprague Dawley rats of the test article LINPAR 10 administered by oral route at the dosages of 0, 25, 150 and 1,000 mg/Kg/day. Report of Medici del Vascello. 20138- Milano (Italy), Instituto di Ricerche Biomediche "Antoine Marxer" RBM S.p.A. for the Enichem Augusta Industriale (Currently Sasol Italy).
Other	Updated September 6, 2002

Robust Summary No.: RPTD-3

Repeated Dose Toxicity

Test Substance	n-decane (CAS No. 124-18-15)
Remarks	
Method	
Method/guideline followed	Similar to standard methods
Test type	Subchronic Inhalation
GLP	No
Year	1966
Species	Rat (41-43/group)
Strain	Not specified
Route of administration	Inhalation
Duration of test	123 days
Doses/concentration levels	540pm (3100mg/m^3)
Sex	Not specified
Exposure period	91 days
Frequency of treatment	18hr/day, 7 days/wk
Control group and treatment	20 rats (sex not specified); no exposure one month (approx. 32 days)
Post exposure observation period	None specified
Statistical methods	
Test Conditions	N-decane was used as a single dose comparative control in a 13 wk subchronic inhalation study that compared toxic effects of C9-C10 and C11-C12 aromatic-rich fractions with benzene and n-decane. Forty-one – 43 rats (strain, sex, age not specified) weighing approx. 301g pre-test, were exposed to 540ppm n-decane, 18hr/day, 7 days/wk for 91 days. N-decane vapor was delivered by gravity feed from the vapor generator (temp and pressure not specified) to a Venturi mixing tube and blended with inlet air. Air-vapor mixture was sucked into a surge chamber and through a diffusion plate into the animal chamber. The outlet mixture of vapor and moisture from the exposed animals was exhausted to the outside atmosphere. Air-vapor mixture was sampled through a port in the center of the chamber and atmospheric concentration determinations were made hourly (method not specified). Equipment was constructed of galvanized sheet metal and galvanized hardware screen. Animal cages were made of ¼ inch mesh hardware cloth and held 6

	rats/cage. Cages were placed into and removed from the inhalation chamber through a 2 ft square door on top of the chamber. Air flow into the chamber was measured by thermo-anemometer and a dry-test meter. Animals were monitored for appearance and behavior, body wt gain, organ wt, hematologic findings, gross and microscopic pathological changes. Sampling intervals were not specified in text but estimated from the figures appeared to be 0, 12, 24 hours, 7, 10, 14, 16, days and weekly thereafter. At exposure termination some rats (number not specified) were set aside without additional exposure for one months (est. 32 days).
Results **NOAEL (NOEL)** **LOAEL (LOEL)**	NOEL<540ppm, NOAEL=540ppm (3100mg/m^3)
Remarks	Significant increase in body wt gain was observed during exposure and recovery. (Reviewer's comment: Increased body wt gain may have been caused by metabolism of n-decane as a fatty acid by oral ingestion during inhalation exposure.) Total WBC count was lower than controls showing a –17% decrease at 57 days, with recovery in count to exceed controls by 6% at day 91 of exposure. Although statistically significant, changes in WBC counts were slight and of doubtful biological significance. No changes were seen in polymorphonuclear leukocyte-lymphocyte ratio; no adverse effects on bone marrow, organ wt, or gross and microscopic tissue examination. Rats retained for 1 month without treatment show no adverse effects.
Conclusions **(study authors)**	Inhalation of n-decane at 540ppm (3100mg/m^3) caused increased body wt gain and increased total WBC counts at day 91 of exposure. These changes were not toxicologically significant. No other systemic effects were observed.
Quality **Reliabilities**	2. Reliable with restrictions. Method and study details probably adequate in 1966 are insufficient by current standards. Analytic data from hourly chamber sampling was not presented. There are inconsistencies in text and tables. Number of animals varied slightly in different tables from 41-43 rats; dose was reported variously as 540ppm (3100mg/m3) or 560ppm (3200mg/m3). The Results section of text stated 123 days of exposure, but actual exposure was 91 days with 1-month recovery. Data in tables and figures for n-decane were presented to 91 days only. Sufficient actual data is presented to support the conclusions for n-decane.
References	Nau, C.A., Neal, J., and Thorton, M. 1966. C9-C12 fractions obtained from petroleum distillates. Arch Environ Health 12: 382-393.
Other **Last changed**	Revised 10/11/2002

Robust Summary No.: RPTD-4

Repeated Dose Toxicity

Test Substance	n-decane (CAS No. 124-18-15)
Remarks	
Method	Similar to standard methods
Method/guideline followed	
Test type	One year Dermal
GLP	No
Year	1966
Species	Mice (65)
Strain	C3H
Route of administration	Dermal
Duration of test	50wk
Doses/concentration levels	100-150mg/application
Sex	Male
Exposure period	91 days
Frequency of treatment	3 times/wk on alternate days
Control group and treatment	763 male mice, no chemical applied to skin one month (approx. 32 days)
Post exposure observation period	None specified
Statistical methods **Test Conditions**	N-decane was used as a single dose comparative control in a 50 wk dermal toxicity study that compared toxic effects of C9-C10 and C11-C12 aromatic-rich fractions with benzene and n-decane. N-decane was applied to the backs of 65 male C3H mice (shaving not specified but standard practice), using a ¼ inch brush, making one stroke up the middle of the back from the base of tail to base of neck, 3 times/wk on alternate days for 50wks. Mice were observed closely for any gross changes. At study termination, body wt., hematology and postmortem evaluations were performed. All tissues and organs were examined microscopically.
Results **NOAEL (NOEL)**	NOEL<100mg/application; LOEL= 100-150mg/application Body weight gain and hematology parameters were not adversely

LOAEL (LOEL)	affected. Grossly, treated skin was thick, dry and scaly; microscopically fibrosis of dermis appeared in 43% of mice, ulceration in 18%, hyperkeratosis in 7%. In kidney, hemorrhage and pigmentation was seen in 33% and inflammation in 18%; amyloidosis in spleen occurred in 10% of mice; and in the lung, hemorrhage in 55% of mice, inflammation in 28% and necrosis in 11% were seen.
Remarks	
Conclusions (study authors)	Dermal application of n-decane at 100-150mg/application three times a wk for 50 wks induced pathological changes in skin, kidney, spleen and lung to varying degrees but did not adversely affect body wt gain or hematological parameters.
Quality Reliabilities	2, Reliable with restrictions. Method and study details are insufficient by current standards.
References	Nau, C.A., Neal, J., and Thorton, M. 1966. C9-C12 fractions obtained from petroleum distillates. Arch Environ Health 12: 382-393.
Other	
Last changed	Revised 10/11/2002

Robust Summary No.: RPTD-5

Combined Repeated Dose and Reproductive and Developmental Screening Test

Test Substance:	CAS No. 1120-21-4, undecane (= or > 99%)
Vehicle:	Olive oil
Type of Study:	A combined Repeated Oral Dose and Reproductive/Developmental toxicity screening study
Species/strain:	Rat / Crj:CD® (SD)
Age at study Initiation:	10 weeks
Route of administration:	Oral Gavage
Duration of test	Males, 46 days; females, from 14 days before mating to day 3 of lactation
Dose/Conc. Levels:	0, 100, 300, 1000 mg/kg (5 mL/kg dose volume
No. of animals/sex/dose:	12/sex/dose group (including controls)
Exposure period	Single daily injection
Frequency of treatment:	7 days per week
Control group and treatment:	Olive Oil- vehicle control

Statistical methods:	Sexual cycle, copulation index (mating index), fertility index, gestation index and nursing index for the test and control groups were analyzed by Fisher's accuracy probability test. Other parameters were analyzed by Bartlett's homogeneity of variance followed by single dimension configuration variance analysis or Kruskal-Wallis method. If the results were significant, either Dunnett's method or the Mann-Whitney U-test was applied to compare the treated groups with the control. Qualitative urinary measurements were analyzed using the Kruskal-Wallis method and the Mann Whitney U-test. Viability and body weight of offspring were analyzed using the litter as the test unit. Results with statistical p-values of < 0.05 were considered statistically significant.
Remarks on Test Conditions:	Males were dosed for 46 days including 14 days prior to mating and during the mating period; females were dosed for 14 days prior to mating, during the mating and gestation periods and postnatally until the third day of nursing.
Method/Guideline:	OECD Guideline 422
GLP:	GLP
Date (Year):	1996
Results (NOEL):	Repeat Dose: 100 mg/kg (males and females) Developmental: 300 mg/kg Reproductive: 300 mg/kg
Toxic response/effects by dose level:	**Repeat dose toxicity:** Salivation was observed in males and females in the 300 and 1000 mg/kg dose groups. A statistically significant suppression of body weight gain was observed in males at the 1000 mg/kg dose level. The 1,000 mg/kg female dose group exhibited a statistically significant increased body weight gain during the lactation period. Food consumption decreased in males at the 300 and 1000 mg/kg dose levels in the first half of the administration period. In contrast, food consumption was increased in males at the 1000 mg/kg dose group in the second half of the administration period, and in females at the 1000 mg/kg level in the second half of pregnancy and during lactation. High dose males (1000 mg/kg) exhibited decreased hemoglobin and albumin concentrations, and increased white cell count, Alpha-2μ-globulin, GPT, cholinesterase and total cholesterol. Relative liver weights, and relative and absolute thymus weights, were increased in males at 1000 mg/kg. Absolute and relative liver weights were elevated in females at the 1000 mg/kg dose level. No gross or histopathological effects were observed at any dose level. No effects were noted at the 100 mg/kg dose level. **Reproductive/developmental toxicity:** No effects on reproductive ability and reproductive organ weights were observed. There were no gross or histological findings of toxicity to reproductive organs of either sex. There was no apparent effect on deliveries or maternal behavior dams. Body weight gain was decreased in male and female offspring at the 1000 mg/kg dose level. No effects were noted in terms of viability, general condition or gross observation of offspring.

Remarks:	None
Conclusions:	The administration of undecane at doses of 300 and 1000 mg/kg resulted in changes in body weight gain and food consumption. Changes in liver and thymus weights were also noted for males and females, respectively, at the 1000 mg/kg dose level only. Some changes hematological and blood chemistry parameters were noted in males at the 1000 dose level. No gross or histopathological effects were noted at the 100 mg/kg dose level. The NOEL for repeat dose toxicity is 100 mg/kg. Decreased body weight gain was noted in offspring, at the 1,000 mg/kg dose level only, however, no others effects were noted on reproductive parameters, including gross or histopathological evaluation of reproductive organs. The NOEL for reproductive and developmental toxicity is 300 mg/kg.
Remarks:	None
Data Quality:	1, no restrictions
References:	Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Combined repeat Dose and Reproductive/Developmental Toxicity Screening test of Undecane by Oral Administration. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

Robust Summary No.: RPTD-6

Repeated Dose Toxicity

Test Substance:	CAS No. 64771-72-8, C12-C14 normal paraffins
Vehicle:	N/A
Type of Study:	28-day repeated dose dermal toxicity study with neurotoxicity evaluation
Species/strain:	Rabbit / New Zealand White
Age at study initiation:	13-14 weeks
Route of administration:	Dermal
Duration of test:	28-days
Dose/Conc. Levels:	0, 100, 500, 2000 mg/kg
Sex:	5 males and 5 females per dose group
Exposure period:	At least 6 hours.
Frequency of treatment:	Daily (7 days per week for a minimum of 28 days)

Control group and treatment:	Sham treatment, No material was applied to the animals, but the action of dosing was simulated and animals were wrapped in the same manner as treated animals.
Post exposure observation period:	None: all surviving rabbits were sacrificed after 28 days of dosing.
Statistical methods:	Bartlett's test was performed to determine if the dose groups had equal variance. If the variances were equal, statistical evaluation of equality of means was conducted using a standard one way ANOVA. If the variances were not equal, the Kruskal-Wallis Test and the Jonckheere's Test were performed. If significant differences among the means were indicated, Dunn's Summed Rank Test was used to determine which treatment groups differed significantly from the control.
Remarks on Test Conditions:	The primary objective of this study was to assess neurotoxicity since neurologic effects had been reported in acute dermal studies in rabbits. Therefore, a reference control group receiving 2000 mg/kg of n-hexane (solvent control material) which is known to cause peripheral neuropathy was added to this study. Whole blood samples were analyzed for the blood concentrations of the test material. Neuropathological examination was conducted from tissue samples from 20 sites in the peripheral and central nervous system. Samples were fixed, and immersed in epoxy resin blocks. Sites selected for examination included optic nerve, frontal cortex, thalamus, basal ganglia, hippocampus, cerebellar vermis, meddula oblongata, 3-4 levels of spinal cord (to include cervial, thoracic and lumbar regions), brachial plexus, selected cervial and lumbar dorsal root ganglia, dorsal roots, ventral roots, sciatic n. at notch, sciatic n. mid-thigh, tivial n. at trifurcation, tibial n. at ankle and gastrocnemius/soleus muscle complex. All slides were examined by light microscopy, and the tissue source was not revealed until all samples had been examined and scored. Pathological changes were scored on a 0-5 scale (no change to severe change) and all scores were recorded on raw data sheets and computer tabulated. Questionable slides were evaluated by 2 examiners (including a board-certified veterinary pathologist) and a consensus reached.
Method/Guideline:	Other, Similar to OECD Guideline 410
GLP:	In the spirit of GLP
Date (Year):	1992
Results (NOAEL, LOAEL):	NOEL = 100 mg/kg (dermal irritation); NOAEL = 500 mg/kg (neurotoxicity)
Actual dose received by dose level by sex:	
Toxic response/effects by	Mortality / Clinical In-Life / Hematology and Serum Chemistry

dose level:

100 mg/kg: All animals survived to study termination. Poor food consumption and abnormal stool were observed. There were no statistically significant differences in mean body weight, mean organ weight, and food consumption compared to controls. All animals displayed increased in body weight over initial values. There were no statistically significant differences in mean hematological and serum chemistry parameters.

500 mg/kg: All animals survived to study termination. Poor food consumption and abnormal stool were observed. No statistically significant differences in mean body weight or mean organ weight compared to controls was noted during the majority of the study. An 11% decrease in mean body weights was noted on Day 27. No difference in food consumption was observed. Statistically significant difference was observed in an increase in the mean percentage of neutrophils and a decrease in mean percent lymphocytes in females at study termination.

2000 mg/kg: All animals were euthanized for humane reasons due to severe dermal irritation, between Day 7 and 14. In addition to the severe irritation, enlarged/thickened and/or discolored liver were the most significant postmortem findings. One control male was observed with an enlarged liver. Two animals were observed with enlarged spleen.

2000 mg/kg n-hexane: One female was found dead on Day 8. The remaining 9 animals were sacrificed in moribund condition. The majority of these animals exhibited severe dermal irritation. In addition to the severe irritation, enlarged/thickened and/or discolored liver were the most significant postmortem findings. Two animals were observed with enlarged spleen.

Prior to sacrifice, all animals in the high dose and n-hexane dose group showed decreased food consumption, extremely poor condition, abnormal stool, emaciation, abdominal griping, hypopnea, hypothermia, and hypoactivity. Statistically significant decreases in serum chemistry parameters were noted which were probably related to malnutrition or severe dermal irritation.

Kidney abnormalities (enlarged, discolored, roughened, or irregular shape) were observed in all groups, including controls.

Dermal Observations

The severity and frequency of erythema and edema increased in a dose-related fashion. Erythema ranged from very slight to severe and edema ranged from very slight to moderate.

Histopathological Examination

Histopathology revealed changes in the skin that correlated with the in-life dermal observations. Extramedullary hematopoiesis, a phenomenon secondary to an active inflammatory process was observed in the adrenal glands, kidneys, spleen and liver of the n-hexane animals and in the spleen of the 2000 mg/kg dose group.

Neuropathological Evaluations:

Neuropathological evaluation showed no marked abnormalities nor degenerative changes. This evaluation suggests no relationship between tissue changes and exposure to the test material. There was

	no pattern to suggest either an active pathological process or a dose-response effect.
Statistical results:	Statistical analyses on the neuropathological data showed statistically higher abnormality scores in the medulla oblongata of treated animals, with the effect apparently greater in females than in males. The changes observed in the spinal cord and medulla oblongata were found in control and treated animals and there was no obvious pattern which would associate their incidence to dose or treatment therefore, these findings were not considered to be treatment-related.
Remarks:	Dermal irritation and possibly overt toxicity were limiting factors to the amount of test material that could be topically applied to the animals. The severe dermal irritation affected how the animal moved and made in-life neurological evaluations difficult.
Conclusions:	Repeated dermal exposure to high levels of the test material did not induce neuropathological lesions. However, this study did produce the minor effects (i.e., decreased righting reflex, staggered gait) seen in previous acute studies. These effects may have been influenced by the severe dermal irritation, thus hindering animal movement. Under the conditions of this study, the NOEL for dermal irritation was 100 mg/kg. Since the 2000 mg/kg group had to be euthanized early, the NOAEL (500 mg/kg) for neurotoxicity is based on the highest dose that completed the study. At 500 mg/kg, the pathology review did not indicate any signs of neurotoxicity.
Data Quality:	2, with restrictions (no recovery group)
References:	ExxonMobil Biomedical Sciences, Inc. 1995. 28-day repeated dose dermal toxicity study in rabbits with neurotoxicity evaluation. Study No. 14051B. O'Connor et al. 1997. Subchronic Toxicity With Neurotoxicity Evaluation of C_{12-14} Normal Paraffinic Fluid in Rabbits. *The Toxicologist.* 36(No. 1, Part 2). Presented at the 1997 Society of Toxicology Meeting, Cincinnati, OH.

Robust Summary No.: RPTD-7

Repeated Dose Toxicity

Type of Study:	90-day oral toxicity
Species/strain:	Rat / Harlan Sprague-Dawley
Age at study initiation:	Approximately 6 weeks
Route of administration:	Oral Gavage
Duration of test:	90 days

Dose/Conc. Levels:	100, 500, 1000 mg/kg at a dose volume of 5 mL/kg
Sex:	10 animals / sex / dose
Exposure period:	90 days
Frequency of treatment:	7 days per week
Control group and treatment:	Control group received carrier (corn oil) only by oral gavage
Post exposure observation period:	28 days post-treatment observation for satellite high dose group
Statistical methods:	Comparisons were limited to within sex analysis. Bartlett's test for equal variances. For parametric procedures, a standard one way ANOVA, Dunnett's test, and standard regression analysis. For nonparametric procedures, Kruskal-Wallis test, Dunn's Summed Rank test and Jonckheere's test.
Remarks on Test Conditions:	A satellite group was dosed at the high dose level for 7 days a week for 13 weeks and were observed for reversibility, persistence or delayed occurrence of toxic effects for 28 days post-treatment.
Method/Guideline:	Other, similar to OECD guideline 408
GLP:	GLP equivalent
Date (Year):	1991
Test Substance:	CAS No. 64742-47-8, C11-C14 multiconstituent alkanes (n-, iso- and cycloparaffins)
Vehicle:	Corn oil (carrier)
Results (NOAEL, LOAEL):	NOAEL > 1000 mg/kg Overall, the blood and liver weight effects noted showed some indication of recovery in the satellite animals. In addition, these effects were not supported by abnormal findings in microscopic examination suggesting an adaptive rather than a treatment-related effect. The kidney effects are consistent with $\alpha_2\mu$-globulin induced nephropathy, effects in male rats which have been determined to have no relevance to humans.
Actual dose received by dose level by sex:	
Toxic response/effects by dose level:	**100 mg/kg, 500 mg/kg and 1000 mg/kg dose groups:** No treatment-related mortality was observed in this study. Two control female animals died prior to termination as a result of a non-treatment related urinary tract abnormality and dosing trauma. The majority of animals in all groups displayed no observable abnormalities during the study. Body weight, food consumption and ophthalmoscopic data displayed no notable trends in either sex. Interim hematology data revealed a spurious decrease in red blood

cells for low dose females. Terminal hematology data revealed a statistically significant increase in platelets for high dose males. However the values were within the normal range for this strain and are not considered to be biologically significant.

Statistically significant difference were observed in some clinical chemistry parameters, including a dose-related increase in male urea nitrogen and male creatinine, but all clinical chemistry values were within the normal physiological ranges.

A linear dose-related increase in male kidney weights at the mid and high dose and an increase in female liver weights at the high dose. Relative organ weight data revealed statistically significant increases in male kidney body weight ratios at the mid and high dose levels, male and female liver/body weight ratios at the mid and high dose levels, and in the male high dose testes/body weight ratios. Satellite recovery group relative organ weight data revealed a recovery trend.

No notable trends were observed at gross postmortem evaluation. Kidney changes were limited to the males and included accumulations of hyaline droplets in the cytoplasm of the proximal tubules of the cortex, an increased incidence of multifocal cortical tubular basophilia with changes consistent with both degeneration and regeneration of tubular epithelium, and dilated medullary tubules with granular casts. Reversibility for kidney changes was evident upon microscopic examination of tissues from the satellite recovery group. These findings are consistent with $\alpha_2\mu$-globulin induced nephropathy.

Microscopic examination of the liver revealed minimal to slight centrilobular hepatocellular hypertrophy in the high dose males and the mid and high dose females. However, reversibility for liver changes was evident upon microscopic examination of the tissues from the satellite recovery group. Hepatocellular hypertrophy was not evident in any satellite group animals.

Statistical results:

Remarks: 28-day satellite high dose group used

Conclusions: Under the conditions of this test, the test substance has a low order of toxicity. Overall, the blood and liver weight effects noted showed some indication of recovery in the satellite animals. These effects were not supported by abnormal findings in microscopic examination suggesting an adaptive rather than a treatment-related effect. The kidney effects are consistent with $\alpha_2\mu$-globulin induced nephropathy, effects in male rats which have been determined to have no relevance to humans. Based on these findings, the NOAEL is > 1000 mg/kg.

Data Quality: 1, no restrictions

References: ExxonMobil Biomedical Sciences, Inc. 1991. 90-Day Oral Toxicity Study in the Rat. Study No. 186870.

Robust Summary No.: RPTD-8

Repeated Dose Toxicity

Test Substance:	Dearomatized white spirit (DAWS) (<0.5%aromatic, 58% alkanes, 42%cycloalkanes)
Vehicle:	None
Type of Study:	12-Week Inhalation
Species/strain:	Rats / Sprague-Dawley
Age at study initiation:	6 – 7 wks
Route of administration:	Inhalation
Duration of test:	12 weeks
Dose/Conc. Levels:	DAWS: 1.89 g/m3 (300 ppm); 5.67 g/m3 (900 ppm)
Sex:	15 males and females / dose group, for each test material (excluding interim sacrifice groups)
Exposure period:	12 weeks
Frequency of treatment:	6 hours/day, 5 days/week
Control group and treatment:	Yes; 0 ppm
Post exposure observation period:	No
Statistical methods:	Bartlett's test for variance. If variances were equal, ANOVA using F distribution to determine significance; if differences significant, Dunnet's test. If variances unequal, Kruskal-Wallis and if differences indicated, summed rank test to determine which treatment groups differed from control.
Remarks on Test Conditions:	Interim sacrifice groups, no recovery group.
Method/Guideline:	Similar to OECD Guideline 413
GLP:	Not specified
Date (Year):	1978; year of publication1984
Results (NOAEL, LOAEL):	DAWS: NOAEL – 1.8 g/m3 (300 ppm) (based on decreased body wt at the high dose, and excluding male rat

	kidney effects, and excluding increased liver wt based on no histopathological effects)
Actual dose received by dose level by sex:	DAWS: 312 ppm, 890 ppm (mean chamber concs)
Toxic response/effects by dose level:	DAWS: Body wt: males decreased from week 5 at top dose only Hematology: no dose-related effect Clinical Chemistry: no consistent effects Organ wts: males - increased absolute and/or relative kidney wts both doses; males and females - increased liver wts at high dose Histopathology: male, focal dilated tubules in kidney corticomedulla both doses
Statistical results:	
Remarks:	Interim sacrifice data are not included, but show no additional effects. Authors conclude “Effects observed at relatively high levels…with the exception of male rat kidney effects were not remarkable”.
Conclusions:	DAWS: NOAEL. 1.8 g/m3. (excluding male rat kidney effects) IPH: LOAEL 1.8 g/m3 (300 ppm) excluding male rat kidney effects. Based on minimal hematological changes and decreased body weights at both doses. However, authors consider effects unremarkable, other than for male rat kidney effects. These are discussed at length and not considered to be relevant for human health assessment.
Data Quality:	1 with restrictions (GLP not specified)
References:	Phillips RD and Egan GF (1984) Subchronic Inhalation Exposure of Dearomatized White Spirit and C10-C11 Isoparaffinic Hydrocarbon in Sprague-Dawley Rats. Fundamental and Applied Toxicology, 4, 808 – 818.

Robust Summary No.: RPTD-9

Repeated Dose Toxicity

Type of Study:	90-day subchronic oral
Species/strain:	Rat / Harlan Sprague-Dawley
Age at study initiation:	Approximately 8 weeks
Route of administration:	Oral gavage

Duration of test:	13 weeks
Dose/Conc. Levels:	0, 500, 2500, 5000 mg/kg
Sex:	10 animals / sex / dose
Exposure period:	13 weeks
Frequency of treatment:	7 days per week
Control group and treatment:	Control group received carrier (corn oil) only by oral gavage
Post exposure observation period:	28 days post-treatment observation for satellite high dose group
Statistical methods:	Comparisons were limited to within sex analysis. Bartlett's test for equal variances. For parametric procedures, a standard one way ANOVA, Dunnett's test, and standard regression analysis. For nonparametric procedures, Kruskal-Wallis test, Dunn's Summed Rank test and Jonckheere's test.
Remarks on Test Conditions:	A satellite group was dosed at the high dose level for 7 days a week for 13 weeks and were observed for reversibility, persistence or delayed occurrence of toxic effects for 28 days post-treatment.
Method/Guideline:	Other, similar to OECD guideline 408
GLP:	EPA GLP 40 CFR Part 160
Date (Year):	1991
Test Substance:	C10-C13 multiconstituent alkanes (n-, iso- and cycloparaffins)
Vehicle:	Corn oil (carrier)
Results (NOAEL, LOAEL):	The NOAEL is > 5000 mg/kg The effects observed appear to be an adaptive response to the irritation of the test substance and not a treatment-related effect. Most effects were reversible. The kidney effects are consistent with $\alpha_2\mu$-globulin induced nephropathy, effects in male rats which have been determined to have no relevance to humans.
Toxic response/effects by dose level:	**500 mg/kg, 2500 mg/kg and 5000 mg/kg dose groups:** Fourteen animals died prior to study termination; 13 of these deaths were attributed to dosing trauma and/or aspiration of the test material. **Mortality Data:** 0 mg/kg: 2 males, 1 female 500 mg/kg: no deaths 2500 mg/kg: 2 females 5000 mg/kg: 4 females

Satellite: 2 males, 3 females

The majority of the animals in the control, low and mid dose groups displayed no observable abnormalities during the test period. The most notable clinical sign during the study was swollen anus in the high dose and satellite groups.

A decrease in mean body weight was noted with increasing dose during the later stages of the study in both the male and female mid- and high dose groups. This effect may be related to the stomach irritation noted at pathology. However, body weights recovered slightly during the recovery period. Also during the second half of the study, an increase in food consumption was noted with increasing dose for both males and females, primarily in the mid-and high dose groups.

Absolute and relative liver and kidney weights for male rats in the mid- and high dose groups were increased relative to controls. Female absolute and relative liver weights were also increased compared to controls, but only the relative kidney weights were increased compared to control values.

Hematology studies revealed an increase in platelets compared to control for both males and females. Serum chemistry values revealed increases in alanine aminotransferase, glutamyl transferase and bilirubin in both male and female animals.

Microscopic examination: Examination of required tissue at terminal sacrifice revealed changes in the male kidneys which were consistent with $\alpha_2\mu$-globulin induced nephropathy. These changes included hyaline droplets in the proximal convoluted tubules, dilation and granular cast formations in the medullary tubules and increased basophilia of cortical tubules representing areas of degeneration and regeneration of cortical tubular epithelium. Liver effects consisted of a dose-related increase in incidence and intensity of centrilobular hepatocellular hypertrophy. Stomach effects consisted of hyperplasia and hyperkeratosis of the squamous mucosa. Anus effects consisted of hyperplasia and hyperkeratosis of the epidermis, focal necrosis and neutrophilic inflammatory cell infiltrations with pustule formation.

Examination of required tissue in the satellite group after a 28-day recovery period revealed complete reversibility of the hepatic changes. Evidence of reversibility was also noted for male kidney effects, except for dilation and cast formation in the medullary tubules in half of the males. Again, these effects are consistent with $\alpha_2\mu$-globulin induced nephropathy. The incidence and intensity of the gastric changes diminished after recovery period and these effects were also reversible. Gross changes in the anus were not observed at the recovery termination.

Remarks:

Microscopic examination from the satellite animals sacrificed after a 28-day recovery period revealed complete reversibility of the liver changes. Evidence of reversibility was also noted for the male kidney effects, however, dilation and cast formation in the medullary tubules were still evidence in half of the males. The incidence and intensity of the gastric changes were diminished after the recovery period and these effects were also reversible. Gross changes seen in the anus were not observed at the recovery sacrifice. The increased number of segmented neutrophils may have been related to infection of the lesions seen in the anus. The increase in platelets for both sexes may

	have been related to the stomach irritation. Serum chemistry values in satellite group were same as terminal control values representing reversibility of effects.
Conclusions:	Under the conditions of this test, the test substance had a low order of toxicity. The gastrointestinal effects observed appear to be an adaptive response to the irritation of the test substance and not a treatment-related effect. Most effects were reversible. The kidney effects are consistent with $\alpha_2\mu$-globulin induced nephropathy, effects in male rats which have been determined to have no relevance to humans. Based on these findings, the NOAEL is > 5000 mg/kg disregarding the gastrointestinal irritation and male rat specific nephropathy.
Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1991. 90-Day Subchronic Oral Toxicity Study in Rats. Study No. 158270. Unpublished Study.

Robust Summary No.: RPTD-10

Repeated Dose Toxicity

Test Substance:	C10-C11 Isoparaffinic Hydrocarbon (IPH)
Vehicle:	None
Type of Study:	12-Week Inhalation
Species/strain:	Rats / Sprague-Dawley
Age at study initiation:	6 – 7 wks
Route of administration:	Inhalation
Duration of test:	12 weeks
Dose/Conc. Levels:	IPH 1.83 g/m3 (300 ppm); 5.48 g/m3 (900 ppm)
Sex:	15 males and females / dose group, for each test material (excluding interim sacrifice groups)
Exposure period:	12 weeks
Frequency of treatment:	6 hours/day, 5 days/week
Control group and treatment:	Yes; 0 ppm
Post exposure observation period:	No

Statistical methods:	Bartlett's test for variance. If variances were equal, ANOVA using F distribution to determine significance; if differences significant, Dunnet's test. If variances unequal, Kruskal-Wallis and if differences indicated, summed rank test to determine which treatment groups differed from control.
Remarks on Test Conditions:	Interim sacrifice groups, no recovery group.
Method/Guideline:	Similar to OECD Guideline 413
GLP:	Not specified
Date (Year):	1978; year of publication1984
Results (NOAEL, LOAEL):	IPH: LOAEL 1.8 g/m3 (300 ppm) (based on 10% decreased red cell counts and slight deceased body wt gain at both doses, excluding male rat kidney effects, and excluding increased liver wt based on no histopathological effects)
Actual dose received by dose level by sex:	IPH: 314 ppm; 022 ppm (mean chamber concs)
Toxic response/effects by dose level:	IPH: Body wt: males decreased body wt in both doses after wk 6 Hematology: males, approx 10% decrease in erythrocyte counts at both doses, not dose related Clinical Chemistry: no consistent effects Organ wts: males - increased absolute and/or relative kidney wts both doses; males and females - increased liver wts at high dose Histopathology: male, focal dilated tubules in kidney corticomedulla both doses
Statistical results:	
Remarks:	Authors conclude "Effects observed at relatively high levels…with the exception of male rat kidney effects were not remarkable". "…the statistically significant (hematological) changes in these studies (IPH) …were spurious and offer little significance of a hematological effect…).
Conclusions:	IPH: LOAEL 1.8 g/m3 (300 ppm) excluding male rat kidney effects. Based on minimal hematological changes and decreased body weights at both doses. However, authors consider effects unremarkable, other than for male rat kidney effects. These are discussed at length and not considered to be relevant for human health assessment.
Data Quality:	1 with restrictions (GLP not specified)

References:	Phillips RD and Egan GF (1984) Subchronic Inhalation Exposure of Dearomatized White Spirit and C10-C11 Isoparaffinic Hydrocarbon in Sprague-Dawley Rats. Fundamental and Applied Toxicology, 4, 808 – 818.

3.0 Genetic Toxicity

3.1 *in vitro* Genetic Toxicity

Robust Summary No.: GTVT-1

Genetic Toxicity In Vitro

Test Substance:	CAS No. 64771-72-8, C10-C13 normal paraffins
Type of Study:	Reverse Mutation, Ames Assay
System of testing (bacterial/nonbacterial):	Bacterial
Species/strain (or cell type or cell line):	Salmonella typhimurium / TA98, TA100, TA1535, TA1537, TA1538
Concentrations tested:	100, 320, 1000, 3200, 10000 μg/plate
Metabolic activation:	Liver homogenate from the livers of aroclor pretreated Sprague Dawley rats.
Remarks on Test Conditions:	
Method:	OECD Guideline 471
GLP:	GLP equivalent
Date (Year):	1991
Statistical methods:	In accordance with published procedures (Snedecor and Cochran, 1967), the mean plate count and standard deviation for each dose point were determined. Any test value which was equal to or greater than 3 times the mean value of the concurrent vehicle control was considered to be a positive dose.
Results:	Test material did not induce a dose-related increase in revertant colonies in any of the five tester strains either with or without metabolic activation.
Cytotoxic concentration w/, w/o metabolic activation	No toxicity observed in the pretest using strain TA98 at a dose range from 1 to 10,000 μg/plate.

Genotoxic effects:	No dose-related increase in the mutation frequencies in any of the tester strains.
Statistical results:	N/A
Remarks:	-
Conclusions:	Under the condition of this assay, this test material is not mutagenic for the Salmonella test strains at doses up to and including 10,000 µg /plate.
Remarks:	Positive and negative controls performed as expected.
Data Quality:	1, no restrictions
References	ExxonMobil Biomedical Sciences, Inc. 1991. Microbial Mutagenesis in Salmonella Mammalian Microsome Incorporation Assay, Unpublished study.
Other	Last Update December 20, 2002

Robust Summary No.: GTVT-2

Genetic Toxicity In Vitro

Test Substance:	N-nonane (CAS RN 111-84-2)
Type of Study:	Ames
System of testing (bacterial/nonbacterial):	Bacterial
Species/strain (or cell type or cell line):	*Salmonella typhiurium* / TA98, TA100, TA1535, TA97, TA1537
Concentrations tested:	Up to 10 mg/plate
Metabolic activation:	Yes
Remarks on Test Conditions:	
Method:	Similar to OECD Guideline 471
GLP:	Yes
Date (Year):	1992
Statistical methods:	
Results:	Negative

Cytotoxic concentration w/, w/o metabolic activation	
Genotoxic effects (e.g., positive, negative, unconfirmed, dose-response, equivocal) w/, w/o metabolic activation:	Negative with and without metabolic activation
Statistical results:	
Remarks:	
Conclusions:	Under the conditions of this assay, there was no evidence of mutagenic activity.
Remarks:	Limited information provided in reference.
Data Quality:	1, without restrictions
References	Zeiger, E, et al. 1992. Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ. Mol. Mutagen. 19(suppl 21): 2-141.

Robust Summary No.: GTVT-3

Genetic Toxicity In Vitro

Test Substance:	PETREPAR® n-C10 (97% 1-decane)
Type of Study:	Reverse mutation assay
System of testing (bacterial/nonbacterial):	Bacterial
Species/strain (or cell type or cell line):	Salmonella typhimurium/ TA 1535, TA 1537, TA 1538, TA 98, TA 100
Concentrations tested:	5,000, 1,500, 500, 150 and 50 μg/plate
Metabolic activation:	With and without metabolic activation(rat S9)
Remarks on Test Conditions:	No protocol deviations were reported
Method:	OECD 471
GLP:	Yes
Date (Year):	1985
Statistical methods:	Not specified

Results:	Negative- no evidence of mutagenic activity
Cytotoxic concentration w/, w/o metabolic activation	The test material was noncytotoxic both with and without metabolic activation at the highest concentration tested (5,000 μg/plate)
Genotoxic effects (e.g., positive, negative, unconfirmed, dose-response, equivocal) w/, w/o metabolic activation:	There were no substantial increases in revertant colony numbers of any of the five tester strains following treatment with the test material at all dose levels, with or without metabolic activation. Positive controls responded as anticipated.
Statistical results:	No statistically significant dose-related increases in reversions were observed
Remarks:	None
Conclusions:	The test material was not mutagenic under test conditions
Remarks:	None
Data Quality:	1
References	PETRESA (Petroquimia Espanola S.A.) (1985). Ames Metabolic Activation Test to Assess the Potential Mutagenic Effect of PETREPAR® C10.

Robust Summary No.: GTVT-4

Genetic Toxicity In Vitro

Test Substance:	LINPAR® 10 (97% 1-decane)
Type of Study:	Cytogenetic Assay
System of testing	nonbacterial
Species/strain	V79 Chinese Hamster Lung Cells
Concentrations tested:	5-5,000 μg/ml Test concentrations analyzed for metaphase analysis: 5, 15, and 50 μg/ml (without activation), 50, 150 and 500 μg/ml (with activation)
Metabolic activation:	With and without metabolic activation (rat S9)
Remarks on Test Conditions:	No protocol deviations
Method:	Directive 84/449/EEC. B. 10
GLP:	Yes
Date (Year):	1994
Statistical methods:	Not specified

Results:	Negative- no evidence of chromosomal aberrations
Cytotoxic concentration w/, w/o metabolic activation	The test material was cytotoxic with activation at 5,000, 3,000 and 1,500 μg/ml and without activation at 5,000, 3,000, 1,500 and 150 μg/ml.
Genotoxic effects (e.g., positive, negative, unconfirmed, dose-response, equivocal) w/, w/o metabolic activation:	Negative for genotoxic activity at 5, 15, and 50 μg/ml (without activation), and 50, 150 and 500 μg/ml (with activation). Reference mutagens (ethylmethane sulfonate and cyclophosphamide) produced expected increases in percentage of cells with chromosomal aberrations.
Statistical results:	At no test article concentration (with and without activation) was the incidence of chromosomal aberrations statistically significantly different from the control (acetone).
Remarks:	none
Conclusions:	The test material did not produce Chromosomal aberrations under these test conditions
Remarks:	none
Data Quality:	1
References	Sasol Italy (Enichem Augusta) (1994). Study of the Capacity of the Test Article LINPAR® 10 to Induce Chromosome Aberrations in V79 Chinese Hamster Lung cells.

Robust Summary No.: GTVT-7

Genetic Toxicity In Vitro

Test Substance:	PETREPAR® n-C14 (99% n-tetradecane)
Type of Study:	Reverse mutation assay (Ames)
System of testing (bacterial/nonbacterial):	Bacterial
Species/strain (or cell type or cell line):	Salmonella typhimurium/ TA 1535, TA 1537, TA 1538, TA 98, TA 100
Concentrations tested:	5,000, 1,500, 500, 150 and 50 μg/plate
Metabolic activation:	With and without metabolic activation (rat S9)
Remarks on Test Conditions:	No protocol deviations were reported
Method:	OECD 471
GLP:	Yes

Date (Year):	1985
Statistical methods:	Not specified
Results:	Negative- no evidence of mutagenic activity
Cytotoxic concentration w/, w/o metabolic activation	The test material was noncytotoxic both with and without metabolic activation at the highest concentration tested (5,000 μg/plate)
Genotoxic effects (e.g., positive, negative, unconfirmed, dose-response, equivocal) w/, w/o metabolic activation:	There were no substantial increases in revertant colony numbers of any of the five tester strain following treatment with the test material at any dose level, with or without metabolic activation.
Statistical results:	No statistically significant dose-related increases in reversions were observed
Remarks:	none
Conclusions:	The test material was not mutagenic under test conditions
Remarks:	none
Data Quality:	1
References	Petroquimia Espanola S.A. (1985). Ames Metabolic Activation Test to Assess the Potential Mutagenic Effect of PETREPAR® C14.

3.2 *in vivo* Genetic Toxicity

Robust Summary No.: GTVI-1

Genetic Toxicity In Vivo

Test Substance:	CAS No. 6477-72-8, C10-C13 normal paraffins
Vehicle:	Corn oil
Type of Study:	Mouse Micronucleus Assay
Species/strain:	Mouse / CD-1
Sex:	Males and Females
Route of administration:	Oral gavage
Exposure period:	24, 48, 72 hour
Dose/Conc. Levels:	5.0, 2.5, 1.0 g/kg

Statistical methods:	Statistical analysis included calculation of means and standard deviations of the micronuclei data and a test of equality of group means by a standard one way analysis of variance at each time period (Snedecor and Cochran, 1971). When the ANOVA was significant, comparisons of vehicle control to dosed group means were by Duncan's Multiple Range Test. A standard regression analysis was performed to test for a dose response. Residuals from the ANOVA were analyzed for normality by Wilk's Criterion (Shapiro and Wilk, 1965). The residuals were normally distributed (Values were greater than 0.01 level of significant) in more than 25% of the analyses. Therefore, nonparametric analysis was not performed. Sexes were analyzed separately.
Remarks on Test Conditions:	
Method:	OECD Guideline 474
GLP:	In the spirit of GLP
Date (Year):	1991
Results (NOAEL/NOEL/LOAEL/LOEL):	NOAEL > 5.0 g/kg
Effects on mitotic index or PCE/NCE ratios by dose level by sex:	
Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal):	This test material did not induce a statistically significant increase in the mean number of micronucleated polychromatic erythrocytes.
Statistical results:	As discussed above.
Remarks:	This test material did not induce a statistically significant decrease in the mean percent of polychromatic erythrocytes which is a measure of bone marrow toxicity.
Conclusions	Under the condition of this assay, this test material was not clastogenic in mouse bone marrow at doses up to and including 5.0 g/kg.
Remarks	
Data Quality:	1, no restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1991. In vivo Mammalian Bone Marrow Micronucleus Assay. Unpublished Study.

4.0 Reproductive Toxicity

Robust Summary No.: RPRO-1

Reproductive Toxicity

Test Substance	CAS No.: 124-18-5
Remarks	LINPAR 10 (commercial Decane) approx. composition: 97% 1-decane
Method	
Method/guideline followed	OECD 422
Test type	A Combined Repeated Dose Toxicity Study With The Reproduction/Developmental Toxicity Screening Test In Sprague Dawley Rats By The Oral Route
GLP	Yes
Year	1995
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) BR
Route of administration	Oral (gavage)
Duration of test	Males were treated from day 14 prior to the mating phase until the end of the mating phase and then killed. Females were treated from day 14 prior to mating, through day 4 of lactation and then killed along with the pups.
Doses/concentration levels	0, 25, 150, or 1,000 mg/kg/day (10 ml/kg dosing volume)
Sex	10 male, 10 female per group
Exposure period	Single daily injection
Frequency of treatment	7 days/week
Control group and treatment	10 male, 10 female, 0.5% methylcellulose
Post exposure observation period	Not applicable
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, gestation length and pup body weights were analyzed by ANOVA. Mean mating time was analyzed via the Kaplan Meier method. Pregnancy rates and mating, conception, viability index, post implantation losses, fertility and gestation indices were analyzed by the trend test, Chi-square 2XN and Fisher's exact test

	(all one tailed).
Test Conditions	Groups of 10 male and 10 female CD rats were dosed via gavage with test material daily by gavage at exposure levels of 0, 25, 150, or 1,000 mg/kg/day. Males were dosed from the 14th day prior to mating, during mating until the end of the mating period. Females were dosed from the 14th day prior to the start of the mating phase to day 4 of lactation. Reproductive assessment of included mating, conception and fertility indices, reproductive organ weights and gross and histologic examination of the reproductive tract (special emphasis on stages of spermatogenesis in male gonads and interstitial testicular cell structure).
Results	
NOAEL (NOEL)	NOEL = 1,000 mg/kg/day (Parental)
LOAEL (LOEL)	Not applicable.
Remarks	With the possible exception of fertility index, there were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The mean mating time of the 1000 mg/kg/day groups was slightly longer than of the control, however, the increase was not statistically significant and within the normal range of variability for this strain of rats. There was a, non dose-related, decrease in fertility (decreased fertility index) was observed in all treated groups (not statistically significant) compared to controls. However, this effect took place in the absence of any adverse effects on reproductive organs and may have resulted from changes in mating behavior due related to stomach irritation experienced by the treated animals.
Conclusions	Oral dosing of Linpar 10 to male and female Sprague Dawley rats at levels of 0, 25, 150, or 1,000 mg/kg/day resulted in no statistically significant treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. Based on these data, the no-observable-effect level (NOEL) for reproductive toxicity was 1000 mg/kg/day.
Data Quality	
Reliabilities	1
References	Maraschin, R., Comotto, L., R., Conz, A. (1995) LINPAR 10: Combined repeated dose toxicity study with the reproduction/developmental screening test in Crl:CD (SD) BR male and female rats Sprague Dawley rats of the test article LINPAR 10 administered by oral route at the dosages of 0, 25, 150 and 1,000 mg/kg/day. Report of Medici del Vascello. 20138- Milano (Italy), Instituto di Ricerche Biomediche "Antoine Marxer" RBM S.p.A. for

	the Enichem Augusta Industriale (Currently Sasol Italy).
Other	Updated August 27, 2003

Robust Summary No.: RPRO-2

Combined Repeated Dose and Reproductive and Developmental Screening Test

Type of Study:	A combined Repeated Oral Dose and Reproductive/Developmental toxicity screening study
Species/strain:	Rat / Crj:CD® (SD)
Age at study Initiation:	10 weeks
Route of administration:	Oral Gavage
Duration of test	Males, 46 days; females, from 14 days before mating to day 3 of lactation
Dose/Conc. Levels:	0, 100, 300, 1000 mg/kg (5 mL/kg dose volume
No. of animals/sex/dose:	12/sex/dose group (including controls)
Exposure period	Single daily injection
Frequency of treatment:	7 days per week
Control group and treatment:	Olive Oil- vehicle control
Statistical methods:	Sexual cycle, copulation index (mating index), fertility index, gestation index and nursing index for the test and control groups were analyzed by Fisher's accuracy probability test. Other parameters were analyzed by Bartlett's homogeneity of variance followed by single dimension configuration variance analysis or Kruskal-Wallis method. If the results were significant, either Dunnett's method or the Mann-Whitney U-test was applied to compare the treated groups with the control. Qualitative urinary measurements were analyzed using the Kruskal-Wallis method and the Mann Whitney U-test. Viability and body weight of offspring were analyzed using the litter as the test unit. Results with statistical p-values of < 0.05 were considered statistically significant.
Remarks on Test Conditions:	Males were dosed for 46 days including 14 days prior to mating and during the mating period; females were dosed for 14 days prior to mating, during the mating and gestation periods and postnatally until the third day of nursing.
Method/Guideline:	OECD Guideline 422

GLP:	GLP
Date (Year):	1996
Test Substance:	CAS No. 1120-21-4, undecane (= or > 99%)
Vehicle:	Olive oil
Results (NOEL):	Repeat Dose: 100 mg/kg (males and females) Developmental: 300 mg/kg Reproductive: 300 mg/kg
Toxic response/effects by dose level:	**Repeat dose toxicity:** Salivation was observed in males and females in the 300 and 1000 mg/kg dose groups. A statistically significant suppression of body weight gain was observed in males at the 1000 mg/kg dose level. The 1,000 mg/kg female dose group exhibited a statistically significant increased body weight gain during the lactation period. Food consumption decreased in males at the 300 and 1000 mg/kg dose levels in the first half of the administration period. In contrast, food consumption was increased in males at the 1000 mg/kg dose group in the second half of the administration period, and in females at the 1000 mg/kg level in the second half of pregnancy and during lactation. High dose males (1000 mg/kg) exhibited decreased hemoglobin and albumin concentrations, and increased white cell count, Alpha-2μ-globulin, GPT, cholinesterase and total cholesterol. Relative liver weights, and relative and absolute thymus weights, were increased in males at 1000 mg/kg. Absolute and relative liver weights were elevated in females at the 1000 mg/kg dose level. No gross or histopathological effects were observed at any dose level. No effects were noted at the 100 mg/kg dose level. **Reproductive/developmental toxicity:** No effects on reproductive ability and reproductive organ weights were observed. There were no gross or histological findings of toxicity to reproductive organs of either sex. There was no apparent effect on deliveries or maternal behavior dams. Body weight gain was decreased in male and female offspring at the 1000 mg/kg dose level. No effects were noted in terms of viability, general condition or gross observation of offspring.
Remarks:	None
Conclusions:	The administration of undecane at doses of 300 and 1000 mg/kg resulted in changes in body weight gain and food consumption. Changes in liver and thymus weights were also noted for males and females, respectively, at the 1000 mg/kg dose level only. Some changes hematological and blood chemistry parameters were noted in males at the 1000 dose level. No gross or histopathological effects were noted at the 100 mg/kg dose level. The NOEL for repeat dose toxicity is 100 mg/kg. Decreased body weight gain was noted in offspring, at the 1,000 mg/kg dose level only, however, no others effects were noted on reproductive parameters, including gross or histopathological evaluation of reproductive

	organs. The NOEL for reproductive and developmental toxicity is 300 mg/kg.
Remarks:	None
Data Quality:	1, no restrictions
References:	Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Combined repeat Dose and Reproductive/Developmental Toxicity Screening test of Undecane by Oral Administration. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

5.0 Developmental Toxicity

Robust Summary No.: DEVL-1

Developmental Toxicity

Test Substance	LINPAR 10 (commercial Decane)
Remarks	approx. composition: 97% 1-decane CAS No.: 124-18-5
Method	
Method/guideline followed	OECD 422
Test type	A Combined Repeated Dose Toxicity Study With The Reproduction/Developmental Toxicity Screening Test In Sprague Dawley Rats By The Oral Route
GLP	Yes
Year	1995
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) BR
Route of administration	Oral (gavage)
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4.
Doses/concentration levels	0, 25, 150, or 1,000 mg/kg/day (10 ml/kg dosing volume)

Sex	10 male, 10 female per group
Exposure period	Single daily injection
Frequency of treatment	7 days/week
Control group and treatment	10 male, 10 female, 0.5% methylcellulose
Post exposure observation period	Not applicable
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, gestation length and pup body weights were analyzed by ANOVA. Mean mating time was analyzed via the Kaplan Meier method. Pregnancy rates and mating, conception, viability index, post implantation losses, fertility and gestation indices were analyzed by the trend test, Chi-square 2XN and Fisher's exact test (all one tailed). The probability of survival per group was calculated by the product-limit procedure of Kaplan-Meier. Both a trend test and a log-rank test were used to analyze differences in survival among groups.
Test Conditions	Groups of 10 male and 10 female CD rats were dosed via gavage with test material daily by gavage at exposure levels of 0, 25, 150, or 1,000 mg/kg/day. Males were dosed from the 14th day prior to mating, during mating until the end of the mating period at which time they were killed. Females were dosed from the 14th day prior to the start of the mating phase to day 4 of lactation and subsequently killed on day 5 of lactation with their pups. Developmental toxicity assessment included, observations of external abnormalities, number of live and still births, mortality, sex determination and weights of pups.
Results	
NOAEL (NOEL)	NOEL = 1,000 mg/kg/day (F1)
LOAEL (LOEL)	Not applicable.
Remarks	There were no treatment-related effects at any dose level on any of the developmental parameters evaluated in this study.
Conclusions	Oral dosing of Linpar 10 to male and female Sprague Dawley rats at levels of 0, 25, 150, or 1,000 mg/kg body weight /day produced no evidence of developmental toxicity or teratogenicity. Based on these data, the no-observable-effect level (NOEL) for developmental toxicity was 1,000 mg/kg/day, the highest dose tested.
Data Quality	
Reliabilities	1
References	Maraschin, R., Comotto, L., R., Conz, A. (1995) LINPAR 10: Combined repeated dose toxicity study with the

	reproduction/developmental screening test in Crl:CD (SD) BR male and female rats Sprague Dawley rats of the test article LINPAR 10 administered by oral route at the dosages of 0, 25, 150 and 1,000 mg/kg/day. Report of Medici del Vascello. 20138- Milano (Italy), Instituto di Ricerche Biomediche "Antoine Marxer" RBM S.p.A. for the Enichem Augusta Industriale (Currently Sasol Italy).
Other	Updated September 6, 2002

Robust Summary No.: DEVL-2

Combined Repeated Dose and Reproductive and Developmental Screening Test

Test Substance:	CAS No. 1120-21-4, undecane (= or > 99%)
Vehicle:	Olive oil
Type of Study:	A combined Repeated Oral Dose and Reproductive/Developmental toxicity screening study
Species/strain:	Rat / Crj:CD® (SD)
Age at study Initiation:	10 weeks
Route of administration:	Oral Gavage
Duration of test	Males, 46 days; females, from 14 days before mating to day 3 of lactation
Dose/Conc. Levels:	0, 100, 300, 1000 mg/kg (5 mL/kg dose volume
No. of animals/sex/dose:	12/sex/dose group (including controls)
Exposure period	Single daily injection
Frequency of treatment:	7 days per week
Control group and treatment:	Olive Oil- vehicle control
Statistical methods:	Sexual cycle, copulation index (mating index), fertility index, gestation index and nursing index for the test and control groups were analyzed by Fisher's accuracy probability test. Other parameters were analyzed by Bartlett's homogeneity of variance followed by single dimension configuration variance analysis or Kruskal-Wallis method. If the results were significant, either Dunnett's method or the Mann-Whitney U-test was applied to compare the treated groups with the control. Qualitative urinary measurements were analyzed using the Kruskal-Wallis method and the Mann Whitney U-test. Viability and body weight of offspring were analyzed using the litter as the test unit. Results with statistical p-values of < 0.05 were considered statistically

	significant.
Remarks on Test Conditions:	Males were dosed for 46 days including 14 days prior to mating and during the mating period; females were dosed for 14 days prior to mating, during the mating and gestation periods and postnatally until the third day of nursing.
Method/Guideline:	OECD Guideline 422
GLP:	GLP
Date (Year):	1996
Results (NOEL):	Repeat Dose: 100 mg/kg (males and females) Developmental: 300 mg/kg Reproductive: 300 mg/kg
Toxic response/effects by dose level:	**Repeat dose toxicity:** Salivation was observed in males and females in the 300 and 1000 mg/kg dose groups. A statistically significant suppression of body weight gain was observed in males at the 1000 mg/kg dose level. The 1,000 mg/kg female dose group exhibited a statistically significant increased body weight gain during the lactation period. Food consumption decreased in males at the 300 and 1000 mg/kg dose levels in the first half of the administration period. In contrast, food consumption was increased in males at the 1000 mg/kg dose group in the second half of the administration period, and in females at the 1000 mg/kg level in the second half of pregnancy and during lactation. High dose males (1000 mg/kg) exhibited decreased hemoglobin and albumin concentrations, and increased white cell count, Alpha-2μ-globulin, GPT, cholinesterase and total cholesterol. Relative liver weights, and relative and absolute thymus weights, were increased in males at 1000 mg/kg. Absolute and relative liver weights were elevated in females at the 1000 mg/kg dose level. No gross or histopathological effects were observed at any dose level. No effects were noted at the 100 mg/kg dose level. **Reproductive/developmental toxicity:** No effects on reproductive ability and reproductive organ weights were observed. There were no gross or histological findings of toxicity to reproductive organs of either sex. There was no apparent effect on deliveries or maternal behavior dams. Body weight gain was decreased in male and female offspring at the 1000 mg/kg dose level. No effects were noted in terms of viability, general condition or gross observation of offspring.
Remarks:	None
Conclusions:	The administration of undecane at doses of 300 and 1000 mg/kg resulted in changes in body weight gain and food consumption. Changes in liver and thymus weights were also noted for males and females, respectively, at the 1000 mg/kg dose level only. Some changes hematological and blood chemistry parameters were noted in males at the 1000 dose level. No gross or histopathological effects were noted at the 100 mg/kg dose level. The NOEL for repeat dose toxicity is 100 mg/kg. Decreased body

	weight gain was noted in offspring, at the 1,000 mg/kg dose level only, however, no others effects were noted on reproductive parameters, including gross or histopathological evaluation of reproductive organs. The NOEL for reproductive and developmental toxicity is 300 mg/kg.
Remarks:	None
Data Quality:	1, no restrictions
References:	Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Combined repeat Dose and Reproductive/Developmental Toxicity Screening test of Undecane by Oral Administration. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

Robust Summary No.: DEVL-3

Developmental Toxicity

Test Substance:	CAS No. 64742-47-8, C9-C13; mixed alkanes (n-, iso- and cycloparaffins)
Vehicle:	N/A
Type of Study:	Segment II teratology study
Species/strain:	Rats / Sprague Dawley
Route of administration:	Inhalation
Sex:	21 mated females / dose group
Duration of test:	Day 6 through 15 of gestation
Frequency of treatment:	6 hours per day
Dose/Conc. Levels:	0, 300, 900 ppm (nominal) 311, 866 ppm (mean actual)
Exposure period:	Daily (days 6-15 of gestation)
Control group and treatment:	Chamber exposed group and a positive control group. The positive control group received 400 mg/kg/day of acetylsalicyclic acid (ASA) via gastric intubation on Gestation Days 6-15.
Statistical methods	Comparisons between control and treated groups and between control and ASA-treated groups were made when applicable by the chi-square method. Body weights, body weight gains, numbers of corpora lutea, implantations, resorptions, fetuses per dam, fetal and litter weights and crown-rump distances were compared to control by the F-test and

	Student's t-test. When variances differed significantly, Student's t-test was appropriately modified using Cochran's approximation.
Remarks on Test Conditions:	Only one species tested, administered by inhalation route
Method:	Designed in accordance with FDA 1966 Guidelines for Reproductive Studies for Safety Evaluation of Drugs for Human Use, Segment II (Teratology Study).
GLP:	GLP equivalent
Date (Year):	1978
Results (NOAEL/NOEL and LOAEL/LOEL for maternal and developmental toxicity):	NOAEL > 866 ppm (mean actual) for maternal and developmental toxicity
Actual dose received by dose level and sex:	304 –318 ppm and 854 to 878 ppm.
Maternal data with dose level:	**311 ppm and 866 ppm dose groups (mean actual):** Pregnancy rate, mortality, body weight gain and gross postmortem observations were not affected by treatment. Females at the high dose exhibited a slight increase in excessive lacrimation during the treatment and post-treatment period.
Fetal data with dose level:	**311 ppm and 866 ppm dose groups (mean actual):** No treatment-related effect on reproductive data, fetal size and sex distribution data, ossification variation data or fetal examination data was reported.
Statistical results:	
Remarks:	
Conclusions:	Under the conditions of this test, inhalation exposure to did not result in any embryotoxic or teratogenic effects.
Remarks:	Only one species tested, administered by inhalation route
Data Quality:	2, with restrictions
References:	ExxonMobil Biomedical Sciences, Inc. 1978. A Segment II Teratology Study in Rats Following Inhalation Exposure. Study No. 77-1567. Unpublished Study.

6.0 Toxicity - Other

Robust Summary No.: Other-1

Tumor Promotion Assay

Type of Study:	Tumor Promotion Assay in Mouse Skin
Method/Guideline:	Other
GLP:	Yes
Date (Year):	1994
Species/strain:	Mice/Crl: CD-1 (ICR)BR VAF/Plus
Route of administration:	Dermal
Duration of test:	54 weeks
No. of animals/sex/dose:	30/Males/dose
Age at initiation:	Approximately 7 weeks
Frequency of Treatment:	7, 4, or 2 times per week for 54 weeks
Dose/Concentration:	37.5 µl / 28.6%, 50% and 100% v/v
Doses per time period:	Single
Vehicle/Carrier:	100 LP Solvent Neutral
Control group and treatment:	Carrier Control: 100 LP Solvent Neutral Initiator: DMBA (9,10-Dimethyl-1,2-benzanthracene) Positive Control: PMA (Phorbol 12-myristate 13-acetate)
Remarks on Test Conditions:	The backs of the mice were clipped prior to dose initiation, and weekly until study termination. All animals were clipped a minimum of five hours prior to dosing. All animals were treated with initiator (DMBA) on Day 0 with the exception of the 100 LP Solvent Neutral control group. The test substance was applied to intact skin of the animals at various concentrations (100%, 50% and 28.6%). The frequency of application of the test substance (2, 4, or 7 times per week) was varied so that lower concentrations of the test substance in carrier was applied more frequently. In this way, an equivalent total weekly dose of the test substance was maintained for each group. The appropriate volume of test substance (neat or diluted) was applied to the clipped dorsal area of each mouse by means of a calibrated automatic pipette with a clean disposable tip used for each group.
Remarks on Test Conditions (cont'd):	The animals were examined for viability twice daily on Monday through Friday, and once daily on Saturday, Sunday, and holidays. Observations were made weekly as to the nature, onset, severity and duration of toxicological signs, dermal irritation and dermal growths. Bodyweights were recorded the week prior to dosing, on the day of dose initiation and every four weeks thereafter. Body weights were also recorded on the day of terminal sacrifice. Animals were sacrificed when judged to be in moribund condition,

when suspected to have a carcinoma, for humane reasons, or after approximately 54 weeks. Necropsy was performed on all animals, and skin tumors, treated/untreated skin, and grossly observable masses were collected and preserved in 10% neutral buffered formalin. Skin and skin tumors were examined microscopically.

Temperature ranged from 68 to 76 deg. F. Relative humidity was between 40 and 70%. Lighting was controlled by automatic timer in a 12 hours light, 12 hours dark photoperiod.

Test animals weighed between 25.6 to 33.3g at initiation.

Test substance: CAS No. 64771-72-8 C10-C13 normal paraffins

Statistics: Fisher's Exact Test

Result: Mortality Data

Group	Carrier Control	Initiator Control	Initiated Carrier	Test Substance 100%	50%	28.6%
Mortality	1	27*	8	25*	4	3
Estimated Median Survival (days)	615	300	427	322	486	511

* Indicates significantly different from the initiated carrier control at $p<0.01$

Tumor Promotion Data

Group	Carrier Control	Initiator Control	Initiated Carrier	Test Substance 100%	50%	28.6%
Animals w/tumors	0	29**	1	15**	1	3
Estimated Median time to first tumor (days)	689	171	594	318	606	503

** Indicates significantly different from the carrier control at $p<0.01$

Remarks: Unscheduled mortality occurred in all groups. Statistically reduced survivorship occurred at the 100% dose level compared to the carrier control group.

There were no biologically meaningful or statistically significant differences in mean body weights between the treated groups and the carrier control group.

There was a statistically significant increase in the incidence of microscopically confirmed papillomas and squamous cell carcinomas in the PMA (29/30) and the 100% test substance (15/30) test animals. The incidence of tumors or the median time to tumor in the 50% and 28.6% dose groups was not statistically different from

	the initiated carrier control group.
Conclusions:	Under the conditions of this study, C10-C13 normal paraffins exhibited clear evidence of increased tumor promotion in mouse skin at a concentration of 100% of the neat test substance. A low tumor incidence occurred in the groups receiving 50% and 28.6% of the test substance. However, the tumor incidence and estimated time to tumor of these two groups was not significantly different from the initiated carrier control group.
Data Quality:	(1) valid without restrictions
References:	ExxonMobil Biomedical Sciences Inc. 1997. Tumor Promotion Assay in Mouse Skin. Study No. 168399B. Unpublished Study

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Robust Summary No.: Other-2

Neurotoxicity

Type of Study:	Acute neurotoxicity screen: Functional observational battery and motor activity; visual discrimination performance
Species/strain:	Male WAGR/RijCrlBR rats
No. of animals/sex/dose:	4 Males
Route of administration	Whole body inhalation, vapor
Frequency of Treatment:	8 hr/day for three consecutive days
Dose/Concentration:	0 (control); 0.5 g/m3 (85 ppm); 1.5 g/m3 (260 ppm); 5 g/m3 (860 ppm)
Doses per time period:	One 8 hr exposure
Control group and treatment:	Concurrent; no n-decane exposure
Remarks on Test Conditions:	Tests were conducted at the end of exposure on each treatment day, and one day after the end of exposure.
Method/Guideline:	WHO/IPCS Collaborative Study on Neurotoxicity Assessment
GLP:	OECD Principles of Good Laboratory Practice
Date (Year):	1989
Test substance	CAS No. 124-18-5 n-decane
Vehicle:	n/a
Result:	Functional observations indicated a significant reduction in forelimb grip strength in the highest exposure group after the third exposure period, but not in hind limb grip strength or 14 other behavioral

	endpoints. Visual discrimination testing indicated mild n-decane-induced disturbances in measures of learned performance, but not in 11 other parameters of learned performance; performance speed was sensitive to the effects of n-decane. The effects were reversible as demonstrated by the absence of significant differences in one-day post-test measurements.
Remarks:	No neurohistopathological examination was conducted. Effects were slight and reversible one day after exposure, possibly indicating a pharmacological rather than a toxicological effect on behavior.
Conclusions:	Short-term high-level exposure to n-decane induced mild reversible neurobehavioral effects on functional observations and measures of learned performance. **LOAEL**: Effects were observed during or after 3 consecutive daily 8 hr exposures to 5 g/m3 n-decane. **NOAEL**: 1.5 g/m3 (260 ppm).
Data Quality:	1, without restrictions
References:	Lammers, JHCM. TNO Report V98.549. Model studies for evaluating the behavioral effects of petroleum solvents and the role of toxicokinetic factors: The effects of n-decane on behavior in the rat.

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ACTO-2 PETRESA (Petroquimia Espanola S.A.) (1984). Acute Oral Toxicity to Rats of PETREPAR® n-C10 (C10).

ACTO-3 Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Single Dose Oral Toxicity Test of Undecane in Rats. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

ACTO-4 ExxonMobil Biomedical Sciences, Inc. 1983. Acute Oral Toxicity Study in the Rat. Study No. 320701. Unpublished Study.

ACTO-5 Exxon Biomedical Sciences, Inc. 1983. Acute Oral Toxicity Study in the Rat. Study No. 320601A. Unpublished Study.

ACTO-6 Petroquimia Espanola S.A. (1984). Acute Oral Toxicity to Rats of PETREPAR® n-C14 (C14).

1.2 Acute Toxicity – Inhalation:

ACTI-1 Carpenter, C.P. *et al*. 1978. Petroleum Hydrocarbon Toxicity Studies XVII. Animal Response to n-Nonane Vapor. Tox and Appl. Pharmacology. 44:53-61.

ACTI-2 Nilsen, O. G. et al. 1988. Toxicity of n-alkanes in the rat on short term inhalation. Pharmacol. & Toxicol. 62:259-266.

1.3 Acute Toxicity – Dermal:

ACTD-1 ExxonMobil Biomedical Sciences, Inc. 1983. Acute Dermal Toxicity Study in the Rabbit. Study No. 320506. Unpublished Study.

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RPTD-2 Maraschin, R., Comotto, L., R., Conz, A. (1995) LINPAR 10: Combined repeated dose toxicity study with the reproduction/developmental screening test in Crl:CD

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RPTD-3 Nau, C.A., Neal, J., and Thorton, M. 1966. C9-C12 fractions obtained from petroleum distillates. Arch Environ Health 12: 382-393.

RPTD-4 Nau, C.A., Neal, J., and Thorton, M. 1966. C9-C12 fractions obtained from petroleum distillates. Arch Environ Health 12: 382-393.

RPTD-5 Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Combined repeat Dose and Reproductive/Developmental Toxicity Screening test of Undecane by Oral Administration. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

RPTD-6 Exxon Biomedical Sciences, Inc. 1995. 28-Day Repeated Dose Dermal Toxicity Study in Rabbits with Neurotoxicity Evaluation. Study No. 140510B. O'Connor et al. 1997. Subchronic Toxicity With Neurotoxicity Evaluation of C_{12-14} Normal Paraffinic Fluid in Rabbits. *The Toxicologist.* 36(No. 1, Part 2). Presented at the 1997 Society of Toxicology Meeting, Cincinnati, OH.

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GTVT-2 Zeiger, E, et al. 1992. Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ. Mol. Mutagen. 19(suppl 21): 2-141.

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GTVT-4 Sasol Italy (Enichem Augusta) (1994). Study of the Capacity of the Test Article LINPAR® 10 to Induce Chromosome Aberrations in V79 Chinese Hamster Lung cells.

GTVT-7 Petroquimia Espanola S.A. (1985). Ames Metabolic Activation Test to Assess the Potential Mutagenic Effect of PETREPAR® C14.

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RPRO-1 Maraschin, R., Comotto, L., R., Conz, A. (1995)
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RPRO-2 Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Combined repeat Dose and Reproductive/Developmental Toxicity Screening test of Undecane by Oral Administration. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614.

5.0 Developmental Toxicity

DEVL-1 Maraschin, R., Comotto, L., R., Conz, A. (1995)
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APPENDIX C
Excerpt from Documentation for Proposed Group Guidance Values for OEL Setting for Hydrocarbon Solvents

Group: C_9-C_{15} Aliphatics/Cycloaliphatics Guidance Value: 1200 mg/m^3

Basis:

For C_9-C_{15} Aliphatics/Cycloaliphatics, a 1200 mg/m^3 mass-based value equates to a range of volume-based values from 229 ppm for C9 to 138 ppm for C_{15}. The only pure aliphatic hydrocarbon in this range for which an OEL exists is nonane. The ACGIH TLV recommendation of 200 ppm (1050 mg/m^3) for nonane is slightly more stringent than the proposed Group Guidance Value of 1200 mg/m^3. The EU, MAK and HSE do not have any OELs for substances in this group. The limited scientific data on n-decane and isodecane does not indicate any effects in animals at doses less than 540 ppm (3100 mg/m^3). The database on C_{11}+ aliphatic compounds is very limited. As noted by the UK HSE, the low vapor pressures of these substances minimize concern over inhalation of vapors in the workplace.

Fewer inhalation toxicity data are available on compounds in this carbon range than for lighter hydrocarbons (i.e., C_5-C_8). Nonetheless, those data that exist do not suggest that CNS depression, irritation, or other adverse effects will occur at concentrations less than 1200 mg/m^3. As with the C_5-C_8 hydrocarbons, the proposed guidance value for the C_9-C_{15} group combines aliphatics with cycloaliphatics. This is based on the absence of any toxicological data suggesting that these two isomeric classes should be differentiated, and on comparisons of toxicological data on C_5 and C_6 compounds indicating that such grouping is justified.

The guidance value for the C_9-C_{15} aliphatic/cycloaliphatic group is lower than that for the C_5-C_8 group based on two primary considerations. The first derives from toxicological data, and the second is based on vapor pressure and exposure potential. Generally speaking, CNS depressant potency and respiratory irritation among C_5-C_9 alkanes increases with increasing molecular weight. This pattern is reflected in the progressively lower ACGIH TLVs for alkanes in this carbon range (i.e., pentane, 1770 mg/m^3; heptane, 1640 mg/m^3; nonane, 1050 mg/m^3). Although fewer comparative data on CNS depressant potency and irritancy are available on higher weight homologues, a lower value for the C_9-C_{15} group (compared to the C_5-C_8 group) is in keeping with this trend of decreasing TLVs with increasing molecular weight. In addition, C_9-C_{15} aliphatics/cycloaliphatics will have a lower vapor pressure than comparable C_5-C_8 compounds, and therefore, a lower potential for exposure. In fact, the saturated vapor concentration for the C_{13}-C_{15} compounds will approach the Guidance Value of 1200 mg/m^3. Inasmuch as it can be confusing to have a vapor-based OEL that exceeds the saturated vapor concentration, the Guidance Value of 1200 mg/m^3 does not extend beyond C_{15}.

A brief summary of studies supporting this recommendation is provided below, along with pertinent reference citations.

- *Nonane*

Carpenter et al. (1978) conducted acute and subchronic inhalation studies in rats with relatively pure n-nonane (98.4%). The 4-hour LC_{50} was 17,000 mg/m^3. The response pattern during inhalation of the highest concentration (23,000 mg/m^3) progressed from early lacrimation, salivation, and coordination loss to tremors, convulsions, and death. Rats tolerated 4600 mg/m^3 (880 ppm) for 4 hours without visible discomfort. In the subchronic study, rats were exposed to concentrations of 1900, 3100, and 8400 mg/m^3 for 6 hrs/day, 5 days/week, for 13 weeks. Rats at the 8400 mg/m^3 concentration exhibited salivation, mild coordination loss and fine tremors. No such signs of distress were noted among rats exposed at the mid- and low concentrations. Body weights of rats exposed to 8400 mg/m^3 were significantly lower than controls during the study. Microscopic evaluation of tissues from exposed rats revealed no treatment-related lesions. The authors concluded that the NOAEL from this study was 3100 mg/m^3 (590 ppm).

Nilsen et al. (1988) evaluated the acute inhalation toxicity of n-C_9 to n-C_{13} alkanes in rats at nearly saturated air concentrations. Rats were exposed to vapors for 8 hours, followed by a 14 day observation period. Exposure concentrations of n-nonane ranged from 2414-5280 ppm (12,675-27,720 mg/m^3), and an LC_{50} of 4467 ppm was estimated. No deaths occurred at 2414 ppm, and only a single death occurred at 3560 ppm. The achievable saturated vapor concentrations were significantly lower for the higher molecular weight n-C_{10} to n-C_{13} compounds. Maximum achievable concentrations were 1369 ppm for n-decane, 442 ppm for n-undecane, 142 ppm for n-dodecane, and 41 ppm for n-tridecane. Neither deaths nor adverse behavioral effects were observed during exposure to these compounds.

- *Decane*

There is limited toxicological data available on n-decane. Rats exposed to 540 ppm (3100 mg/m^3) for 18 hrs/day, 7 d/week for 123 days had a significant increase in organ weight and total leukocytes, but no signs of organ toxicity (Nau et al., 1966). Saturated vapor concentrations (approximately 1800 ppm; 10,900 mg/m^3) caused a slight decrease in respiration rate in mice (Kristianen and Nielsen, 1988).

More recently, a neurobehavioral study was conducted by TNO to evaluate the effects of short-term, high-level exposure to n-decane on functional observational measures, motor activity, and learned performance. Rats were exposed to 500, 1500, or 5000 mg/m^3 (85, 260 or 860 ppm) n-decane 8 hours/day for 3 consecutive days. Decane did not cause any effects on measures of sensorimotor reactivity, excitability, or motor activity. Tests for two behavioral endpoints found mild reversible effects from the high dose exposure. A statistically significant decrease in forelimb gripstrength, one of the neuromuscular endpoints, was observed after the third exposure. In learned

performance tests, n-decane did not affect discrimination accuracy or measures of stimulus control, but there was an increase in the number of long response latencies (> 6 sec) in the high dose group. Based on the mild reversible effects on some parameters of neuromuscular activity and learned performance observed in this study, the NOAEL for n-decane is 1500 mg/m^3.

- *VM&P Naphtha*

Carpenter et al. (1975) tested a sample of Varnish Makers' and Painters' (VM&P) Naphtha in rats, dogs, cats, and humans. The sample tested had the following composition: 48% light hydrocarbons (to C_8), 27% C_9 hydrocarbons, 14% C_{10} and higher molecular weight hydrocarbons, and 11% aromatics (predominantly C_7 to C_9). The 4-hour LC_{50} for rats was 16,000 mg/m^3 (3400 ppm), and the highest concentration producing no visible signs of distress in rats was 4,400 mg/m^3 (940 ppm). In a subchronic study, rats and dogs were exposed to 1300, 2800, or 5800 mg/m^3 vapor for 6 hrs/day, 5 days/week for 13 weeks. At the high concentration, there appeared to be some indication of hematological effects in rats and elevated serum alkaline phosphatase levels in dogs. The mid- and low concentrations were judged to be without effect, so the NOAEL was 2800 mg/m^3. In studies with human subjects exposed for 15 minutes, concentrations up to and including 2100 mg/m^3 caused only slight or transitory eye and throat irritation in two of seven individuals. As these effects were seen at a similar incidence at doses as low as 660 mg/m^3, the authors attributed the results to the sporadic sensory response of humans.

Based on the overall database, the authors suggested a tentative "hygienic standard" of 2000 mg/m^3 (430 ppm) for VM&P naphtha vapors in humans for repeated daily inhalation.

- *Isoparaffinic Hydrocarbon Solvent Products*

A variety of commercial hydrocarbon solvents in the C_9-C_{15} molecular weight range have undergone inhalation toxicity testing in order to provide data to support company-recommended exposure limits. Among these are numerous isoparaffinic solvents spanning a range of approximately C_8 to C_{15}. The physical properties and available toxicity data for these isoparaffinic solvents have been summarized by Mullin et al. (1990). Isoparaffins have a very low order of acute toxicity, being practically non-toxic by oral, dermal, and inhalation routes. Subchronic and chronic studies on C_{10}-C_{11} isoparaffins in animals at doses up to 900 ppm (5620 mg/m^3) showed few toxicological effects. The one major finding was renal tubular damage in kidneys of male rats (Phillips and Egan, 1984; Phillips and Cockrel, 1984). This effect does not occur in mice or in female rats. The male rat nephropathy has been observed with a number of hydrocarbons and the mechanism of action has been extensively studied. The finding is not considered to be of biological significance to humans (U.S. EPA, 1991).

When evaluated for developmental toxicity in rats, C_{10}-C_{11} isoparaffins were neither embryotoxic nor teratogenic at doses up to 900 ppm (5620 mg/m^3), the highest level tested. Isoparaffins are consistently negative on genotoxicity assays.

Several studies have evaluated sensory irritation in laboratory animals or odor and sensory response in humans. When evaluated by a standard procedure to assess upper airway irritation, a C_{10}-C_{11} isoparaffin did not produce sensory irritation in mice exposed to up to 400 ppm (2500 mg/m^3).

Recently, a neurobehavioral study was conducted on a C_{10}-C_{11} isoparaffinic product. Rats were exposed to 500, 1500, or 5000 mg/m^3 (85, 260, or 860 ppm) for 8 hours per day for 3 consecutive days. C_{10}-C_{11} isoparaffins did not cause any effects on measures of neuromuscular response, sensorimotor reactivity, excitability, or motor activity. Mild reversible effects from exposure to 5000 mg/m^3 isoparaffins were observed on one measure of learned performance (psychomotor slowing). C_{10}-C_{11} isoparaffins did not affect discrimination accuracy or measures of stimulus control, but did result in a slightly increased response latency. Based on the mild reversible effect on learned performance observed in this study, the NOAEL for C_{10}-C_{11} isoparaffins is 1500 mg/m^3.

- *Mixed C9-C15 Aliphatic Solvents with Limited Aromatics*

Stoddard Solvent, also known as mineral spirit or white spirit, is a mixture of straight and branched chain aliphatics (primarily C_9-C_{12}), cycloaliphatics, and aromatic hydrocarbons. Typically, the aromatic content of mineral spirits is in the range of 20-25%. Since a large fraction of Stoddard Solvent consists of aliphatic hydrocarbons in the C_{10}-C_{15} range, toxicity data on Stoddard Solvent were deemed to be pertinent for the present guidance value.

Carpenter et al. (1975) studied the response to vapors of Stoddard solvent (8% light hydrocarbons (up to C_8), 47% C_9-C_{12} aliphatics, 31% C_9-C_{12} cycloaliphatics, 14% aromatics) in rats, dogs, cats, and humans. Inhalation of 8200 mg/m^3 (1400 ppm) caused death of 1 of 15 rats in 8 hours. The rats exhibited eye irritation, bloody exudate around the nostrils, and slight ataxia. Dogs and cats showed signs of CNS effects and died between 2 and 7 hours after inhalation of roughly equivalent concentrations. Inhalation of 2400-4000 mg/m^3 did not cause any effects in rats and dogs. In a subchronic inhalation study, no significant effects were observed in dogs exposed to 480, 1100, or 1900 mg/m^3 (84, 190, or 330 ppm, respectively) for 6 hrs/day, 5 days/week for 13 weeks (NOAEL: 1900 mg/m^3). Rats exposed at the high concentration exhibited slight pathological changes in the kidney. However, this effect was related at least in part to the susceptibility of the strain of rats (Harlan-Wistar) (Carpenter et al., 1975). Among human subjects, no one exposed to a concentration of 140 mg/m^3 experienced any irritation, but 1 of 6 individuals exposed to 850 mg/m^3 had slight and transitory eye irritation. At 2700 mg/m^3, all 6 individuals experienced eye irritation. Based on the data, the authors suggested a hygienic standard of 1200 mg/m^3 for inhalation of Stoddard Solvent by humans.

- *Cycloparaffinic Hydrocarbon Solvent Product*

A neurobehavioral study was recently conducted by TNO to assess the effects of a C_{10} cycloaliphatic product on functional observational measures, motor activity, and visual discrimination performance. Rats were exposed to 1000, 2500, or 5000 mg/m^3 (170, 430, or 860 ppm) 8 hours per day on 3 consecutive days. Endpoints were measured at the end of each 8-hour exposure period and at completion of the study. C_{10} cycloaliphatics did not cause any effects on measures of sensorimotor reactivity, excitability, or motor activity. Minimal effects of C_{10} cycloaliphatics on gait and learned performance were observed in the high dose group. The toxicological relevance of the learned performance response from exposure to C_{10} cycloaliphatics was considered questionable. C_{10} cycloaliphatics caused an improved response in the number of repetitive errors (less errors from 2500 and 5000 mg/m^3 exposure than controls) and a very mild increase in psychomotor response latency. These effects were reversible after cessation of exposure. No neurobehavioral effects were observed following exposure to 1000 mg/m^3 or 2500 mg/m^3 C_{10} cycloaliphatics. Hence, the NOAEL observed in this study was 2500 mg/m^3.

- OEL Documentation for Nonane

For nonane, ACGIH recommends a TLV of 200 ppm (1050 mg/m^3). ACGIH notes that the primary effect associated with inhalation of high concentrations of aliphatic hydrocarbons is depression of the central nervous system, and that the acute toxicity and narcotic potential of the alkanes increase with an increase in carbon chain length. Accordingly, the TLV of 200 ppm is not based on specific toxicological data, but is recommended by comparison with that for octane (TLV of 300 ppm). In fact, the justification of this TLV has been called into question by the UK HSE, who noted that the 100 ppm stepwise decrease in the TLVs from heptane to nonane appears to be an extrapolation of convenience.

Summary:

An exposure limit of 1200 mg/m^3 for C_9-C_{15} aliphatic and cycloaliphatic hydrocarbons will provide adequate protection from respiratory tract irritation, CNS depression, and any other adverse health effects.

Animal data indicate that C_9-C_{15} aliphatic and cycloaliphatic hydrocarbons are of low acute and subchronic toxicity, with NOAELs of 3100 - >5620 mg/m^3. In addition, data on isoparaffinic hydrocarbon solvent products indicate that they are neither mutagenic nor developmental toxicants.

The TNO/HSPA acute neurobehavioral test program found that C_{10}-C_{11} aliphatic and cycloaliphatic hydrocarbons caused very mild neurobehavioral effects in rats at 5000 mg/m^3. Effects were generally limited to changes in response times in learned performance tests, with little effect on measures of neuromuscular response,

sensorimotor reactivity, excitability, or motor activity. No effects were seen at doses up to 2500 mg/m^3. These data are consistent with a 13-week study on nonane in rats that showed CNS effects at 8400 mg/m^3, but no effects at 3100 mg/m^3 nonane.

There is limited human data on C_9-C_{15} aliphatic and cycloaliphatic hydrocarbons, but human data are available on irritant effects of mixed aliphatic hydrocarbon solvents containing 10-15% aromatics.

Nonane is the only C_9-C_{15} aliphatic hydrocarbon with an OEL. The ACGIH TLV for nonane is 1050 mg/m^3, but this value does not appear to be based on specific toxicological data, but is recommended by comparison with that for octane (TLV of 300 ppm). The UK HSE guidance values for aliphatics and cycloaliphatics with 7 carbons or more are 1200 mg/m^3 and 800 mg/m^3, respectively.

The available database on C_9-C_{15} aliphatics and cycloaliphatics is limited, with most relevant data on complex hydrocarbon solvent products, including some containing aromatic hydrocarbons. One reason for the lack of data on C_{11}+ hydrocarbons is the low vapor pressure of these materials which minimizes the concern for toxic effects by inhalation.

Summary Table
C_9-C_{15} Aliphatics/Cycloaliphatics (1200 mg/m^3)

Existing OELs (mg/m^3):

	ACGIH	Germany	UK	EU
Nonane	1050	---	800-1200*	---

*Group Guidance Value

Key Studies:

Test Material	Study	NOAEL (mg/m^3)
N-Nonane	13 week inhalation (rats)	3100
VM&P naphtha[1]	13 week inhalation (rats, dogs)	2800
C10-C11 Isoparaffin	12 week inhalation (rats)	5620 (highest dose tested)
C10-C11 Isoparaffin	Neurobehavioral (rats)	1500
n-Decane	Neurobehavioral (rats)	1500
C10 Cycloaliphatics	Neurobehavioral (rats)	2500
Stoddard solvent[2]	13 week inhalation (dogs)	1900 (highest dose tested)

[1]48% light hydrocarbons (to C8), 27% C9, 14% C10+, 11% aromatics
[2]8% light hydrocarbons (to C8), 47% C9-C12 aliphatics, 31% C9-C12 cycloaliphatics, 14% aromatics

References:

Carpenter et al. (1978). Petroleum hydrocarbon toxicity studies. XVII. Animal response to n-nonane vapor. Toxicol Appl. Pharmacol. 44: 53-61.

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APPENDIX D:

Calculation of a 6-Hour Inhalation Concentration Equivalent to An Oral Dose of 1000 mg/kg of n-Decane

Assumptions:

1) 100% of the oral dose is absorbed;
2) 50% of the inhalation dose is absorbed;

Parameters:

1) Rat weight is 250 g (0.25 kg);
2) Inhalation rate (in minutes) is 200 mL/min;
3) Inhalation period is 6 hours;
4) 1 ppm decane = 5.81 mg/m^3;

A. Oral dose is 1000 mg/kg or **250 mg/rat** (1000 mg/kg X 0.25 kg/rat).

B. Inhalation volume in 6 hr is 200 mL/min X 60 min/hr X 6hr = 72,000 mL or **0.072 m^3**.

C. 6-hour air concentration equivalent for a dose of 1,000 mg/kg/day in rats (assuming 50% inhalation absorption) is:
250 mg ÷ 0.072 m^3 X 100/50 **= 7,000 mg/m^3** or **1200 ppm**.

APPENDIX E

Ambient Air n-decane Concentrations: Trends Over Time

Decrease in National Emissions

National air emissions for most pollutants peaked around 1970 (EPA, 2000). The decrease in VOC emissions is largely attributable to the Clean Air Act of 1970 (CAA), Clean Air Act Amendments of 1990 (CAAA) and voluntary emissions reductions. Programs created to implement the CAAA including inspection and maintenance programs, reformulated gasoline (RFG) programs, tail pipe emission standards and new car technology. These ongoing programs will continue to decrease the amount of VOC released. Because of these programs EPA has projected that VOCs will decline an additional 20% between 1999 and 2010 (EPA, 2001).

Information regarding the national decreases of n-decane and n-undecane ambient concentrations is available for the years 1993 – 2001 from EPA's AirData Database. During this time frame, the arithmetic average ambient n-decane concentration has decreased by 84% (http://www.epa.gov/aqspubl1/annual_summary.html; accessed 3/16/04). Figure I.1 graphically depicts the decline in ambient air concentrations of n-decane. During the same period average n-undecane concentrations declined by 88%. This is illustrated in Figure I.2

The decline in ambient concentrations is largely due to a decrease in mobile source emissions resulting from the introduction of Tier 1 car emission standards, and the replacement over time of older cars with cars that meet new emission standards (fleet turnover). Given the continued phase in of mobile source regulations through 2010 (See Table I.1), ambient air n-alkane levels are likely to continue to decline. Additionally, voluntary emissions reductions and the implementation of the maximum achievable control technology (MACT) standards for the petroleum and chemical processing industries have brought about a decrease in n-alkane emissions from stationary sources.

This downward trend in ambient air concentrations has two implications. First, motor vehicles are major contributors to outdoor urban air levels and to indoor air levels (especially for homes with attached garages). Thus, in considering the ambient outside and indoor air exposure pathways, it is important to recognize that studies from the 1980s and early 1990s are likely to be overestimates of the current exposures. Second, future n-decane exposure from these microenvironments are likely to be lower then current levels.

FIGURE E.1

Trends in U.S. Air Concentrations for n-decane
(Data taken from EPA AirData Database)
(http://www.epa.gov/aqspub1/annual_summary.html)
Accessed 3/16/04

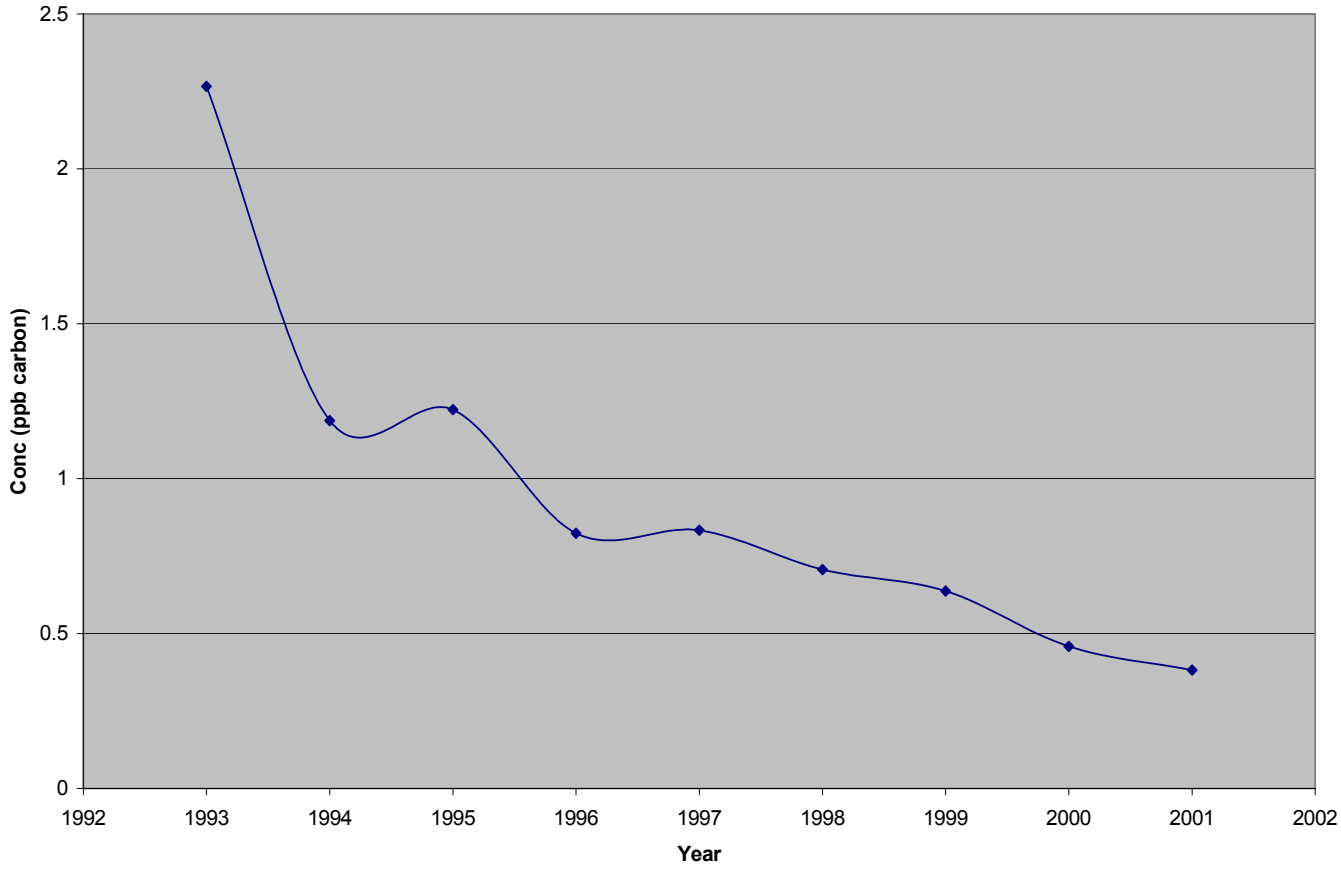


Table E.2

Trends in U.S. Air Concentrations for n-undecane
(Data taken from EPA AirData Database) (http://www.epa.gov/aqspub1/annual_summary.html)
Accessed 3/17/04

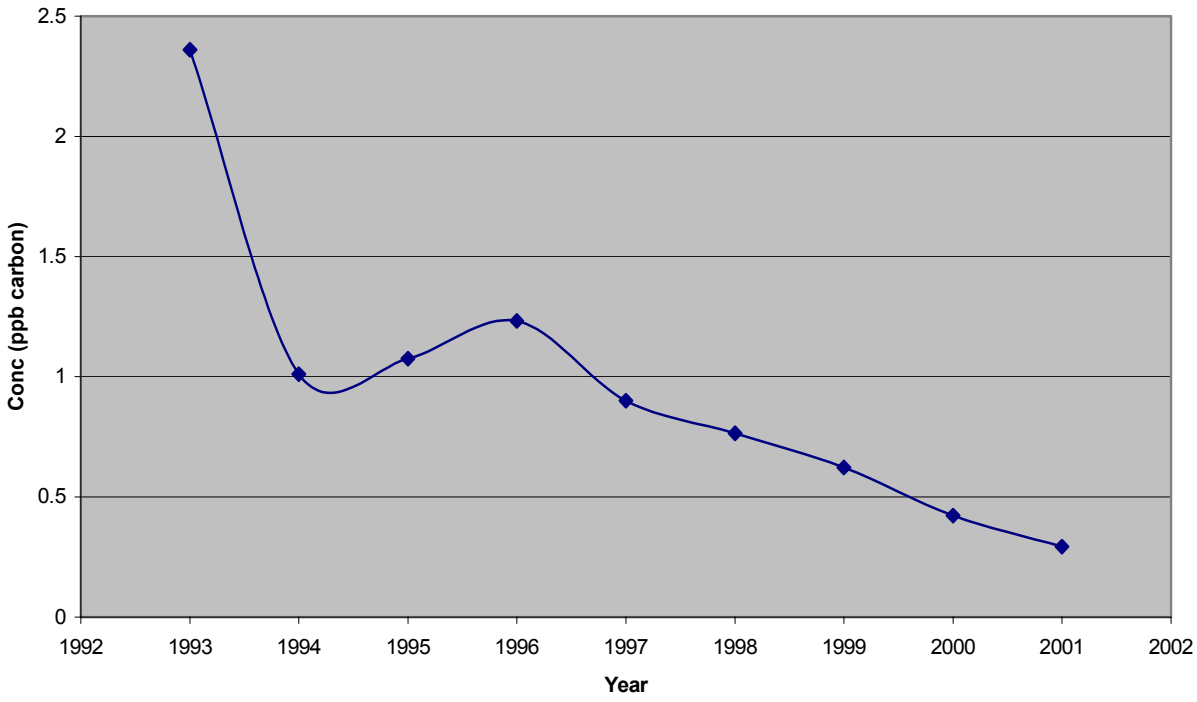


Table E.1: Timeline of Mobile Source Regulatory Actions Resulting in Reductions of VOCs in Emissions

Year	Description
1970	The Clean Air Act Amendments of 1970 - sets the first standards for emissions from motor vehicles. The standards are phased in over the next 5 years.
1971	New cars must meet evaporative emissions standards for the first time.
1975	New cars are required to use catalytic converters.
1981	New cars meet the amended Clean Air Act standards for the first time.
1983	Second generation catalytic converters required for new cars.
1983	First inspection and maintenance programs established in areas with air pollution problems.
1989	EPA sets first fuel volatility limits aimed at reducing evaporative emissions.
1990	Clean Air Act Amendments of 1990 require further reductions in hydrocarbons, lower tailpipe standards, more stringent emission testing procedures, expanded I/M programs, new vehicle technologies, and clean fuels programs. California adopts a low emission vehicle (LEV) program.
1991	EPA establishes lower tailpipe standards for hydrocarbons.
1992	Winter oxygenated fuel program begins in cities with high carbon monoxide levels. California has a similar "Phase I gasoline" program (oxygenated fuel required to limit carbon monoxide emissions also has a lower hydrocarbon content).
1994	Progressive introduction begins of national Tier 1 emission limits for light duty vehicles. On board diagnostic systems become a requirement for light duty vehicles and trucks.
1995	Phase I RFG is required to be sold in areas of ozone non-attainment (Phase I RFG has lower volatility, contain oxygenated compounds, and lower hydrocarbons). California transitional gasoline introduced as a transition from Phase I to Phase II RFG.
1996	California Phase II RFG is introduced (Phase II RFG has reduced vapor pressure and lower hydrocarbon and). National Tier 1 emission limits introduced progressively from 1996 for light duty trucks. Phase-in begins of revised procedures and limits for evaporative emissions for light and heavy-duty vehicles. Dispensing rates for gasoline and methanol pumps are regulated.
1998	Federal Tier 1 tailpipe emissions standards go into effect. California's Low Emission Vehicles (LEV) fleet averaging program begins. National hydrocarbon emission limits introduced for vehicles using clean alternative fuels (provisions under LEV program). Voluntary Agreement for Cleaner Cars: Northeastern states agree to put cleaner cars on the road before they could be mandated under the CAAA. The first NLEVs under this agreement were released in New England in 1999 and were available nationwide in 2001.
1998	Phase-in begins of on-board refueling controls (1998 - 2000).
2000	National Low Emissions Vehicle (NLEV) program starts. California hydrocarbon emission limits introduced for vehicles using clean alternative fuels - provisions under LEV program.
2001	Japanese electric-gasoline hybrid automobiles become available.
2003	Federal Tier 2 tailpipe emissions standard phase-in begins.

Year	Description
2003	Phase-in of California's LEV II program begins.
2003	California requires a maximum level of sulfur in RFG of 600 ppm.
2004	For refiners and importers, EPA requires a maximum level of sulfur in gasoline of 300 ppm, and an average of 120 ppm.
2005	For refiners, EPA requires an average level of sulfur in gasoline of 30 ppm. For importers, the average requirement is 90 ppm, and the maximum is 300 ppm.
2006	For refiners, EPA requires a maximum level of sulfur in gasoline of 80 ppm. For importers, the average is set at 150 ppm.
2005	California requires a maximum level of sulfur in RFG of 30 ppm.
2007	Importers must meet the 30 ppm average and 80 ppm maximum sulfur content in gasoline.
2006	Phase-in of California's LEV II program complete.
2010	Federal Tier 2 tailpipe emissions standard phase-in complete.

This list also includes regulatory actions that reduce sulfur in gasoline. Lower sulfur content increases catalytic converter efficiency, thus decreasing hydrocarbon emissions. Therefore, the new sulfur regulations have also been included in the table

APPENDIX F

EVALUATION OF HUMAN MILK AS AN EXPOSURE ROUTE

Erickson et al (1980), and Pellizzari et al (1982) have reported the detection of the n-alkanes of interest in human milk and are based on the same study. The report of Erickson et al is the more comprehensive and includes chromatograms. This study collected 42 samples of human milk in women living in 4 urban areas containing chemical manufacturing plants: Bridgeville PA, Bayonne NJ, Jersey City NJ, and Baton Rouge LA. All 42 samples were analyzed, then of these the 8 samples with the greatest number of peaks or very intense unique peaks were selected for qualitative identification. Isomers of decane, undecane and dodecane were identified but not quantified in 7 of the 8 samples. Identification was by professional judgment rather than by comparison with standards. Over 100 compounds were manually identified but not quantified and background contamination was not fully characterized. From this analysis, 9 compounds (none of them alkanes) were selected for quantitation but only four were reported, as the results for the other 5 were "not judged sufficiently greater than background to be reliable." The low levels of C_{10}-C_{12} alkane isomers detected but not quantified imply even lower levels of the specific normal isomers under consideration.

An evaluation of the data was performed to estimate possible levels of the n-alkanes actually detected. This analysis is presented below and used to estimate an upper bound on potential infant exposure through mother's milk.

The analytical method employed was thermal desorption GC/MS analysis without standards for identification verification. Quantitation was only done for four halogenated compounds.

Identification Issues:

Eight of the 42 samples with the greatest number of peaks or those containing very intense unique peaks were selected for manual mass spectral interpretation.

The initial identification of the unknown compounds involved the use of the Eight Peak Index of Mass Spectra. During this step, the analyst or interpreter compared the spectra of the unknowns to those of standard compounds tabulated in the Index. If the interpreter determined that a clear match existed, the compound was given a positive identification status. If the peak intensities varied from those of the standards, but the compound appeared to be an isomer of the compounds found in the Index, then the compound was listed as an “isomer.” A “tentative” (tent.) label was used to flag compounds whose identification was uncertain due to background peak interference. When fragments characteristic of a certain class of compounds were identified, but no standard spectra was found in the Index that matched the unknown, the compounds were labeled “tent.” In the case of tentatively identified compounds, these compounds

were alkyl derivatives or homologs of classes of compounds that were positively identified in the same sample. The Registry of Mass Spectral Data was also used during data interpretation. To obtain a library match of an unknown spectrum, the masses and relative abundance of the ions of the unknown spectrum are compared to the masses and abundance of ions of reference standards found in electronic or bound libraries. The quality of the match indicates the probability of a tentative identification. Most matches, even those with a high quality score, are often rejected after further scrutiny by experienced analyst.

Furthermore, the identification of specific hydrocarbons is particularly difficult because of the number of potential isomers with the same molecular weight. Mass spectrometry is not capable of identifying specific isomers without further steps. Correct identification is only possible with actual analysis of the particular compound to determine its retention time. This was not done in this study. The identification of n-decane, n-undecane, and n-dodecane in this report was obtained through a "Level II" review involving manual interpretation of the data. During this process, a skilled interpreter compares the spectra of the unknown material to spectra compiled in one or more data compendiums such as the Eight Peak Index of Mass Spectra. This level of interpretation does not involve comparison of retention times of the unknowns, or potential positively identified compounds, to those of standards. The key to obtaining reliable positive identification of unknowns using the Level II approach relies in the experience of the interpreter. Interpretation is subjective and dependent upon the analyst's and/or interpreter's judgment. There is no way to determine the quality of the interpretation in this report.

For a molecule with 10 carbons and 22 hydrogens, there are 75 potential isomers, for 15 carbons and 32 hydrogens, the number of potential isomers is 4,347.

Many factors can contribute to the degree of difficulty of interpretation of spectral data. Instrument conditions, matrix complexity and low analyte concentration are perhaps the three main contributors to increased uncertainty in the identification of unknowns. In this study, only four of nine compounds that were quantified were summarized (see Table 17) while the levels in milk of the remaining five compounds were deemed insufficiently greater than background to be reliable. The four quantified compounds are chlorinated compounds. Chlorinated species are easier to identify due to their characteristic spectra. It is unclear which compounds were quantified but not reported. All other positively and tentatively identified compounds, possibly including n-decane, n-undecane, and n-dodecane, would have been present in lower concentrations making them insufficiently greater than background to be reliable.

In this study, identification of n-C_{10}, n-C_{11}, and n-C_{12} is extremely questionable for the following reasons:

- Isomer identification issues as stated above
- No actual analysis of standards to verify retention time

- Obvious coelution with other compounds in the samples. In many cases, the coelution is with major peaks like dichlorobenzene. Coelutions impair the MS library search routines. To produce a library match for an unknown spectrum, the computer compares the masses and relative abundances of the ions in the sample spectrum to the masses and relative abundance of the ions in candidate library spectra. The matches are scored and if the score are high enough to justify confidence. Small differences in the sample spectra can have drastic effects in the scoring. Even if the matches are reproducible and high scoring, they are often poor. Manual inspection often results in rejection of most matches.
- It is often the case that there is no real peak in the chromatogram where the report states that one of these n-alkanes is expected. Only baseline is seen.

Estimated Quantitation

There was no attempt to quantify most of the peaks in these samples. Only four chlorinated compounds were quantified. The report provides information pertaining what the analysts think a certain amount of a compound is required for detection. Based on that information, we made the following conclusions:

Volatile Organics in Milk:

30ng is required for ID by GC/MS. If 50g milk is used, then about 0.6 ng/g could be detected.

Normal C_{10}, n-C_{11} and n-C_{12} potential concentrations were estimated by comparison of peak heights with the peak heights of PCE and dichlorobenzene and using the geometric mean for the particular cities for calculations. All were either ND (not detected) or <1 or up to <10ppb.

Using the geometric mean calculated for perchloroethylene and dichlorobenzene (Table 19) and assuming a similar response factor for the n-alkanes, we did a very rough estimate of what the potential concentration of the n-alkanes could be in these eight samples. Such an estimate is summarized in the table below and in the attached Excel file. It must be noted that nearly all of these peaks are clearly coeluting with other peaks with the exception of n-dodecane in some of the samples.

Estimated Potential Concentration of Selected n-Alkanes.
Units are ng/mL (ppb)

Compound /Sample #	1081	1040	1107	1115	2048	2071	3053	3111
n-Decane	<1	<1	<10	<10	<1	<1	<5	<1
n-Undecane	<1	<1	<10	<10	<1	<1	~10	<1
n-Dodecane	<1	<1	~5	~5	<1	<1	~10	<1

Semivolatile Organics in Milk:

These were almost always siloxane hits (column bleeding). nC10, nC11, nC12 were not detected, therefore must have been <20ppb. The semivolatile analysis starts with toluene and the n-alkanes of interest would have been picked up by this analysis if present above detection.

Estimation of dose based on 60 ug/kg C_{10}-C_{12} n-alkanes in milk:

We will conservatively assume that all three target chemicals were present at the higher detection level in the semi-volatile analysis level (where no detections were reported) for a total milk concentration of 60 ppb (60 ug/kg).

A bounding estimate on infant exposure via human milk can be calculated as:

$$Dext = \frac{C \times IR \times EF \times ED \times UCF}{BW \times AT}$$

Where
D = External Dose (mg/kg/day)
C = Concentration (mg/kg)
IR = Ingestion Rate of human milk (g/day)
EF = Exposure Frequency (365days/year)
ED = Exposure Duration (1 year)
AT = Averaging Time (365 days)
UCF = Unit Conversion Factor, here 1 kg/1000 g
BW = Body Weight (infant) (kg)

From the USEPA Child Specific Exposure Factors Handbook, average human milk intake for ages birth to 12 months is 688 ml/day (709 g/day), with an upper 95th percentile of 980 ml/day (1009 g/day). The same report indicates a mean weight for infants 6-11 months of 9.1 kg. Conversion from ml/day to g/day is made using a density of 1.03 g/ml (USEPA 2002b)

Assuming a human milk concentration for C_{10}-C_{12} normal alkanes equal to 60 ppb yields a potential exposure of 0.0047 mg/day (mean intake) or 0.0067 mg/day (upper bound intake) for infants. This compares with an RfD of 0.1 mg/kg/day indicating a 14 to 20 fold Margin of Safety. It should be emphasized that these margins of safety are based on detection limits and not on actual detections which, when they occurred, were estimated to be less than 1-10 ppb. Realistically, it would be expected that Margins of Safety would exceed 100.

Intakes from mothers milk from the heavily industrialized areas sampled do not indicate infants to be significantly exposed through human milk based on this study. There are

no data on occupationally exposed mothers. Results are summarized in Table F.1 and in a separate spreadsheet that is attached.

Table F.1
Calculation of Infant Dose from Human Milk based on the Erickson et al (1980) Study

Human Milk Intake

1. Representative Intake:

Dext= Conc*IR*EF*ED*UCF/(BW*AT)

Conc	Concentration	0.06 mg/kg
IR	Ingestion rate	709 g/day
EF	Exposure Frequency	365 days/year
ED	Exposure Duration	1 year
AT	Averaging Time	365 days
UCF	Unit Conversion Factor	0.001 kg/1000g
BW	Infant Bodyweight	9.1 kg
Dext	Dose	0.0047 mg/kg/d
MOE*	Margin of Exposure	213,000

2. Upper Bound intake (95%)

Dext= Conc*IR*EF*ED*UCF/(BW*AT)

Conc	Concentration	0.06 mg/kg
IR	Ingestion rate	1009 g/day
EF	Exposure Frequency	365 days/year
ED	Exposure Duration	1 year
AT	Averaging Time	365 days
UCF	Unit Conversion Factor	0.001 kg/1000g
BW	Infant Bodyweight	9.1 kg
Dext	Dose	0.0067 mg/kg/d
MOE*	Margin of Exposure	150,000

*MOE based on subchronic NOAEL of 1,000 mg/kg/d

NOTES:

Section 6.4.3 of the EPA report - "Qualitative Data Interpretation" includes a statement dealing with the use of retention times to assist in the interpretation procedure (p 117). However, the authors mentioned on page 44 that all identifications were Level II.

Nora P. Castillo and Kent W. Thomas: mass spectral interpretation

Pamela A. Gentry, Fred A. McKinney, Stephen P. Burke, and Barbara L. Bickford: mass spectrometry analysis

Kathleen c. Swallow, Neil S. Shifrin, Phillip J. Doherty, “Hazardous Organic Compound Analysis”, Env. Sci. Technol., Vol. 22, No. 2, 1988

APPENDIX G
Analysis of EPA Research House Data

An EPA sponsored study of a test house has provided data on exposure levels resulting from application of an alkyd based primer and paint to gypsum walls of a bedroom (USEPA, 2001). A primer coat (AP-F) was applied followed 2 days later by a coat of alkyd paint (ASG-G). Concentrations of decane, undecane, and dodecane (speciation of isomers not reported as discussed below) were measured over a period of up to 23 days and compared with the predictions of the Wall Paint Exposure Model (WPEM). The house was unoccupied and sealed. It had a volume of 11,272 ft^3, the bedroom constituted 9.5% of the house volume, and walls of area 318 ft^2 were painted. The Air Exchange Rate was measured as 0.48 air changes per hour.

Paint composition in regard to the C10-C12 aliphatics were reported as follows in mg/g:

Chemical	Primer (AP-F)	Paint (ASG-G)
Decane	11.80	21.40
n-Decane	---	---
Branched Decane A	---	---
Branched Decane B	---	---
Undecane	8.76	16.50
n-Undecane	---	---
Branched Undecane A	---	---
Branched Undecane B	---	---
Branched Undecane C	---	---
Branched Undecane D	---	---
Branched Undecane E	---	---
Branched Undecane F	---	---
Dodecane	1.85	2.40

As reported, there do not appear to be any normal C10-C12 alkanes present in the paint so its specific relevance to this submission is doubtful. However, in the absence of more information, as a screening exercise, reported concentrations of decane, undecane, and dodecane were treated as if they were normal isomers.

The spreadsheet data from the EPA Research House study was examined and the following analyses were performed:

1. Concentration-time data for the sum of the alkanes of interest were tabulated and plotted.
2. Time weighted Average (TWA) concentrations were calculated for 24 hour periods starting from application of the primer and plotted.

Results are summarized below.

Concentrations of three alkanes **combined** peaked at about 480 mg/m^3 during priming and 620 mg/m^3 during painting in the bedroom with corresponding values in the den (at the other corner of the house) of 80 mg/m^3 and 140 mg/m^3. The 24 hour time weighted average (TWA) concentration reached about 50 mg/m^3 in the 24 hour periods during priming or painting. Peak levels reached during application of primer or paint rapidly dropped in a matter of hours by over 2 orders of magnitude. After 2 weeks, levels of 109 μg/m^3 were recorded in the bedroom and, after 3 weeks the combined concentrations of decane, undecane, and dodecane had dropped to 40 μg/m^3 in the painted bedroom. This is within the range of mean values reported in various surveys of normal homes (Samfield, 1992, Brown et al, 1994, BRE, 1996, Brown and Crump, 1995, Kostianinen, 1995, Wallace, 1991 and Heavner, 1996). This exposure concentration in the painted bedroom is also less than the means reported for new homes (Crump, 1997, Rothweiler, 1992) and even in homes undergoing renovation (Brown and Crump, 1998, Wallace, 1989). The apparently strange result that levels dropped below levels commonly found in dwellings may be related to the fact the house is a research facility, was not occupied, and there were no other sources of alkanes in the house. Such a finding supports the conclusion that the model home experiment did not reflect real world conditions but may provide some perspective on possible acute short-term exposures in situations where recommended procedures are not followed during painting.

This EPA Research House study was undertaken to validate a model and is not relevant to normal practice and indeed did not follow paint manufacturers recommendations regarding ventilation. The house was sealed for the duration and no windows were opened. However, the model appeared to be reasonably well validated under the controlled conditions of the study. In reality, if normal practice had been followed, such as opening windows and doors to increase ventilation, peak values would have been less and reduced to background even more rapidly than they did.

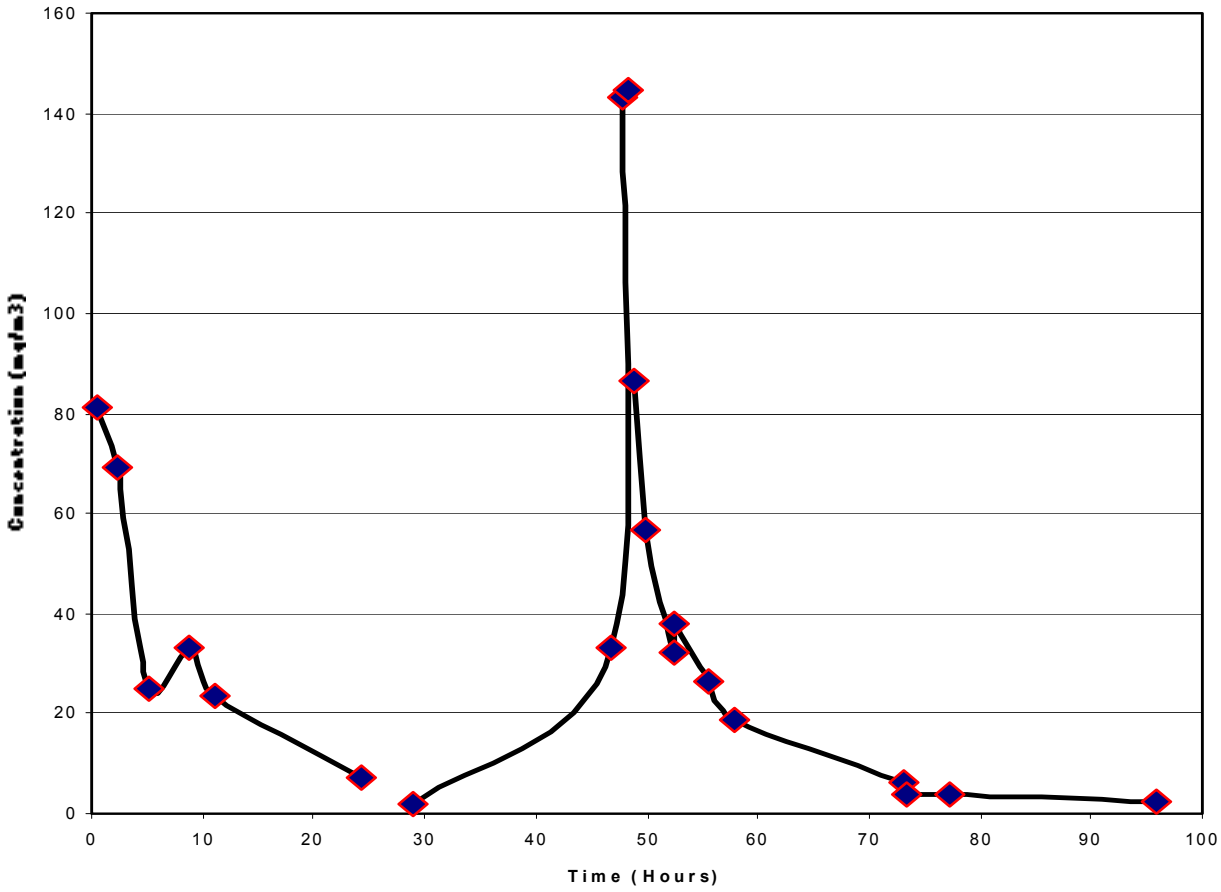
The data and calculations are summarized below.

Test House Alkyd Paint Test 1

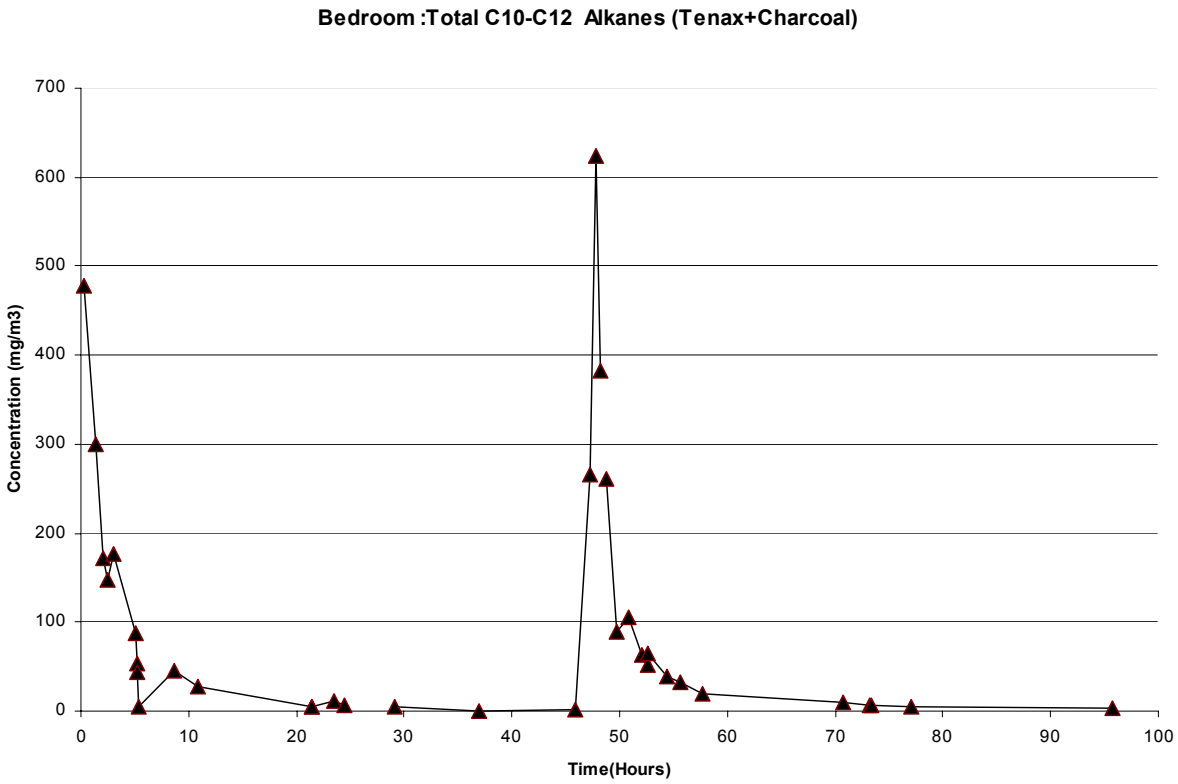
Sheet 1: Summary of Test Conditions

Parameter	Value	Units
Internal test ID	Test House A1	
Primer tested	AP-F	Alkyd Primer
Paint tested	ASG-G	Alkyd Semi-gloss PL-044
Substrate	Gypsum Board	
Application room	Front Corner BR	
Wall area primed then painted	29.5	m2
Application method	Roller	
Primer Application Date	9/9/1997	
Start primer application	11:12:42	
Finished primer application	11:56:04	
Amount of primer applied	6.96	kg
Paint application date	9/11/1997	
Start paint application	10:41:17	
Finished paint application	11:15:00	
Elapsed time for paint application	47.32	hr
Amount of paint applied	4.93	kg
Air exchange rate -average in FCBR	0.48 +/- 0.06	/hr
Air velocity over source	Not measured	
House air handler fan	On constant	
Average temperature	N/A	
Average relative humidity	N/A	

Concentration Vs Time in Den (Primed at 24 hours; painted at 48 hours)



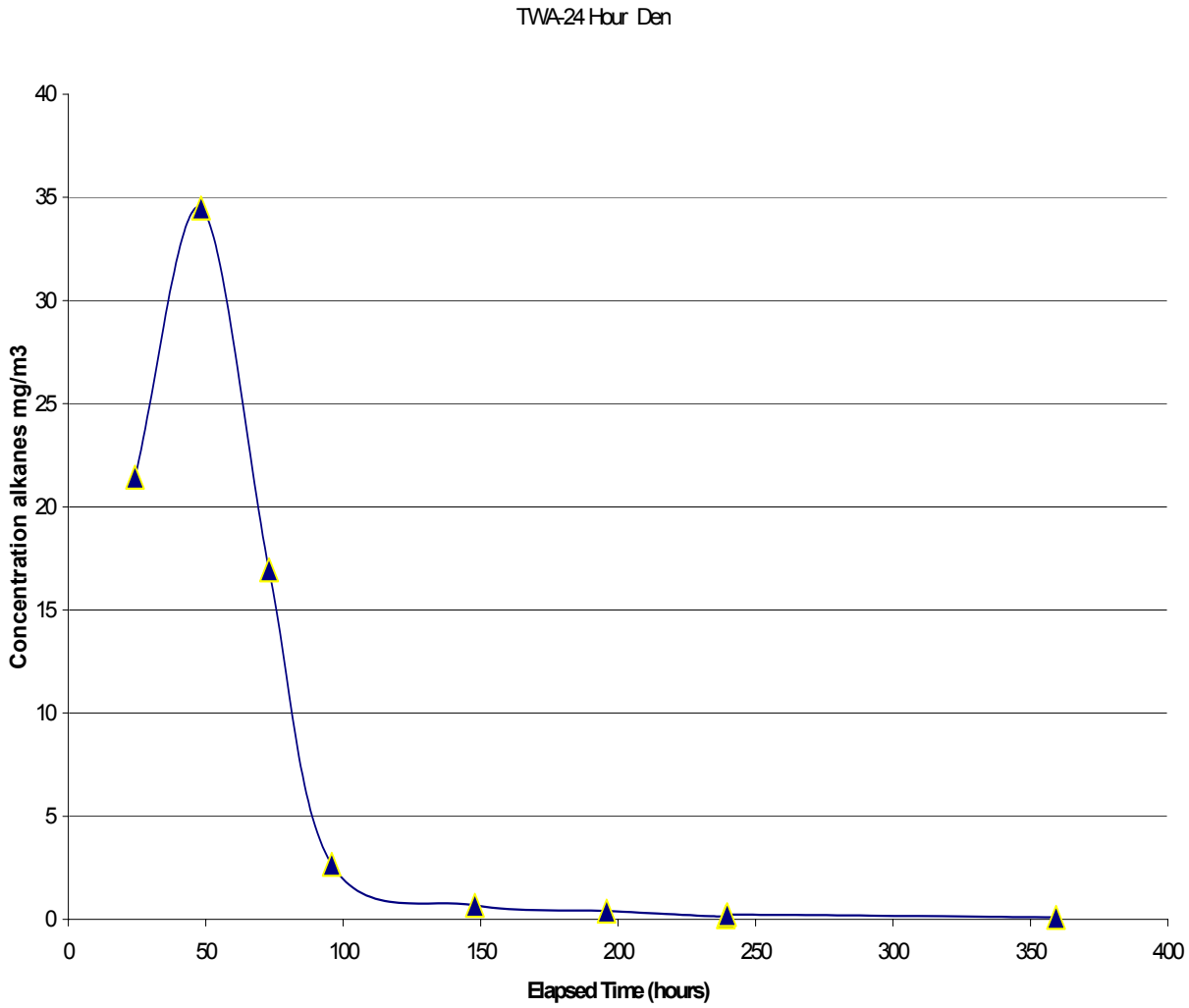
Concentration Vs Time in Bedroom (Primed at 24 hours; painted at 48 hours)



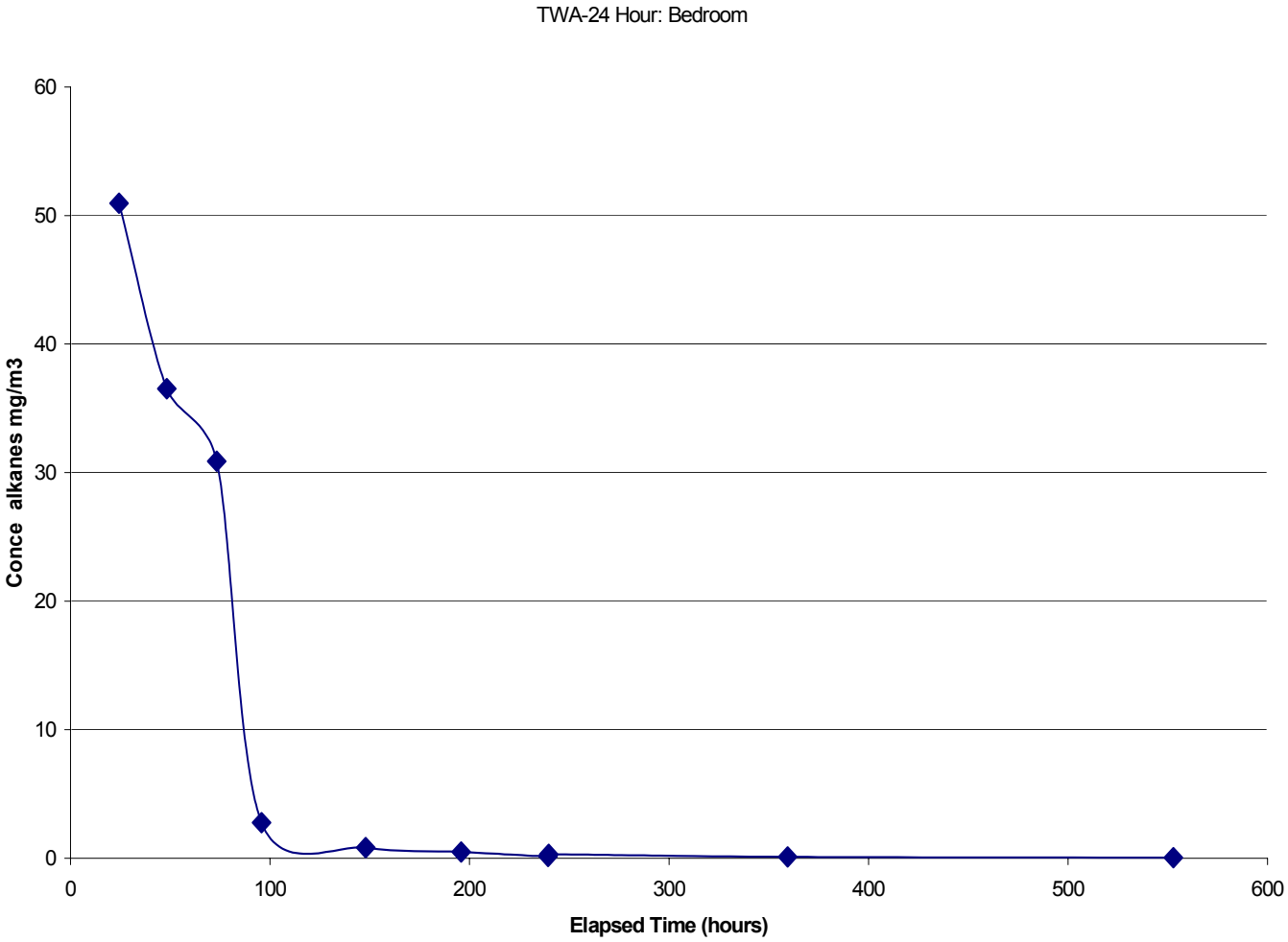
Measured Air Concentrations and Time-Weighted Averages (TWA) for EPA Test House Experiments with Alkyd Paint and Primer

Coating Type	Location	Elapsed Time hours	Decane mg/m^3	Undecane mg/m^3	Dodecane mg/m^3	TOTAL mg/m^3	24-hour TWA mg/m^3
Paint	Den	24	2.66E+00	3.81E+00	5.38E-01	7.01E+00	21
Paint	Den	48	9.23E+01	4.87E+01	3.49E+00	1.44E+02	34
Paint	Den	73	2.32E+00	3.22E+00	6.02E-01	6.14E+00	17
Paint	Den	96	7.22E-01	1.47E+00	3.50E-01	2.54E+00	2.7
Paint	Den	148	1.93E-01	3.69E-01	1.21E-01	6.82E-01	0.682
Paint	Den	196	1.12E-01	2.07E-01	7.46E-02	3.94E-01	0.394
Paint	Den	239	3.61E-02	5.80E-02	2.13E-02	1.15E-01	0.115
Paint	Den	240	7.04E-02	1.17E-01	4.57E-02	2.33E-01	0.233
Paint	Den	359	2.87E-02	4.18E-02	1.70E-02	8.74E-02	0.087
Primer	FCBR	24	2.24E+00	3.32E+00	5.11E-01	6.07E+00	51
Paint	FCBR	48	2.10E+02	1.59E+02	1.36E+01	3.83E+02	37
Paint	FCBR	73	2.60E+00	3.94E+00	7.31E-01	7.27E+00	31
Paint	FCBR	96	6.69E-01	1.40E+00	3.84E-01	2.46E+00	2.8
Paint	FCBR	148	2.19E-01	4.41E-01	1.67E-01	8.27E-01	0.827
Paint	FCBR	196	1.24E-01	2.48E-01	9.97E-02	4.72E-01	0.472
Paint	FCBR	239	4.17E-02	7.26E-02	3.03E-02	1.45E-01	0.145
Paint	FCBR	240	8.57E-02	1.52E-01	6.74E-02	3.05E-01	0.305
Paint	FCBR	359	3.18E-02	5.31E-02	2.39E-02	1.09E-01	0.109
Paint	FCBR	553	1.37E-02	2.10E-02	7.84E-03	4.25E-02	0.043

24 hour Time Weighted Average vs. Time in Den
(Primed at 24 hours; painted at 48 hours)



24 hour Time Weighted Average vs. Time in Bedroom
(Primed at 24 hours; painted at 48 hours)



Appendix H

Summary Tables

Margins of Exposure (MOE) and Margins of Safety (MOS) [1]

1. Chronic Domestic Exposure

MARGIN OF EXPOSURE BASED ON NOAEL

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOE	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOE
Infant	42	6,000	129	1,900
Children	42	6,000	129	1,900
Adults	42	6,000	129	1,900

MARGIN OF SAFETY BASED ON RfC

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOS	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOS
Infant	42	24	129	8
Children	42	24	129	8
Adults	42	24	129	8

2. Short Term Exposure at Home During Renovation

MARGIN OF EXPOSURE BASED ON NOAEL

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOE	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOE
Infant	122	2,000	910	275
Children	122	2,000	910	275
Adults	122	2,000	910	275

MARGIN OF SAFETY BASED ON RfC*

Receptor	Representative Exposure Concentration ($\mu g/m^3$)	MOS	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOS
Infant	122	8	910	1.1
Children	122	8	910	1.1
Adults	122	8	910	1.1

***** The RfC addresses chronic exposure therefore exceedance in a short tern or sub-chronic scenario does not necessarily imply a risk. An acute or sub-chronic benchmark is more appropriate in such cases.

1. Based on the following benchmarks discussed in Sections 7 and 8.
   NOAEL: 2.5×10^5 ug/m^3; RfC: 1,000 ug/m^3; OEL: 1,200 mg/m^3

Short Term Exposure at Home During Renovation (Cont)

MARGIN OF EXPOSURE BASED ON NOAEL (EPA Research House)

Time After painting	Representative Exposure Concentration ($\mu g/m^3$)	MOE
1 day	8,400	30
2 days	2,460	100
4 days	827	300
15 days	109	2,300
23 days	43	5,800

3. Occupational Exposure:

MARGIN OF EXPOSURE BASED ON NOAEL

Prospective Parent Occupationally Exposed in Fuel Related Operations	Representative Exposure Concentration ($\mu g/m^3$)*	MOE	Upper Bound Exposure Concentration ($\mu g/m^3$)*	MOE
8 hour exposure (adjusted to continuous exposure)	1,160	200	3,850	65

*Total concentrations of the three alkanes adjusted to continuous exposure through the relation: Exposure Concentration x (8hr/24hr) x (5days/7Days) x50wks/52 wks

MARGIN OF SAFETY BASED ON OEL

Prospective Parent Occupationally Exposed in Fuel Related Operations	Representative Exposure Concentration ($\mu g/m^3$)*	MOS	Upper Bound Exposure Concentration ($\mu g/m^3$)	MOS
8 hour exposure	5,060	237	16,800	71

*Total concentrations of the three alkanes 8 hour exposure