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Provisional Peer-Reviewed Toxicity Values for

n-Decane
(CASRN 124-18-5)

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Commonly Used Abbreviations

BMD	Benchmark Dose
IRIS	Integrated Risk Information System
IUR	inhalation unit risk
LOAEL	lowest-observed-adverse-effect level
$LOAEL_{ADJ}$	LOAEL adjusted to continuous exposure duration
$LOAEL_{HEC}$	LOAEL adjusted for dosimetric differences across species to a human
NOAEL	no-observed-adverse-effect level
$NOAEL_{ADJ}$	NOAEL adjusted to continuous exposure duration
$NOAEL_{HEC}$	NOAEL adjusted for dosimetric differences across species to a human
NOEL	no-observed-effect level
OSF	oral slope factor
p-IUR	provisional inhalation unit risk
p-OSF	provisional oral slope factor
p-RfC	provisional inhalation reference concentration
p-RfD	provisional oral reference dose
RfC	inhalation reference concentration
RfD	oral reference dose
UF	uncertainty factor
UF_A	animal to human uncertainty factor
UF_C	composite uncertainty factor
UF_D	incomplete to complete database uncertainty factor
UF_H	interhuman uncertainty factor
UF_L	LOAEL to NOAEL uncertainty factor
UF_S	subchronic to chronic uncertainty factor

PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR *n*-DECANE (CASRN 124-18-5)

Background

On December 5, 2003, the U.S. Environmental Protection Agency's (U.S. EPA) Office of Superfund Remediation and Technology Innovation (OSRTI) revised its hierarchy of human health toxicity values for Superfund risk assessments, establishing the following three tiers as the new hierarchy:

1) U.S. EPA's Integrated Risk Information System (IRIS).
2) Provisional Peer-Reviewed Toxicity Values (PPRTVs) used in U.S. EPA's Superfund Program.
3) Other (peer-reviewed) toxicity values, including
   - Minimal Risk Levels produced by the Agency for Toxic Substances and Disease Registry (ATSDR),
   - California Environmental Protection Agency (CalEPA) values, and
   - EPA Health Effects Assessment Summary Table (HEAST) values.

A PPRTV is defined as a toxicity value derived for use in the Superfund Program when such a value is not available in U.S. EPA's IRIS. PPRTVs are developed according to a Standard Operating Procedure (SOP) and are derived after a review of the relevant scientific literature using the same methods, sources of data, and Agency guidance for value derivation generally used by the U.S. EPA IRIS Program. All provisional toxicity values receive internal review by two U.S. EPA scientists and external peer review by three independently selected scientific experts. PPRTVs differ from IRIS values in that PPRTVs do not receive the multiprogram consensus review provided for IRIS values. This is because IRIS values are generally intended to be used in all U.S. EPA programs, while PPRTVs are developed specifically for the Superfund Program.

Because new information becomes available and scientific methods improve over time, PPRTVs are reviewed on a 5-year basis and updated into the active database. Once an IRIS value for a specific chemical becomes available for Agency review, the analogous PPRTV for that same chemical is retired. It should also be noted that some PPRTV documents conclude that a PPRTV cannot be derived based on inadequate data.

Disclaimers

Users of this document should first check to see if any IRIS values exist for the chemical of concern before proceeding to use a PPRTV. If no IRIS value is available, staff in the regional Superfund and Resource Conservation and Recovery Act (RCRA) program offices are advised to carefully review the information provided in this document to ensure that the PPRTVs used are appropriate for the types of exposures and circumstances at the Superfund site or RCRA facility in question. PPRTVs are periodically updated; therefore, users should ensure that the values contained in the PPRTV are current at the time of use.

It is important to remember that a provisional value alone tells very little about the adverse effects of a chemical or the quality of evidence on which the value is based. Therefore, users are strongly encouraged to read the entire PPRTV document and understand the strengths

and limitations of the derived provisional values. PPRTVs are developed by the U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center for OSRTI. Other U.S. EPA programs or external parties who may choose of their own initiative to use these PPRTVs are advised that Superfund resources will not generally be used to respond to challenges of PPRTVs used in a context outside of the Superfund Program.

Questions Regarding PPRTVs

Questions regarding the contents of the PPRTVs and their appropriate use (e.g., on chemicals not covered, or whether chemicals have pending IRIS toxicity values) may be directed to the U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300), or OSRTI.

INTRODUCTION

n-Decane (CASRN 124-18-5) is a high production volume (HPV) chemical constituent of the paraffin fraction of petroleum and natural gas. A very small volume (estimated at less than 20,000 pounds) is produced in pure form for use as a laboratory reagent. There are no known consumer product applications for pure *n*-decane, but, their large production volumes and wide usage make the petroleum distillates the primary sources of exposure. Toxicity information is scant, and there is a paucity of quantitative reference values in the *n*-decane literature. No RfD, RfC, or carcinogenicity assessment for *n*-decane is available on IRIS (U.S. EPA, 2008). *n*-Decane is not included on the Health Effects Assessment Summary Tables (HEAST; U.S. EPA, 1997), the Drinking Water Standards and Health Advisory list (U.S. EPA, 2006), or the Chemical Assessments and Related Activities (CARA) list (U.S. EPA, 1991, 1994). The Agency for Toxic Substances and Disease Registry (ATSDR, 2008) has not produced a Toxicological Profile for *n*-decane. Toxicological Profiles for mixtures containing *n*-decane, such as Total Petroleum Hydrocarbons (TPH) (ATSDR, 1999) and Stoddard Solvent (a low aromatic hydrocarbon solvent containing C10-C14 n-, iso-, and cycloalkanes) (ATSDR, 1995), do exist, but they do not derive oral or inhalation MRLs for any of the individual compounds. Staats Creative Sciences (SCS) for the United States Air Force (Staats, 1994) derived a chronic oral RfD of 1.332 mg/kg-day based on a route-to-route extrapolation from an inhalation NOAEL of 540 ppm, which, in turn, was derived from a subchronic inhalation study in rats by Nau (1966) described below.

No Environmental Health Criteria Document is available for *n*-decane from the World Health Organization (WHO, 2008). The Occupational Safety and Health Administration (OSHA, 2008), the National Institute for Occupational Safety and Health (NIOSH, 2008), and the American Conference for Governmental Industrial Hygienists (ACGIH, 2007) have not established occupational health standards for *n*-decane. The carcinogenicity of *n*-decane has not been assessed by the International Agency for Research on Cancer (IARC, 2008) or the National Toxicology Program (NTP) (2005, 2008). NTP has conducted subchronic inhalation and carcinogenicity studies in rats and mice on Stoddard Solvent (mixture containing *n*-decane, as mentioned above), but they did not evaluate the individual compounds (NTP, 2004).

To identify toxicological information pertinent to the derivation of provisional toxicity values for *n*-decane, a literature search was conducted through December 2008 using the following databases: MEDLINE, TOXLINE (Special), BIOSIS, TSCATS1/TSCATS2, CCRIS, DART/ETIC, GENETOX, HSDB, RTECS, and Current Contents. Additionally, a Voluntary Children's Chemical Evaluation Program (VCCEP) Tier-1 Pilot Submission on the *n*-Alkane Categories of decane, undecane, and dodecane (CASRNs 124-18-5, 1120-21-4, and 112-40-3), from the American Chemistry Council *n*-Alkane VCCEP Consortium (ACCVC, 2004), was reviewed.

REVIEW OF PERTINENT DATA

Human Studies

No information was located regarding the subchronic or chronic oral or inhalation toxicity of *n*-decane in humans. Some information is available for several complex mixtures, for example, white spirits, or Stoddard solvent (ATSDR, 1995), but none of these are directly applicable here because of the problems inherent in dealing with complex mixtures of variable composition.

Animal Studies

Oral Exposure

Data on the effects of repeated oral exposure to *n*-decane in animals are available from a single study, initially submitted on behalf of Sasol North America, Inc., under the Toxic Substances Control Act to the U.S. EPA Office of Pollution Prevention and Toxics, evaluating the effects of commercial *n*-decane on general, reproductive, and developmental toxicity (Sasol NA, 1995). This study is also included as Maraschin et al. (1995) in the VCCEP Tier-1 Pilot Submission for the *n*-alkane category as a robust summary (ACCVC, 2004). Sasol NA (1995) treated groups of 20 Sprague-Dawley rats (10/sex) with doses of 0, 25, 150, or 1000 mg/kg-day (10 mL/kg dosing volume) of commercial *n*-decane (Linpar 10; approximately 97% *n*-decane) in 0.5% methylcellulose aqueous solution by gavage. Dosing was conducted 7 days/week from Day 14 prior to mating through to the end of the mating phase for males for a total duration of approximately 4 weeks, and through Day 4 of lactation for females for a total duration of up to approximately 8 weeks. The dosages were established in accordance with the sponsorship of Italy in the Organization for Economic Co-operation and Development Screening Information Datasets (OECD SIDS) program; further detail on how the dose levels were chosen is not reported. The study authors determined pregnancy based on the presence of spermatozoa in vaginal smears collected. For females demonstrating a positive smear that did not give birth, treatment was continued until presumed Day 27 of pregnancy when these rats were then sacrificed. For females that did not demonstrate positive smears, treatment continued up until Day 27 after the end of the mating period when these rats were then sacrificed. Initial body weights were 0.20−0.225 kg for female rats and 0.275−0.30 kg for male rats. Rats were allowed free access to food and water and were housed two to a cage by sex prior to mating, one to a cage after mating and gestation, and dams were housed in a cage with their litter through the first 4 days of lactation. A control group consisted of 10 males and 10 females treated with 0.5% methylcellulose following the same treatment schedule as described above. Each animal

was fasted for about 16 hours overnight before killing and the fasted body weight was recorded. Male rats were killed the day after the end of the mating period, and dams and pups were killed on Day 5 of lactation.

Effects on general toxicity, neurobehavioral activity (startle reflex, grip reflex, and open field tests performed in five adult males and females of each group), clinical chemistry (glucose, urea, creatinine, alanine aminotransferase [ALT, formerly serum glutamic oxalacetic transaminase, or SGOT], and aspartate aminotransferase [AST, formerly serum glutamic pyruvic transaminase, or SGPT], total cholesterol, total protein, protein electrophoresis, albumin/globulin [A/G] ratio, sodium, potassium, and bile acids examined in five adult males and females of each group) and hematology (erythrocytes, total and differential leukocytes, and platelet count, as well as measures of hemoglobin volume, mean corpuscular volume [MCV], mean corpuscular hemoglobin concentration [MCHC], mean corpuscular hemoglobin [MCH], and prothrombin time in five adult male and female rats of each group) were evaluated (Sasol NA, 1995). Urinalysis (diuresis and specific gravity, semiquantitative examination for leukocytes, nitrites, pH, protein, glucose, ketone bodies, urobilinogen, and bilirubin), and blood and microscopic examination (for epithelial cells, leukocytes, erythrocytes, crystals, casts, bacteria, and other abnormal components) was only conducted in males that were also used for blood collection. Reproductive and developmental effects were evaluated by measuring mating, fertility, gestation, and birth indices, conception, gestation length, litter size, offspring survival, pup body weight, sex ratio, and developmental abnormalities in pups at birth. Gross necropsies, including examination of the external surface of the body, all orifices and the cranial, thoracic, and abdominal cavities and their contents, were conducted on each adult rat. Whenever possible, the study authors examined the dead pups externally and internally in an attempt to determine the cause of death. In the adults of the high-dose group, the study authors conducted histopathological examination of tissues (bladder, prostate, testes, epididymides, seminal vesicles, uterus, ovaries, spleen, stomach, intestine, mesenteric lymph nodes, liver, kidneys, adrenals, submandibular lymph nodes, sternum, heart, thymus, lungs, trachea, brain, peripheral nerve, spinal cord, and gross lesions). In the adults of the low- and intermediate-dose groups, the study authors evaluated the male reproductive tract, the stomach, kidneys, and gross lesions.

The study authors noted no mortalities, clinical signs, or treatment-related changes in behavior or body weight were observed throughout the study in parental rats (Sasol NA, 1995). There were no differences in the functional neurobehavioral tests (startle reflex, forelimb grip strength, open field test) between treated and control rats. The study authors noted no significant urological findings in male rats (not examined in female rats). Hematology and serum chemistry parameters in treated animals were comparable to controls. Although serum creatinine in male rats exhibited a trend towards an increase in all treated groups, it is not statistically significant. This change is considered incidental because (1) it was slight in degree, (2) not clearly dose-related, and (3), while some individual values were above the range for controls, the values were still within the normal clinical ranges. Female rats exhibited a nonsignificant trend towards an increase in total cholesterol across all treated groups, indicating a possible dose-response relationship (very slight variation, compared to controls, at the low dose and of moderate degree at the highest dose); some individual animals given the intermediate dose (Group 3 female number 51) and the highest does (Group 4 females 72 and 80) showed concentrations above 100 mg/dL. Except for the slight changes noted in the nonglandular stomach mucosa of treated rats (data presented in Table 1), no changes in organ weights or gross pathology were observed. Upon gross examination, thickening of the nonglandular mucosa of the stomach was noted in

rats from the 150-mg/kg-day (3/20) and 1000-mg/kg-day (10/20) dose groups. Some of the animals in these groups also demonstrated slight erosion of the nonglandular mucosa and/or thickening of the cuticular ridge. Sasol NA (1995) considered these findings to be related to the bolus dosing method. Histopathology confirmed treatment-related slight-to-moderate hyperplasia of the nonglandular mucosa of the stomach associated with degeneration, hyperkeratosis, and submucosal subacute inflammation (see Table 1). The authors reported that these changes of the nonglandular mucosa of the stomach were not dose-related in degree, frequency, or diffusion (i.e., focal, multifocal, or diffuse) (diffusion data are presented in the Sasol NA [1995] Appendix and are not shown in Table 1). Sasol NA (1995) considered the additional findings observed upon gross or microscopic examination to be incidental and not related to treatment. Despite the author's statements, there does appear to be a dose related increase in incidence, though not severity of these lesions.

Table 1. Stomach Gross Pathology and Histology Incidence and Severity[a,b]

Pathology	Dose (mg/kg-day)							
	0		25		150		1000	
	Male	Female	Male	Female	Male	Female	Male	Female
Gross Pathology								
Nonglandular mucosa, erosion	0/10	0/10	2/10 (1.5)	0/10	2/10 (1.0)	1/10 (1.0)	1/10 (2.0)	1/10 (1.0)
Nonglandular mucosa, thickened	0/10	0/10	0/10	0/10	2/10 (1.0)	1/10 (1.0)	6/10 (1.0)	4/10 (1.3)
Histology								
Nonglandular mucosa, degeneration	0/5	0/5	5/5 (1.0)	1/5 (2.0)	4/5 (1.5)	5/5 (1.6)	7/7 (1.6)	6/6 (1.3)
Nonglandular mucosa, erosion	0/5	0/5	1/5 (2.0)	0/5	0/5	2/5 (1.5)	1/7 (2.0)	1/6 (2.0)
Nonglandular mucosa, hyperkeratosis	0/5	0/5	3/5 (1.0)	1/5 (1.0)	4/5 (1.0)	5/5 (1.0)	7/7 (1.1)	5/6 (1.2)
Nonglandular mucosa, hyperplasia	0/5	0/5	5/5 (1.8)	2/5 (1.0)	5/5 (1.8)	5/5 (1.2)	7/7 (1.8)	6/6 (2.2)
Nonglandular submucosa, Inflammation-subacute	0/5	0/5	3/5 (1.7)	1/5 (1.0)	5/5 (1.4)	5/5 (1.2)	7/7 (1.1)	5/6 (1.8)

[a]Sasol NA, 1995
[b]Incidence (mean severity); Severity: 0 (very slight), 1 (slight), 2 (moderate), 3 (severe)

The mean mating time of rats in the high-dose group was slightly longer than that of the control group, but this difference was still within the normal range of variability for this strain of rat according to Sasol NA (1995). A decrease in fertility—evaluated as a decreased fertility index in all treated rats—was observed compared to controls (see data presented in Table 2). However, the differences between the treated and control rats are not statistically significant and there is not a clear dose-response relationship among these data.

Table 2. Fertility Index[a]	
Dose (mg/kg-day)	**Incidence of Gravid Females**
0	7/10
25	5/10
150	6/10
1000	4/10

[a]Sasol NA, 1995

Sasol NA (1995) noted that the decrease in fertility index occurred in the absence of any adverse effects on reproductive organs and considered that this effect may be related to stomach irritation in treated rats, as described above. No other treatment-related effects on any of the reproductive parameters are noted; there are no treatment-related effects at any dose level on any of the developmental parameters evaluated in this study.

Based on the findings described above, the NOAEL was the highest dose of 1000 mg/kg-day.

Inhalation Exposure

Data on the subchronic inhalation effects of *n*-decane in animals come from a single, poorly reported subchronic study by Nau (1966). Nau (1966) exposed groups of 43 rats (strain and sex not specified) to 540 ppm (3140 mg/m^3) *n*-decane (purity not reported) via whole-body inhalation in an exposure chamber for 18 hours per day, 7 days per week, for up to 91 days. The study authors measured vapor concentrations via a sampling port in the chamber each hour during exposure to ensure that the rats were exposed to a constant concentration of *n*-decane. Some rats (number not specified) were set aside without additional exposure for 32 days, while the rest of the animals were presumably sacrificed immediately following the exposure period—although details of animal treatment are lacking. Nau (1966) does not discuss how the exposure concentration of 540 ppm was chosen and reports the tested concentration inconsistently in the text and tables of the report as 540 ppm and 560 ppm (3260 mg/m^3). The number of rats exposed is also inconsistently reported as 43 rats and 41 rats in different tables of the report. Study details regarding maintenance of the rats during the experiment are not reported. Initial average rat body weight was 301 ± 40 grams. In addition to the inhalation exposures in rats using *n*-decane, Nau (1966) also exposed rats via inhalation to benzene and other aromatic-rich fractions of reformed naphthas for 105 days. A control group of 20 rats was maintained simultaneously through 105 days (longer than the 91-day exposure of *n*-decane treated rats) for comparison to all of the exposure groups evaluated by this study.

Nau (1966) monitored rats for changes in general appearance and behavior, body-weight gain, organ weights (specific organs not specified), limited hematology (total leukocytes, polymorphonuclear-lymphocyte ratio, and total lymphocytes), and changes in bone marrow (myelocytic and erythrocytic activity). Gross necropsies and histopathological examination of the tissues were conducted following inhalation exposure. However, in their report, the study authors did not disclose which specific tissues were evaluated following exposure to *n*-decane.

Significant gains in body weight were observed during exposure in comparison to controls ($p < 0.001$) (Nau 1966). Methods of statistical analysis performed by Nau (1966) are not reported. Table 3 shows the changes in body weight over the exposure period in comparison to the control group. After 57 days of exposure, the mean body weight of the treated rats was approximately 36% higher than the control rats. However, at the end of the 91-day exposure period the mean body weight of the treated rats was only about 12% higher than that of the control rats, suggesting that this response may be reversible. Nau (1966) reported that the increase in weight gain among treated rats compared to the control rats was maintained through the 32-day recovery period, although the magnitude of the increase is not reported and neither is the mean body weight of the treated rats at the end of recovery period.

Table 3. Body Weights in Rats Following Inhalation of *n*-Decane[a]

Exposure Period	0 ppm		540 ppm	
	N Rats	Mean ± SD (g)	N Rats	Mean ± SD (g)
Preexposure	20	295 ± 33	43	301 ± 40
End of 57 days	20	335 ± 94	31	456 ± 26 [c]
End of 91 days[b]	17	423 ± 23	18	476 ± 38 [c]

[a]Nau, 1966
[b]end of 105 days for control rats
[c]significantly different from controls ($p < 0.001$)
SD-standard deviation

Table 4 presents changes in hematology (Nau, 1966). After 57 days of exposure, mean counts of total leukocytes were significantly decreased in the treated rats ($p < 0.001$). However, by the end of the 91-day exposure, the mean number of total leukocytes measured in treated rats was significantly increased compared to controls. No significant changes were observed in numbers of lymphocytes or polymorphonuclear-lymphocyte ratio. Although specific data are not reported, Nau (1966) states that there were no significant gross or microscopic changes or changes in bone marrow observed in rats exposed to 540-ppm *n*-decane for 91 days. Organ weight results are not reported.

The only changes associated with exposure to *n*-decane in rats reported in this study are increased body weight and altered total leukocyte counts (decreased at 57 days, increased at 91 days) (Nau, 1966). Neither of these changes was considered toxicologically significant by the authors. Due to the limited endpoints examined and the poor reporting of methods and results, this study is considered inadequate for identification of effect levels.

Table 4. Hematological Changes in Rats Following Inhalation of *n*-Decane[a]

Hematology Measure	Exposure Period	0 ppm		540 ppm	
		N Rats	Mean ± SD	N Rats	Mean ± SD
Total leukocytes	Preexposure	20	22,760 ± 3060	43	21,490 ± 730
	End of 57 days	20	21,055 ± 1610	31	17,765 ± 1600 [c]
	End of 91 days [b]	17	20,510 ± 2120	18	22,815 ± 1530 [c]
Poly. leukocytes	Preexposure	20	16 ± 5	43	18 ± 8
	End of 57 days	20	18 ± 8	31	22 ± 6
	End of 91 days [b]	17	22 ± 7	18	28 ± 14
Total lymphocytes	Preexposure	20	82 ± 6	43	81± 8
	End of 57 days	20	81 ± 9	31	76 ± 6
	End of 91 days [b]	17	77 ± 6	18	72 ± 14

[a]Nau, 1966
[b]hematology values at the end of 105 days for the control rats (0 ppm)
[c]significantly different from controls ($p < 0.001$)

Other Studies

Acute Studies

Petresa (1984) reported an acute oral LD_{50} value of >5000 mg/kg. The study authors derived this value from a single dosing of 5 male and 5 female Sprague-Dawley rats by gavage with 5000 mg/kg *n*-decane. During a 3-day observation period, no deaths were recorded. Terminal necropsy findings are reported as normal. The study authors noted piloerection shortly following treatment in all animals. External appearance and behavior appeared normal by the end of the study.

Nau (1966) exposed 25 CFW mice for 3.75 hours to 540 ppm (3140 mg/m^3) *n*-decane vapor and notes that all mice survived the exposure period and through the next 24 hours postexposure, but 4 mice died before the end of the fourth day after the exposure. Nilsen et al. (1988) exposed 10 male Sprague-Dawley rats to *n*-decane near the saturation concentration at 1368 ppm (7967 mg/m^3) for 8 hours and did not observe any signs of toxicity (no deaths or adverse behavioral effects and no pathological changes), resulting in an 8-hour acute LC_{50} in rats of >1368 ppm (7967 mg/m^3). Carreón (2001) reported a 2-hour LC_{50} of 12,400 ppm (72,300 mg/m^3) in mice. Based on the saturation concentration for *n*-decane reported by Nilsen et al. (1988), it is unclear how the value reported in Carreón (2001) was achieved, and details of the methodology used to derive the 2-hour LC_{50} value of 12,400 ppm (72,300 mg/m^3) are unavailable. Thus, confidence in the 2-hour LC_{50} value is low.

Dermal Studies

Nau (1966) applied 0.1 to 0.15 g of *n*-decane to the skin of 65 male C3H mice 3 times per week on alternate days for a total of 16.53 g per mouse over the course of approximately 150 applications. The mice demonstrated gross and microscopic evidence of skin irritation and kidney and lung hemorrhage, pigmentation, and inflammation. The study authors observed no significant changes in body weight gain or hematology, and they reported no skin tumors. Absorption through the skin is negligible; studies have shown that alkanes having eight or more carbons penetrate the skin with difficulty (Tsuruta, 1982).

Toxicokinetics

Zahlsen et al. (1992) studied the inhalation kinetics of *n*-decane by exposing male Sprague-Dawley rats to an average of 100 ppm for 3 consecutive days and measuring the concentration in blood, brain, liver, kidney, and peripheral fat. The study authors concluded that *n*-alkanes show very low concentrations in the blood, but *n*-alkanes do have relatively elevated concentrations in the brain and exhibit a potential for accumulation in fat with repeated exposures. The acute neurotoxicity study described below (TNO, 1999) reports that the concentration of *n*-decane in the brain was approximately 12- to 23-fold higher than the concentration in blood following a single 8-hour exposure. This is corroborated by Lammers et al. (2007), which studied blood and brain levels of *n*-decane after inhalation exposure to white spirits (nondearomatized). The brain:blood ratio was 15 for a single 8-hour exposure (ratio not dose dependent) and 16 after 3 consecutive days of 8-hour exposures (ratio not dose dependent). The blood levels of human subjects were similar to that of rats exposed to similar concentrations (adjusted for slight differences in dosing). Peak blood concentrations in the Lammers et al. (2007) study decrease after the initial exposures, which is consistent with the explanation that exposures induce metabolism in the treated animals. A physiologically based pharmacokinetic (PBPK) model (for inhalation exposures [not oral]) exists (Hissink et al., 2007) for *n*-decane that allows predictions of blood, expired air, and brain levels. The model predicts an *n*-decane level that is 20% lower in the human brain than the rat brain at a dose near the no-effect level for inhalation exposures.

Neurotoxicity

TNO (1999) exposed rats for 8 hours each day for 3 successive days to *n*-decane at concentrations of 85, 260, and 860 ppm (0.5, 1.5, and 5 g/m^3 respectively). The study authors evaluated the rats 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 3 days and 24 hours after the last exposure. In a separate study, the study authors evaluated response speed and accuracy 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. This decrease was noted only after the third day of exposure. The effect was not apparent 24 hours 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 is reported to be 1.5 g/m^3. In the Maraschin et al. (1995) rat subchronic oral study of commercial decane, startle reflex, an open field test, and forelimb grip strength were examined. The study authors reported no effects at any dose up to 1000 mg/kg-day.

Mutagenicity

Genotoxicity studies summarized by ACCVC (2004) indicate that the potential for *n*-decane to induce any significant mutagenic or cytogenetic activity is low. *n*-Decane produced uniformly negative results in bacteria assays—including negative results in TA1535, 1537, 97, 98, and 100 ± S9 (rat, hamster) (Petresa, 1985; Zeiger, 1992). Negative results have also been obtained in mammalian systems including gene mutation studies in Chinese hamster lung V79 cells, both with or without metabolic activation (enhanced mutant frequency of methylazoxy-methanol (Lankas et al., 1978), and in cytogenetic studies involving chromosomal aberrations with or without metabolic activation (Sasol Italy, 1994) in V79 Chinese hamster lung cells in vitro. *n*-Decane also failed to induce DNA adducts in P-32 postlabeling studies in the skin of treated mice (Shell, 1998). In the mouse micronuclei assay, mice given up to 5.0 g/kg in corn oil gavage showed no increase in micronuclei/PCE in bone marrow (ExonMobil Biomedical Science Inc., 1991). One additional in vitro study on V79 Chinese hamster cells showed that *n*-decane, as a component of mineral spirits, could be considered a tumor promoter because the frequency of mutations caused by methylazoxymethanol, a complete carcinogen in several species, increased in the presence of *n*-decane (ATSDR, 1995). This however, appears to be related to its efficacy as a solvent and primary irritant (see text below).

Carcinogenicity

Little information is available on the carcinogenic potential for *n*-decane. *n*-Decane did not produce skin tumors when tested alone in initiation/promotion studies conducted in mice (Van Duuren and GoldSchmitt, 1976). *n*-Decane does not promote morphological transformation or inhibit intercellular communication in primary Syrian hamster embryo cells in culture (Rived et al., 1992).

There is, however, evidence for a cocarcinogenic effect with some agents. Bingham and Nord (1977) compared the effects of repeated topical applications to mice of 3 *n*-paraffins (*n*-decane, *n*-dodecane, and *n*-tetradecane) on the carcinogenic potential of UV light at 3 wavelength regions: 254 nm, 290−320 nm, and greater than 350 nm. All three *n*-alkanes had a cocarcinogenic effect at 254 nm, whereas only *n*-dodecane was effective from 290 to 320 nm. Radiation at wavelengths longer than 350 nm, generally considered noncarcinogenic, produced tumors on the backs of mice treated with *n*-decane or *n*-tetradecane. According to Horton et al. (1957) *n*-decane can also act as a cocarcinogen with agents such as 3-methylcholanthrene or benzo[a]pyrene. For example, solutions of polycyclic carcinogens in solvents having long-chain structures (e.g., *n*-dodecane and dodecylbenzene) induce tumors of the skin of mice at a much higher rate for a given concentration of carcinogen than do solutions in hydrocarbon solvents of lower molecular weight. Solutions in such accelerating solvents also show an unusual capacity to spread upon the skin. An additional study, Nessel et al. (1999), provides evidence that the skin-tumor-promoting effects of C10−C14 normal alkanes is secondary to skin irritation by showing that undiluted C10−C14 alkanes produced irritation and significant increases in tumor incidence in dimethylbenzanthracene pretreated mice. When applied in mineral oil diluent, skin irritation was ameliorated and tumor incidence dropped to an insignificant level. The available evidence indicates that these solvents, when free of polycyclic impurities, are not carcinogenic for the skin of mice, although they are primary irritants.

FEASIBILITY OF DERIVING OF PROVISIONAL SUBCHRONIC AND CHRONIC ORAL RfD VALUES FOR *n*-DECANE

Sasol NA (1995) is the only study located that reports data on the toxicity of *n*-decane following repeated oral exposure. As this study was not reported in the peer-reviewed literature, but rather as an industry study reported to EPA, any reference values derived from it must be used only as screening values (see Appendix).

FEASIBILITY OF DERIVING PROVISIONAL SUBCHRONIC AND CHRONIC INHALATION RfC VALUES FOR *n*-DECANE

Nau (1966) is the only study that reports data on the subchronic inhalation toxicity of *n*-decane. This is a poorly reported study that features investigation of limited endpoints. The only reported changes (increased body-weight gain and variable alterations in total leukocyte count) were not considered to be toxicologically significant. Thus, this study is inadequate to identify a point of departure for derivation of p-RfC values.

PROVISIONAL CARCINOGENICITY ASSESSMENT FOR *n*-DECANE

Weight-of-Evidence Descriptor

Studies evaluating the carcinogenic potential of oral or inhalation exposure to *n*-decane in humans or animals are not available. Mutagenicity data suggest that the potential for *n*-decane to induce any significant mutagenic or cytogenetic activity is low. Under the 2005 Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005), there is *"Inadequate Information to Assess the Carcinogenic Potential"* of *n*-decane.

Quantitative Estimates of Carcinogenic Risk

The lack of suitable data precludes derivation of quantitative estimates of cancer risk.

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APPENDIX. DERIVATION OF A SCREENING p-RfD VALUE FOR n-DECANE (CASRN 124-18-5)

For reasons noted in the main PPRTV document, it is inappropriate to derive provisional toxicity values for *n*-decane. However, information is available for this chemical which, although insufficient to support derivation of a provisional oral or inhalation toxicity values, under current guidelines, may be of limited use to risk assessors. In such cases, the Superfund Health Risk Technical Support Center summarizes available information in an Appendix and develops a "screening value." Appendices receive the same level of internal and external scientific peer review as the PPRTV documents to ensure their appropriateness within the limitations detailed in the document. Users of screening toxicity values in an appendix to a PPRTV assessment should understand that there is considerably more uncertainty associated with the derivation of an appendix screening toxicity value than for a value presented in the body of the assessment. Questions or concerns about the appropriate use of screening values should be directed to the Superfund Health Risk Technical Support Center.

Sasol NA (1995) is the only study located that reports data on the toxicity of *n*-decane following repeated oral exposure. As this study was not reported in the peer-reviewed literature, but rather as an industry study reported to EPA, any reference values derived from it must be used only as screening values. This study found hyperplastic changes of the nonglandular mucosa of the stomach in male and female rats treated by daily gavage with commercial *n*-decane (approximately 97% *n*-decane) for 4−8 weeks. The effects were not statistically significant although there was a trend. No other systemic effects are reported. Although there is some indication of reduced fertility in treated rats, the differences from controls are not statistically significant, the observations are not clearly related to dose, and there are no corresponding histological changes in the reproductive organs. Therefore, a NOAEL of 1000 mg/kg-day, the highest dose tested, is identified for repeated-dose toxicity in this study.

Screening Subchronic p-RfD Value

Although the duration of oral exposure in the Sasol NA (1995) study is only 4−8 weeks, 10 rats of each sex were tested at multiple doses and evaluated for multiple endpoints, as described above. The NOAEL of 1000 mg/kg-day in rats from Sasol NA (1995) is used to calculate a screening subchronic value for *n*-decane. The only other data regarding oral toxicity of *n*-decane come from an acute study that derived an LD_{50} value of >5000 mg/kg based on the absence of mortality in rats treated with a single dose of *n*-decane at 5000 mg/kg (Petresa, 1984).

A screening **subchronic screening p-RfD of 1 mg/kg-day** is derived by dividing the NOAEL of 1000 mg/kg-day by an UF of 1000, as shown below:

Screening Subchronic p-RfD Value	=	NOAEL ÷ composite UF
	=	1000 mg/kg-day ÷1000
	=	**1.0 mg/kg-day**

The composite UF of 1000 encompasses the following:

- A UF of 10 is applied for interspecies extrapolation to account for potential pharmacodynamic and pharmacokinetic differences between rodents and humans.
- A UF of 10 is applied for intraspecies differences to account for potentially susceptible individuals in the absence of quantitative information or information on the variability of response in humans.
- A UF of 10 is applied for database insufficiencies. A single, short-term-oral toxicity study in one animal species (rat) is available (Sasol NA, 1995). Although the principal study (Sasol NA, 1995) did evaluate systemic, neurological, reproductive, and developmental effects, the database lacks studies of subchronic and chronic toxicity, a study in another species, a supporting developmental toxicity study, and a multigenerational reproduction study.

Confidence in the principal study (Sasol NA, 1995) is moderate because, despite investigation of multiple endpoints at multiple dose levels with sample sizes of 10 rats/sex/dose, the experiment only lasted 4 to 8 weeks depending on the sex of the rat. Confidence in the database is low because the data set includes only short-term and acute animal studies. Reflecting medium confidence in the principal study and low confidence in the database, confidence in the subchronic value is low to medium.

Screening Chronic Value

A chronic p-RfD is not derived from the previous data due to the lack of any data on the effects of longer-term exposure. The only repeated-dose oral study is the 4−8 week study in rats (Sasol NA, 1995), which is used to derive the subchronic screening value. While repeat dosing induces metabolism, and blood and brain levels decline relatively quickly, the compound does partition to fat, and levels there accumulate with time in repeat dosing experiments (Lammers et al., 2007).