# Ground Water Quality Standard for
# n-Heptane

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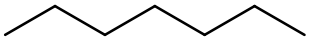
**Summary of Decision:** In accordance with the New Jersey Ground Water Quality Standards rules at N.J.A.C. 7:9C-1.7, the Department of Environmental Protection (Department) has determined that insufficient information is available to develop a specific or interim specific ground water quality criterion for n-heptane at this time. Since n-heptane is a synthetic organic chemical not listed in Appendix Table 1, and has not been determined to be a carcinogen, **the applicable constituent standard is the interim generic ground water quality criterion of 100 µg/L**. The basis for this criterion and PQL are discussed below.

**n-Heptane**
(Dipropylmethane)
**Molecular Formula: $C_7H_{16}$**
**Molecular Structure:**



**Background:** Although some chemical-specific risk data are available for the ingestion route of exposure to nheptane, these data are quite limited and carry a large quantitative uncertainty leading to a larger than acceptable overall uncertainty factor adjustment to support a data-based risk assessment.

The generic criterion for non-carcinogens is protective relative to the available (but inadequate) toxicological data. The Department considered ingestion as well as inhalation exposure under a screening-level showering scenario at 100 ppb n-heptane in water. On the basis of this analysis, inhalation showering exposure is predicted to be more than two orders of magnitude below occupational exposure limits and the odor threshold for n-heptane.

**Literature Search:** Pharmacokinetic studies have been summarized by the U.S.EPA (1989). n-Heptane appears to share narcotic, central nervous system depressing properties with other volatile alkanes. These effects have been reported in acute inhalation studies, and to a lesser extent, during the course of somewhat longer duration exposures (Biodynamics Inc., 1980). It is not clear whether decreased auditory sensitivity observed by Simonsen and Lund (1995) is a central nervous system effect. No central nervous system-related effects were observed with either ingestion or intraperitoneal exposure.

Most studies of n-heptane toxicology have focused on inhalation exposure since occupational inhalation exposure to n-heptane vapor released from its use as a solvent is the most common exposure. It is necessary to consider whether such studies can be useful in assessing the ingestion toxicity of n-heptane. In general, inhaled gases that are systemically absorbed from the lungs into blood are transported to the brain before returning to the heart from where the enter the circulatory system as a whole. On the

other hand, substances absorbed from the gastro-intestinal tract generally pass through the liver before entering the general circulation. This distinction is potentially important for substances that are metabolized in the liver. Such metabolism can either enhance or reduce the toxicity observed with ingestion relative to inhalation. In the case of n-heptane, the liver is a major site of metabolism (U.S.EPA, 1989; EC, 1996). Thus, for an equivalent mass of n-heptane systemically absorbed by ingestion and inhalation, adverse endpoints that proceeds through metabolic products will likely occur at a lower dose with ingestion. Adverse effects that do not require metabolism, including, but not limited to narcotic effects and other effects on axon membranes, will likely occur at lower doses with inhalation. Therefore, it may be possible to draw qualitative conclusions about the type of adverse effects that could occur with ingestion based on evaluation of inhalation studies. However, extrapolation of ingestion dose-response relationships from inhalation data cannot be made without reference to physiologically based pharmacokinetic (PBPK) model. No such model appears to be available for heptane at the present time.

There are no chronic ingestion studies available. Relevant studies include only the 90-day gavage ingestion study by O'Donoghue and Krasavage (1980), and two closely related intraperitoneal injection studies (Goel et al. 1982; 1988). The O'Donoghue and Krasavage (1980) study employed only a single dose level, plus controls. The study was severely compromised by the premature death of 5 of the 8 exposed animals as a result of gavage errors. Thus, the one ingestion study available is both sub-chronic in duration and severely compromised. It is of marginal use in deriving a health-based exposure guideline. However, it is clear that the single dose in that study is a Low Observed Adverse Effect Level (LOAEL) rather than a No Observed Adverse Effect Level (NOAEL). The usefulness of that study is supported somewhat by its consistency with the intraperitoneal and inhalation studies in not showing clear signs of unusual systemic toxicity. Given the relatively large body of knowledge regarding the toxicity of similar length alkanes, and given lack of clear evidence for the occurrence of 2,5-dione peripheral neuropathy, the Department has determined that the LOAEL from the ingestion study of O'Donoghue and Krasavage (1980) can be used with a low-degree of confidence, and has made an appropriate adjustment for uncertainty in the derivation of health-based drinking water guideline.

**Reference Dose:** There are no data to support the construction of a dose-response curve; therefore, benchmark-dose modeling is not an option. The single oral dose of 4,000 mg/kg body wt/day from O'Donoghue and Krasavage (1980) is identified as a LOAEL.

**Uncertainty Factor (UF) Adjustment:**

$UF_{LOAEL - NOEL} = 10$
$UF_{subchronic - chronic} = 10$
$UF_{animal - human} = 10$
$UF_{sensitive\ human} = 10$
$UF_{database\ insufficiency} = 3$

$UF_{total} = UF_{LOAEL - NOEL} \times UF_{subchronic - chronic} \times UF_{animal - human} \times UF_{sensitive\ human} \times UF_{db.\ ins.}$
**UF** = $UF_{total}$ = 10x10x10x10x3 = 30,000

The UF for database insufficiency reflects the lack of data for evaluation of

developmental and reproductive endpoints, and the uncertainty regarding the potential for peripheral neuropathy with chronic ingestion exposure. A (half) factor of 3 is assigned in light of the relatively strong and generalizable database for toxicology of the short-chain alkanes, and the lack of a clear indication of the occurrence of peripheral neuropathy associated with the minor 2,5-heptanedione metabolite.

Overall this UF value should be viewed as having low certainty and is based on a weak database. Current risk assessment practice for non-carcinogens suggests not deriving a data-based Reference Dose (RfD) or similar risk-based criterion when the total UF exceeds 10,000 (U.S.EPA, 2002). This is because such a value would only be obtained when there is significant uncertainty in more than four specific categories of uncertainty. In such a case, the available data are deemed too uncertain to be quantitatively useful.

**Derivation of Ground Water Quality Criterion:** The Department has determined that insufficient information exists for n-heptane to develop a specific or interim specific health-based ground water quality criterion. The Ground Water Quality Standards at N.J.A.C 7:9C-1.7(c)6 establish that for synthetic organic chemicals (SOC) not listed in Appendix Table 1, the interim generic ground water quality criterion of 5 µg/L applies to SOCs defined as carcinogens at N.J.A.C. 7:9C-1.4 (generally, chemicals categorized by USEPA carcinogen risk assessment as Group A, B, or C), and the interim generic ground water quality criterion of 100 µg/L applies to SOCs defined as non-carcinogens at N.J.A.C. 7:9C-1.4 (generally, chemicals categorized by USEPA carcinogen risk assessment as D or E). Since there is no data indicating that n-heptane is a carcinogen, the interim generic ground water quality criterion of 100 µg/L applies to this constituent.

**Derivation of PQL:** The method detection limit (MDL) and the practical quantitation level (PQL) are performance measures used to estimate the limits of performance of analytic chemistry methods for measuring contaminants. The MDL is defined as "the minimum concentration of a substance that can be measured and reported with 99 percent confidence that the analyte concentration is greater than zero" (40 CFR Part 136 Appendix B). USEPA recommends that the MDL be multiplied by a factor of five or 10 to account for the variability and uncertainty that can occur at the MDL. The Department uses a value of five as the median upper boundary of the inter-laboratory MDL distribution from the New Jersey certified laboratory community and multiplies the MDL by five to derive the PQL. Establishing the PQL at a level that is five times the MDL provides a reliable quantitation level that most laboratories can be expected to meet during day-to-day operations.

n-Heptane appears as a listed parameter in a Standard Operating Procedure (SOP) developed by the New Jersey Department of Health and Senior Services (NJDHSS) state primacy laboratory analytical method – "USEPA 524.2, Volatile Organic Compounds by GC/MS" (see National Environmental Methods Index (NEMI)). The limit of detection in the method is not specified. The limit of detection specified by NJDHSS laboratory is 0.1 ppb. As explained above, a more conservative detection limit is established using a multiplier of five. 0.1 ppb x 5 = 0.5 ppb. Therefore, the Department has established a PQL of 0.5 ppb (µg/L) for n-heptane.

**Conclusion:** Based on the information provided above (and cited below), the Department has determined that insufficient information is available to develop a specific or an interim specific ground water quality criterion for n-heptane at this time; therefore, the applicable constituent standard is the interim generic ground water

quality criterion of 100 µg/L for a non-carcinogen.

**Technical Support Documents:** *Interim Specific Ground Water Quality Criterion Recommendation Report for n-Heptane*, Dr. Alan Stern, NJDEP, May 11, 2005; *Procedure for Describing Process for Development of Analytical Practical Quantitation Levels (PQLs) for n-Heptane*, R. Lee Lippincott, Ph.D., NJDEP, May 18, 2005.

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