5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

4,4´-Methylenedianiline is released to air and water during industrial production and use of this compound (IARC 1986). 4,4´-Methylenedianiline may also be released in water as a result of hydrolysis of treated and untreated 4,4´-methylenediphenyl diisocyanate wastewater discharged into surface water or public sewers. However, there are no monitoring data that confirm the presence of 4,4´-methylenedianiline in waste effluents from the plants that manufacture and use 4,4´-methylenedianiline, or in natural waters where the treated or untreated wastewaters from these plants are discharged. 4,4´-Methylenedianiline may be found in soils of controlled or uncontrolled hazardous waste sites as a result of disposal of wastes containing either 4,4´-methylenedianiline or products such as 4,4´-methylenediphenyl diisocyanate. 4,4´-Methylenedianiline may also be released to soil as a result of accidental spillage during storage or transport. Smaller amounts of 4,4´-methylenedianiline may be released to water and soil as a result of terrestrial and hydrospheric precipitation and scavenging of atmospheric 4,4´-methylenedianiline. However, very few monitoring data are available that confirm the presence of 4,4´-methylenedianiline in soil.

Experimental data on the environmental fate of 4,4´-methylenedianiline are scarce. Most conclusions about the environmental fate and transport of 4,4´-methylenedianiline are estimated, based on its physical and chemical properties. In air, the compound will primarily exist as particulate matter and will be removed from the atmosphere by dry deposition and scavenging by rain and snow. The small amount of 4,4´-methylenedianiline present in the vapor phase in the atmosphere will be transformed by reaction with hydroxyl radicals with an estimated half-life of 1.6 hours. In water and soil, the material will be degraded primarily via biodegradation. The estimated half-lives of biodegradation in surface water, groundwater and soil are l-7 days, 2-14 days, and l-7 days, respectively. 4,4´-Methylenedianiline will covalently bind with humic materials in soil and water. As a result, it will be present predominantly in the bound form in sediment and suspended solids in water, and its leaching from most soils will not be important. Three factors indicate that 4,4´-methylenedianiline will neither bioconcentrate in aquatic organisms nor biomagnify in terrestrial or aquatic food chains: (1) the experimental bioconcentration factor in carp (Caprinus carpio); (2) the estimated bioconcentration factor and octanol/water partition coefficient (indicator of lipid solubility), and (3) the fact that it is metabolized quickly in higher trophic level animals.

No monitoring data exist on the levels of 4,4′-methylenedianiline in ambient air, surface water, industrial effluents, soil or any fruits and vegetables. Levels of the compound in occupational air have been measured; and the levels rarely exceed the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value of 0.8 mg/m^3 for an 8-hour weighted average concentration. 4,4′-Methylenedianiline and its metabolites have also been measured in urine of workers. The maximum urinary 4,4′-methylenedianiline concentration of 6,871 nmol/mmol cretinine was detected in a worker at a manufacturing plant in Britain (Cocker et al. 1994).

4,4′-Methylenedianiline has been found in none of the 1,445 current or former EPA National Priorities List (NPL) hazardous wastes sites (HazDat 1997). However, the number of sites evaluated for methylenedianiline is not known.

5.2 RELEASES TO THE ENVIRONMENT

Anthropogenic releases of 4,4′-methylenedianiline are primarily to the soil via underground injection. According to the Toxics Chemical Release Inventory, in 1994, a total of 36,531 pounds of 4,4′-methylenedianiline were released to the environment (air, water, soil) from 27 large processing facilities (TR194 1996). Table 5-l lists the amounts released from these facilities. In addition, an estimated 1,889 pounds of 4,4′-methylenedianiline were released by these manufacturing and processing facilities to publicly owned treatment works (POTWs), and an estimated 184,458 pounds were transferred off-site (TR194 1996). The data listed in the TRI should be used with caution because only certain types of facilities are required to report (EPA 1996). This is not an exhaustive list. Manufacturing and processing facilities are required to report information to the Toxics Release Inventory if they employ 10 or more full-time employees; if their facility is classified under Standard Industrial Classification (SIC) codes 20 through 39; and if their facility produces, imports, or processes 25,000 or more pounds of any TRI chemical or otherwise uses more than 10,000 pounds of a TRI chemical in a calendar year (EPA 1996).

5.2.1 Air

4,4′-Methylenedianiline is released to the air during the industrial production of this compound (IARC 1986). It is also released into the air during industrial production processes that use 4,4′-methylenedianiline as a component. For example, it is released to the air during the production of reinforced

Table 5-1. Releases to the Environment from Facilities That Manufacture or Process 4,4'-Methylenedianiline

			Reported amounts released in pounds per year						
State[a]	City	Facility	Air	Water	Land	Underground injection	Total environment[b]	POTW transfer	Off-site waste transfer
AL	MC INTOSH	CIBA GEIGY CORP.	4				4		
AR	LITTLE ROCK	A. O. SMITH CORP.	1				1		2,700
AR	LITTLE ROCK	A. O. SMITH CORP.							180
AR	MAGNOLIA	NA	1,000				1,000		750
CA	CHATSWORTH	HEXCEL CORP.	255				255		2,708
CA	LOS ANGELES	AIR PRODS. & CHEMICALS INC.	28				28	72	34,680
CT	NAUGATUCK	UNIROYAL CHEMICAL CO. INC.	500				500	402	10,650
IL	ELK GROVE VILLAGE	ALLCO ACQUISITIONS							
IL	MC COOK	UOP	250				250	250	250
KS	WICHITA	AIR PRODS. & CHEMICALS INC.	2,400			64	2,464		56
KS	WICHITA	A. O. SMITH CORP.							
LA	GEISMAR	BASF CORP.	11				11		6,900
LA	GEISMAR	RUBICON INC.	20			26,000	26,020		27,910
MO	NORTH KANSAS CITY	COOK COMPOSITES & POLYMERS CO.	10				10		5
MO	SAINT LOUIS	NA	255				255		750
NC	GASTONIA	UNIROYAL CHEMICAL CO. INC.	250				250		250
NC	GRANITE FALLS	COOKSON AMERICA							319
SC	PIEDMONT	AMOCO CORP.	18				18	5	118
SC	SPARTANBURG	AMERON INC.	296				296		

Table 5-1. Releases to the Environment from Facilities That Manufacture or Process 4,4'-Methylenedianiline

			Reported amounts released in pounds per year						
State[a]	City	Facility	Air	Water	Land	Underground injection	Total environment[b]	POTW transfer	Off-site waste transfer
TX	BAYTOWN	NA	1,505	250			1,755		8,600
TX	BURKBURNETT	AMERON INC.	120				120		
TX	LA PORTE	DOW CHEMICAL CO.	95				95		9,732
UT	CLEARFIELD	HERCULES INC.							57,910
WI	GREEN BAY	RPM INC.	250				250		500
WI	PRAIRIE DU CHIEN	3M CO.	5				5		18,000
WV	HUNTINGTON	BASF CORP.	310				310	1,160	1,240
WV	NEW MARTINSVILLE	NA	2,159	475			2,634		250
		Totals	9,742	725		26,064	36,531	1,889	184,458

Source: TRI94 1996

[a] Post office state abbreviations used
[b] The sum of all releases of the chemical to air, land, water, and underground injection wells by a given facility

NA = not available; POTW = publicly owned treatment works plastics, during encapsulation of instruments with polyurethane mixture, and during coremaking of iron and steel foundries where 4,4´-methylenedianiline polymers are used as binders in molding (IARC 1986).

According to the Toxics Chemical Release Inventory (TRI) in 1994, releases of 4,4´-methylenedianiline to the air from 27 large processing facilities were 9,742 pounds (4,419 kg) (TR194 1996). Release to the air constituted 26.7% of the total environmental release. Table 5-l lists amounts released from these facilities. The TRI data should be used with caution because only certain types of facilities are required to report. This is not an exhaustive list (EPA 1996).

5.2.2 Water

4,4´-Methylenedianiline is released to water as aqueous effluents from industries that produce or use it, for example, from methylenediphenyl diisocyanate manufacturing plants. The source of 4,4´-methylenedianiline in treated and untreated waste water from methylenediphenyl diisocyanate plants may be due to release of the starting material (4,4´-methylenedianiline) in waste water or from the hydrolysis of methylenediphenyl diisocyanate. Small amounts of 4,4´-methylenedianiline may also be released to surface water via storm water runoff from waste sites containing this compound. However, there is no monitoring data that confirm the presence of the compound in waste effluents from the plants that manufacture and use it, or in natural waters where the treated or untreated wastewaters from these plants are discharged.

According to the TRI, in 1994 releases of 4,4´-methylenedianiline to water from the 27 large processing facilities totaled 725 pounds (329 kg) (TR194 1996). Release to water constituted 2% of the total environmental release. An additional 1,889 pounds (857 kg) were released indirectly to POTWs and some of this volume ultimately may have been released to surface waters. Table 5-l lists amounts released from these facilities. The TRI data should be used with caution because only certain types of facilities are required to report. This is not an exhaustive list (EPA 1996).III

5.2.3 Soil

4,4´-Methylenedianiline may be found in soils of controlled or uncontrolled hazardous waste sites as a result of disposal of wastes containing either 4,4´-methylenedianiline or reaction products, such as methylenediphenyl diisocyanate. Products such as polyurethane foams which contain the reactant diphenylisocyanate moiety (NIOSH 1976) can break down into 4,4′-methylenedianiline either chemically or biologically in soil. 4,4′-Methylenedianiline may also be released to soil as a result of accidental spillage during storage or transport. However, very few monitoring data are available that confirm the presence of 4,4′-methylenedianiline in soil.

According to the TRI, in 1994 there were no releases of 4,4′-methylenedianiline to soil from the 27 large processing facilities (TR194 1996). However, an additional 26,064 pounds (11,818 kg) was released by underground injection. These releases represent 71% of all environmental releases. Table 5-l lists amounts released from these facilities. The TRI data should be used with caution because only certain types of facilities are required to report. This is not an exhaustive list (EPA 1996).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

The vapor pressure of 4,4′-methylenedianiline at 25 ^{o}C has been estimated to be $2.82x10^{-10}$ atm ($2.15x10^{-7}$ mm Hg) by multiplying its water solubility of 5.04 moles/m^3 by its Henry's law constant (II) of $5.6x10^{-11}$ atm-m^3/mole (H = vapor pressure/water solubility) (Thomas 1990a). This is comparable to an estimated vapor pressure of $1.5x10^{-7}$ mm Hg at 25 ^{o}C (NIOSH 1986). Organic compounds with a vapor pressure of $2.15x10^{-7}$ mm Hg will exist in the air mostly as an aerosol and partly in the vapor phase (Eisenreich et al. 1981). In a test atmosphere generated by vaporization of epoxy resin containing 4,4′-methylenedianiline hardener, no difference in the sample collection efficiency for 4,4′-methylenedianiline was observed when sulfuric acid-coated glass-fiber filters and simple Teflon filters were used (Gunderson and Anderson 1988). This indicates that 4,4′-methylenedianiline will exist primarily in the aerosol phase in the atmosphere and, like other atmospheric aerosol, will be removed from the atmosphere by rain/snow scavenging and dry deposition (Bidleman 1988).

4,4′-Methylenedianiline has an estimated K_{oc} value of 174 (see Table 3-2). It will be weakly to moderately adsorbed to suspended solids and sediment in water (Swarm et al. 1983), and a large percentage of 4,4′-methylenedianiline may exist in water in the dissolved state where it is susceptible to degradation via chemical/biological processes. As the water solubility of amine salts is higher than the free base, the concentration of dissolved 4,4´-methylenedianiline will increase in natural waters as the pH decreases below 7. However, aromatic amines, particularly primary aromatic amines, covalently and irreversibly bind to humic substances present in most natural waters (Parris 1980). Therefore, in deference to moderate/low physical adsorption, 4,4´-methylenedianiline will become strongly bound (through covalent bonds) to humic materials in suspended solids and sediment present in most waters. Therefore, the percentage of 4,4´-methylenedianiline present in water may be much lower than is expected from simple physical adsorption of the compound. Organic compounds with Henry's law constants <3.7x10^{-7} atm-m^3/mole are essentially non-volatile in water (Thomas 1990b). Therefore, 4,4´-methylenedianiline, with an estimated H of 5.99x10^{-11} atm-m^3/mole (see Table 3-2), will remain essentially non-volatile in water.

Based on a value of 1.59 for log K_{ow} and a regression equation (Bysshe 1990), the estimated bioconcentration factor for 4,4´-methylenedianiline in fathead minnow, bluegill sunfish, rainbow trout, and mosquitofish is 9.5. Therefore, 4,4´-methylenedianiline will not bioconcentrate in aquatic organisms. Carp (Cyprinus *carpio)* were grown in a model river consisting of natural river water, 0.5% volume per volume (v/v) river bottom sludge, and 0.1 mg/L methylene-di-p-phenylene isocyanate (MDI) in an outdoor stainless steel tank for 8 weeks with water flowing in the tank at rates of 4-14 cm/sec (III 1981). Neither MD1 nor its decomposition product, 4,4´-methylenedianiline, was detected (detection limit <0.1 mg/kg) in the whole body of fish. It was concluded that MD1 and 4,4´-methylenedianiline do not bioaccumulate in carp (III 1981). No data were located in the literature that would suggest that 4,4´-methylenedianiline will biomagnify in animals of higher trophic level via food chain biotransfer (e.g., bioaccumulation in algae < bioaccumulation in fish < bioaccumulation in human). This is not surprising, considering the low K_{ow} value (indicative of low accumulation in lipids) and easy metabolism of the compound (Cocker et al. 1994) in higher trophic level animals.

The estimated K_{oc} value of 174 indicates that the mobility of 4,4´-methylenedianiline in soils having low organic carbon content will be moderate to high (Swarm et al. 1983). However, besides the physical adsorption to organic matter in soils, the compound will also become bound to organic matter (humates) by stronger covalent bonds (Parris 1980). In soils that exhibit this covalent bonding behavior, the mobility of 4,4´-methylenedianiline will be low and the rate of leaching from soil to groundwater will not be important.

5.3.2 Transformation and Degradation

5.3.2.1 Air

Reactions with hydroxyl radicals, ozone and nitric acid may be important for 4,4′-methylenedianiline in the atmosphere (Atkinson 1985). The rate constant for the homogeneous vapor phase reaction of 4,4′-methylenedianiline with hydroxyl radicals at 25 ^oC is estimated to be 2.4lx 10^{-10} cm^3/molecule-sec (HSDB 1996). The estimated value is in conformity with a value of $1.18x10^{-10}$ for reaction of aniline with hydroxyl radicals (Atkinson 1985). Assuming the atmospheric concentration of hydroxyl radicals to be constant at $5x10^{-5}$ molecules/cm^3, the half-life of 4,4′-methylenedianiline for this pseudo first order reaction is 1.6 hours. However, since the compound will be present predominantly in the aerosol phase (see Section 5.3.1), the importance of the heterogeneous reaction of particulate 4,4′-methylenedianiline with gas phase hydroxyl radicals cannot be ascertained. Based on the rate constants for the reactions of primary amines with ozone (Atkinson and Carter 1984), the atmospheric reaction of 4,4′-methylenedianiline with ozone will not be important. On the other hand, based on the reaction of amines with atmospheric nitric acid (Atkinson 1985), the reaction of 4,4′-methylenedianiline with gas phase nitric acid may be an important loss process in urban atmospheres (where the concentration of atmospheric nitric acid is much higher than the concentration of nitric acid in rural atmospheres). But the importance of the heterogeneous reaction of particulate 4,4′-methylenedianiline with gas phase nitric acid in the atmosphere cannot be quantitatively ascertained.

5.3.2.2 Water

The ultraviolet absorption spectra of 4,4′-methylenedianiline solution in methanol shows an absorption maximum at 243 nm, and a much weaker maximum at 289 nm (Sadtler 1974). The weaker absorption extends well into wavelengths >290 nm. Therefore, solutions of 4,4′-methylenedianiline in water will absorb some sunlight (wavelength >290 nm) and may undergo photolysis in water. In water with pH <7, the absorption maximum shifts from 289 nm to a lower wavelength (261 nm), with little absorption at wavelengths 2290 nm (Sadtler 1974). Therefore, in water with pH <7, photolysis of 4,4′-methylenedianiline will not occur. Even in natural surface waters having pH ≥7, photolysis may not be important because 4,4′-methylenedianiline will be present predominantly in the adsorbed form in the sediment (see Section 5.3.1).

The hydrolysis of 4,4´-methylenedianiline in water will not be important because aromatic amines are generally resistant to hydrolysis (Harris 1990). Aromatic amines react with hydroxyl and peroxy radicals present in most waters found in the environment, and the pseudo-first-order half-lives of 4,4´-methylenedianiline due to these reactions are estimated to be upwards of 2.6 days (Howard et al. 1991). Based on aqueous screening test data for toluidines, the half-lives for biodegradation of 4,4´-methylenedianiline in surface waters under aerobic and anaerobic conditions have been estimated to be 1-7 days and 4-28 days, respectively (Howard et al. 1991). Similarly, the half-life for biodegradation of 4,4´-methylenedianiline in groundwater has been estimated to be 2-14 days (Howard et al. 1991). In an experimental biodegradation study in water, it was concluded that 4,4´-methylenedianiline (concentration 1.35 mg/L) was not biodegradable in 87 days with activated sludge alone (III 1986). Biodegradation occurred when the sludge was adapted with aniline and 4,4´-methylenedianiline and the rate of biodegradation was maximum when the adaptation period was >200 days. The biodegradation of 4,4´-methylenedianiline was concluded to be a co-metabolic process (III 1986) and the adapted sludge biodegraded 4,4´-methylenedianiline from its initial concentration of 12.7 mg/L to undetectable levels (detection limit <0.02 mg/L) in 8 days (III 1987). Under aerobic conditions, the nitrogen in 4,4´-methylenedianiline oxidized to ammonia and finally to nitrate (III 1987). There was some evidence of phenol formation, but this could not be confirmed. The degradation of 4, 4'-methylenedianiline in water was studied in a model river system (for a description of the model river, see Section 5.3.1). Methylene-di-p-phenylene isocyanate (MDI) was first added to the water; it degraded to form 4,4´-methylenedianiline at an initial concentration of 0.1 mg/L. After 4 days, the concentration of 4,4´-methylenedianiline was below the analytical methods detectable limit (<0.02 mg/L) (III 1980). It was concluded that 4,4´-methylenedianiline will biodegrade rapidly in most natural bodies of water. The main drawbacks of the International Isocyanate Institute (III 1980) study are inadequacy of the performed control tests, failure to identify the products of biodegradation, and failure to provide any mass balance of the original substrates with the products formed.

5.3.2.3 Sediment and Soil

No data, either experimental or estimated, were located for the rate of 4,4´-methylenedianiline loss from soil by reaction with oxidants and natural sunlight. The importance of photolysis beyond the surface layer of soil can be ruled out because of lack of light availability. The reaction of 4,4´-methylenedianiline with nitric acid (see Section 5.3.2.1) in soil, particularly in soil having pH <7, is an interesting subject that needs investigation. The pseudo-first-order aerobic biodegradation half-life of 4,4′-methylenedianiline in soil has been estimated to be l-7 days (Howard et al. 1991). In deeper soil or sediment where there is a lack of oxygen, 4,4′-methylenedianiline may be degraded by anaerobic biodegradation, but the rate of this reaction was not located in the literature.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

No monitoring data for the levels of 4,4′-methylenedianiline in ambient air were located in the literature.

5.4.2 Water

No data regarding the level of 4,4′-methylenedianiline in surface water, industrial effluents, groundwater, or drinking water were located in the literature.

5.4.3 Sediment and Soil

No data were located on the level of 4,4′-methylenedianiline in contaminated soil or sediment.

5.4.4 Other Environmental Media

No data were located in the literature on the levels of 4,4′-methylenedianiline in edible fish or aquatic organisms from contaminated water, fruits, or vegetables grown on contaminated land, and in other related environmental media. No residue of MD1 or 4,4′-methylenedianiline was found at a detection limit of 0.01 mg/kg (fresh weight) in tomato, cucumber, melon, and lettuce grown on soilless reconstituted polyurethane foam with or without nutrient solutions (Rouchaud et al. 1992).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The consumption of bread accidentally contaminated with 4,4′-methylenedianiline led to an outbreak of 84 cases of jaundice in Eppin, England, in the early 1960s (Kopelman et al. 1966). Six young people developed acute jaundice and may have suffered severe liver damage when they ingested an alcoholic beverage spiked with 4,4´-methylenedianiline, which they assumed was the psychometric drug methylendioxyamphetamine; both have the same abbreviation, MDA (Tillmann et al. 1997). Consumer products that contain 4,4´-methylenedianiline are polyurethane foam, Spandex® fiber, and epoxy-containing products (see Section 4.3). Under normal use conditions, very little 4,4´-methylenedianiline is present in the free state in these consumer products. Potential consumer exposure may occur via dermal contact with trace amounts of free 4,4´-methylenedianiline found in automobile cushioning or epoxy-containing products (NIEHS 1994). It has been reported that the levels of the compound in food, food additives, and food packaging are so low that the potential daily intake via food is virtually zero (NIEHS 1994). With the exception of certain medical devices, there is no documentation of exposure to 4,4´-methylenedianiline from any consumer products. Polyurethane is widely used in such medical devices as potting materials for components of plasma separators and artificial dialyzers (Shintani 1991). Although polyurethane in these materials contains methylene diphenyldiisocyanate, polyurethane releases free 4,4´-methylenedianiline during sterilization by gamma irradiation or autoclaving (Shintani 1991). Therefore, there is a potential risk of exposure to 4,4´-methylenedianiline for patients with kidney disease or patients who receive frequent blood transfusions (Shintani 1991). The relative potential of sterilization methods to release 4,4´-methylenedianiline and mutagenic compounds from polyethylene foam potting material has been studied (Shintani 1995a). Gamma-ray irradiation sterilization at 2.5 Mrad produced a few ppm of the compound, but more importantly, produced unknown compounds which proved to be mutagenic in the absence of metabolic activity. On the other hand, no formation of 4,4´-methylenedianiline was observed in autoclaved thermosetting polyurethane potting material (heated at 12 l°C for 60 minutes) and smaller amounts of mutagenic compounds were determined. Thus, autoclave sterilization is more appropriate, provided materials can withstand the process. Another sterilization technique, ethylene oxide gas, produced the least amount of 4,4´-metbylenedianiline and other compounds, but the residue of ethylene oxide gas is itself problematic (Shintani 1995b).

Occupational exposure to 4,4´-methylenedianiline can occur during its production; during its use in the manufacture of insulation materials (e.g., plastic insulating materials and polyurethane), eoremaking in iron and steel foundries, and encapsulation of instruments with polyurethane mixture; and during use of epoxy resins in the construction of nuclear power plants (NIOSH 1976). The major routes for occupational exposure to 4,4´-methylenedianiline are dermal and inhalation (Cocker et al. 1994; Peterson et al. 1991). The occupational exposure to 4,4´-methylenedianiline can be assessed both by air monitoring and biological monitoring of urinary 4,4´-methylenedianiline and its metabolites in workers. However, air monitoring alone would underestimate occupational exposure to the compound by failing to consider exposure from skin absorption (Peterson et al. 1991). There is some evidence which showed that when exposure to 4,4′-methylenedianiline was via inhalation, postshift urine samples of workers had higher concentrations of the compound than samples taken preshift next day (Cocker et al. 1994). When the exposure was mostly via the dermal route, urine samples taken preshift the next day had higher concentrations of 4,4′-methylenedianiline than urine samples collected immediately postshift (Cocker et al. 1994). Therefore, urine collection strategies may provide some clue about the route of entry into the body. Workers' exposure to 4,4′-methylenedianiline used in an epoxy mixture to insulate electrical cables was monitored by analysis of the compound in blood and urine (Dalene 1995). At the end of the workday, workers removed material from their skin with a cleaning solution containing mainly butyl acetate. Some results suggested that using such cleaning solutions may enhance the absorption of 4,4′-methylenedianiline (compared to washing with soap and water).

Occupational exposure to 4,4′-methylenedianiline has been assessed by monitoring workplace air, analysis of the substance collected on dermal pads, and analysis of urine. The concentrations of 4,4′-methylenedianiline in the air of working areas for some of these industries are given in Table 5-2. A concentration of ≤29 mg/m^3 was detected in the occupational air of a facility where workers were blending and bagging a hardener containing 4,4′-methylenedianiline (Shuker et al. 1986). In a survey conducted in Britain, postshift urine samples were taken from 111 workers at 5 factories that used 4,4′-methylenedianiline (Cocker et al. 1986a). The urinary concentrations (both free and conjugated 4,4′-methylenedianiline) in 77.2% of the samples were below the detection limit (<5 nmol 4,4′-methylenedianiline/mmol creatinine) and the concentration range was 6- 175 nmol 4,4′-methylenedianiline/mmol creatinine in the rest of the samples. In a more recent survey (1989-1990) by the same group, 960 preshift and postshift urine samples from 411 workers from 45 factories that manufactured or used 4,4′-methylenedianiline were analyzed for total 4,4′-methylenedianiline (Cocker et al. 1994). The compound was not detected in 57% of postshift and 42% of the preshift urine samples. The concentrations of 4,4′-methylenedianiline in about 95% of urine samples were below 100 nmol/mmol creatinine. However, the concentration of 4,4′-methylenedianiline in 3 postshift urine samples exceeded 1,300 nmol/mmol creatinine and the concentration in one sample was 687 1 nmol/mmol creatinine. The maximum urinary 4,4′-methylenedianiline levels were found among manufacturers and formulators. In a Swedish study of 8 epoxy resin workers, the urinary total 4,4′-methylenedianiline concentrations (not standardized with creatinine level in urine) were in the

Table 5-2. Concentrations of 4,4′-Methylenedianiline in Air/Dermal Pad in Some Working Areas

Industry	Sample type	Concentration range ($\mu g/m^{3}$)	Reference
4,4′-Methylenedianiline production	Personal area	5–74	Boeniger 1984a
	Dermal pad	13–651	Boeniger 1984a
		4.2–54[a]	Boeniger 1984a
Plastic insulating materials	Personal area	1–690	IARC 1986
		<0.3–99	IARC 1986
Coremaking in iron and steel foundries	Area	Up to 1,600	Toeniskoetter 1981
Coremaking in aluminum foundries	Area	>1,600	Toeniskoetter 1981
Encapsulation of instruments with polyurethane	Area	10	IARC 1986

[a]This value is in $\mu g/cm^3$

range of l0-3,026 nmol/L (2-600 μg/L) (Tiljander et al. 1989). 4,4´-Methylenedianiline was detected (detection limit < 1.7 nmol/mmol creatinine) in <20% of urine samples from more than 160 workers at 10 industrial sites in the United States at a concentration range of 1.7-119.8 nmol 4,4´-methylenedianiline/ mmol creatinine (2.9-210 μg/g creatinine) (Peterson et al. 1991). The National Occupational Exposure Survey (NOES) conducted by NIOSH during 1981-83 estimated that a total of 15,178 workers in different industries are potentially exposed to 4,4´-methylenedianiline (NIOSH 1989). However, the NOES database does not contain data on the frequency, duration, concentration, or route of exposure of workers to 4,4´-methylenedianiline (or any other chemical). German researchers (Sepai 1995) found that a hemoglobin adduct of an acetylated metabolite of 4,4´-methylenedianiline can be detected after occupational exposure to MDI. The authors consider this evidence for the biological availability of 4,4´-methylenedianiline from *in vivo* hydrolysis of MDI.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Within the general population, there are a few groups that are potentially exposed to 4,4´-methylenedianiline at higher levels than the background population. In addition to individuals exposed to the compound in the workplace, these groups include: patients with kidney disease, patients who receive frequent blood transfusions (Shintani 1991), and people who live in the vicinity of 4,4´-methylenedianiline disposal facilities. With the exception of occupational groups, the levels of exposure in other potentially high exposure groups have not been documented either by measuring levels in the contaminated media (e.g., air, transfused plasma) or the levels in tissues or body fluids of the exposed persons.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, 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 4,4´-methylenedianiline is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of 4,4´-methylenedianiline.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Identification of Data Needs

Physical and Chemical Properties. Data on physical and chemical properties are available for 4,4′-methylenedianiline (HSDB 1996; IARC 1986; Moore 1978), although some of these data (vapor pressure, pb, and Henry's law constant) are estimated by reliable methods. The available data will permit the prediction of environmental fate processes for 4,4′-methylenedianiline. Therefore, a data need has not been identified.

Production, Import/Export, Use, Release, and Disposal. Five companies that manufacture 4,4′-methylenedianiline for sale and/or distribution also utilize the predominant amount of manufactured material captively for the production of other products (IARC 1986; TR194 1996). Therefore, data on recent production volumes or the trend in yearly production volume for 4,4′-methylenedianiline remain unavailable. The availability of this data could be important, because it provides indirect evidence of environmental release. Information regarding the recent trend in import/export volumes and its use is well documented in the literature (IARC 1986; NTDB 1994). Since medical devices such as plasma separators or artificial dialyzers are often fabricated with polyurethane as a potting material, they release 4,4′-methylenedianiline during sterilization (Shintani 1991). This is one of the documented sources of consumer exposure to the compound. Although some information regarding the method of disposal is available (HSDB 1996), it would be helpful to obtain more information on the methods currently used by industries for the disposal of 4,4′-methylenedianiline wastes that are transferred off-site. 4,4′-Methylenedianiline itself is used to prepare other chemicals or products; it is not used in the home or the general environment and thus, would not contaminate any home or environmental media. No literature data were found on 4,4′-methylenedianiline as a food contaminant. Levels of the compound in food, food additives, and food packaging are so low that potential daily intake via these routes is virtually zero (NIEHS 1994). No residue of the compound was found on vegetables grown on soilless reconstituted polyurethane foam with or without nutrient solutions (Rouchaud et al. 1992). Consumer products that contain

4,4´-methylenedianiline are polyurethane foam, Spandex® fiber, and epoxy-containing products (see Section 4.3). Under normal use conditions, very little 4,4´-methylenedianiline is present in the free state in such products.

According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxics Release Inventory (TRI), which contains this information for 1992, became available in May of 1994. This database will be updated yearly and should provide a list of industrial production facilities and emissions.

Environmental Fate. Experimental data on the fate of 4,4´-methylenedianiline in air, water, and soil are scarce. Homogeneous reaction of vapor-phase 4,4´-methylenedianiline with the hydroxyl radical in the atmosphere is known to be an important removal mechanism (half-life estimated at 1.6 hours). However, 4,4´-methylenedianiline exists in the atmosphere predominantly as either a solid aerosol or adsorbed on other particles. Very little is known about the reaction mechanisms, rate of removal, or degradation products formed when 4,4´-methylenedianiline reacts heterogeneously with hydroxyl radical or gas-phase nitric acid. Based on its low estimated vapor pressure of 2.15×10^{-7} mm Hg at 25 ^{o}C, and its ability of form covalent bonds with humic substances present in soil and sediment (Parris 1980), 4,4´-methylenedianiline will partition into sediment of surface water and in soil. The strong binding of the compound with humic substances in soil will retard its mobility, resulting in low leachability in most soils. However, it would be important to verify experimentally the sorption behavior of 4,4´-methylenedianiline in sediment and soil. The half-lives of 4,4´-methylenedianiline due to biodegradation in aerobic soil and anaerobic sediment/soil are predicted to be l-7 days and 4-28 days, respectively (Howard et al. 1991). Therefore, the compound will persist in deeper soil and sediment where there is a lack of oxygen. However, these estimated halflives and the prediction that biodegradation will be the most important fate of 4,4´-methylenedianiline in water and soil need further experimental verification.

Bioavailability from Environmental Media. People who live in the vicinity of disposal facilities may be exposed to 4,4´-methylenedianiline by inhalation of airborne dust, ingestion of soil (children), and dermal contact with soil (children). However, no monitoring data on levels of the compound in air, water, or sediment and soil were located in the literature search. Analyses of fish and vegetables have been conducted, but no residues were found at the detection limits attained (see

Section 5.4). Thus, no information on the absorption of 4,4´-methylenedianiline from contaminated air, water, soil, or plant material is available. In order to estimate the uptake of the substance as a result of exposure, it is important that the bioavailability of 4,4´-methylenedianiline from each route of entry be known. The bioavailability may not depend entirely on the sorption coefficient of 4,4´-methylenedianiline on soil or air particles, but may also depend on the pH of the media of contact. Because 4,4´-methylenedianiline is a weak base, its bioavailability may increase as the medium becomes more and more acidic. Since no data on the bioavailability of 4,4´-methylenedianiline from contaminated air and soil are available, it would be helpful to develop this information.

Reliable monitoring data for the levels of 4,4´-methylenedianiline in contaminated media at hazardous waste sites are needed so that the information obtained on levels of 4,4´-methylenedianiline in the environment can be used in combination with the known body burdens of 4,4´-methylenedianiline to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Food Chain Bioaccumulation. Both the experimentally determined K, value (HSDB 1996) and the estimated bioconcentration value indicate that 4,4´-methylenedianiline will not bioconcentrate in lipids and will not bioconcentrate in aquatic organisms or animals. Experimental study also supports this conclusion (III 1981). No data located in the literature suggest that 4,4´-methylenedianiline will biomagnify in animals of higher trophic levels through aquatic or terrestrial food chains. Since experimental data on the bioaccumulation and biomagnification potential of 4,4´-methylenedianiline are lacking, it would be helpful to develop these data in both aquatic and terrestrial food chains.

Exposure Levels in Environmental Media. Other than in occupational air, measured values for the levels of 4,4´-methylenedianiline in ambient air, water, soil, plant materials, and foodstuffs have not been reported. Consequently, no estimate of human intake of the compound from various environmental media was located in the literature. Reliable monitoring data for the levels of 4,4´-methylenedianiline in contaminated media at hazardous waste sites are needed so that the information obtained on levels in the environment can be used in combination with the known body burden of the substance to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Reliable monitoring data for the levels of methylenedianiline in contaminated media at hazardous waste sites are needed so that the information obtained on levels of 1,4-dichlorobenzene in the environment can be used in combination with the known body burdens of 1,4-dichlorobenzene to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Exposure Levels in Humans. Data on the levels of 4,4′-methylenedianiline in urine of occupationally exposed workers are available (Cocker et al. 1994; Peterson et al. 1991; Tiljander et al. 1989). No data were located on the levels in other tissues or body fluids of exposed or unexposed people. Similarly, no biological monitoring study has been conducted for populations in the vicinity of hazardous waste sites. This information is necessary for assessing the need to conduct health studies on these populations.

Exposure Registries. No exposure registries for 4,4′-methylenedianiline were located. This substance is not currently one of the compounds for which subregistry has been established in the National Exposure Registry. The substance will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to exposure to this substance.

5.7.2 Ongoing Studies

A search of the Federal Research in Progress (FEDRIP) database did not identify any ongoing studies that could be useful in filling the data gaps discussed in Section 5.7.1.