United States Environmental Protection Agency | Pollution Prevention and Toxics (7407) | February 1995 EPA 749-F-95-015a

OPPT Chemical Fact Sheets

Nitrobenzene Fact Sheet: Support Document (CAS No. 98-95-3)

This summary is based on information retrieved from a systematic search limited to secondary sources (see Appendix A). These sources include online databases, unpublished EPA information, government publications, review documents, and standard reference materials. The literature search was done in February of 1995. No attempt has been made to verify information from these databases or secondary sources.

I. CHEMICAL IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

The chemical identity and physical/chemical properties of nitrobenzene are summarized in Table 1.

TABLE 1. CHEMICAL IDENTITY AND CHEMICAL/PHYSICAL PROPERTIES OF NITROBENZENE

Characteristic/Property	Data	Reference
CAS No.	98-95-3	
Common Synonyms	nitrobenzol; oil of mirbane	U.S. EPA 1994
Molecular Formula	$C_6H_5NO_2$	
Chemical Structure		
Physical State	liquid	U.S. EPA 1985
Molecular Weight	123.06	U.S. EPA 1985Melting
Point	5.85°C @ 760 Torr	U.S. EPA 1985
Boiling Point	210.9°C @ 1 atm	U.S. EPA 1985
Water Solubility	1.9 g/L @ 20°C; 2.1 g/L @ 25°C	U.S. EPA 1985
Specific Gravity	1.199 @ 24/4°C	U.S. EPA 1985
Vapor Density (air = 1)	4.1	U.S. EPA 1985
K_{OC}	36-650 (estimated)	U.S. EPA 1987
Log K_{OW}	1.85	U.S. EPA 1987
Vapor Pressure	0.15 mm Hg @ 20°C; 0.27 mm Hg @ 25°C	U.S. EPA 1987
Reactivity	flammable	
Flash Point	88°C (closed cup)	Budavari 1989
Henry's Law Constant	2.3×10^{-5} atm-m^3/mole @ 25°C	U.S. EPA 1985
Fish Bioconcentration Factor	<10-15 (measured in the golden orfe)	U.S. EPA 1985
Odor Threshold	perception, 0.0182 mg/m^3 (3.6 ppb)	Verschueren 1983
	threshold, 1.9 ppm	U.S. EPA 1985
Conversion Factors (in air)	1 ppm = 5.12 mg/m^3; 1 mg/m^3 = 0.20 ppm	Verschueren 1983

II. PRODUCTION, USE, AND TRENDS

A. Production

There were four producers of nitrobenzene in the United States in 1991: First Chemicals Corp, Mobay, DuPont Chemicals, and Rubicon, Inc. In 1991, the estimated total production capacity of nitrobenzene in the U.S. was 1,360 million pounds (Mannsville 1991).

Table 2 shows the producers, plant locations, and 1991 plant production capacities of nitrobenzene.

TABLE 2. U. S. PRODUCERS OF NITROBENZENE AND THEIR PRODUCTION CAPACITIES

Producer	Location	1991 Capacity (Millions of Pounds)
DuPont	Beaumont, TX	375
First Chemical Corp.	Pascagoula, MS	425
Mobay (now Bayer)	New Martinsville, WV	60
Rubicon, Inc.	Geismar, LA	500
TOTAL		1,360

Source: Mannsville 1991.

B. Uses

While nitrobenzene is primarily used in the production of aniline and aniline derivatives, such as methyl diphenyl diisocyanate (MDI), it also finds use in the manufacture of rubber chemicals, pesticides, dyes, and pharmaceuticals. Nitrobenzene is also used in shoe and floor polishes, leather dressings, paint solvents, and other materials to mask unpleasant odors. Substitution reactions with nitrobenzene are used to form m-derivatives (Mannsville 1991; Sittig 1991). Redistilled, as oil of mirbane, nitrobenzene has been used as an inexpensive perfume for soaps. A significant merchant market for nitrobenzene is its use in the production of the analgesic acetaminophen (Mannsville 1991). Table 3 presents the estimated 1991 U. S. end-use pattern for nitrobenzene.

TABLE 3. END-USE PATTERN OF NITROBENZENE--1991 ESTIMATE

Derivative (Typical Standard Industrial Classification (SIC) Code)[1]	Percent
Aniline (production, SIC 2865)	97
Other	3

Source: Mannsville 1991.

[1] The Standard Industrial Classification (SIC) code is the statistical classification standard for all Federal economic statistics. The code provides a convenient way to reference economic data on industries of interest to the researcher. SIC codes presented here are not intended to be an exhaustive listing; rather, the codes listed should provide an indication of where a chemical may be likely to be found in commerce.

C. Trends

Future demand for nitrobenzene is almost exclusively dependent on demand for aniline. Overall U.S. long-term aniline demand, and therefore nitrobenzene demand, will probably increase at about 3 to 4 percent per year (Mannsville 1991).

The USITC has not reported production statistics for nitrobenzene since 1986. Nitrobenzene output is generally in the range of 1.4 times derivative aniline output. The USITC (1994) reported the production of aniline to be 1005 million pounds for 1992. There is adequate capacity to meet domestic demand for nitrobenzene for several years. Both Rubicon and First Chemical have expanded their nitrobenzene production capacities in recent years (Mannsville 1991).

III. ENVIRONMENTAL FATE

A. Environmental Release

Depending on its purity, nitrobenzene is a pale yellow to yellow-brown, oily liquid at room temperature. It has a characteristic odor that has been associated with bitter almonds and shoe polish (vapor pressure, 0.27 mm Hg @ 25°C) (U.S. EPA 1985; Budavari 1989). It is released into the environment primarily from industrial uses but can also be formed in the atmosphere by the nitration of benzene, a common air pollutant (ATSDR 1990). The largest sources of nitrobenzene release are from its manufacture and primary use as a chemical intermediate in the synthesis of aniline (U.S. EPA 1985). The amounts of nitrobenzene released to surface water and to land by industry have been greatly reduced since 1988 (TRI92 1994). Smaller amounts are also released from consumer products in which nitrobenzene is used as a solvent. The most familiar of these are metal and shoe polishes (ATSDR 1990).

Nitrobenzene levels in air have been measured in urban, rural, and waste disposal areas in New Jersey. Most air samples taken in 1982 were negative for nitrobenzene, and the positive samples taken from residential areas were about 0.3 parts per billion (ppb) or less. Samples from industrial areas were 0.9 ppb or more with the highest samples being 3.5 to 5.7 ppb. The atmospheric nitrobenzene concentration was higher in the summer than winter and lower during periods of heavy rain or snow. Air samples taken over landfills in 1985, contained a maximum of 14.48 ppb nitrobenzene. Nitrobenzene has been detected in samples taken during rain or snow (ATSDR 1990). In surface water, nitrobenzene was detected in only 0.4% of 836 ambient surface water stations, and in 1.8% of 1245 reporting stations on industrial waste waters (ATSDR 1990). Soil samples taken along the banks of the Buffalo River in New York contained 8 ppm nitrobenzene in 1980, but the chemical was not found in sediment samples (ATSDR 1990).

In 1992, releases of nitrobenzene to environmental media, as reported to the Toxic Chemical Release Inventory by certain types of U.S. industries, totaled about 917 thousand pounds. Of this amount, 52 thousand pounds (5.6%) were released to the atmosphere; 442 pounds (0.05%) were released to surface water; and 865 thousand pounds (94.32%) were released in underground injection sites; no nitrobenzene was reported to have been released to land (TRI92 1994).

B. Transport

Nitrobenzene will volatilize slowly from soil and surface water (vapor pressure, 0.27 mm Hg @ 25°C) and is subject to biodegradation (U.S. EPA 1985). Adsorption to sediment and bioconcentration are not thought to be significant fate processes in water. Nitrobenzene may leach through the soil and is considered to have intermediate mobility (ATSDR 1990).

C. Transformation/Persistence

1. Air — Nitrobenzene apparently undergoes direct photolysis in the atmosphere. Photoproducts formed from nitrobenzene in the atmosphere include *ortho*- and *para*-nitrophenols, and nitrosobenzene. Phenol was found as a photodegradation product of nitrobenzene in the absence of oxygen (U.S. EPA 1985; ATSDR 1990). In laboratory tests,

38% of nitrobenzene in air was photochemically degraded in 5 hours by irradiation from a xenon lamp (U.S. EPA 1985; Howard 1989). The chemical reacts slowly with hydroxyl radicals and ozone. The half-lives calculated for reactions of nitrobenzene with hydroxyl radicals and ozone in moderately polluted air are 90 days and 2 years, respectively (ATSDR 1990). Removal of nitrobenzene from the atmosphere by wet deposition is not believed to be significant (U.S. EPA 1985).

2. Soil — Nitrobenzene is subject to biodegradation in the soil, but the rates of decomposition based on screening tests are conflicting. Results range from 98% removal in 5 days with activated sludge inoculum, to no degradation in 10 days with activated sludge inoculum. Higher concentrations of nitrobenzene have been shown to be toxic to microorganisms, but this explanation alone cannot account for the varying results (Howard 1989; ATSDR 1990).

3. Water — Nitrobenzene in solution is subject to biodegradation and photodegradation; small amounts also adsorb to sediment or volatilize from the surface. The half-life of nitrobenzene in model waste stabilization ponds was measured at 3.8 days; 89.5% of the added chemical was degraded, 4.9% volatilized, 2.3% adsorbed to sediment, 2.3% was lost in effluent, and 1% remained (Howard 1989). The half-life of nitrobenzene in aquatic environments has been estimated at 0.3 days by the U.S. EPA (1987).

4. Biota — The bioconcentration factors in two species of fish, *L. idus* (golden orfe) and *P. promelas* (fathead minnow), have been estimated at 15 and less than 10, respectively (U.S. EPA 1987). A bioconcentration factor of 3 has also been calculated for *P. reticulata* (guppy) (Howard 1989). Nitrobenzene is not expected to accumulate significantly in aquatic organisms, however, it has been shown to be taken up and may bioconcentrate in terrestrial plants (ATSDR 1990).

IV. HUMAN HEALTH EFFECTS

A. Pharmacokinetics

1. Absorption — Studies in humans and animals have demonstrated that nitrobenzene is absorbed through the skin, the lungs, and the gastrointestinal tract. The maximum dermal absorption of liquid nitrobenzene was 0.2 - 3.0 mg/cm^2/hour (U.S. EPA 1985). When volunteers were exposed to 1 or 5.5 ppm nitrobenzene in air, it was estimated that about half of the absorbed dose of nitrobenzene was absorbed through the skin (ATSDR 1990). Volunteers breathing 6 ppm nitrobenzene had an average absorption rate of 80% (ATSDR 1990; U.S. EPA 1985). Animal experiments have shown that nitrobenzene is metabolized and excreted following oral administration. Absorption from the gastrointestinal tract can also be inferred from animal and human studies that demonstrate toxic effects following the ingestion of nitrobenzene (U.S. EPA 1985).

2. Distribution — Two days after oral administration of ^{14}[C]-nitrobenzene to rabbits, about 56% of the radioactivity was bound by the tissues, localized primarily in fat and the intestinal tract. After 8 days, about 8% of the original dose remained in the fat tissues. Analysis of the tissue indicated that the radioactivity represented metabolites of nitrobenzene rather than unaltered nitrobenzene (U.S. EPA 1985). The day after the oral administration of radiolabeled nitrobenzene to rats the amount of radioactivity bound to various tissues included 229 mmol/mol bound to hemoglobin in the blood, 129 mmol/kg bound in liver, 204 mmol/kg bound in kidney, and 62 mmol/kg bound in lung (ATSDR 1990).

3. Metabolism — The primary metabolite of nitrobenzene in rabbits was reported to be *p*-aminophenol (U.S. EPA 1985). This urinary metabolite accounted for 31-56% of the administered oral dose within 2-5 days. Other metabolites representing 3-9% of the oral dose included *m*-aminophenol, *o*-aminophenol, *p*-nitrophenol, and *m*-nitrophenol. Minor metabolites accounting for less than 1% of the administered dose were identified as aniline, *o*-nitrophenol, 4-nitrocatechol, nitroquinol, and *p*-nitrophenylmercapturic acid (U.S. EPA 1985). *p*-Aminophenol was a major urinary metabolite in mice, but did not appear in the urine of either CD or Fischer 344 rats following oral exposure to nitrobenzene. U.S. EPA (1995) has suggested this species difference in nitrobenzene metabolism be considered when discussing possible metabolism of nitrobenzene in humans. Other urinary metabolites

identified in rat and mouse studies include *p*-hydroxyacetanilide, *p*-aminophenol, *p*-nitrophenol, and *m*-nitrophenol. These metabolites have been found in the free state and conjugated with glucuronide and sulfate with varying frequencies in rats and different strains of mice (U.S. EPA 1985). The reduction of nitrobenzene by microflora of the intestinal tract appears to occur following oral exposure. Sterilization of the intestinal tract altered the proportion of urinary metabolites excreted by rats, decreasing the excretion of *p*-hydroxyacetanilide and an unidentified metabolite by 94 and 86%, respectively (U.S. EPA 1985).

4. Excretion — Nitrobenzene metabolites are excreted in the urine predominantly with smaller amounts excreted in feces and in expired air. *p*-Nitrophenol and *p*-aminophenol and their glucuronate and/or sulfate conjugates have been identified in the urine of humans and mice; *p*-aminophenol was apparently not excreted by the rat strains tested. Rats eliminated a total of 75-79% of the initial dose in 72 hours following oral administration of ^{14}[C]nitrobenzene; 60.8-65.8% of the dose was found in the urine. Mice were able to eliminate 54.3% of the administered dose in 72 hours with 34.7% found in the urine. The rest of the radioactivity recovered was found in the feces (11.8-21.4%) and in expired air (0.8-2.5%) from the rats and mice tested (U.S. EPA 1985). The major urinary metabolites in humans are *p*-nitrophenol and *p*-aminophenol; however, the metabolites are excreted more slowly than in rats, mice, or rabbits. Urinary *p*-nitrophenol, which can be utilized to estimate the nitrobenzene exposure level, reached peak levels about 4 days after exposure (U.S. EPA 1985).

B. Acute Toxicity

The primary toxic effect resulting from acute exposure to nitrobenzene by inhalation, oral or dermal routes is methemoglobinemia and accompanying anoxia and erythrocyte damage. Nervous system effects may also be experienced, but may be partially due to the anoxia from the methemoglobinemia (see section IV.G.).

1. Humans — Inhalation exposure to nitrobenzene concentrations equal to or greater than 6 ppm in air (30.72 mg/m^3; 4.4 mg/kg/day)[2] was reported to result in nervous system effects (see section IV.G.) and methemoglobin production (U.S. EPA 1985). Sulfhemoglobinemia has also been observed following nitrobenzene poisoning (U.S. EPA 1985). Atmospheric concentrations of nitrobenzene resulting in these effects are well above the odor threshold of 1.9 ppm, which may help limit human exposures (U.S. EPA 1985). Oral exposures to nitrobenzene have been reported, although rare and poorly documented. Methemoglobinemia is the primary acute effect following nitrobenzene ingestion. The dose resulting in methemoglobinemia was estimated in one case study at 4.3 to 11 g based on urinary p-nitrophenol levels. A latency period of 30 minutes to 12 hours, varying inversely with the dose, followed ingestion (ATSDR 1990). Nitrobenzene is rapidly absorbed through the skin and is a contact irritant (Keith and Walters 1985).

2. Animals — Increased methemoglobin production has been reported in mice, rats, rabbits, and dogs following acute exposure to nitrobenzene. Mice appear to be the most resistant to methemoglobinemia probably because of a higher level of methemoglobin reductase activity. However, germ-free or antibiotic-treated rats do not develop methemoglobinemia, which demonstrates a likely role of intestinal bacteria in methemoglobin production in the rat (U.S. EPA 1985). Hepatic lesions were recorded following a single oral dose of nitrobenzene in rats (amount not given in the secondary source) (U.S. EPA 1985).

   LD_{50} values for various routes of administration have been calculated for rats including 640 mg/kg for oral administration and 2100 mg/kg for dermal administration (U.S. EPA 1985). An inhalation LC_{50} value of 556 ppm was calculated for Crl:CD rats exposed for 4 hours.

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[2]For dose comparison purposes, this has been calculated by multiplying by 0.143 (the adult occupational breathing rate, 10 m^3/day, divided by the assumed adult body weight, 70 kg) to obtain the dose in mg/kg/day assuming 100% absorption (U.S. EPA 1988).

Clinical observations reported during exposure included cyanosis, weakness, chromodacryorrhea, slight reddish-brown nasal discharge, slight corneal clouding, and lacrimation. Following exposure, survivors exhibited tremors, tachypnea, weight loss, diarrhea, and prostration. Some animals were hyperactive and exhibited aggressive behavior (TSCATS 1994).

C. Subchronic/Chronic Effects

Limited evidence suggests that the liver may be a target organ in humans following extended inhalation exposure to nitrobenzene. Adverse effects on the liver and kidneys have been reported in animal studies. A lowest-observed-adverse-effect level of 25 mg/m^3 was identified in rats and mice based on hematologic, adrenal, renal, and hepatic lesions. This value was converted to an equivalent continuous oral dose for mice and utilized by the U.S. EPA (1994) to derive an oral reference dose (RfD)[3] of 0.0005 mg/kg/day for nitrobenzene exposure.

1. Humans — An enlarged liver, jaundice, and a decreased liver function test (bromosulfophthalein retention) were reported in a case history of a woman occupationally exposed to unspecified concentrations of nitrobenzene for 17 months. The exposure concentration for 2 of the 17 months has been qualitativiely described as "high" (U.S. EPA 1985). The consumption of alcohol has been reported to result in an acute crisis including coma in individuals previously exposed chronically or subchronically to nitrobenzene. In one case history, an acute crisis was precipitated by the consumption of one beer 6 weeks after recovering from a subchronic nitrobenzene poisoning episode; however, no numerical data on nitrobenzene exposure were given (U.S. EPA 1987).

2. Animals — Groups of 10 male and 10 female Fischer 344 rats, Sprague-Dawley CD rats, and $B6C3F_1$ mice were exposed by inhalation to nitrobenzene concentrations of 0, 5, 16, or 50 ppm (0, 25, 81, or 252 mg/m^3), 6 hours/day, 5 days/week for 90 days. Increased methemoglobin levels were seen in Fischer rats at 25 mg/m^3, in Sprague-Dawley rats at 81 mg/m^3, and in mice at 252 mg/m^3. Hemosiderosis was seen in the spleens of both rats and mice, but was mild in mice and also occurred in the control group. Increased hematopoiesis and hemolytic anemia including reticulocytosis was observed at 81 mg/m^3 in Fischer rats and at 252 mg/m^3 in Sprague-Dawley rats. Very slight to minimum nephrosis was recorded for both rat strains at 25 mg/m^3. Increased kidney weights were seen at 252 mg/m^3. No kidney effects were recorded in mice. Nitrobenzene treatment resulted in liver lesions in both rats and mice. Hepatocellular hypertrophy and Kupffer cell pigmentation were observed in Sprague-Dawley rats at 25 mg/m^3. At 81 mg/m^3, increased periportal basophilia and enlarged nucleoli were seen in rats, and centrilobular hepatocellular hyperplasia was recorded for mice. Increased severity and incidence of vacuolization of the adrenal zona reticularis in female mice were also observed at 25 mg/m^3 (U.S. EPA 1985). The 25 mg/m^3 concentration defined a lowest-observed-adverse level (LOAEL) for rats and mice based on hematologic, adrenal, renal, and hepatic lesions (U.S. EPA 1994). This value in mice was converted to an equivalent continuous oral dose of 4.6 mg/kg/day and was utilized by the U.S. EPA (1994) to calculate a chronic oral RfD of 0.0005 mg/kg/day for nitrobenzene.

   Inhalation exposure to 35 ppm for 2 weeks resulted in hepatocyte necrosis in male Sprague-Dawley rats (ATSDR 1990).

D. Carcinogenicity

Nitrobenzene causes in rats and mice in lifetime inhalation studies. This has been used as a basis for a recommendation to classify nitrobenzene as a B2, probable human carcinogen.

1. Humans - No information was found in the secondary sources search on the carcinogenicity

[3]The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of the exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during the time period of concern.

of nitrobenzene in humans.

2. Animals - A recent assessment of the carcinogenicity of nitrobenzene has been completed by U.S. EPA (1995). The assessment is based on a single 1983 Chemical Industry Institute of Toxicology inhalation study of both sexes of B6C3F, F344/N rats, and Sprague-Dawely (CD strain) rats.[4] Mice were exposed to 0, 5, 25, and 50 ppm; rats, to 0, 1, 5, and 25 ppm. Exposures were for 6 hours per day, 5 days per week, for 104 weeks. Nitrobenzene induced tumors in several sites over different species, sexes, and doses. Significant increases in tumors were observed in the alveolus and bronchus, the thyroid, and the mammary gland of mice. F344/N rats showed significant increases in tumors of the liver, the thyroid, the kidney, and the endometrium. Sprague-Dawley (CD) rats showed significant increases in tumors of the liver.

E. Genotoxicity

Results of short term mutagenicity testing show nitrobenzene is not genotoxic. Nitrobenzene was negative in the Ames assay with *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, TA1537, and TA1538 with, or without metabolic activation (U.S. EPA 1987). Intragastric treatment of mice with nitrobenzene did not result in micronuclei or chromosome aberrations in bone marrow cells or dominant lethal mutations. No increase in unscheduled DNA synthesis in rat hepatocytes was seen 12 hours following gavage treatment with 200 or 500 mg/kg nitrobenzene (U.S. EPA 1987).

F. Developmental/Reproductive Toxicity

Animal studies have shown that inhalation exposure to nitrobenzene can cause adverse testicular effects resulting in decreased fertility index.

1. Humans — No information was found in the secondary sources searched on the developmental/reproductive toxicity of nitrobenzene to humans.

2. Animals — A decrease in fertility indices was recorded following inhalation exposure to 40 ppm nitrobenzene, 6 hours/day, 7 days/week for 12 weeks prior to and including the mating period in a two-generation study in rats. Exposure was continued with the females through day 19 of gestation. Microscopic examination revealed atrophy of the seminiferous tubules, spermatocyte degeneration, absence of mature sperm in the epididymis, and decreased testicular and epididymal weights in both F_0 and F_1 generations. The fertility index increased five-fold during 9 weeks of recovery following exposure to nitrobenzene. There was no observed maternal toxicity, and no effects on survival or lactation indices at any dose tested (0, 1, 10, or 40 ppm) (U.S. EPA 1987). Inhalation exposure of $B6C3F_1$ mice, and Fischer 344 and Sprague-Dawley rats to nitrobenzene concentrations of 0, 5, 16, or 50 ppm, 6 hours/day, 5 days/week for 90 days resulted in severe degeneration of the spermatogenic epithelium with decreased testicular weight, and an absence of mature sperm in the epididymis of both rat strains. Only slight effects were observed at the lower doses, and no testicular changes were seen in the mice (U.S. EPA 1987).

   Inhalation studies have shown no fetotoxic, embryotoxic, or teratogenic effects at concentrations up to 40 ppm in rats and 100 ppm in rabbits. Maternal toxicity did occur at these levels, demonstrated by increased methemoglobin levels and increased spleen and liver weights (ATSDR 1990; U.S. EPA 1987).

   Treatment of Fischer 344 and Sprague-Dawley rats with a single oral dose of 300 mg/kg nitrobenzene resulted in necrotic primary and secondary spermatocytes, multinucleated giant cells, and decreased numbers of spermatocytes in the epididymis within 1-4 days after treatment. These effects were not seen at 50-200 mg/kg (U.S. EPA 1985).

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[4] The study was finalized in 1993.

G. Neurotoxicity

Adverse central nervous system effects can occur in humans and animals following nitrobenzene exposure. Many of these effects may be secondary to the anoxia resulting from methemoglobinemia.

1. Humans — Exposure to nitrobenzene for up to 17 months was reported to cause headache, nausea, vertigo, confusion, hyperalgesia, and paresthesia (U.S. EPA 1985; ATSDR 1990). Acute nervous system effects include nausea, nystagmus, convulsions, and coma. Exposure to concentrations greater than 40 ppm has resulted in intoxication. Methemoglobinemia has also been shown to occur, and the resulting anoxia may partially account for the nervous system effects (U.S. EPA 1985).

2. Animals — Bilateral cerebellar perivascular hemorrhage and cell breakdown in the hindbrain (cerebellar peduncle) were seen in $B6C3F_1$ mice and Sprague-Dawley rats exposed to 125 ppm nitrobenzene for two weeks. Fischer rats given nitrobenzene at the same exposure level and duration did not develop any brain lesions (ATSDR 1990).

V. ENVIRONMENTAL EFFECTS

Available information indicates that nitrobenzene is moderately toxic to aquatic life. Several reported 96-hour LC_{50} values are in the range of >1 mg/L to 100 mg/L.

A. Toxicity to Aquatic Organisms

Ninety-six-Hour LC_{50} values for fish are: 42.6 mg/L for *Lepomis macrohirus* (bluegill sunfish), 117 mg/L for *Pimephales promelas* (fathead minnow), 112.5 mg/L for *Brachydanio rerio* (zebrafish), and 58.6 for *Cyprinodon variegatus* (sheepshead minnow). Forty-eight-Hour LC_{50} values for fish are: 105 mg/L for *Lepomis macrohirus* (bluegill sunfish), 156 mg/L for *Pimephales promelas* (fathead minnow), 60-89 mg/L for *Leuciscus idus melanotus* (golden orfe), 20 mg/L for *Oryzias latipes* (medaka), and >120 mg/L for *Cyprinodon variegatus* (sheepshead minnow) (U.S. EPA 1985).

B. Toxicity to Terrestrial Organisms

Nitrobenzene is unlikely to exist in U.S. terrestrial environments in sufficient concentrations to cause serious acute or chronic effects to terrestrial organisms. Toxicity information reported for rats, mice, and rabbits (see sections IV.B.2., IV.C.2. and IV.G.) suggest that no acute effects would be seen at normally expected U.S. environmental concentrations.

C. Abiotic Effects

Nitrobenzene reacts with hydroxyl radicals and ozone in the atmosphere. In moderately polluted conditions the half-life of nitrobenzene in the atmosphere may be reduced by a factor of 10. The rate constant calculated for the reaction with ozone ($5x10^{23}$ cm^3/molecule-sec) indicates that the reaction has no environmental significance (U.S. EPA 1985).

VI. EPA/OTHER FEDERAL/OTHER GROUP ACTIVITY

The Clean Air Act Amendments of 1990 list nitrobenzene as a hazardous air pollutant. Occupational exposure to nitrobenzene is regulated by the Occupational Safety and Health Administration (OSHA). The OSHA permissible exposure limit (PEL) is 1 part per million parts of air (ppm) as an 8-hour time-weighted average (TWA) (29 CFR 1910.1000). In addition to OSHA, other federal agencies and groups may develop recommendations to assist in controlling workplace exposure. These agencies and groups (listed in Tables 4 and 5) should be contacted regarding workplace exposures, and for additional information on nitrobenzene.

TABLE 4. EPA OFFICES AND CONTACT NUMBERS INFORMATION ON NITROBENZENE

EPA Office	Statute	Contact Number
Pollution Prevention & Toxics	EPCRA (§313/TRI)[a]	(800) 535-0202
	TSCA (§8A, §8D, §4)[b]	(800) 554-1404
Air	Clean Air Act (§111, §112B)[c]	(919) 541-0888
Solid Waste & Emergency Response	RCRA (Action levels: 2.0 µg/m^3, air 0.02 mg/L, water 40 mg/kg, soil)[d]	(800) 535-0202
	CERCLA (RQ, 1000 pounds)[e] SARA (§110, §302A, §313)	(800) 535-0202
Water	Clean Water Act (§304b, §307a, §311, CWA Priority) WQC (17 µg/L [ao/do]; 1900 µg/L [ao])[f]	(202) 260-7588

[a]EPCRA: Emergency Planning and Community Right to Know Act of 1986

[b]TSCA: Toxic Substances Control Act

[c]Listed as hazardous air pollutant under § 112 of Clean Air Act [42 U.S.C. 7401 et seq.]

[d]RCRA: Resource Conservation and Recovery Act (40 CFR 264.94). Action Level: Health and environmental-based levels used by the EPA as indicators for the protection of human health and the environment and as triggers for a Corrective Measure Study.

[e]CERCLA: Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended. RQ: level of hazardous substance, which, if equaled or exceeded in a spill or release, necessitates the immediate reporting of that release to the National Response Center (40 CFR Part 302).

[f]WQC: Federal ambient water quality criteria for the protection of human health (56 FR 58420). Ambient Water Quality Criteria standards: established pursuant to the Clean Water Act, 57 FR 60848, December 22, 1992. ao/dw: protection for consuming aquatic organisms and drinking water; ao: protection for consuming aquatic organisms.

TABLE 5. OTHER FEDERAL OFFICES/CONTACT NUMBERS FOR INFORMATION ON NITROBENZENE

Other Agency/Department/Group	Contact Number
Agency of Toxic Substances & Disease Registry	(404) 639-6000
American Conference of Governmental Industrial Hygienists [TLV-TWA, 1 ppm (5 mg/m^3),*][a]	(513) 742-2020
Consumer Product Safety Commission	(301) 504-0994
Food & Drug Administration	(301) 443-3170
National Institute for Occupational Safety & Health [TWA, 1 ppm (5 mg/m^3); IDLH, 200 ppm; *][b]	(800) 356-4674
Occupational Safety & Health Administration [TWA, 1 ppm (5 mg/m^3][c]	(202) 639-7960

[a]**TLV-TWA**: Time-weighted-average concentration for a normal 8-hour workday and a 40-hour workweek to which nearly all workers may be repeatedly exposed without adverse effects; *****: Skin designation, air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required (ACGIH 1994-1995).

[b]**TWA**: Time-weighted-average concentrations for up to a 10-hour workday during a 40-hour workweek; **IDLH**: immediately dangerous to life or health concentration, the maximum concentration from which, in the event of respirator failure, one could escape within 30 minutes without a respirator and without experiencing any escape-impairing or irreversible health effects; *****: Skin designation, air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required (NIOSH 1990; 1992).

[c]**TWA**: Time-weighted-average that must not be exceeded during any 8-hour work shift of a 40-hour workweek. Standard promulgated pursuant to the Occupational Safety and Health Act, 29 CFR 1910 (OSHA 1993).

VII. CITED REFERENCES

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