

## 5. POTENTIAL FOR HUMAN EXPOSURE

### 5.1 OVERVIEW

1,2-Diphenylhydrazine oxidizes rapidly in the environment under aerobic conditions, with a half-life in water as short as 15 minutes. This rapid oxidation coupled with the lack of straightforward sampling methods makes the assessment of the literature difficult. For example, while a few monitoring papers report the detection of 1,2-diphenylhydrazine in the environment, their analytical methodology suggests that it is unlikely that 1,2-diphenylhydrazine would have been detected even if present. In addition, little information is available to assess the potential for environmental contamination, making the estimation of environmental releases difficult. Therefore, not only is the significance of reported environmental concentrations difficult to interpret, environmental concentrations are difficult to predict. The fate, transport, and distribution of 1,2-diphenylhydrazine in the environment are uncertain. 1,2-Diphenylhydrazine has been reported at 7 of 1177 sites in the National Priority List database (ATSDR 1990); the frequency of these sites within the United States can be seen in Figure 5-1.

### 5.2 RELEASES TO THE ENVIRONMENT

#### 5.2.1 Air

No information concerning the release of 1,2-diphenylhydrazine to air was located in the literature. The vapor pressure of 1,2-diphenylhydrazine is low ( $2.6 \times 10^{-5}$  mmHg at 25 C), indicating that little 1,2-diphenylhydrazine will volatilize from manufacturing and use operations. Dust generated from the loading and off-loading of 1,2-diphenylhydrazine during use may cause local atmospheric concentrations. If present in water, 1,2-diphenylhydrazine will probably oxidize to azobenzene before it volatilizes. Volatilization of 1,2-diphenylhydrazine is not expected to be an environmentally relevant fate process given the low Henry's Law constant ( $9.42 \times 10^{-8}$  atm-m<sup>3</sup> mol<sup>-1</sup>).

#### 5.2.2 Water

No information concerning the release of 1,2-diphenylhydrazine to water was located in the literature. If discharged to water, detectable concentrations will probably persist for only a short time, since the halflife of (100 µg/L) 1,2-diphenylhydrazine in wastewater is about 15 minutes (Riggin and Howard 1979, 1982)

#### 5.2.3 Soil

No information concerning the release of 1,2-diphenylhydrazine to soil was located in the literature. The manufacturing process for 1,2-diphenylhydrazine generates a sludge containing iron and/or zinc

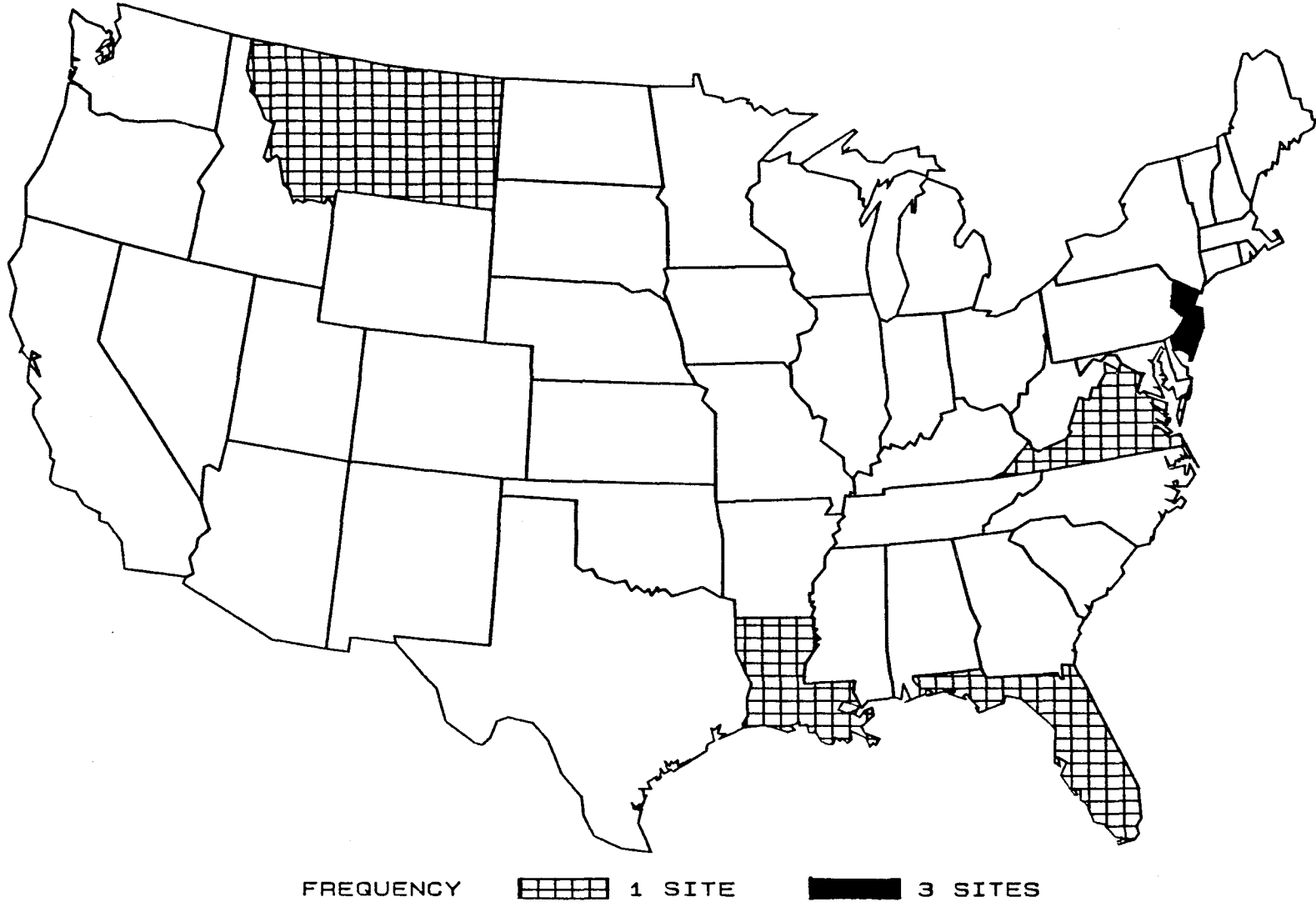


FIGURE 5-1. FREQUENCY OF NPL SITES WITH 1,2-DIPHENYLHYDRAZINE CONTAMINATION

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compounds, probably along with small amounts of unextracted 1,2-diphenylhydrazine. Some of this material may be disposed of in landfills, but no information is available concerning the 1,2-diphenylhydrazine disposal practices of the manufacturing industry.

### 5.3 ENVIRONMENTAL FATE

#### 5.3.1 Transport and Partitioning

No information concerning the transport and partitioning of 1,2-diphenylhydrazine in the environment was located in the literature. In water, 1,2-diphenylhydrazine is not expected to volatilize because of its rapid oxidation in aerated water (near-surface water) to azobenzene and its low calculated Henry's Law constant ( $9.42 \times 10^{-8} \text{ atm}\cdot\text{m}^3 \text{ mol}^{-1}$ ) (Lyman et al. 1982). The calculated  $\log K_{oc}$  (2.76) suggests that 1,2-diphenylhydrazine may sorb to sediments or suspended particles. This is based on the analysis of Kenaga (1980), who stated that chemicals with a  $K_{oc} < 100$  tend to be mobile in soil, while those with a  $K_{oc} > 1000$  tend to sorb. In soil, 1,2-diphenylhydrazine is not expected to leach to groundwater, based on its physical and chemical properties (i.e., 1,2-diphenylhydrazine reacts rapidly under environmental conditions and, based on its  $K_{oc}$ , will not rapidly leach downward in the soil column).

#### 5.3.2 Transformation and Degradation

##### 5.3.2.1 Air

No studies were located regarding the rates or products of reaction of 1,2-diphenylhydrazine in the atmosphere. Based on its behavior in aerated water, 1,2-diphenylhydrazine may react rapidly in air to form azobenzene as well as other products resulting from the abstraction of a hydrogen from a nitrogen by hydroxyl radical. Atkinson (1987) developed a method to estimate the hydroxyl radical ( $\text{HO}\cdot$ ) reaction rate based on structure. This method, an overall reaction rate of  $211 \times 10^{-12} \text{ cm}^3 \text{ molecule}^{-1} \text{ sec}^{-1}$  was calculated, which yields a half-life of less than 2 hours for an atmospheric  $\text{HO}\cdot$  concentration of  $0.5 \times 10^6 \text{ molecules cm}^{-3}$ . This is an estimated annually averaged concentration for a 24-hour period (Atkinson 1985). 1,2-Diphenylhydrazine also absorbs light above 290 nm (Sadler Index, no date) and may be susceptible to photolysis. No information was found concerning the characteristics of this potential reaction.

##### 5.3.2.2 Water

Very little information was located concerning the fate of 1,2-diphenylhydrazine in water. Riggan and Howard (1979, 1982) reported the results of a study on the stability of 1,2-diphenylhydrazine in a number of solvents including distilled water and wastewater. In distilled water at pH values of 2, 4.7, 7, and 10 and at 4°C or at room temperature, less than 10% of the initial 10 µg/L of 1,2-diphenylhydrazine remained in the water after

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1 day. At pH 2, 1,2-diphenylhydrazine degraded to benzidine, while at pH 7 it degraded to an unidentifiable oxidizable product. At pH 10, 1,2-diphenylhydrazine degraded to azobenzene, and at pH 4.7, it degraded into two unidentifiable products, which were not azobenzene or benzidine. In secondary municipal sewage effluent, Riggin and Howard (1979, 1982) reported that 100 µg/L of 1,2-diphenylhydrazine had a half-life of about 15 minutes in the presence of oxygen, and about 60 minutes when no oxygen was present. These results suggest that 1,2-diphenylhydrazine is unlikely to persist in the environment, particularly under aerobic conditions.

Weber and Wolfe (1986, 1987) reported that azobenzene, when incubated in air with four anaerobic lake sediments containing about 2-4% organic matter, was reduced to aniline with a reaction half-life of about 2700-5700 minutes, depending on the source and date of specimen collection. 1,2-Diphenylhydrazine was not detected as an intermediate. The authors postulate a four-electron mechanism involving the intermediate formation of 1,2-diphenylhydrazine.

In reporting the same data, Tabak et al. (1981a,b) and Patterson and Kodukala (1981) stated that 5 or 10 mg/L of 1,2-diphenylhydrazine was degraded up to 80% when initially cultured with settled domestic wastewater. This degradation rate, however, was reduced to 40% in the case of the 10 mg/L concentration, after the third subculture. The authors suggested that a de-adaptive and toxification process was occurring with 1,2-diphenylhydrazine. It is unclear if the analytical methods used by these authors would have been able to detect 1,2-diphenylhydrazine if present. Both dissolved organic carbon and gas chromatography (GC) analyses were performed on the samples. Considering the sample preparation procedures, however, the compound detected might not have been 1,2-diphenylhydrazine, but a decomposition product such as azobenzene.

### 5.3.2.3 Soil

No information concerning the fate of 1,2-diphenylhydrazine in soil was located in the literature. Based on the fate of 1,2-diphenylhydrazine in water and sediment, detectable concentrations probably will not persist for long periods, but this may depend on the initial concentration.

## 5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

The rapid oxidation of 1,2-diphenylhydrazine in water to form azobenzene and other compounds makes its sampling and analysis difficult. Storing a sample containing 1,2-diphenylhydrazine for even short periods can result in complete oxidation; in gas chromatography, 1,2-diphenylhydrazine is oxidized to azobenzene upon injection onto the chromatographic column (Riggin and Howard 1982). Therefore, unless sampling and analysis are performed under conditions that will prevent oxidation or unless concentrations of 1,2-diphenylhydrazine in the sample are very high, analyses of environmental samples for 1,2-diphenylhydrazine are inaccurate

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(Ahuja et al. 1988; Riggin and Howard 1979). It is doubtful that the concentrations measured reflect on the concentrations present in the sample at the time of collection (i.e., measured concentrations would underestimate actual concentrations (Riggin and Howard 1982)).

### 5.4.1 Air

No ambient air monitoring for 1,2-diphenylhydrazine was located in the literature. This may be due to both the rapid oxidation of 1,2-diphenylhydrazine and its low vapor pressure, which limit the amount of 1,2-diphenylhydrazine entering the atmosphere. In addition, no information was located suggesting that any studies have sought but not found 1,2-diphenylhydrazine.

### 5.4.2 Water

Two reported identifications of 1,2-diphenylhydrazine in water samples were located in the literature. Melton et al. (1981) reported that 1,2-diphenylhydrazine was present in Cincinnati, OH, drinking water (river water treated by coagulation, sand filtration, and chlorination). 1,2-Diphenylhydrazine was reported at a concentration of 1 ng/L. Since the sample preparation involved aeration and the original sample was chlorinated, it is unclear if the detected material was 1,2-diphenylhydrazine. Riggin and Howard (1982) found that, in addition to injection onto a GC column, either chlorination or aeration of a sample resulted in total disappearance of 1,2-diphenylhydrazine. Tang et al. (1983) reported 1,2-diphenylhydrazine in coal gasification wastewater at concentrations of 0.149 and 1.786 µg/L. Sample preparation in this case involved separation into classes by pH, liquid-liquid extraction, concentration, and gas chromatography/mass spectroscopy (GC/MS) analysis. No precautions were taken to reduce the aeration of the sample. Also, the analytical procedure indicates that no 1,2-diphenylhydrazine would have been able to survive the conditions of the sample preparation and the detection may be of another chemical or of 1,2-diphenylhydrazine from another source (e.g., decomposition of another compound to 1,2-diphenylhydrazine).

Hall et al. (1985) reported that no 1,2-diphenylhydrazine (less than 1 µg/L) was detected in the Nanticoke River near the Chesapeake Bay. The analytical method involved liquid-liquid extraction, concentration, and analysis by GC/MS. The Contract Laboratory Program statistical database (queried April 13, 1987) reported that 1,2-diphenylhydrazine has been detected in water at 1 of 357 hazardous waste sites at a concentration of 96 ppb (CLPSDB 1987), and has been reported at 7 of 1177 sites in the National Priority List database (ATSDR 1990). The U.S. EPA Contract Laboratory Program uses GC methods to analyze the contaminants of interest. Since 1,2-diphenylhydrazine oxidizes to azobenzene in the GC injector port and both 1,2-diphenylhydrazine and azobenzene have the same GC retention time and mass spectra, reports of 1,2-diphenylhydrazine from the Contract

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Laboratory Program may actually represent detections of 1,2-diphenylhydrazine, azobenzene, or both (see Chapter 6 for more details).

### 5.4.3 Soil

1,2-Diphenylhydrazine has been identified in soil only at hazardous waste sites. The Contract Laboratory Program statistical database (queried April 13, 1987) reported that 1,2-diphenylhydrazine has been detected in the soil at 2 of 357 hazardous waste sites in both cases at 18,200 ppm (CLPSDB 1987). The Contract Laboratory Program uses GC methods to analyze the contaminants of interest. As discussed in Section 5.4.2, this may actually represent detections of either 1,2-diphenylhydrazine or azobenzene (see Chapter 6 for more details). Furthermore, the fact that identical concentrations were reported increases uncertainty about the validity of the data.

### 5.4.4 Other Media

1,2-Diphenylhydrazine has been assayed but not detected in fish samples from the Great Lakes area. Camanzo et al. (1987) reported that no 1,2-diphenylhydrazine was detected in fish samples from 13 Lake Michigan tributaries and Grand Traverse Bay fish. Analyses were made by GC/MS and no detection limits were given. Similarly, DeVault (1985) reported that a GC/MS did not identify any of the peaks present in fish samples from Great Lakes Harbors and Tributaries as 1,2-diphenylhydrazine.

Phenylbutazone and sulfinpyrazone can hydrolyze to yield 1,2-diphenylhydrazine and these drugs may contain some 1,2-diphenylhydrazine (Ahuja et al. 1988; Fabre et al. 1984; Matsui et al. 1983). Phenylbutazone is a drug used for the treatment of inflammatory conditions (e.g., arthritis) and sulfinpyrazone is used to treat gouty arthritis. Although potential exists for exposure to 1,2-diphenylhydrazine via from treatment with these drugs, no information regarding body burden was located in the literature.

## 5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Virtually no information concerning general population or occupational exposure was located in the literature. General population exposure may come from those on phenylbutazone or sulfinpyrazone therapy, since these drugs may contain some 1,2-diphenylhydrazine (Fabre et al. 1984; Matsui et al. 1983). The National Institute for Occupational Safety and Health (NIOSH), National Occupational Exposure Survey (NOES) reported as of May 1988 that 977 total employees and 154 female employees are potentially exposed to 1,2-diphenylhydrazine (100% from actual observations) (NIOSH 1988).

The available database limits analysis of exposures in two ways. First, very little information is available concerning the manufacturing

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processes used in the production of phenylbutazone and sulfinpyrazone, the two drugs that use 1,2-diphenylhydrazine as a starting material. A better understanding of these processes would allow the estimation of worker exposure potentials. Second, dye manufacturers in the United States no longer produce benzidine based dyes (the last manufacturer stopped production in 1988) and the number of workers potentially exposed to 1,2-diphenylhydrazine is now less than at the time of the NOES survey cited above. Thus, the survey may no longer accurately reflect the number of workers potentially exposed to 1,2-diphenylhydrazine.

### 5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURE

The only populations with potentially high exposure appear to be persons receiving phenylbutazone or sulfinpyrazone therapy, those living near hazardous waste sites, and those in occupations that manufacture or use 1,2-diphenylhydrazine. Very little information concerning these populations, however, is available to clearly understand the extent of these potential exposures.

### 5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-diphenylhydrazine 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 1,2-diphenylhydrazine.

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 or eliminate the uncertainties of human health assessment. 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.** Physical and chemical properties are essential for estimating the partitioning of a chemical in the environment. Data are available for only a few physical and chemical properties of 1,2-diphenylhydrazine, and most of these have limited experimental descriptions. Therefore, an evaluation of the accuracy of the data is difficult. Specifically, measured solubility, vapor pressure,  $K_{oc}$ , pKa, and Henry's Law constant at environmentally significant temperatures would help to remove any doubt concerning the accuracy of the partitioning estimates, especially in circumstances where 1,2-diphenylhydrazine does not oxidize rapidly (such as when high concentrations are present). These data form the

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basis of much of the input requirements for environmental models that predict the behavior of a chemical under specific conditions including hazardous waste landfills. In addition, the uncertainty in these measurements can be used to estimate the sensitivity of these properties in determining the overall fate of 1,2-diphenylhydrazine in the environment.

**Production, Use, Release, and Disposal.** Production methods for 1,2-diphenylhydrazine are well described in the literature (including the patent literature); there does not appear to be a need for further information in this area. Uses of 1,2-diphenylhydrazine are documented but no recent production figures or detailed descriptions of uses are available. This information is useful for estimating the potential for environmental releases from manufacturing and use industries as well as the potential environmental burden, but it is difficult to obtain in the detail desired since it is considered confidential business information for those industries that manufacture 1,2-diphenylhydrazine. Release information is similar to use information in that it is not obtained easily and can be used to estimate environmental burdens and potentially exposed populations. A Toxic Release Inventory will provide some of this information in the future. Disposal information is useful for determining environmental burden and potential concentrations where environmental exposures may be high. Data on different disposal methods for 1,2-diphenylhydrazine are lacking. According to the Emergency Planning and Community Right to Know Act of 1986 (EPCRTKA), (§313), (Pub. L. 99-499, Title III, §313), industries are required to submit release information to the EPA. The Toxic Release Inventory (TRI), which contains release information for 1987, became available in May of 1989. This database will be updated yearly and should provide a more reliable estimate of industrial production and emission.

**Environmental Fate.** Photolysis, photooxidation, and chemical oxidation studies in air and water are lacking, as are persistence studies in soil and groundwater. These kinds of studies are important since they address the fundamental removal mechanisms available to 1,2-diphenylhydrazine in the environment. In addition, removal mechanisms such as atmospheric photooxidation may be several orders of magnitude faster than any other removal mechanism; understanding these reactions is crucial to an understanding of the fate of 1,2-diphenylhydrazine in the environment. Biodegradation studies in water may not be important, even though they are lacking, since 1,2-diphenylhydrazine oxidizes rapidly.

**Bioavailability from Environmental Media.** No studies were located regarding the bioavailability of 1,2-diphenylhydrazine from environmental media, but lack of these data does not necessarily indicate a lack of bioavailability. As exposure to 1,2-diphenylhydrazine could occur at waste sites by dermal contact with contaminated soil or by ingestion of contaminated soil, it would be useful to know if dermal or oral absorption of 1,2-diphenylhydrazine from environmental media could occur. Information on dermal absorption of 1,2-diphenylhydrazine from other media is not



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available, but qualitative evidence indicates that 1,2-diphenylhydrazine in diet or oil media is absorbed from the gastrointestinal tract (Section 2.3).

**Food Chain Bioaccumulation.** 1,2-Diphenylhydrazine reacts rapidly in water to form azobenzene and other oxidation products (half-life in wastewater is 60 minutes). Because of this and based upon the log octanol/water partition coefficient, no bioaccumulation is expected in any aquatic organism.

**Exposure Levels in Environmental Media.** Environmental monitoring data are not available or are of questionable accuracy for water, soil, and air. These data would be helpful in determining the ambient concentrations of 1,2-diphenylhydrazine so that exposure estimates for the general population could be made as well as 1,2-diphenylhydrazine exposure estimates for terrestrial and aquatic organisms.

**Exposure Levels in Humans.** The database for exposure levels in humans is very limited, and it is unclear if an exposed population exists given the rapid disappearance of 1,2-diphenylhydrazine from the environment. While a more complete database would be helpful in determining the current exposure levels and thereby estimating the average daily dose associated with various scenarios (e.g., living near a hazardous waste site, taking phenylbutazone), a number of factors limit establishing such a program, including the lack of appropriate analytical methods.

**Exposure Registries.** An exposure registry is not available. The development of such a registry would be a useful reference tool in assessing exposure levels and frequency. In addition, a registry would allow an assessment of the variations in exposure concentrations from, for example, geography, season, regulatory actions, presence of hazardous waste landfills, or manufacturing and use facilities. These assessments, in turn, would provide a better understanding of the need for research or data acquisition based on the current exposure concentrations.

### 5.7.2 On-Going Studies

No on-going studies were located in the literature.