

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

N-nitrosodi-n-propylamine is not an industrially or commercially important chemical. It is produced in small, laboratory-scale quantities for research purposes. It is also produced inadvertently during certain manufacturing processes, occurring as an impurity in some dinitroaniline pesticides and during manufacture of some extruded rubber products. Nitrosodi-n-propylamine could also be present in certain secondary amines (di-n-propylamine, tri-n-propylamine and the N-oxide of tri-n-propylamine) as an impurity or due to inadvertent nitrosation of these amines in industrial processes other than those mentioned above. Low levels of Nitrosodi-n-propylamine may be released to the environment from contaminated products, from industrial sites of inadvertent production or from disposal of wastes containing this chemical. N-nitrosodi-n-propylamine could also be released to the environment from waste disposal sites where the precursor secondary amines have been discharged, but the potential for human exposure from nitrosation of precursors at waste sites has not been evaluated.

N-Nitrosodi-n-propylamine is not expected to be a persistent environmental contaminant. If released to the ambient atmosphere, it should be degraded by direct photolysis and/or reaction with sunlight-produced hydroxyl radicals (overall half-life typically on the order of several hours). In water with significant exposure to sunlight, N-nitrosodi-n-propylamine would be subject to rapid photolysis (half-life about 2-3 hours). On soil surfaces, N-nitrosodi-n-propylamine would be subject to rapid removal by photolysis and volatilization. The volatilization half-life of N-nitrosodi-n-propylamine from soil surfaces after spray application of a dinitroaniline herbicide was found to be between 2 to 6 hours. In subsurface soil and in water beyond the penetration of sunlight, N-nitrosodi-n-propylamine would be susceptible to biodegradation under both aerobic and anaerobic conditions. In subsurface soil, the half-life of N-nitrosodi-n-propylamine has been found to range from 14 to 40 days under aerobic conditions and 47 to 80 days under anaerobic conditions. At this time, N-nitrosodi-n-propylamine has been found in at least 1 of 1177 hazardous waste sites on the National Priorities List (NPL) in the United States (VIEW Database 1989).

Limited data are available concerning exposure of the general population to N-nitrosodi-n-propylamine. It appears that exposure possibly results from formation in the upper gastrointestinal tract during digestion of certain foods or drugs that contain secondary amines, ingestion of some foods containing N-nitrosodi-n-propylamine (e.g., certain cheeses, cured meats and fishes and alcoholic beverages), and inhalation of cigarette smoke.

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5.2 RELEASES TO THE ENVIRONMENT

5.2.1 Air

Occurrence of part per million levels of N-nitrosodi-n-propylamine in various dinitroaniline herbicides may result in release of small amounts of the nitrosamine into the atmosphere during and after application (Cohen et al. 1978, Crosby 1979, Oliver 1981). Occurrence of N-nitrosodi-n-propylamine in air in the production area of a rubber products plant where common nitrosating agents (e.g., oxides of nitrogen) were used in conjunction with rubber formulations containing secondary amine-based compounds, suggests that plants using this type of production process are a potential source of N-nitrosodi-n-propylamine emissions (NIOSH 1982).

5.2.2 Water

N-Nitrosamines may be formed inadvertently in situations in which amines come in contact with nitrogen oxides, nitrous acid, nitrite salts, nitro compounds or nitroso compounds (Fajen et al. 1980). This suggests that under appropriate industrial conditions where di-n-propylamine is present, N-nitrosodi-n-propylamine could be formed inadvertently and released to the environment via effluent discharges. Limited monitoring data which support this supposition indicate that N-nitrosodi-n-propylamine has been released in wastewater from some textile plants and manufacturers and/or users of amines. Small amounts of N-nitrosodi-n-propylamine may also be released to surface waters either directly or indirectly (e.g., in runoff) as a result of using dinitroaniline herbicides containing the nitrosamine as an impurity.

5.2.3 Soil

Small amounts of N-nitrosodi-n-propylamine may be released to soil during the application of some dinitroaniline herbicides. For example, a typical 1 kg per hectare application of trifluralin containing 1 part per million (ppm) N-nitrosodi-n-propylamine would result in application of 0.01 ng nitrosamine per square centimeter (Oliver 1979). Federal regulations require trifluralin formulations to contain <1 ppm N-nitrosodi-n-propylamine (EPA 1979). Data pertaining specifically to the formation of N-nitrosodi-n-propylamine in soil were not found in the literature; however, formation of N-nitrosodimethylamine (NDMA) in soil containing dimethylamine and nitrate or nitrite suggests that a similar mechanism may exist for N-nitrosodi-n-propylamine (Mills and Alexander 1976, Oliver 1981, Pancholy 1976).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Organics having a vapor pressure of $>10^{-4}$ mm Hg should exist almost entirely in the vapor phase in the atmosphere (Eisenreich et al. 1981). The

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estimated vapor pressure of N-nitrosodi-n-propylamine [0.086 mm Hg at 25°C (see Table 3-2)] indicates that this compound should not partition from the vapor phase to particulates in the atmosphere.

Using linear regression equations based on $\log K_{ow}$ data [$\log K_{ow} = 1.36$ (see Table 3-2)], a bioconcentration factor of 6 and an adsorption coefficient (K_{oc}) of 129 have been estimated for N-nitrosodi-n-propylamine (Bysshe 1982; Hansch and Leo 1985; Lyman 1982). These values indicate that bioaccumulation in aquatic organisms and adsorption to suspended solids and sediments in water would not be important fate processes. The low Henry's Law constant for N-nitrosodi-n-propylamine [1.47×10^{-6} atm-m³/mol (see Table 3-2)] suggests that volatilization would be a relatively insignificant fate process in water.

If a herbicide containing N-nitrosodi-n-propylamine were applied to warm, moist soil surfaces, most of the nitrosamine would be expected to volatilize. The volatilization half-life from soil surfaces under field conditions is estimated to be on the order of 2 to 6 hours (Berard and Rainey 1979, Oliver 1979). If a herbicide containing N-nitrosodi-n-propylamine were incorporated into soil (below the soil surface), volatilization would be of minor importance (Oliver 1979). When incorporated into soil, N-nitrosodi-n-propylamine is expected to be highly mobile and it has the potential to leach into shallow groundwater supplies (Saunders et al. 1979, Swann et al. 1983).

5.3.2 Transformation and Degradation

5.3.2.1 Air

In the atmosphere, N-nitrosodi-n-propylamine vapor would be rapidly degraded by direct photolysis and/or reaction with photochemically-generated hydroxyl radicals. Crosby et al. (1980) determined a pseudo-first order half-life of 5 to 7 hours for photolysis of N-nitrosodi-n-propylamine vapor in air exposed to sunlight. Although experimental conditions did not closely simulate environmental conditions (the concentration of N-nitrosodi-n-propylamine was relatively high), results of this study did indicate that N-nitrosodi-n-propylamine is susceptible to rapid photolysis. The half-life for the reaction of N-nitrosodi-n-propylamine vapor with photochemically-generated hydroxyl radicals has been estimated to be about 16 hours in typical ambient air. This value is based on a reaction rate constant of 2.42×10^{-11} cm³/molecules-sec at 25°C which was estimated using the method of Atkinson (1987).

5.3.2.2 Water

N-nitrosodi-n-propylamine is not expected to undergo abiotic degradation under the conditions found in natural waters (Callahan et al. 1979, Oliver et al. 1979, Saunders and Mosier 1980). The dominant removal process for N-nitrosodi-n-propylamine in surface water is probably

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photolysis. A study of low levels (0.65 ppm) of N-nitrosodi-n-propylamine in lake water resulted in a photolytic half-life of about 2.5 hours. The major photoproduct was found to be n-propylamine, but the formation of di-n-propylamine was also observed (Saunders and Mosier 1980). Beyond the reach of sunlight it appears that N-nitrosodi-n-propylamine would be subject to slow microbial degradation in aerobic waters (Tabak et al. 1981, Tate and Alexander 1975). Insufficient data are available to predict the rate at which this would occur.

5.3.2.3 Soil

It appears that microbial degradation would be the dominant removal process for the nitrosamine in subsurface soil under aerobic conditions. Half-lives ranging from 14 to 40 days have been observed in aerobic subsurface soil and from 47 to 80 days in anaerobic subsurface soil (Oliver et al. 1979, Saunders et al. 1979, Tate and Alexander 1975). Initial losses were due primarily to volatilization; however, biodegradation was the dominant fate process. Available data on the degradation of the nitrosamine in water and air, indicate that photolysis may be an important removal process on soil surfaces.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

There is no indication in the available literature that N-nitrosodi-n-propylamine has been detected in ambient air in the United States. Air samples collected above agricultural fields before, during, and after application of the pesticide trifluralin contained no detectable levels of N-nitrosodi-n-propylamine (detection limit 50 ng/m^3) (Day et al. 1982, West and Day 1979).

5.4.2 Water

No data were available regarding the monitoring and detection of N-nitrosodi-n-propylamine in ambient surface water, groundwater, or drinking water in the United States except at EPA National Priorities List (NPL) hazardous waste sites. There were only a couple of monitoring studies available pertaining to the occurrence N-nitrosodi-n-propylamine in treated wastewater. In a survey of 32 U.S. textile plants, N-nitrosodi-n-propylamine was detected at concentrations of 2-20 $\mu\text{g/L}$ in 2 out of 32 samples of secondary effluent, while no detectable levels were found in samples of raw wastewater from these same plants (Rawlings and Samfield 1979). This suggests that N-nitrosodi-n-propylamine was formed during the treatment process. N-nitrosodi-n-propylamine has also been detected at a maximum concentration of 1.2 $\mu\text{g/L}$ in the final effluent from a German chemical manufacturing plant involved in the manufacture and/or use of amines (Hartmetz and Slemrova 1980). A survey of stormwater runoff samples collected from 15 cities geographically located across the U.S. revealed

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that N-nitrosodi-n-propylamine is not a typical contaminant of stormwater runoff (Cole et al. 1984). Water samples collected from agricultural fields immediately following application of the pesticide trifluralin contained no detectable levels of N-nitrosodi-n-propylamine (detection limit 0.01-0.02 µg/L) (Ross et al. 1978, West and Day 1979).

5.4.3 Soil

Soil samples collected from agricultural fields immediately following application of the pesticide trifluralin contained no detectable levels of N-nitrosodi-n-propylamine (detection limit 0.2-1 ng/g) (Ross et al. 1978, West and Day 1979). It has been detected in at least 1 of 1177 NPL hazardous waste sites (VIEW 1989).

5.4.4 Other Media

A number of studies have focused on the monitoring of volatile N-nitrosamines in various foodstuffs, including cheese, cured meats, cooked fish, and alcoholic beverages; however, N-nitrosodi-n-propylamine has rarely been detected (Alliston et al. 1972, Gavinelli et al. 1988, Goff and Fine 1979, Gross and Newberne 1977, Huang et al. 1981, Sen et al. 1987). The nitrosamines appear to have formed in these foods as the result of the reaction of secondary amines with the preservative sodium nitrite (Gray and Dugan 1974). N-nitrosodi-n-propylamine has been monitored in food at the following levels: salt-preserved fish (steamed), 0.050 µg/kg; salt-preserved fish (fried), 0.030 µg/kg; salt-preserved fish (raw), not detected; cheese, 5-30 µg /kg; apple brandy, up to 3.6 µg/kg; cognac, rum and whiskey, up to 0.2 µg /kg (Cerutti et al. 1975, Gross and Newberne 1977, Huang et al. 1981, IARC 1978). A study of cigarette smoke condensate from European cigarettes showed that N-nitrosodi-n-propylamine was found at a level equivalent to 1 ng per cigarette in smoke condensate from 1 out of 11 types of cigarettes, while condensate from 10 out of 11 cigarettes had levels below the detection level of 0.5 ng per cigarette (McCormick et al. 1973). Although a number of volatile N-nitrosamines have been identified in children's pacifiers and baby-bottle nipples, N-nitrosodi-n-propylamine was not among them (Billedeau et al. 1986, Gavinelli et al. 1988, Westin et al. 1987). Crops and plants harvested from fields treated with the pesticides trifluralin, benefin, or oryzalin contained no detectable levels of N-nitrosodi-n-propylamine (detection limit 0.2 ng/g) (Ross et al. 1978, West and Day 1979).

In the mid-to-late 1970s, N-nitrosodi-n-propylamine was detected in the herbicide trifluralin at levels as high as 154 mg/L, oryzalin at <1 mg/L and isopropalin at 39-87 mg/L (Cohen et al. 1978, Ross et al. 1977). Subsequent to these findings, the production process for trifluralin was modified; current levels of the nitrosamine in technical trifluralin are <1 mg/L (EPA 1979, Maybury and Grant 1983, Wotherspoon and Hindle 1988).

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5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The potential for inhalation of N-nitrosodi-n-propylamine during application and soil incorporation of trifluralin containing N-nitrosodi-n-propylamine is extremely low; N-nitrosodi-n-propylamine levels in breathing zone air of field workers should be on the order of several parts per trillion or less (Day et al. 1982). During 1982, NIOSH carried out a monitoring study at a plant where workers were involved in the production of extruded rubber parts for automobile part interiors. Samples of personal breathing-zone air were found to contain N-nitrosodi-n-propylamine at concentrations ranging from 1.3 to 3.3 $\mu\text{g}/\text{m}^3$ (241-611 ppt), with a mean concentration of 2.3 $\mu\text{g}/\text{m}^3$ (430 ppt). Airborne nitrosamine levels at this plant were consistent with those found by NIOSH in other rubber industries where the same type of extruding process was used. Volatile nitrosamines, such as N-nitrosodi-n-propylamine, are emitted from heated rubber after formation by the reaction of common nitrosating agents (e.g., oxides of nitrogen) with secondary amine-based compounds frequently used in rubber formulations (NIOSH 1982). N-nitrosodi-n-propylamine has been detected in soil samples from at least one NPL site, and workers at NPL sites or other hazardous waste sites could potentially be exposed to this compound by inhalation and dermal contact. It is not certain whether direct skin contact with N-nitrosodi-n-propylamine would allow the chemical to enter the body.

Based on limited data it appears that the general population may be exposed to part per trillion levels of N-nitrosodi-n-propylamine in some sodium nitrite-treated foods and certain alcoholic beverages. The general population may be exposed to N-nitrosodi-n-propylamine as a result of its in vivo formation during digestion in the upper gastrointestinal tract of nitrite-containing and secondary amine-containing foods or drugs, especially those containing di-n-propylamine (Groenen PJ et al. 1980, Magee et al. 1976; Sakai et al. 1984). One study pertaining to exposure to N-nitrosodi-n-propylamine through inhalation of cigarette smoke suggests that there is a possibility that low levels of this compound (on the order of 1 ng per cigarette) may occur in cigarette smoke. There is no evidence of general population exposure to N-nitrosodi-n-propylamine through ingestion of contaminated drinking water or through dermal contact.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURE

Data are not available for determining those segments of the general population with potentially high exposure.

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5.7 ADEQUACY OF THE DATA BASE

Section 104 (i) (5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of N-nitrosodi-n-propylamine is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

5.7.1 Data Needs

Physical and Chemical Properties. Physical and chemical properties are essential for estimating the partitioning of a chemical in the environment. Many physical and chemical properties are available for N-nitrosodi-n-propylamine, but most do not have extensive experimental descriptions accompanying the data so that an evaluation of the accuracy of the data is difficult to make. Specifically, measured water solubility, vapor pressure, K_{oc}) and Henry's Law constant would be helpful in removing any doubt concerning the accuracy of the data as well as provide information concerning the uncertainty of these types of data. These data form the basis for much of the input requirements for environmental models that predict the behavior of a chemical under specific conditions including hazardous waste landfills.

Environmental Fate. Data are available to establish, in general, the environmental fate of N-nitrosodi-n-propylamine. It has been predicted that in surface waters, beyond the reach of sunlight, N-nitrosodi-n-propylamine would be subject to slow microbial degradation; however, data are needed to determine its degradation rate in unlit surface water under aerobic or anaerobic conditions. Natural water grab sample biodegradation studies and soil metabolism studies carried out in the dark under both aerobic and anaerobic conditions would be useful in establishing the persistence of N-nitrosodi-n-propylamine in the environment. The dominant removal mechanisms for N-nitrosodi-n-propylamine in air are expected to be photolysis and reaction with photochemically generated hydroxyl radicals; however, no data are available concerning the reaction pathway and the products of these types of reactions. These types of data would be useful in establishing what happens to this compound when it is released to the environment.

Exposure Levels in Environmental Media. Data are needed to relate the levels of N-nitrosodi-n-propylamine found at hazardous waste landfills to

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levels of exposure resulting from its occurrence at these sites. Studies in which air monitoring (ambient and personal air) in the vicinity of contaminated sites and water sampling (groundwater and drinking water) at locations where contamination from the site is most likely to occur would be useful in establishing the extent of human exposure from contaminated sites. N-Nitrosodi-n-propylamine has been detected on a few occasions in some sodium nitrite-treated foods and alcoholic beverages and ingestion appears to be a potential route of exposure; although, recent comprehensive data regarding the occurrence of N-nitrosodi-n-propylamine in foods were not available. A comprehensive survey of those food items in which N-nitrosodi-n-propylamine may occur, including cheese, cured meats and fish, and alcoholic beverages, would be useful in understanding the potential for human exposure to N-nitrosodi-n-propylamine. Only one study was available regarding the occurrence of N-nitrosodi-n-propylamine in cigarette smoke. Results of this study do not provide strong conclusive evidence for occurrence of measurable levels of N-nitrosodi-n-propylamine in cigarette smoke and further studies need to be carried out before any conclusions can be made.

Exposure Levels in Humans. Limited data were available regarding human exposure to N-nitrosodi-n-propylamine. It appears that the general population may be exposed to N-nitrosodi-n-propylamine through various foodstuffs, some alcoholic beverages, and possibly cigarette smoke; however, data are needed to predict with certainty the frequency and level of exposure. A few broad-based monitoring studies of air, water, and typical diets would be useful in deriving estimates of typical exposure levels in humans.

Exposure Registries. An exposure registry currently is not available. The development of a registry for exposures would provide a useful reference tool in assessing exposure levels and frequency. In addition, a registry would allow an assessment of the variations in exposure concentrations from, for example, geography, season, regulatory actions, presence of hazardous waste landfills, or manufacturing facilities. These assessment would, in turn, provide a better understanding of the needs for some type of research or data acquisition based on current exposure concentrations. Occupational exposure to this compound is mainly through its inadvertent formation, so an occupational exposure registry would be difficult to obtain.

5.7.2 On-going Studies

There is no indication that there are any studies currently in progress which are related to the level of N-nitrosodi-n-propylamine in environmental media, environmental fate of N-nitrosodi-n-propylamine, or general population or occupational exposure to N-nitrosodi-n-propylamine.