6. POTENTIAL FOR HUMAN EXPOSURE

6.1 OVERVIEW

Since benzidine may only be produced for captive use in the United States, its direct release to the environment is expected to be low. Benzidine-based dyes may still be imported into the country (Anonymous 1999; Pfaltz and Bauer 1999; Weber 1991). These dyes can undergo microbial degradation and release free benzidine to the environment (Weber 1991; Yoshida et al. 1981). In the past, benzidine's production and use may have led to its release to the environment from waste waters and sludges. Relatively high benzidine levels have been detected in soils and water in the vicinity of industrial sources (Boyd et al 1984; Zhao et al. 1998).

Benzidine is a moderately persistent compound in the environment, but it may readily partition from solution to soils and sediments, which reduces the potential for human exposure. In the atmosphere, benzidine exists in both the particulate and vapor phases (Kelly et al. 1994). Particulate-phase benzidine may be removed from the atmosphere by wet and dry deposition, while vapor-phase benzidine will be readily degraded by reaction with photochemically-produced hydroxyl radicals. Benzidine may undergo direct photolysis in the atmosphere, but the kinetics of this reaction are unknown. In water, benzidine does not significantly volatilize or hydrolyze, but it may be oxidized by cations. Benzidine may undergo photolysis in sunlit surface waters. Benzidine may be strongly adsorbed from solution by soils, sediments, and clays, depending on the pH of the soil-water system. It may also be oxidized at clay surfaces. Benzidine does not seem to be readily biodegradable in soil, but does degrade at low concentrations in acclimated sludges. Benzidine may be bioconcentrated by aquatic organisms, but it appears that the extent of concentration is not significant and that it will not be transferred through the food chain to higher levels.

The direct risk of benzidine exposure to the general population appears to be low. Concern for human health is primarily focused on populations living near former manufacturing or disposal sites where benzidine or benzidine-based dyes may have been manufactured or disposed of. Impurities contained in certain food dyes may also be metabolized once inside the body and release free benzidine.

Benzidine has been identified in at least 28 of the 1,585 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (HazDat 2001). However, the number of sites evaluated for benzidine is not known. The frequency of these sites within the United States can be seen in Figure 6-1.

6.2 RELEASES TO THE ENVIRONMENT

Benzidine is a synthetic chemical and has not been reported to occur naturally in the environment (EPA 1986c). It is released to the environment only through industrial production and use, and through the degradation of benzidine-based dyes. Since 1976, releases of benzidine have decreased because it is only produced for captive consumption in the United States (see Section 5.1).

6.2.1 Air

No data were located documenting current benzidine emissions to the atmosphere. Prior to 1974, benzidine and its derivatives were manufactured and used in open systems that permitted atmospheric releases at the workplace. Based on the current regulations restricting the production and use of benzidine (see Table 8-1), atmospheric emissions of benzidine are expected to be low.

No emissions of benzidine to air from manufacturing and processing facilities in the United States from 1987 to 1996 were reported on the TRI (TRI87 1989; TRI90 1992; TRI92 1994; TRI96 1999). It was reported that 13 pounds of benzidine were released to the air from four facilities in the United States in 1999 (TRI99 2001). These emissions resulted from the incineration of hazardous waste and not from the manufacture, production, or use of benzidine.

Benzidine was not identified in air samples collected from the 28 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2001).

6.2.2 Water

No data were located documenting current benzidine emissions to water. In the past, benzidine was released into the environment in waste waters generated by its production or its use in the synthesis of azo dyes (EPA 1980a). Industrial reports have claimed that benzidine discharges at any production facility generally did not exceed approximately 0.45 kg/day (EPA 1979d), and that the discharged benzidine concentrations in the dye wastes were generally less than 10 ppm. Benzidine was estimated to be a

Figure 6-1. Frequency of NPL Sites with Benzidine Contamination

Derived from HazDat 2001

potential hazard only in the vicinity of dye and pigment plants (EPA 1980a). Waste effluent from factories where textiles were dyed with benzidine-based dyes contained an average benzidine concentration of 3.5 ppb (µg/L), effluents from a leather factory contained an average of 0.25 ppb (µg/L) benzidine (EPA 1979b), and effluents from a foundry contained up to 10 ppb (µg/L) benzidine (EPA 1986c). Benzidine was detected in 1.1% of 1,235 effluent samples reported on the Storage and Retrieval (STORET) database maintained by EPA (Staples et al. 1985). The median concentration of all samples was less than 10 ppb (µg/L). These STORET results must be used with some caution, since many of the analysis methods through the early 1980s used techniques that could not distinguish between benzidine and a variety of related aromatic amines and metabolites (EPA 1978c). In some cases, therefore, the STORET data may overestimate the reported benzidine levels. Benzidine was detected in the waste water of a dye manufacturing plant in Dalian, China, at a concentration of 23 ppb (µg/L) (Zhao et al. 1998).

It was demonstrated that anaerobic sediment-water systems were able to biodegrade benzidine-based dyes to benzidine (Weber 1991). Direct Red 28 was degraded in an anaerobic sediment-water slurry and about 5% of the degradation products were shown to be benzidine (Weber 1991). Although the amount of benzidine produced was not quantified, the dye Deep Black EX was shown to biodegrade in river water, and benzidine was a metabolite (Yoshida et al. 1981).

Benzidine was not reported to be discharged to surface water or by underground injection from manufacturing and processing facilities in the United States from 1987 to 1999 according to TRI records (TRI87 1989; TRI90 1992; TRI92 1994; TRI96 1999; TRI99 2001). Since only certain types of facilities are required to report, it is possible that some benzidine has been released to water in small quantities or from other types of facilities.

Benzidine was identified in surface water collected at 5 sites and in groundwater collected at 10 of the 28 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2001).

6.2.3 Soil

No data were located documenting current benzidine emissions to soil surfaces. There is a potential for soils to become contaminated with benzidine if waste water treatment sludge or industrial wastes containing benzidine or benzidine-based dyes are land disposed. The dye Deep Black EX was shown to biodegrade in soils, and one of the degradation products was benzidine (Yoshida et al. 1981). The improper disposal of industrial sludges from a benzidine-manufacturing plant in Michigan resulted in soil, groundwater, and surface water contamination (Boyd et al. 1984). According to TRI, benzidine was not discharged to land from manufacturing and processing facilities in the United States from 1987 to 1999 (TRI87 1989; TRI90 1992; TRI92 1994; TRI96 1999; TRI99 2001).

Benzidine has been identified in soil samples collected from 9 sites and in sediment samples from 4 of the 28 NPL hazardous waste sites where it was detected in some environmental media (HazDat 2001).

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

Benzidine is expected to exist in both the particulate and vapor phases in the ambient atmosphere (Kelly et al. 1994). Particulate-phase benzidine is subject to atmospheric dispersion, gravitational settling, and wash-out by rain. Vapor-phase benzidine reacts rapidly with photochemically generated hydroxyl radicals, and thus, its transport in the atmosphere is limited. The Henry's law constant for benzidine is estimated as 5.2×10^{-11} atm-m^3/mol using a fragment constant estimation method (Meylan and Howard 1991). Based on this Henry's law constant, volatilization from moist soils and water surfaces is not expected to be an important environmental fate process and only minor amounts of benzidine can be expected to partition to the atmosphere.

In water, benzidine may be adsorbed by soils and sediments. The extent of adsorption of hydrophobic (sparingly water soluble) compounds has been shown to be highly correlated with the organic carbon content of the adsorbents (Hassett et al. 1983). When adsorption is expressed as a function of organic carbon content, an organic-carbon/water partition coefficient (K_{oc}) is generated, which is a unique property of the compound and may be used to rank the relative mobility of organic contaminants in saturated soil-water systems. EPA (1981b) calculated a K_{oc} value for benzidine of 10.5, based on an octanol-water partition coefficient (K_{ow}) of 21.9. This relatively low value implies that benzidine is a "very highly mobile" compound in saturated soil-water systems (Roy and Griffin 1985). However, benzidine is a weak base in solution, and exists in both neutral and cationic forms. Written as hydrolysis reactions, the amine groups on the benzidine molecule may be protonated (Korenman and Nikolaev 1974), as follows:

$$\text{benzidine} + H_2O \text{ W } \text{benzidineH}^+ + OH^- \quad pK_{a1} = 4.3 \text{ at 20 EC}$$

$$\text{benzidineH}^+ + H_2O \text{ W } \text{benzidineH}_2^{++} + OH^- \quad pK_{a2} = 3.3 \text{ at 20 EC}$$

At low pH, as in the case of acidic soils, benzidine will partially exist in the protonated form and can bind strongly to cation exchange sites in soils. As the pH increases, the proportion of cationic benzidine decreases, and the extent of adsorption via Coulombic interactions would decrease. This was demonstrated by Zierath et al. (1980), who found that the adsorption of benzidine by soils and sediments was controlled primarily by the concentration of the ionized species, which in turn, was highly correlated with pH. As the pH decreased, the magnitude of adsorption increased because of the increase in cationic forms which, via Coulombic interactions, would have a greater affinity for charged surfaces than would the neutral form. A recent study has supported these conclusions. Sorption of benzidine to three silt clay loams was measured from $CaCl_2$ electrolyte solutions at pH ranges of 4.4–7.2 (Lee et al. 1997). It was determined that the magnitude of sorption increased with decreasing pH, decreased with increasing $CaCl_2$ electrolyte concentration, and was affected by competition with other organic amines that competed with benzidine for cation exchange sites (Lee et al. 1997).

Benzidine is an aromatic amine that can also form covalent bonds with humic material in soils (Lee et al. 1997; Ononye and Gravel 1994; Ononye et al. 1989). This reaction usually involves imine formation between the amine group of benzidine and a carbonyl group of soil humic material. This reaction is reversible, and is partly responsible for the rapid binding of primary aromatic amines in soils. Benzidine may also undergo another type of binding involving a nucleophillic substitution reaction with quinone type residues in the soil matrix. This type of adsorption may be irreversible or only slowly reversible. Lee et al. (1997) have provided evidence that benzidine undergoes both of these reactions in soil, but the primary mechanism for the initial adsorption of benzidine is through the interaction of the protonated species with cation exchange sites in the soil matrix. The reported K_{oc} for benzidine on estuarine colloidal organic matter was 3,430 at pH 7.9 (Means and Wijayaratne 1989), indicating that benzidine will adsorb strongly to suspended solids and sediment in the water column.

Four aquatic organisms were exposed to radiolabeled benzidine in laboratory model ecosystems for 33 days by Lu et al. (1977). Bioconcentration factors (BCFs) were calculated for each organism: fish, 110; mosquito, 1,180; snail, 370; and algae, 160. In a 42-day experiment, bluegills were exposed to ^{14}C-benzidine in a flow-through tank. The BCF was 44 for the edible portion of the fish (EPA 1978c). Although benzidine does bioconcentrate to some degree, it is not strongly bioaccumulated by the lower forms of aquatic organisms or transferred through food chains to higher trophic levels (EPA 1986c).

6.3.2 Transformation and Degradation

6.3.2.1 Air

Benzidine is expected to exist in both the particulate and vapor phases in the ambient atmosphere (Kelly et al. 1994). The rate constant for the vapor-phase reaction of benzidine with photochemically-produced hydroxyl radicals has been estimated as 1.54×10^{-10} cm^3/molecule-sec at 25 EC using a structure estimation method (Meylan and Howard 1993). This corresponds to an atmospheric half-life of about 2.5 hours at an atmospheric concentration of 5×10^5 hydroxyl radicals/cm^3 (Meylan and Howard 1993). Particulate-phase benzidine is not expected to react with photochemically-produced hydroxyl radicals, and therefore, will not be readily degraded in the atmosphere. Benzidine absorbs light greater than 290 nm, and thus, may also undergo direct photolysis in the environment (Banerjee et al. 1978), but the kinetics of this reaction are unknown.

6.3.2.2 Water

Studies conducted by the Synthetic Organic Chemical Manufacturer's Association (SOCMA) indicated that the half-life of benzidine in dilute aqueous solution was 4 hours (EPA 1976a). However, neither reaction mechanisms nor degradation products were determined, and only the disappearance of benzidine itself from solution was an empirical observation.

Other than the hydrolysis (or protonation) of the amine groups, no data were located to suggest that the hydrolysis of benzidine is significant (EPA 1979c). A hydrolysis-rate constant of 0/mol-hour has been proposed (EPA 1981b, 1987c).

There is some evidence that benzidine may degrade in water by oxidation, but actual data on reaction rates were not available. Based solely on reaction rates with peroxy radicals, the half-life of benzidine in water has been estimated to be 100 days (range of 10–1,000 days) (EPA 1978c). Based on oxidation rates of similar compounds, the oxidation rate of benzidine with peroxy radicals was estimated to be approximately 1.1×10^8/mol-hour (EPA 1981b). However, there is a paucity of data to actually demonstrate that these reactions are environmentally significant. The available literature, therefore, offers widely disparate findings (e.g., EPA 1976a; EPA 1978c) on the fate of benzidine in water. Since the SOCMA studies were based in large measure on lake water samples, one possible explanation might be the tendency of benzidine to oxidize in the presence of certain clay minerals as described below in

Section 6.3.2.3 or to adsorb to suspended solids as described in Section 6.3.1. Other SOCMA test data involved chlorinated water or vigorously aerated water samples, which could have led to rapid oxidation of the benzidine parent materials (EPA 1976a). It was determined that the photolysis half-life of benzidine in methanol was about 2 hours when irradiated at 254 nm (Lu et al. 1977). Furthermore, it was determined that the disappearance quantum yield for benzidine at 300 nm was essentially identical to the disappearance quantum yield at 254 nm (Banerjee et al. 1978). Based upon this data, it is reasonable to conclude that photolysis of benzidine in sunlit surface waters may occur.

6.3.2.3 Sediment and Soil

Benzidine may be oxidized when mixed with some clay minerals in solution (Lahav and Raziel 1971; Solomon et al. 1968; Tennakoon et al. 1974a, 1974b; Theng 1971). When aqueous solutions containing benzidine are mixed with montmorillonite, pyrophyllite, hectorite, muscovite, illite, and kaolinite, the solution may turn blue. Benzidine blue, a monovalent radical cation, may form by the oxidation of benzidine by iron(III) in the silicate lattice and by aluminum(III) at crystal edges.

Previous assessments (e.g., EPA 1979c) generalized that cations in solution oxidize benzidine. However, it should be noted that these oxidation observations were made with benzidine-clay slurries. It has not been shown that ambient cations in natural or waste water will significantly oxidize benzidine. The concentrations of iron(III) and aluminum(III) in natural systems are often controlled by sparingly soluble hydroxide and oxide solid phases.

It has not been demonstrated that benzidine biodegrades in natural waters, and it may not readily biodegrade in soil. In one study, Lu et al. (1977) mixed a sample of Drummer soil with 100 µg of benzidine, and incubated it at 26.7 EC. After 4 weeks, only 20.6% of the compound remained in the soil. However, Graveel et al. (1985) generalized that the half-life of benzidine in soil may range from 3 to 8 years. Based on $^{14}CO_2$ evolution, benzidine decomposition averaged only 2% after 84 days of incubation with three soils (a Typic Hapudalf and two Typic Argiaqualls). Additional experiments indicated that after 365 days of incubation, approximately 8–12% of the added benzidine (53.4 µmol/kg dry soil) evolved as $^{14}CO_2$ (Graveel et al. 1986). It should be noted that biodegradation when measured by gas evolution may be a conservative estimate of the extent of decomposition. This technique does not account for carbon that is incorporated into the biomass or the soil organic matter, or if the compound is only partially metabolized (Graveel et al. 1986). Since benzidine may be found in waste water treatment sludges, studies have been conducted to assess whether benzidine would be biodegraded in conventional treatment systems. Benzidine was found to be biodegraded by two activated waste water sludges (Baird et al. 1977). The biodegradation of benzidine tended to be greater at lower benzidine concentrations, ranging from 35–88% depletion at 10 mg/L, 11–93% depletion at 20 mg/L, 21–60% depletion at 40 mg/L, and 9–55% depletion at 100 mg/L after a contact time of 6 hours. Little is known about the toxicity of benzidine to microorganisms; higher concentrations may inhibit bio-oxidation (EPA 1978c).

The extent of biodegradation depended on the concentration of the benzidine in aerobic growth reactors using waste water sludges (Tabak and Barth 1978). Using lower benzidine concentrations and longer contact times, the authors found that benzidine degraded to a greater extent. At concentrations of 0.5 and 1 mg/L, biodegradation was nearly complete after a contact time of 1 week, and was complete after a contact time of 3 weeks. At concentrations of 5 and 10 mg/L, 94 and 77%, respectively, of the benzidine was biodegraded after a contact time of 7 weeks. Acclimated sludges can completely degrade continuous low doses (#1 mg/L) of benzidine. They further concluded that ambient concentrations that are <1 than 1 mg/L will be degraded in natural ecosystems. Possible biodegradation products included 4,4'-dihydroxybiphenyl, N-hydroxybenzidine, 4-hydroxy-phenylamine, 4-aminobiphenyl, 3-hydroxybenzidine, 4-amino-4'-nitrobiphenyl, aniline, N,N'-dihydroxybenzidine, phenol, 3-3'-dihydroxybenzidine, and catechol (Baird et al. 1977; Tabak and Barth 1978). The environmental fate and pathways of degradation by products have not been assessed.

Laboratory studies of sediment-water systems suggest that the breakdown of various benzidine-based dyes can liberate benzidine (Weber 1991). Up to 5% of the initial amount of benzidine-dye materials may be transformed to benzidine, especially in anaerobic sediments. At lower pHs, however, sorption to sediment particulates was enhanced, and the degree of transformation diminished substantially. Yoshida et al. (1981) studied the disappearance of Deep Black EX from soil surfaces, and noted that benzidine was one of the products of microbial degradation. It was further noted that the resultant benzidine did not biodegrade in the soil after 9 weeks. However, no quantitative data on the conversion of the dye to benzidine was reported.

6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Benzidine does not occur naturally (IARC 1982a), and has been detected only infrequently and at low concentrations in environmental media. The production and use of benzidine-based dyes have decreased in the last 30 years while environmental regulations have been implemented to reduce the release of benzidine to the environment. Concentrations of benzidine still remaining in the environment may be at or below current detection limits or adsorbed to sediments, making it difficult to quantify the amount of benzidine in various environmental media.

6.4.1 Air

Monitoring data for benzidine concentrations in ambient air were not located (EPA 1978c; EPA 1979d, 1986c; Kelly et al. 1994).

6.4.2 Water

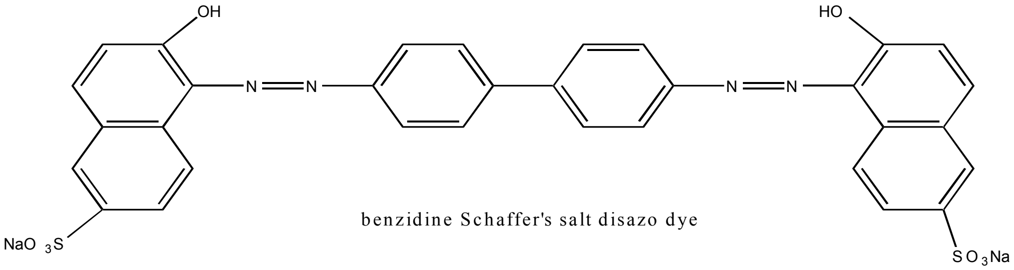
Benzidine is rarely detected in ambient water. It has been analyzed for, but not detected, in several systems (Howard 1989). The median concentration of benzidine in ambient water was less than 10 µg/L, and was detectable in only 1 of 879 samples reported in the STORET database (Staples et al. 1985). In 1990, benzidine was detected at maximum concentrations of 240 µg/L (on-site) and 19 µg/L(off-site) in groundwater at the Nyanza hazardous waste site in Ashland, Massachusetts (ATSDR 1994). This site was formerly the location for Nyanza Company, one of the first and largest dye manufacturers in the United States.

6.4.3 Sediment and Soil

Benzidine was not detected in any of the 3,240 sediment sample analyses reported on the STORET database (Staples et al. 1985). Benzidine was not detected in 21 samples from 7 sites in the Buffalo River upstream and downstream from the Allied Chemical plant where benzidine was believed to have been discharged (EPA 1976a).

6.4.4 Other Environmental Media

No data were located documenting the occurrence of benzidine in foods. An analysis of data from the STORET database indicated that benzidine was not detected in any of the 110 biota samples reported (Staples et al. 1985). Exposure to benzidine through most food products is highly unlikely (EPA 1986c). It is possible that low levels of benzidine or other impurities that can be metabolized to benzidine once inside the body may be found in synthetic coloring agents added to some foods. Although the Delaney Clause of the Food, Drug, and Cosmetic Act bans the use of all carcinogenic agents in food, various synthetic dyes (including those containing small amounts of benzidine-based dye materials and some trace amounts of benzidine impurities) are still in use (NIOSH 1980c). The benzidine concentration in food colorants is limited to 1 ppb by the FDA (see Table 8-1). It was recently determined that an impurity thought to be benzidine Schaeffer's salt disazo dye (shown below), was contained in 34 of 67 lots of FD&C Yellow No. 6 (Sunset Yellow FCF; Colour Index No. 15985) at concentrations of 11–941 ppb (Peiperl et al. 1995).



benzidine Schaffer's salt disazo dye

It is believed that this compound may be reduced in the intestine to release free benzidine (Peiperl et al. 1995). This compound arises during the manufacture of dyes due to free benzidine present as an impurity in the sulfanilic acid starting material. More recent data have also supported these findings. Free and bound benzidine was detected in 7 out of 8 samples of FD&C Yellow No. 6 (Sunset Yellow FCF) manufactured from 1991-1998 at concentrations ranging from 45 to 246 ng/g (Lancaster and Lawrence 1999). Free and bound benzidine was also detected in 2 of 9 samples of tartrazine manufactured from 1990-1998 at concentrations of 8 and 20 ng/g (Lancaster and Lawrence 1999).

Of 26 samples of benzidine-based dyes produced in the United States in the late 1970s, 17 samples contained benzidine concentrations ranging from 1 to 4 mg/kg, 8 samples contained from 10 to 20 mg/kg, and 1 sample was measured at 270 mg/kg (NIOSH 1980c). Although no data are available on the rates of azo reduction of benzidine-based dyes in environmental media, the dye called Direct Black 38 is known to be readily reduced in solution (Gregory 1984; Orzeck and Gregory 1981).

6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Based on the available data, the potential for benzidine exposure via environmental media (air, soil, water, or food) is low. Certain compounds found as impurities in azo food dyes have the potential to be converted to benzidine once inside the body, and represent a possible source of human exposure. There may remain a risk of benzidine exposure to populations near hazardous waste sites from the former disposal of benzidine or benzidine-based dyes.

Since benzidine is no longer commercially produced or used in the United States, the potential for occupational exposure to this compound is low. Workers that are involved in the in-house production of benzidine may be occupationally exposed via dermal contact and inhalation of benzidine vapors or dust particles. In the past, air concentrations at different locations in a benzidine manufacturing plant ranged from 0.007 to 17.6 mg/m^3 (Howard 1989). Benzidine was also reported in the urine of exposed workers at concentrations ranging from 1 to 112 μg/L (Howard 1989). Benzidine has also been detected in the urine of workers in India exposed to Direct Black 38 at concentrations of 2.4 to 362.5 μg/L (Dewan et al. 1988). Workers that are employed at hazardous waste sites may also be exposed to benzidine if it is present. No data were located on current levels of occupational exposure in the United States since, as noted earlier, recent information indicates that benzidine and benzidine-based dyes are no longer used or marketed in significant quantities by dye manufacturers in the United States.

6.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans. Differences from adults in susceptibility to hazardous substances are discussed in 3.6 Children's Susceptibility.

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, put things in their mouths, sometimes eat inappropriate things (such as dirt or paint chips), and spend more time outdoors. Children also are closer to the ground, and they do not use the judgment of adults to avoid hazards (NRC 1993).

At one time, benzidine-based dyes were available for home dyeing of fabrics, and accidental ingestions were reported to have occurred in children (Orzeck and Gregory 1981). These home dyes have since been taken off the market and the potential exposure risks are virtually non existent today. There is no other evidence to indicate that children are directly exposed to benzidine. There are no measurements of benzidine or its metabolites in amniotic fluid, meconium, cord blood or neonatal exposure that indicate prenatal exposure. Furthermore, there are no known studies of benzidine or its metabolites in breast milk.

Although not documented, children residing near hazardous waste sites where benzidine or benzidine-based dyes were disposed of may be exposed to benzidine via pica (dirt eating) if benzidine is present in the soil. Playing in contaminated soil could also lead to dermal exposure. Even though benzidine volatilizes and biodegrades slowly from soil surfaces, the likelihood of exposure from pica is considered low since benzidine has only been detected in 28 of the 1,585 hazardous waste sites that have been proposed for inclusion on the EPA (NPL) (HazDat 2001). Impurities in certain food dyes such as FD&C Yellow No. 6 can be metabolized to benzidine inside the body (Lancaster and Lawrence 1999; Peiperl et al. 1995). Since this dye is used to color medications, soft drinks, and candies, children may be indirectly exposed to benzidine through the ingestion of compounds that contain this dye. It is unknown whether there is a difference between children and adults in their weight adjusted intake of benzidine.

Since benzidine is no longer produced or used commercially in the United States, exposure to benzidine from parents' work clothes, skin, hair, tools, or other work-related items is unlikely.

6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Populations living or working near hazardous waste sites at which benzidine was detected may be exposed to higher levels than the general population. Persons residing near or employed at hazardous waste incinerators may be subject to small amounts of benzidine released to air. Workers in facilities (if any) that manufacture benzidine or benzidine-based dyes for in-house use may also be exposed. During the use of benzidine-based dyes, the greatest potential for exposure would be expected to be among workers who routinely handled the dry powders, which may be readily transformed to an aerosol and inhaled (NIOSH 1980a). Other occupations with potential exposure risks are medical or laboratory technicians where stains are used that may contain benzidine as a trace impurity. During the period 1981–1983 when these types of workplace exposures were still possible, it was estimated that up to 15,554 workers might potentially have been exposed (NIOSH 1990). Of these workers, 830 were in industrial finishing plants, and the remainder were in industries associated with laboratory or medical work. These most recent NIOSH numbers are not based on actual measurements, but rather were extrapolations of surveys, and the precise numbers are best used to make rough estimates of occupations and activities where risks may exist. In light of regulatory changes that went into effect during the 1980s, these NIOSH figures clearly do not provide an accurate basis from which to project current workplace exposure risks.

Workers in the United States currently wear protective equipment to eliminate skin contact with or inhalation of benzidine-containing materials. Worker exposures depend on the specific operations of the facility, but no information on current occupational exposure levels was located.

6.8 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 benzidine is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (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 benzidine.

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.

6.8.1 Identification of Data Needs

Physical and Chemical Properties. The physical and chemical properties necessary to evaluate the environmental fate of benzidine have been measured or estimated (EPA 1987b; Meylan and Howard 1991; Neely and Blau 1985; Schmidt-Blelk et al. 1982; Zierath et al. 1980). However, estimated properties may have a degree of uncertainty; a measured value for the Henry's law constant, for example, would allow more accurate prediction of the environmental fate of benzidine.

Production, Import/Export, Use, Release, and Disposal. Since 1973, benzidine has only been produced in the United States for captive consumption (EPA 1986c). No data were located on current domestic producers, production volumes, or import/export volumes of benzidine-based dyes, but recent information suggests that neither benzidine nor the dyes are currently produced in significant quantities in the United States, although importation of benzidine-based dyes may be continuing (Anonymous 1999; Pfaltz and Bauer 1999; Weber 1991). Ascertaining the quantity of these dyes that are imported would be useful in determining the potential for human exposure to benzidine. The most recent TRI has reported small releases of benzidine emitted to the air as a result of incineration of hazardous waste (TRI99 2001).

Environmental Fate. Benzidine generally partitions into the soil or sediment in the environment and its mobility decreases with decreasing pH (Lee et al. 1997; Ononye and Gravel 1994; Ononye et al. 1989). It has been demonstrated that clays can oxidize benzidine (Lahav and Raziel 1971; Solomon et al. 1968; Tennakoon et al. 1974a, 1974b; Theng 1971), but more information regarding the biodegradation of benzidine in water, soil, and sediment is necessary. It has been shown that benzidine may degrade in sewage treatment systems (Baird et al. 1977), but research on natural ecosystems would be useful. Also, the nature and environmental fate of degradation by products warrants future study. Information on the environmental degradation of benzidine-based dyes to benzidine is also essential.

Bioavailability from Environmental Media. It is generally agreed that benzidine base and salts can be readily absorbed through the intact human skin and through inhalation (Ferber et al. 1976; Meigs et al. 1951, 1954; Zavon et al. 1973), but no quantitative studies were located regarding absorption in humans or animals after oral exposure to benzidine. Studies on the bioavailability of benzidine are needed to determine its risks of entering ecological food chains and potential human exposures. No studies were located regarding the bioavailability of benzidine from environmental media. The lack of data does not necessarily indicate a lack of bioavailability.

Food Chain Bioaccumulation. Limited data have shown that benzidine can bioconcentrate in aquatic organisms (Lu et al. 1977). Studies are needed on the potential for benzidine to bioaccumulate in food chains since this would increase the risks of human exposures. No studies were located regarding the food chain accumulation of benzidine from environmental media. It would be useful to know if benzidine does bioaccumulate in the food chain, and whether there is a potential impact on human exposure levels.

Exposure Levels in Environmental Media. Benzidine has infrequently been detected in the environment (ATSDR 1994; Staples et al. 1985); however, no estimates have been made of the potential human intake of benzidine from environmental media. There is a need to further determine the ambient concentrations of benzidine and/or benzidine-based dyes in the atmosphere, surface water, groundwater, and soil. However, since benzidine is an anthropogenic substance of limited production, the expected concentrations would be at or below analytical detection limits, making it difficult to estimate general benzidine levels in the environment.

Further studies regarding impurities in azo food dyes that have the potential to be metabolized to benzidine once inside the body are needed. Identifying these impurities and monitoring the concentrations of these compounds in food dyes are necessary in order to determine the potential impact on humans.

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

Exposure Levels in Humans. No measurements of benzidine in human tissues have been located for the general population or for those residing near hazardous waste sites. This information is necessary for assessing the need to conduct health studies on these populations. Benzidine has been detected in the urine of workers who were involved in the production of dyes (Dewan et al. 1988). There is a need for further studies on benzidine and benzidine based dyes to document the degree to which exposures to human populations may still be taking place. Impurities found in certain dyes used to color foods may be broken down to benzidine once inside the body. Accurate data on the level of these impurities in food dyes and a better understanding of the amount of dyed foods ingested by the general population will provide a better understanding of the amount of benzidine that humans are exposed to.

Exposure Levels in Children. There is no information available on the exposure of children to benzidine and since it is no longer manufactured or produced in the United States, it is unlikely that children will be exposed to this compound. There do not appear to be unique exposure pathways for children other than pica, but since benzidine is rarely found in the environment, the potential for exposure is considered low. It is not known whether children are different in their weight-adjusted intake of benzidine and no childhood specific means to decrease exposure have been identified. Impurities found in certain dyes used to color foods may be broken down to benzidine once inside the body. Accurate data on the level of these impurities in food dyes and a better understanding of the amount of dyed foods ingested by children will provide a better understanding of the amount of benzidine children are exposed to.

Child health data needs relating to susceptibility are discussed in Section 3.12.2 Identification of Data Needs: Children's Susceptibility.

Exposure Registries. No exposure registries for benzidine were located. This substance is not currently one of the compounds for which a 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.

6.8.2 Ongoing Studies

No information could be identified on ongoing studies related directly to the fate and transport of benzidine.