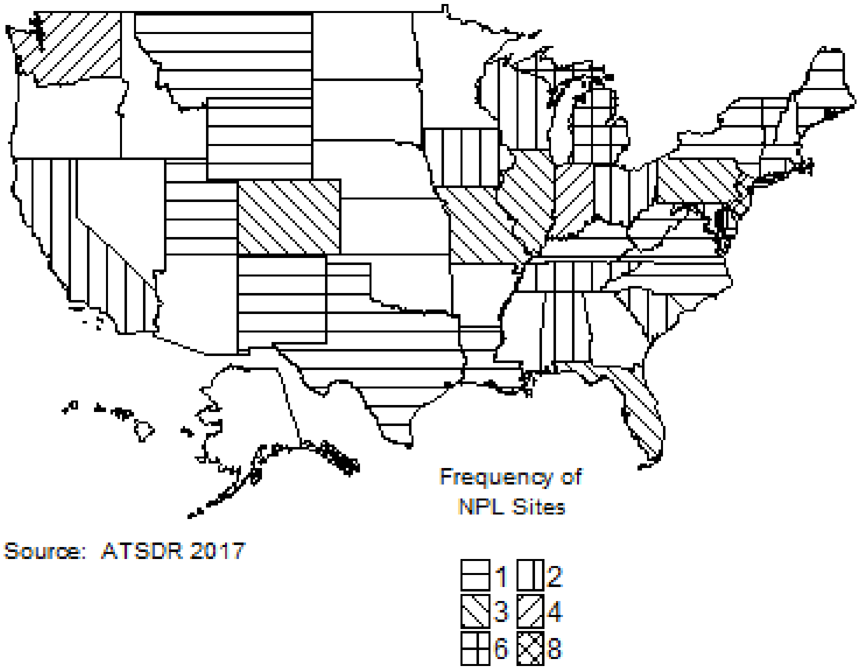
CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

N-Nitrosodi-n-propylamine has been identified in at least 71 of the 1,854 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (ATSDR 2017). However, the number of sites in which N-nitrosodi-n-propylamine has been evaluated is not known. The number of sites in each state is shown in Figure 5-1.

Figure 5-1. Number of NPL Sites with N-Nitrosodi-n-Propylamine Contamination



Source: ATSDR 2017

- N-nitrosodi-n-propylamine 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.

- 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.

- Low levels of N-nitrosodi-n- propylamine may be released to the environment from contaminated products and industrial sites of inadvertent production or disposal of wastes. It may also be released from waste disposal sites where the precursor secondary amines have been discharged.

- N-Nitrosodi-n-propylamine is not expected to be a persistent environmental contaminant. In air and soil surfaces, it is likely degraded by photolysis and volatilization. In water and subsurface soil, N-nitrosodi-n-propylamine would be susceptible to biodegradation under both aerobic and anaerobic conditions.

5.2 PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

5.2.1 Production

N-Nitrosodi-n-propylamine is not produced for commercial use in the United States (HSDB 1988). Table 5-1 contains a list the number of facilities per state that produced, processed, or used N-nitrosodi-n-propylamine in 2016, as well as information on the amount of N-nitrosodi-n-propylamine on site and related activities and uses (TRI16 2017). Manufacturers are required to report Toxics Release Inventory (TRI) data to satisfy EPA requirements. The TRI data should be used with caution since only certain types of facilities are required to report (EPA 2005). This is not an exhaustive list.

Table 5-1. Facilities that Produce, Process, or Use N-Nitrosodi-n-Propylamine

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
IN	1	100	999	12
OH	1	100	999	12

[a] Post office state abbreviations used.
[b] Amounts on site reported by facilities in each state.
[c] Activities/Uses:

1. Produce
2. Import
3. Used Processing
4. Sale/Distribution
5. Byproduct
6. Reactant
7. Formulation Component
8. Article Component
9. Repackaging
10. Chemical Processing Aid
11. Manufacture Aid
12. Ancillary
13. Manufacture Impurity
14. Process Impurity

Source: TRI16 2017 (Data are from 2016)

5.2.2 Import/Export

No U.S. import data were found for N-nitrosodi-n-propylamine.

5.2.3 Use

N-Nitrosodi-n-propylamine is prepared in laboratory-scale quantities solely for use as a research chemical (HSDB 1988).

5.2.4 Disposal

Landfill disposal procedures should be confirmed by responsible environmental engineers and regulatory officials (OHM-TADS 1988). N-Nitrosodi-n-propylamine may be destroyed by high-temperature incineration in an incinerator equipped with a NOx scrubber (OHM-TADS 1988). Chemical treatment methods may also be used to destroy N-nitrosodi-n-propylamine. These methods involve:
(a) denitrosation by reaction with 3% hydrobromic acid in glacial acetic acid; (b) oxidation by reaction with potassium permanganate-sulfuric acid; or (c) extraction of the nitrosamine from the waste using dichloromethane and subsequent reaction with triethyloxonium tetrafluoroborate (TOEF) (Castegnaro et al. 1982).

5.3 RELEASES TO THE ENVIRONMENT

The Toxics Release Inventory (TRI) data, presented in Table 5-2, should be used with caution because only certain types of facilities are required to report (EPA 2005). This is not an exhaustive list. Manufacturing and processing facilities are required to report information to the TRI only if they employ ≥10 full-time employees; if their facility is included in Standard Industrial Classification (SIC) Codes 10 (except 1011, 1081, and 1094), 12 (except 1241), 20–39, 4911 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4931 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4939 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4953 (limited to facilities regulated under RCRA Subtitle C, 42 U.S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited to facilities primarily engaged in solvents recovery services on a contract or fee basis); and if their facility produces, imports, or processes ≥25,000 pounds of any TRI chemical or otherwise uses >10,000 pounds of a TRI chemical in a calendar year (EPA 2005).

Table 5-2. Releases to the Environment from Facilities that Produce, Process, or Use N-Nitrosodi-n-Propylamine[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
IN	1	1	0	0	0	No data	1	0	1
OH	1	No data	No data	No data	No data	No data	No data	No data	No data
Total	2	1	0	0	0	0	1	0	1

[a] The TRI data should be used with caution since only certain types of facilities are required to report. This is not an exhaustive list. Data are rounded to nearest whole number.
[b] Data in TRI are maximum amounts released by each facility.
[c] Post office state abbreviations are used.
[d] Number of reporting facilities.
[e] The sum of fugitive and point source releases are included in releases to air by a given facility.
[f] Surface water discharges, waste water treatment-(metals only), and publicly owned treatment works (POTWs) (metal and metal compounds).
[g] Class I wells, Class II-V wells, and underground injection.
[h] Resource Conservation and Recovery Act (RCRA) subtitle C landfills; other onsite landfills, land treatment, surface impoundments, other land disposal, other landfills.
[i] Storage only, solidification/stabilization (metals only), other off-site management, transfers to waste broker for disposal, unknown
[j] The sum of all releases of the chemical to air, land, water, and underground injection wells.
[k] Total amount of chemical transferred off-site, including to POTWs.

RF = reporting facilities; UI = underground injection

Source: TRI16 2017 (Data are from 2016)

5.3.1 Air

Estimated releases of 1 pound (~0.00045 metric tons) of N-nitrosodi-n-propylamine to the atmosphere from 4 domestic manufacturing and processing facilities in 2016, accounted for about 100% of the estimated total environmental releases from facilities required to report to the TRI (TRI16 2017). These releases are summarized in Table 5-2.

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). The 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).

5.3.2 Water

No releases of N-nitrosodi-n-propylamine to surface water or publicly owned treatment works (POTWs) were reported from facilities required to report to the TRI (TRI16 2017).

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 that support this supposition indicate that N-nitrosodi-n-propylamine has been released in waste water 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.

5.3.3 Soil

No releases of N-nitrosodi-n-propylamine to soils from were reported by facilities required to report to the TRI, and no N-nitrosodi-n-propylamine was released via underground injection (TRI16 2017).

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/hectare application of trifluralin containing 1 ppm N-nitrosodi-n-propylamine would result in application of 0.01 ng nitrosamine/cm^2 (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).

5.4 ENVIRONMENTAL FATE

5.4.1 Transport and Partitioning

Air. 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 estimated vapor pressure of N-nitrosodi-n-propylamine

(0.086 mm Hg at 25°C; see Table 4-2) indicates that this compound should not partition from the vapor phase to particulates in the atmosphere.

Water. Using linear regression equations based on log K_{ow} data [log K_{ow}=1.36; see Table 4-2), 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-m^3/mol; see Table 4-2) suggests that volatilization would be a relatively insignificant fate process in water.

Sediment and Soil. If an 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 2–6 hours (Berard and Rainey 1979; Oliver 1979). If an 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).

5.4.2 Transformation and Degradation

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 5–7 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} cm^3/molecules-see at 25°C, which was estimated using the method of Atkinson (1987).

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 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.

Sediment and 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.

5.5 LEVELS IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to N-nitrosodi-n-propylamine depends, in part, on the reliability of supporting analytical data from environmental samples and biological specimens. Concentrations of N-nitrosodi-n-propylamine in unpolluted atmospheres and in pristine surface waters are often so low as to be near the limits of current analytical methods. In reviewing data on N-nitrosodi-n-propylamine levels monitored or estimated in the environment, it should also be noted that the amount of chemical identified analytically is not necessarily equivalent to the amount that is bioavailable.

Table 5-3 shows the lowest limit of detections that are achieved by analytical analysis in environmental media.

Table 5-3. Lowest Limit of Detection Based on Standards[a]

Media	Detection limit	Reference
Air	<0.04 μg/m^3	Cooper 1987
Drinking water	0.05 μg/L (for 100 mL sample)	Drescher and Frank 1978
Groundwater	10 μg/L	EPA 1986b, 1987; Fisk 1986
Soil	0.025 μg/g	Pancholy 1976
Sediment	330 μg/kg	EPA 1987; Fisk 1986

Table 5-3. Lowest Limit of Detection Based on Standards[a]

Media	Detection limit	Reference
Whole blood	0.6 ng/kg	Maki 1980
Urine	0.05 µg/L (for 100 mL sample)	Drescher and Frank 1978

[a]Detection limits based on using appropriate preparation and analytics. These limits may not be possible in all situations.

Detections of N-nitrosodi-n-propylamine in air, water, and soil at NPL sites are summarized in Table 5-4.

Table 5-4. N-Nitrosodi-n-Propylamine Levels in Water, Soil, and Air of National Priorities List (NPL) Sites

Medium	Median[a]	Geometric mean[a]	Geometric standard deviation[a]	Number of concentrations	NPL sites
Water (ppb)	21	11.4	6,420	8	8
Soil (ppb)	1,900	1,470	3,970	11	10
Air (ppbv)	No data	No data	No data	No data	No data

[a]Concentrations found in ATSDR site documents from 1981 to 2015 for 1,854 NPL sites (ATSDR 2017). Maximum concentrations were abstracted for types of environmental media for which exposure is likely. Pathways do not necessarily involve exposure or levels of concern.

5.5.1 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).

5.5.2 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 NPL hazardous waste sites. There were only a couple of monitoring studies available pertaining to the occurrence N-nitrosodi-n-propylamine in treated waste water. In a survey of 32 U.S. textile plants, N-nitrosodi-n-propylamine was detected at concentrations of 2–20 µg/L in 2 out of 32 samples of secondary effluent, while no detectable levels were found in samples of raw waste water 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 µg/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 United States revealed 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).

5.5.3 Sediment and 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).

5.5.4 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; and 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 herbicides trifluralin, oryzalin, and isopropalin at levels as high as 154, <1, and 39–87 mg/L, respectively (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).

5.6 GENERAL POPULATION 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, the National Institute for Occupational Safety and Health (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 $\mu g/m^3$ (241–611 ppt), with a mean concentration of 2.3 $\mu g/m^3$ (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). Workers at 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 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.

5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

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