TOXICOLOGICAL PROFILE FOR METHYL MERCAPTAN

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

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The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the Federal Register on April 17, 1987; on October 20, 1988; on October 26, 1989; and on October 17, 1990. A revised list of 275 substances was published on October 17, 1991.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the lists. Each profile must include the following content:

(A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and adverse health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicological properties. Other pertinent literature is also presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Foreword

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

William L. Roper, M.D., M.P.H.
Administrator
Agency for Toxic Substances and
Disease Registry

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1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about methyl mercaptan and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,300 sites on its National Priorities List (NPL). Methyl mercaptan has been found in at least 2 of these sites. However, we do not know how many of the 1,300 NPL sites have been evaluated for methyl mercaptan. As EPA evaluates more sites, the number of sites at which methyl mercaptan is found may change. This information is important for you to know because methyl mercaptan may cause harmful health effects and because these sites are potential or actual sources of human exposure to methyl mercaptan.

When a chemical is released from a source, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment as a chemical emission. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous chemical such as methyl mercaptan, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

1.1 WHAT IS METHYL MERCAPTAN?

Methyl mercaptan, also known as methanethiol, is a colorless gas with a smell like rotten cabbage. It is a natural substance found in the blood, brain, and other tissues of humans and other animals, and it is released from animal feces. It occurs naturally in certain foods such as some nuts (filberts) and cheese (Beaufort).

Methyl mercaptan is released from decaying organic matter in marshes and is present in the natural gas of certain regions of the United States, in coal tar, and in some crude oils. Methyl mercaptan is manufactured for use in pesticides, as a jet fuel additive, in the plastics industry, and in making methionine, a nutrient that is added to poultry feed. Methyl mercaptan is also released as a decay product of wood in pulp mills.

We know very little about what happens to methyl mercaptan after it is released to the environment. Because it is a gas, most of it probably goes into the air. Sunlight can break it down into other substances. If methyl mercaptan is released to soil, it probably then goes into the air or is

carried through the soil by rain or any other water that contacts it. More information on the properties and uses of methyl mercaptan and how it behaves in the environment can be found in Chapters 3, 4 and 5.

1.2 HOW MIGHT I BE EXPOSED TO METHYL MERCAPTAN?

Methyl mercaptan is always present in your body and in your urine and feces. It can also be present in the breath of persons with liver damage. You can be exposed to methyl mercaptan in the air if you live near a natural source of this gas, such as a marsh, an underground gas pocket, or a dump site that releases it. We have no information on the levels of methyl mercaptan that come from these sources.

Methyl mercaptan has not been found in drinking water, so you would probably not be exposed to it in this way. Methyl mercaptan is a natural part of certain foods, such as nuts and cheeses. It has also been approved for use as a food additive. Because of its unpleasant smell, very little can be added to food. You could be exposed to small amounts of methyl mercaptan by eating foods that contain it. However, we have no information on the levels of methyl mercaptan in food.

You can be exposed to methyl mercaptan if you work at a wood-pulp mill or sewage treatment plant or if you work in a factory that uses it to make other products such as jet fuel, pesticides, or poultry feed. Measurements of methyl mercaptan in the air inside these mills were lower than 4 ppm (4 parts of methyl mercaptan per million parts of air). Methyl mercaptan has been found in the environmental air at 4 ppb (4 parts of methyl mercaptan per billion parts of air).

Levels of methyl mercaptan in soil are probably very low. Even at hazardous waste sites, the levels were about 83 ppb. More information on how you might be exposed to methyl mercaptan is given in Chapter 5.

1.3 HOW CAN METHYL MERCAPTAN ENTER AND LEAVE MY BODY?

Methyl mercaptan can enter your body when you breathe in air or eat food that contains this chemical. We do not know if methyl mercaptan can enter your body through the skin or what happens to it after it enters your body. Studies in rats suggested it leaves the body quickly. After methyl mercaptan reaches the blood, it is either breathed out unchanged or is broken down to other substances (within one hour). These substances may be breathed out from the lungs or leave the body with the urine within a few hours.

More information on how methyl mercaptan enters and leaves the body is given in Chapter 2.

1. PUBLIC HEALTH STATEMENT

1.4 HOW CAN METHYL MERCAPTAN AFFECT MY HEALTH?

We have very little information on the health effects of exposure to methyl mercaptan. A worker exposed to very high levels (exact amount unknown) of this compound for several days when he opened and emptied tanks of methyl mercaptan went into a coma (became unconscious), developed anemia (a blood disorder) and internal bleeding. He died within a month after this incident.

We do not know whether long-term exposure of humans to low levels of methyl mercaptan can result in harmful health effects such as cancer, birth defects, or problems with reproduction.

Methyl mercaptan can be smelled and recognized in air when it is there at a level of about 1.6 ppb (1.6 parts of methyl mercaptan per billion parts of air). It can be smelled when it is present in water at a level far lower than 1 ppb.

More information on the health effects of methyl mercaptan in humans and animals can be found in Chapter 2.

1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO METHYL MERCAPTAN?

Methyl mercaptan is always present in your body. There is a test that can be used to find out if it is present in your blood at levels that are higher than normal, which may happen if you are exposed to high levels of this substance. This test requires special equipment and is not usually available in a doctor's office. It can be done in a special laboratory. However, this test cannot be used to find out how much methyl mercaptan you were exposed to or to predict whether harmful health effects will occur.

More information on how methyl mercaptan can be measured in exposed humans is given in Chapters 2 and 6.

1.6 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government has set certain regulations and guidelines to help protect people from the possible harmful health effects of methyl mercaptan in the environment. When more than 100 pounds of methyl mercaptan is released to the environment (such as during an industrial accident or spill), the EPA National Response Center must be notified. The Food and Drug Administration (FDA) allows methyl mercaptan to be used as a food additive but does not set specific limits on the levels that can be used. The Occupational Safety and Health Administration (OSHA) has set an average limit of 0.5 ppm for exposure to this chemical in workplace air. The American Conference of

Governmental Industrial Hygienists (ACGIH) has recommended that the average concentration of airborne methyl mercaptan should not be more than 0.5 ppm for each 8-hour exposure (time-weighted average) in a 40-hour work week.

More information on governmental rules for methyl mercaptan can be found in Chapter 7.

1.7 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

This agency can also provide you with information on the location of the nearest occupational and environmental health clinic. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of methyl mercaptan and a depiction of significant exposure levels associated with various adverse health effects. It contains descriptions and evaluations of studies and presents levels of significant exposure for methyl mercaptan based on toxicological studies and epidemiological investigations.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure--inhalation, oral, and dermal--and then by health effect--death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods--acute (less than 15 days), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear. They should also help to determine whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the tables and figures may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons may be interested in levels of exposure associated with "serious" effects. Public health officials and project managers concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) may be of interest to health professionals and citizens alike.

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer effect for each exposure duration. MRLs include adjustments to reflect human variability from laboratory animal data to humans.

2. HEALTH EFFECTS

Although methods have been established to derive these levels (Barnes et al. 1988; EPA 1989b), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

2.2.1 Inhalation Exposure

Very little information is available on the health effects in humans or experimental animals after inhalation exposure to methyl mercaptan. Most studies of occupational exposure to methyl mercaptan in the pulp industry also involve exposure to other sulfur-containing compounds such as hydrogen sulfide, dimethyl sulfide, and sulfur dioxide as well as to methyl mercaptan (Kangas et al. 1984).

2.2.1.1 Death

A single case of death resulting from occupational exposure to methyl mercaptan has been located. A 53-year-old Black male laborer worked for about 1 week emptying tanks containing methyl mercaptan. No details of exposure level were available; however, it is assumed that both inhalation and dermal exposure were probably involved. The man was hospitalized in a coma, developed hemolytic anemia and methemoglobinemia, and died 28 days after admission (Shults et al. 1970). The immediate cause of death was determined to be a massive embolus that occluded both main pulmonary arteries.

An LC_{50} of 675 ppm was reported for male and female rats exposed to methyl mercaptan for 4 hours (Tansy et al. 1981). However, no deaths (O/10) occurred in rats exposed to 400 ppm for 4 hours, and there was 100% mortality at 700 ppm and above. These authors also reported that no mortality was observed in male rats exposed to methyl mercaptan at doses up to 57 ppm for 3 months.

The highest NOAEL values and an LC_{50} for rats in each duration category are recorded in Table 2-l and plotted in Figure 2-1.

2.2.1.2 Systemic Effects

Based on the available information, effects on body weight are the only systemic effects that can be clearly associated with inhalation exposure to methyl mercaptan. No studies were located regarding musculoskeletal effects in humans or animals after inhalation exposure to methyl mercaptan.

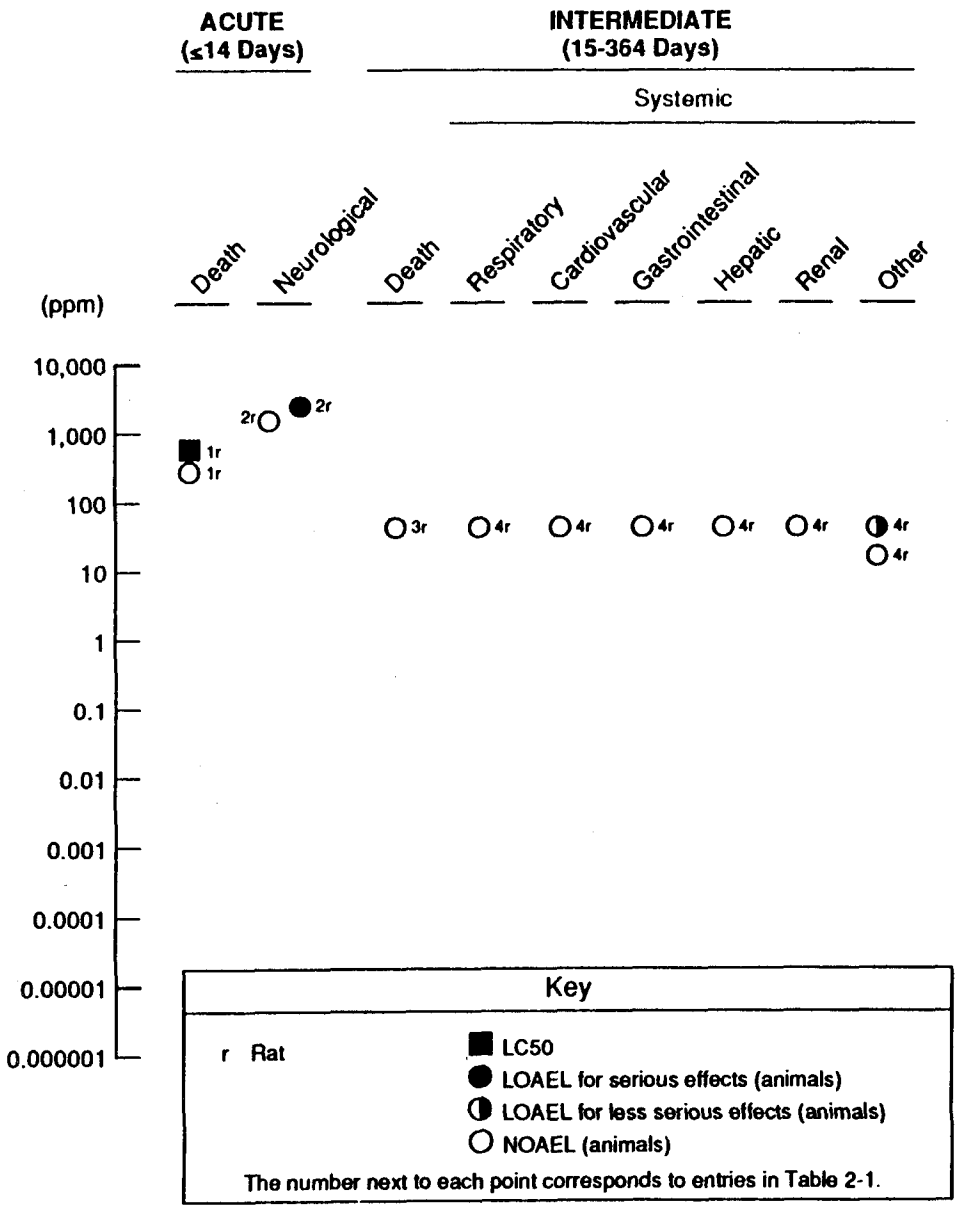
TABLE 2-1. Levels of Significant Exposure to Methyl Mercaptan - Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
ACUTE EXPOSURE							
Death							
1	Rat	1 d 4hr/d		400		675 (LC50)	Tansy et al. 1981
Neurological							
2	Rat	1 d 15 min		1200		1400 (coma)	Zieve et al. 1984
INTERMEDIATE EXPOSURE							
Death							
3	Rat	3 mo 5d/wk 7hr/d		57			Tansy et al. 1981
Systemic							
4	Rat	3 mo 5d/wk 7hr/d	Resp	57			Tansy et al. 1981
			Cardio	57			
			Gastro	57			
			Hepatic	57			
			Renal	57			
			Other	17	57 (decreased body weight)		

[a]The number corresponds to entries in Figure 2-1.

Cardio = Cardiovascular; d = day(s); Gastro = Gastrointestinal; hr = hour(s); LC50 = lethal concentration, 50% mortality; LOAEL = lowest-observed-adverse-effect level; min = minute(s); mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = Respiratory; wk = week(s)

FIGURE 2-1. Levels of Significant Exposure to Methyl Mercaptan – Inhalation



2. HEALTH EFFECTS

A NOAEL and a reliable LOAEL for systemic effects in rats in the intermediate-duration category are recorded in Table 2-1 and plotted in Figure 2-l.

Respiratory Effects. No studies have been located that would be useful in assessing the potential effects on the respiratory system in humans breathing methyl mercaptan. Irritation of mucous membranes of the nose and respiratory tract have been reported by workers exposed to mercaptans in general (Key et al. 1977).

No compound-related histopathological changes were observed in the lungs of male rats exposed to methyl mercaptan at doses up to 57 ppm, 7 hours/day, 5 days/week, for 3 months (Tansy et al. 1981).

Cardiovascular Effects. Increased pulse rate and blood pressure were reported by Shults et al. (1970) in a 53-year-old comatose patient who had been working with tanks of methyl mercaptan. Exposure level data were not available.

No histopathological changes were found in the hearts of male rats exposed to methyl mercaptan at levels up to 57 ppm, 7 hours/day, 5 days/week, for 3 months (Tansy et al. 1981).

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans after inhalation exposure to methyl mercaptan.

No evidence of histopathological changes was found in the small intestines of male rats exposed to methyl mercaptan at levels up to 57 ppm, 7 hours/day, 5 days/week, for 3 months (Tansy et al. 1981). Intestinal transit performance, as measured by the amount of small intestine traversed in 30 minutes, was not found to be affected by exposure in this study. There was, however, a statistically significant dose-related decrease in the length of the small intestines at 17 ppm and above. However, the clinical significance of this observation is not clear, and it is not viewed as a serious adverse effect.

Hematological Effects. The only information on hematologic effects resulting from human inhalation and presumably dermal exposure to methyl mercaptan is a case report by Shults et al. (1970). A Black 53-year-old worker who had been handling and emptying tanks of methyl mercaptan for about 1 week became comatose and developed methemoglobinemia and hemolytic anemia before his death. After transfusions, these conditions were reversed. The authors postulated that the hemolysis may have been due to the oxidant effect of methyl mercaptan on erythrocytes in a person who was deficient in glucose-6-phosphate dehydrogenase (G-6-PD). An inherited deficiency of this

enzyme may be common in American Blacks (Calabrese 1986; Goldstein et al. 1974; Shannon and Buchanan 1982). This worker was found to have some degree of G-6-PD deficiency (Shults et al. 1970).

No studies were located regarding hematological effects in animals after inhalation exposure to methyl mercaptan.

Hepatic Effects. No studies were located regarding hepatic effects in humans after inhalation exposure to methyl mercaptan.

In male rats exposed to methyl mercaptan at levels up to 57 ppm, 7 hours/day, 5 days/week, for 3 months, no compound-related histopathologic changes of the liver were noted (Tansy et al. 1981). The authors stated that results of blood chemistry studies (i.e., increased total protein with decreased serum albumin) were suggestive of liver damage, but that dehydration could not be ruled out as the cause.

Renal Effects. No studies were located regarding renal effects in humans after inhalation exposure to methyl mercaptan. Shults et al. (1970) reported that bilateral polycystic kidneys were found during the autopsy of a 53-year-old man who died after working with tanks of methyl mercaptan. However, it is possible that this was a pre-existing condition.

No compound-related histopathologic changes in the kidneys of male rats exposed to methyl mercaptan at levels up to 57 ppm, 7 hours/day, 5 days/week, for 3 months (Tansy et al. 1981).

Dermal/Ocular Effects. Irritation of the skin and eyes have been reported by workers occupationally exposed to mercaptans in general (Key et al. 1977). However, there is no available information that is specifically related to methyl mercaptan.

No studies were located regarding dermal or ocular effects in animals after inhalation exposure to methyl mercaptan.

Other Systemic Effects. No studies were located regarding other systemic effects in humans after inhalation exposure to methyl mercaptan. Male rats exposed to methyl mercaptan at 57 ppm for 7 hours/day, 5 days/week, for 3 months had significantly decreased body weights (Tansy et al. 1981). This effect was not observed in rats exposed to 17 ppm and below. Decreased levels of food consumption were not observed in rats in the 57-ppm dose group.

2.2.1.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals after inhalation exposure to methyl mercaptan.

2.2.1.4 Neurological Effects

The only available information on neurological effects in humans exposed to methyl mercaptan via inhalation is from a case study by Shults et al. (1970). A 53-year-old man went into an irreversible coma after emptying tanks of methyl mercaptan for about 1 week. Levels of exposure were not estimated.The authors also noted minimal movement in response to painful stimuli, hypoactivity of all deep tendon reflexes, and seizure activity. The patient died about one month after the onset of this coma.

Fifteen-minute exposures to methyl mercaptan at 1,400 ppm have been found to result in lethargy or coma in rats (Zieve et al. 1974). Exposures to 1,200 ppm and below did not result in either of these conditions. A methyl mercaptan concentration of 0.5 nmol/mL in the blood was identified as the level associated with coma. This study also demonstrated that the doses of intraperitoneally injected ammonium acetate or sodium octanoate needed to induce hepatic coma (coma following acute necrosis of the liver) were greatly reduced when animals were exposed to methyl mercaptan at 1,200 ppm within 1 minute after injection. (However, hepatic effects were not actually demonstrated in this study.) The authors suggested that methyl mercaptan exposure may intensify the toxic effects of ammonia and fatty acids in human hepatic failure.

These values are recorded in Table 2-l and plotted in Figure 2-l.

No studies were located regarding the following health effects in humans or animals after inhalation exposure to methyl mercaptan:

2.2.1.5 Developmental Effects
2.2.1.6 Reproductive Effects
2.2.1.7 Genotoxic Effects
2.2.1.8 Cancer
2.2.2 Oral Exposure

No studies were located regarding the following health effects in humans or animals after oral exposure to methyl mercaptan:

2.2.2.1 Death
2.2.2.2 Systemic Effects
2.2.2.3 Immunological Effects
2.2.2.4 Neurological Effects
2.2.2.5 Developmental Effects
2.2.2.6 Reproductive Effects
2.2.2.7 Genotoxic Effects
2.2.2.8 Cancer

2.2.3 Dermal Exposure

Occupational exposure as reported in the case study by Shults et al. (1970) may have involved dermal exposure since the victim's wife noted a repugnant odor on his clothes; however, there is not enough information to assess this possibility.

No studies were located regarding the following health effects in humans or animals after dermal exposure to methyl mercaptan:

2.2.3.1 Death
2.2.3.2 Systemic Effects
2.2.3.3 Immunological Effects
2.2.3.4 Neurological Effects
2.2.3.5 Developmental Effects
2.2.3.6 Reproductive Effects
2.2.3.7 Genotoxic Effects
2.2.3.8 Cancer
2.2.4 Other Routes of Exposure

Because the available data on the toxicity of methyl mercaptan via inhalation, oral, or dermal exposure are extremely limited, studies conducted via intraperitoneal exposure have also been considered. These studies are also limited in number and scope, and serve only to provide additional evidence that coma is associated with exposure to this chemical.

2.2.4.1 Death

No information is available on the levels of methyl mercaptan administered to animals via intraperitoneal injection that would result in death. Studies described in Section 2.2.4.4 have resulted in coma in the test animals; however, recovery and/or death in response to these injections were not among the topics of investigation.

2.2.4.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or dermal/ocular effects in humans or animals after intraperitoneal exposure to methyl mercaptan.

2.2.4.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals after intraperitoneal exposure to methyl mercaptan.

2.2.4.4 Neurological Effects

Two studies that investigated the neurological effects of intraperitoneal administration of methyl mercaptan have been located. An injection equivalent to 4.8 mg/kg was sufficient to induce coma in 100% of treated rats in 2-4 minutes (Zieve et al. 1984). In germ-free rats administered methyl mercaptan at 9.6-28.8 mg/kg, 200 nmol/mL was the minimum blood concentration associated with coma (Al Mardini et al. 1984). It is interesting to note that this level was much higher than the blood level of 0.5 nmol/mL in comatose rats reported by Zieve et al. (1974) in inhalation studies.

In addition, an important observation was made by Al Mardini et al. (1984) who reported that blood methyl mercaptan concentrations were significantly higher in patients with hepatic encephalopathy (coma) than in normal subjects or patients with liver disease without encephalopathy. (Methyl mercaptan was not administered to any of these persons, but presumably resulted from the endogenous breakdown of methionine.) Methyl mercaptan concentrations were also higher (but not significantly) in the blood of liver disease patients without encephalopathy than in normal subjects. These findings, combined with the observations of Zieve et al. (1974) in rats with liver damage from ammonium ion or octanoate (Section 2.2.1.4), suggest that persons with existing liver damage may already have elevated blood levels ofmethyl mercaptan and thus may be at greater risk for the neurological effects of exposure to exogenous methyl mercaptan than would be persons with normal livers.

No studies were located regarding the following health effects in humans or animals after intraperitoneal exposure to methyl mercaptan:

2.2.4.5 Developmental Effects
2.2.4.6 Reproductive Effects
2.2.4.7 Genotoxic Effects
2.2.4.8 Cancer

2.3 TOXICOKINETICS

The only studies located on the toxicokinetics of methyl mercaptan have been conducted via the intraperitoneal route. There is indirect evidence of absorption of methyl mercaptan by humans in a human case study and by rats in a toxicity study.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

Based on adverse effects (hemolysis, methemoglobinemia, coma, and death)reported in a 53-year-old worker exposed to methyl mercaptan via inhalation

(Shults et al. 1970) and on the induction of coma in rats exposed to 1,400 ppm (Zieve et al. 1974), it can be inferred that absorption occurs via this route of exposure. No other data are available.

2.3.1.2 Oral Exposure

No studies were located regarding absorption in humans or animals after oral exposure to methyl mercaptan.

2.3.1.3 Dermal Exposure

No studies were located regarding absorption in humans or animals after dermal exposure to methyl mercaptan.

2.3.2 Distribution

No studies were located regarding distribution in humans or animals after exposure to methyl mercaptan via the following routes:

2.3.2.1 Inhalation Exposure
2.3.2.2 Oral Exposure
2.3.2.3 Dermal Exposure
2.3.2.4 Other Routes of Exposure

After injection of ^{14}C- or 35_S-labeled methyl mercaptan into rats, distribution of the radioactivity that remained in the body (from either the 14C or 35_S label) after 6 hours was: 22.7% in plasma proteins, 17.8% in the liver, 16.7% in the intestinal mucosa, 11.5% in the lungs, 11.4% in the kidneys, 9.8% in the spleen, 8.5% in the testes, and 0% in the erythrocytes (Canellakis and Tarver 1953). No other information on the distribution of methyl mercaptan was located.

2.3.3 Metabolism

Information on the metabolism of methyl mercaptan is available only in studies in rodents using intraperitoneal administration. Susman et al. (1978) injected methyl mercaptan into one mouse and found the unchanged compound and dimethyl sulfide in the expired breath.

In rats, intraperitoneal administration of methyl mercaptan resulted in the excretion of CO_2 and volatile sulfur-containing compounds in the expired breath (Canellakis and Tarver 1953). The ^{35}S from labeled methyl mercaptan in injected rats could be found mostly (94%) as $^{35}S0_4$ in urine (Derr and Draves 1983, 1984).

2. HEALTH EFFECTS

Methyl mercaptan is an intermediate in the catabolism of the amino acid methionine (Blom et al. 1988, 1989). These in vitro studies were conducted with the blood of methionine-loaded patients and with human and rat hepatocytes. Blom and Tangerman (1988) found that, in whole blood, methyl mercaptan is oxidized by the erythrocytes, the carbon-sulfur bond is split, and the resulting products are formic acid, sulfite ion, and sulfate ion.

2.3.4 Excretion

No studies were located regarding excretion by humans or animals after exposure to methyl mercaptan via the following routes:

2.3.4.1 Inhalation Exposure
2.3.4.2 Oral Exposure
2.3.4.3 Dermal Exposure
2.3.4.4 Other Routes of Exposure

The only information available on the excretion of methyl mercaptan or its metabolites is found in studies in rats conducted via intraperitoneal administration. Within 6 hours after administration of ^{14}C-methyl mercaptan, more than 40% of the administered ^{14}C was recovered as CO_2 (presumed to result solely from pulmonary excretion) (Canellakis and Tarver 1953). Another 6.4% was excreted in 1 hour in volatile sulfur compounds (route not stated), and 2.3% was excreted in the urine within 6 hours. Within 8 hours after administration of ^{35}S-methyl mercaptan, 32% of the administered 35S was recovered in sulfur compounds (mostly sulfates) in the urine. Derr and Draves (1983), however, found that within 21 hours, 94% of the ^{35}S-label of ^{35}S-methyl mercaptan intraperitoneally administered to rats was excreted in the urine. No data on fecal excretion have been located.

2.4 RELEVANCE TO PUBLIC HEALTH

As discussed in Section 2.2, estimates of levels of exposure to methyl mercaptan posing minimal risk to humans (MRLs) were to have been made, where data were believed reliable, for the most sensitive noncancer effect for each route and exposure duration. However, no MRLs could be derived for methyl mercaptan. Available data on effects of acute-duration inhalation exposure to methyl mercaptan in humans or animals suggests that neurological effects may be the most sensitive indicator of toxicity, but this information does not reliably identify the threshold for this effect. Available data on effects of intermediate-duration inhalation exposure to methyl mercaptan in animals does not identify the most sensitive effect or the threshold for adverse effects. No data were located on effects of chronic-duration inhalation exposure to methyl mercaptan in humans or animals. Therefore, no inhalation MRLs were derived. No data were located on effects of acute-duration, intermediate duration, or chronic-duration oral exposure to methyl mercaptan in humans or

animals, Therefore, no oral MRLs were derived. Acute-duration, intermediate duration, and chronic-duration dermal MRLs were not derived for methyl mercaptan due to the lack of an appropriate methodology for the development of dermal MRLs.

The observations in a single human case study, combined with the results of studies in animals, suggest that the principal health risk associated with short-term exposure to high levels of methyl mercaptan is coma. Hematological effects such as hemolytic anemia and methemoglobinemia may also result, but there is less information on this topic. In total, the available database on this chemical is so limited that the relevance of methyl mercaptan exposure to public health cannot be determined.

Death. The accidental death of a 53-year-old worker who had been handling tanks of methyl mercaptan for 1 week was reported by Shults et al. (1970). After a month in a coma and despite aggressive medical intervention, the patient died from a massive embolus that occluded both main pulmonary arteries. The exposure level was not known or estimated. An LC_{50} of 675 ppm was determined for a 4-hour exposure in rats (Tansy et al. 1981). However, no deaths (O/10) occurred at 400 ppm. Exposure to 57 ppm for 3 months also resulted in no deaths in rats. The available data indicate that high level exposure to this substance, at least by inhalation, can be lethal to exposed humans and animals.

Systemic Effects.

Hematological Effects. The major systemic effects reported in the case study of the 53-year-old Black worker who died after acute inhalation exposure to methyl mercaptan were methemoglobinemia and hemolytic anemia (Shults et al. 1970). The authors stated that the observed hemolysis may have been due to oxidant stress to erythrocyte membranes with glucose-6-phosphate dehydrogenase deficiency. In an analysis of hospital data on 14 Black children (aged 3 weeks to 11 years) with hemolytic anemia, 7 of these patients were found to be deficient in glucose-6-phosphate dehydrogenase in an initial screening test (Shannon and Buchanan 1982). Similarly, methemoglobinemia susceptibility has been attributed to this enzyme deficiency (Goldstein et al. 1974). It is obviously not possible to draw firm conclusions from the single case study presented by Shults et al. (1970) with no other studies in humans or animals to provide evidence. However, that study does provide consistent preliminary evidence for the potential for hematological effects resulting from inhalation exposure to methyl mercaptan by an individual who may also be deficient in erythrocytic glucose-6-phosphate dehydrogenase.

Other Systemic effects. The only systemic effect clearly associated with methyl mercaptan in an animal study was a significant decrease in body weight in rats exposed to methyl mercaptan by inhalation at 57 ppm for 3 months (Tansy et al. 1981). This suggests that effects on body weight may be of concern for humans exposed to methyl mercaptan.

Immunological Effects. There is currently no information in humans or animals to suggest that exposure to methyl mercaptan is associated with immunological effects.

Neurological Effects. The main neurotoxic effect reported in a human exposed to methyl mercaptan at high levels is coma. Shults et al. (1970) reported that a 53-year-old worker who had been working with tanks of methyl mercaptan for about a week went into an irreversible coma accompanied by convulsions and died about 1 month later. Rats exposed via inhalation to methyl mercaptan at 1,400 ppm, but not 1,200 ppm or below, for 15 minutes became lethargic or comatose (Zieve et al. 1974). Intraperitoneal injections of methyl mercaptan in rats can also induce coma (Al Mardini et al. 1984; Zieve et al. 1984). Although this route of administration is not relevant to potential human exposure to this compound, these studies serve to provide additional evidence that neurological effects are a major risk when methyl mercaptan is absorbed by humans.

Developmental Effects. There is currently no information in humans or animals to suggest that exposure to methyl mercaptan is associated with developmental effects, therefore the relevance to human health is not known.

Reproductive Effects. There is currently no information in humans or animals to suggest that exposure to methyl mercaptan is associated with reproductive effects, therefore the relevance to human health is not known.

Genotoxic Effects. There is currently no information in humans or animals to suggest that exposure to methyl mercaptan is associated with genotoxic effects, therefore the relevance to human health is not known.

Cancer. There is currently no information in humans or animals to suggest that exposure to methyl mercaptan is associated with cancer effects, therefore the relevance to human health is not known.

2.5 BIOMAREERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid(s) or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high

urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time biologic samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to methyl mercaptan are discussed in Section 2.5.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are often not substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by methyl mercaptan are discussed in Section 2.5.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, biologically effective dose, or target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, "POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE."

2.5.1 Biomarkers Used to Identify and/or Quantify Exposure to Methyl Mercaptan

Methyl mercaptan itself and its metabolites, carbon dioxide and sulfate, can be measured in human tissues, fluid, and excreta. However, these compounds are always present in these media regardless of exposure to methyl mercaptan. Elevated blood levels of methyl mercaptan may be detected in persons who have recently been exposed to it, or in nonexposed persons with liver disease or in hepatic coma (Al Mardini et al. 1984; Challenger and Walshe 1955; Zieve 1981). In cases of liver damage, these elevated levels may be the result, rather than the cause, of liver problems.

The best indication of exposure to methyl mercaptan would probably be a combination of elevated levels of the substance itself in the breath and blood along with evidence or suspicion of exposure from environmental sources. There are currently no subtle or sensitive biomarkers of effects associated with exposure to methyl mercaptan.

2.5.2 Biomarkers Used to Characterize Effects Caused by Methyl Mercaptan

As stated previously, no subtle or sensitive biomarkers of effects associated with exposure to methyl mercaptan have been identified.

2.6 INTERACTIONS WITH OTHER CHEMICALS

Interactions between mercaptans, including methyl mercaptan, and Ammonium acetate or sodium octanoate in the induction of coma in rats has been reported (Zieve et al. 1974). The dose of intraperitoneally injected ammonium acetate required to induce coma in 50% of the rats was 1.45 mmols without methyl mercaptan exposure but only 0.46 mmols when the animals were exposed to methyl mercaptan via inhalation at 1,200 ppm within 1 minute after the injection. Similarly, the dose of sodium octanoate decreased from 0.48 to 0.16 mmols to induce coma using the same procedures.

The condition induced in these rats was referred to as "hepatic coma" (Zieve et al. 1974) because it was demonstrated in a previous study that injection of an ammonium salt or fatty acid into rats resulted in coma accompanied by massive hepatic necrosis. In the current study of synergism, Zieve et al. (1974), hepatic damage was assumed but not demonstrated, and it is not clear if methyl mercaptan exposure resulted in increased hepatic damage in these rats. These results suggest, however, that human exposure to methyl mercaptan in conjunction with hepatotoxins may result in exacerbated liver damage and/or neurotoxicity. There is a possibility of these multiple exposures in the workplace and in the vicinity of hazardous waste sites.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A hemolytic response to methyl mercaptan exposure, as reported in the case study by Shults et al. (1970), may be enhanced by the presence of inherited erythrocytic glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. Although hemolysis may occur in any person who is exposed to a sufficiently high dose of methyl mercaptan, this enzyme deficiency may cause some persons to be unusually sensitive, since it results in an inability to maintain reduced glutathione which is needed for the integrity of the erythrocyte membrane (Goldstein et al. 1974). The incidence of the deficiency among Caucasians of European origin is relatively low, whereas there is a higher incidence among certain groups of Asians and Mediterranean (Italians, Sardinians, Greeks), and Middle Eastern populations (Shannon and Buchanan 1982). A study of hemolytic anemia in American Black children with G-6-PD deficiency by Shannon and Buchanan (1982) suggests that this is another population that may be susceptible to the hemolytic effects of methyl mercaptan exposure. Calabrese (1986) estimated that 16% of Black males are G-6-PD-deficient; Berkow et al. (1982) estimated that 10% of American Black

males and fewer Black females have this deficiency. According to Shannon and Buchanan (1982), a syndrome of acute severe hemolysis following exposure to oxidative stress is associated with the Mediterranean variant of the deficiency, whereas the hemolytic anemia seen in American Blacks is generally mild.

The pattern of inheritance for G-6-PD deficiency is that of an autonomous sex-linked defect (Berkow et al. 1982; Goldstein et al. 1974). This is an X-linked disorder and is thus fully expressed in males who carry it on their single X chromosome and in females who carry it on both X chromosomes. Female heterozygotes (who have one normal and one defective gene for this trait) have a wide variety of values for the enzyme which suggests that other factors influence the degree to which this trait is influenced in identical genotypes (Goldstein et al. 1974).

Studies by Zieve et al. (1974) and Al Mardini et al. (1984) suggest that the major neurological effects of methyl mercaptan exposure (i.e., coma) may occur at lower levels of this compound in persons with liver disease. Methyl mercaptan levels may already be higher than normal in these persons and additional exposure may bring their blood concentrations of this compound to a more dangerous level.

2.8 MITIGATION OF EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to methyl mercaptan. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to methyl mercaptan. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

Inhalation is the primary route of human exposure to methyl mercaptan, although dermal absorption or ingestion of small amounts in food or water may occur (see Chapter 5). General procedures following acute, high-level exposure to methyl mercaptan consist of measures to reduce or eliminate further absorption. Following inhalation exposure, these measures include removal of the victim and administration of high-flow, humidified oxygen (Bronstein and Currance 1988; Stutz and Janus2 1988). Following dermal and ocular exposure, contaminated clothing is removed and the skin and eyes thoroughly washed with water (Bronstein and Currance 1988; Stutz and Janusz 1988). Procedures used following acute, high-level oral exposure include emptying the stomach, using care to avoid pulmonary aspiration of the gastric contents, particularly in victims with severe nervous system depression or seizures. Stomach emptying is followed by administration of activated charcoal to bind the methyl mercaptan and a cathartic which may stimulate fecal excretion (Stutz and Janusz 1988).

Supportive measures for symptoms induced by acute, high-level exposure to methyl mercaptan include administration of anticonvulsant drugs to control seizures (Stutz and Janusz 1988) and blood transfusion or alkaline diuresis to alleviate effects of hemolysis (Shannon and Buchanan 1982; Shults et al. 1970). Supportive treatment for noncardiogenic pulmonary edema, central nervous system depression, and hypertension with tachycardia may be required. In patients with methemoglobinemia of approximately 30% or greater methylene blue is administered to reduce methemoglobin levels (Ellenhorn and Barceloux 1988; Goldfrank et al. 1990). However, treatment of G-6-PD deficient individuals with methylene blue may be contraindicated.

Limited information is available regarding the retention in the body or metabolism of methyl mercaptan. Studies in animals demonstrate that carbon dioxide and sulfate are the final metabolites found in the expired breath and/or urine and that methyl mercaptan is cleared from the body within several hours (Canellkis and Traver 1953; Derr and Draves 1983, 1984; Susman et al. 1978). Studies with human blood indicated that methyl mercaptan is oxidized in erythrocytes yielding formic acid and sulfate ion as metabolites in urine (Blom et al. 1988, 1989; Blom and Tangerman 1988). No method is commonly used to enhance the elimination of the absorbed dose of methyl mercaptan.

Acute intoxication with methyl mercaptan may cause methemoglobinemia, hemolytic anemia and neurological effects leading to lethargy, seizures, coma, and death (see Section 2.2). However, because of the lack of information regarding the mechanism of toxicity of methyl mercaptan, no specific method for reducing its toxic effects is available.

2.9 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 methyl mercaptan 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 methyl mercaptan.

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.

2.9.1 Existing Information on Health Effects of Methyl Mercaptan

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to methyl mercaptan are summarized in Figure 2-2. The purpose of this figure is to illustrate the existing information concerning the health effects of methyl mercaptan. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information (i.e., data gaps that must necessarily be filled).

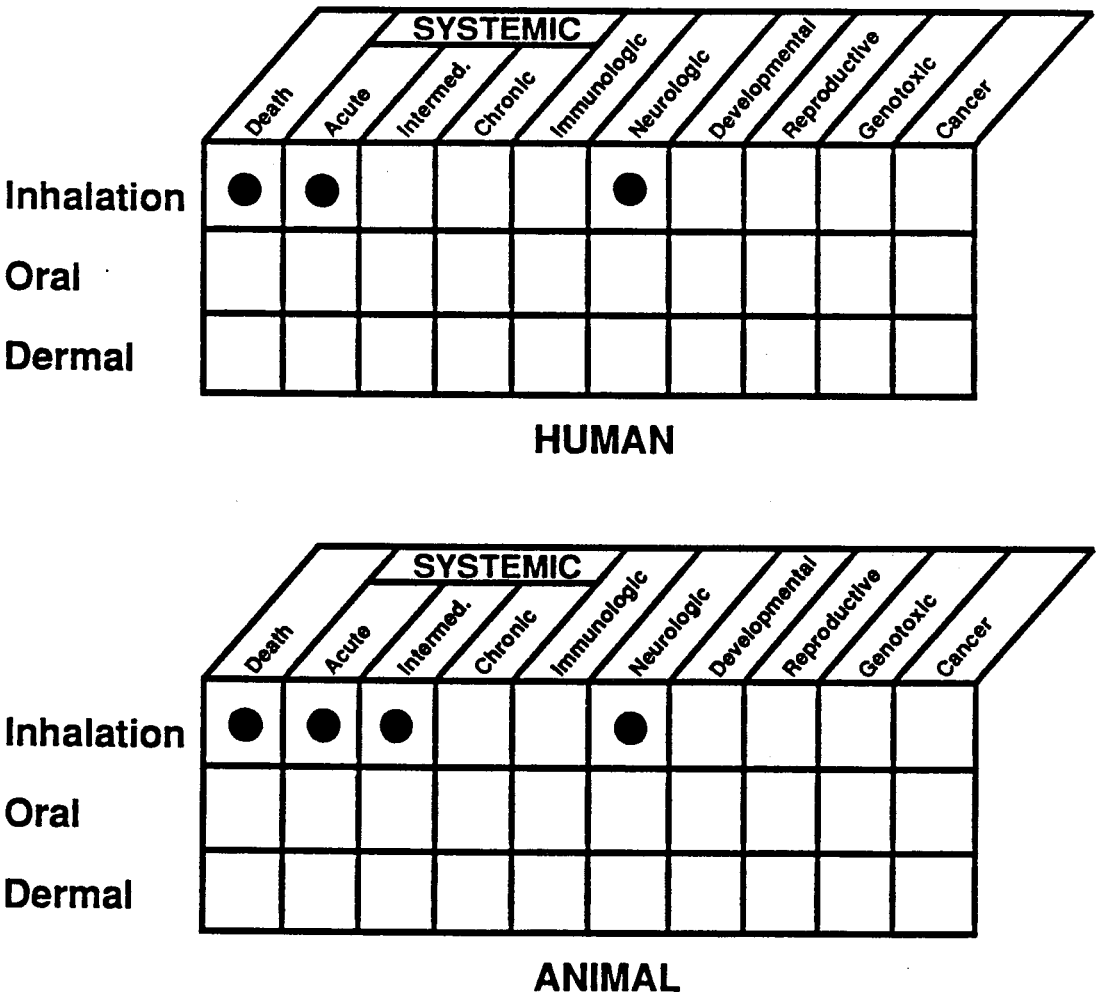
Figure 2-2 graphically depicts the information that currently exists on the health effects that have been observed or studied in humans and animals following inhalation, oral, or dermal exposure to methyl mercaptan. There is little information available on this chemical, and, therefore, almost any additional information would probably be useful. This section, however, will attempt to focus on those areas of investigation that would appear to be the most useful for a chemical about which almost nothing is known.

2.9.2 Data Needs

Acute-Duration Exposure. The available information in humans and animals suggests that the nervous system is the major target organ following acute inhalation exposure (Shults et al. 1970; Zieve et al. 1974). However, quantitative data were available in only one study in rats (Zieve et al. 1974)and this was not considered sufficient to calculate an MRL via this route, and no studies conducted via the oral and dermal routes were available. Although any new data for this exposure duration would be useful, estimates of a lethaldose via inhalation would be most helpful, because a human death has been reported as a result of occupational exposure. Currently, LC,, data are available only for the rat (Tansy et al. 1981). Because there are no data on absorption via the oral and dermal route, it is not known if toxicity studies using these routes would be useful.

Intermediate-Duration Exposure. There are no data on humans exposed tomethyl mercaptan for this duration period. A 3-month study in rats exposed to methyl mercaptan via inhalation (Tansy et al. 1981) comprises virtually the entire useful database for this compound and indicates that decreased body weight is the only compound-related effect that was observed. Data were not considered sufficient to calculate an inhalation MEL for this exposure duration due to an inadequate database. There are no animal studies using the oral route, and, therefore, an intermediate oral MRL has not been calculated. Any further studies using either of these routes should use doses high enough to elicit clinically evident neurological effects and should focus on hematological effects such as hemolytic anemia and methemoglobinemia. The use of an animal model that is susceptible to these hematological effects may be

FIGURE 2-2. Existing Information on Health Effects of Methyl Mercaptan



● Existing Studies

the best choice for these tests. Dose-response information for these effects would be useful in assessing the risks of persons exposed to methyl mercaptan in the vicinity of hazardous waste sites and in the workplace. Studies via the dermal route would also be useful if pharmacologic studies have demonstrated that methyl mercaptan can be absorbed through the skin.

Chronic-Duration Exposure and Cancer. No chronic inhalation, oral, or dermal studies in any species were located for methyl mercaptan. This appears to be the most important category of duration for future study of this compound because low level chronic exposure is likely to occur via the inhalation route in occupational settings and in the vicinity of hazardous waste sites. Although the entire population is exposed via the oral route since methyl mercaptan is naturally present at low levels in certain foods, this compound has not been reported in drinking water. Since the potential for dermal exposure is not known, it is not clear if these studies would be useful.

Evaluations of its carcinogenic potential via the oral and inhalation routes would, therefore, also be useful. Studies using the dermal route would be useful if dermal exposure were first demonstrated to occur in populations living or working in the vicinity of methyl mercaptan emissions.

Genotoxicity. There are currently no genotoxicity data available in humans or animals for methyl mercaptan. A battery of in vitro genotoxicity tests would be useful as a preliminary step in determining its mutagenic potential and the need for further testing.

Reproductive Toxicity. There are no available data on the reproductive toxicity of methyl mercaptan in humans or animals via any route. Available data indicate that when intraperitoneally injected into rats, some methyl mercaptan is distributed to the testes (Canellakis and Tarver 1953). Based on this observation, potential effects on reproductive organs and sperm count should be considered in any future intermediate (go-day) or chronic durationstudies conducted via any route. Studies via inhalation would probably be the most relevant to assessing the potential effects on the fertility of men exposed in the vicinity of hazardous waste sites or in occupational settings. This information would probably also be useful in the development of MRLs for these durations.

Developmental Toxicity. There are currently no available data on this end point in humans or animals. A study in animals exposed via inhalation would be useful in assessing the potential developmental effects on fetuses carried by women exposed to methyl mercaptan in the vicinity of hazardous waste sites and in occupational settings, since this is expected to be themain route of human exposure.

Immunotoxicity. No studies related to the immunological effects of methyl mercaptan in humans or animals have been located. Immunologic

assessments such as effects on peripheral white blood cell counts would provide useful preliminary information on this end point, especially as a part of intermediate or chronic duration exposure studies using the inhalation route since this is the most likely route of exposure of persons in the vicinity of hazardous waste sites and in occupational settings.

Neurotoxicity. The available information in humans and animals indicates that high level exposure to methyl mercaptan via inhalation or intraperitoneal injection can result in irreversible coma (Al Mardini et al. 1984; Shults et al. 1970; Tansy et al. 1981; Zieve et al. 1984). Animal studies that describe neurological effects and assess morphological damage to the brain associated with intermediate or chronic duration inhalation exposure to methyl mercaptan at levels similar to those in the vicinity of hazardous waste sites or in occupational settings would be extremely useful, since inhalation is expected to be the main route of human exposure in those settings.

Epidemiological and Human Dosimetry Studies. Occupational exposure to methyl mercaptan, such as occurs in pulp mills, also involves exposure to other sulfur-containing compounds such as hydrogen sulfide, sulfur dioxide, and dimethyl sulfide. Epidemiological studies of such populations may not provide useful data since observed effects may not clearly be attributable to methyl mercaptan. Human dosimetry studies would be useful, however, because measurement of levels of exposure to methyl mercaptan would help to indicate whether humans were at risk for methyl mercaptan-induced effects associated with those levels (assuming that this toxicity information would eventually become available).

Biomarkers of Exposure and Effect. There are no sensitive biomarkers of methyl mercaptan exposure. This would be useful information, especially for the levels of this compound present in the vicinity of hazardous waste sites and in occupational settings. However, because methyl mercaptan is always present in the human body and blood levels can become elevated as a result of liver damage (without exogenous exposure), progress in this area may not be forthcoming.

Currently, the only effect clearly associated with methyl mercaptan toxicity is coma (Shults et al. 1970). The identification of more subtle effects that might result from chronic low-level exposure would be useful.

Absorption, Distribution, Metabolism, and Excretion. There are no toxicokinetic studies for methyl mercaptan via the inhalation, oral, or dermal routes. These studies would be valuable for tracing its metabolic fate following each route of exposure. Studies of absorption via the oral and dermal routes may be useful in helping to determine if toxicity studies using these routes are warranted.

Comparative Toxicokinetics. There is no available information on the comparative toxicokinetics of methyl mercaptan. Although species differences in response to methyl mercaptan exposure may exist, these studies may not be useful until several other aspects of this chemical's toxicity are first investigated. These comparisons would then serve as an aid in putting the results of animal toxicity data into perspective in relation to its relevance to potential human health effects.

Mitigation of effects. Recommended methods for the mitigation of acute effects of methyl mercaptan poisoning include administration of oxygen if exposure is by inhalation, or thorough washing of the skin and flushing the eyes with water if exposure is to these organs (Bronstein and Currance 1988; Stutz and Janusz 1988). Drugs may also be administered to control seizures and transfusions to alleviate anemia. No information was located concerning mitigation of effects of lower-level or longer-term exposure to methyl mercaptan. Further information on techniques to mitigate such effects wouldbe useful in determining the safety and effectiveness of possible methods for treating methyl mercaptan-exposed populations surrounding hazardous waste sites.

2.9.3 On-going Studies

No studies on toxicity, toxicokinetics, epidemiology, or other topics discussed in Section 2.8.2, above are known to be in progress.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

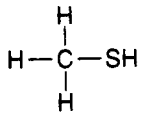
Common synonyms, trade names, and other pertinent identification information for methyl mercaptan are listed in Table 3-1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of methyl mercaptan are listed in Table 3-2.

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-1. Chemical Identity of Methyl Mercaptan

Characteristic	Information	Reference
Chemical name	Methyl mercaptan	Windholz 1983
Synonyms	Methanethiol; thiomethyl alcohol; methyl sulfhydrate; mercaptomethane; thiomethanol	HSDB 1989; Windholz 1983
Trade names	No data	
Chemical formula	CH_4S	Windholz 1983
Chemical structure		
Identification numbers:		
CAS Registry	74-93-1	Sax and Lewis 1987
NIOSH RTECS	PB4375000	HSDB 1989
EPA Hazardous Waste	U153	NLM 1989
OHM/TADS	No data	
DOT/UN/NA/IMCO Shipping	UN 1064	NLM 1989
	IMCO 2.0	HSDB 1989
HSDB	813	NLM 1989
NCI	No data	

CAS = Chemical Abstracts Service; DOT/UN/NA/IMCO = Department of Transportation/United Nations/North America/International Maritime Dangerous Goods Code; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-2. Physical and Chemical Properties of Methyl Mercaptan

Property	Information	Reference
Molecular weight	48.11	Windholz 1983
Color	Colorless	Verschueren 1983
Physical state	Gas	Verschueren 1983
Melting point	-123.1°C	Verschueren 1983
Boiling point	5.95°C	Windholz 1983
Density at 20°C	0.8665	Windholz 1983
Odor	Rotten cabbage	Windholz 1983
Odor threshold:		
Water	0.000024 mg/L	Amoore and Hautala 1983
Air	0.0016 ppm	Amoore and Hautala 1983
Solubility:		
Water at 20°C	23.3 g/L	Windholz 1983
Water at 25°C	15.39 g/L	Hine and Mookerjee 1975
Organic solvents	Soluble in alcohol, ether, petroleum, naphtha	Sax and Lewis 1987
Partition coefficients:		
Log K_{ow}	No data	
Log K_{oc}	No data	
Vapor Pressure at 25°C	1,500 mmHg	EPA 1983
pKa	No data	
Henry's law constant	3.85×10^{-3} atm-m^3/mol	EPA 1983
Autoignition temperature	No data	
Flashpoint	0°F (_-18°C) (open cup)	HSDB 1989
Flammability limits	No data	
Conversion factors	1 ppm = 2.05 mg/m^3 1 mg/m^3 = 0.488 ppm	Verschueren 1983
Explosive limits	3.9%-21.8%	Sax and Lewis 1987

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Methyl mercaptan is produced commercially by the reaction of hydrogen sulfide with methanol (Santodonato et al. 1985; Windholz 1983). Methyl mercaptan is manufactured by the Organic Chemical Division of Pennwalt Corporation in Beaumont and Houston, Texas. Production volumes for these facilities were not located (SRI 1987, 1988, 1989).

4.2 IMPORT/EXPORT

No data were located regarding the import or export of methyl mercaptan.

4.3 USE

Methyl mercaptan is used as a chemical intermediate in the production of jet fuel, certain pesticides, and plastics and in the synthesis of the amino acid methionine (ACGIH 1986; HSDB 1989; Santodonato et al. 1985). Methyl mercaptan is also used to add odor to certain odorless hazardous gases. Methyl mercaptan is not one of the chemicals considered acceptable for use as an odorant in natural gas (AGA 1983; HSDB 1989; Reid 1958; Santodonato et al. 1985; Windholz 1983).

4.4 DISPOSAL

Since methyl mercaptan is listed as a hazardous substance, disposal of wastes containing methyl mercaptan is controlled by a number of federal regulations (see Chapter 7). Land disposal restrictions for methyl mercaptan are among those scheduled for promulgation in 1990 (40 CPR 268.12). Methyl mercaptan may be disposed of by controlled incineration, and it is a potential candidate for fluidized bed and rotary.kiln incineration (HSDB 1989). No quantitative data were located on the amount of methyl mercaptan disposed of in waste sites.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Methyl mercaptan is a naturally occurring gaseous compound produced as a result of microbial degradation and present in trace amounts in natural gas. It is likely to volatilize from soil and water and be photooxidized in the atmosphere. Methyl mercaptan is probably mobile in soils, and it is not likely to bioaccumulate.

Human exposure to trace amounts of methyl mercaptan probably occurs from all environmental media. However, since this compound has an extremely unpleasant odor and the odor threshold is quite low, it is unlikely that significant human exposure to methyl mercaptan will occur, except possibly in the vicinity of sewage treatment plants or industrial facilities or in the workplace.

The EPA has identified 1,177 NPL sites. Methyl mercaptan has been found at 2 of the sites evaluated for the presence of this chemical. However, we do not know how many of the 1,177 NPL sites have been evaluated for this chemical. As more sites are evaluated by the EPA, the number may change (View 1989). The frequency of occurrence at these sites within the United States can be seen in Figure 5-l.

5.2 RELEASES TO THE ENVIRONMENT

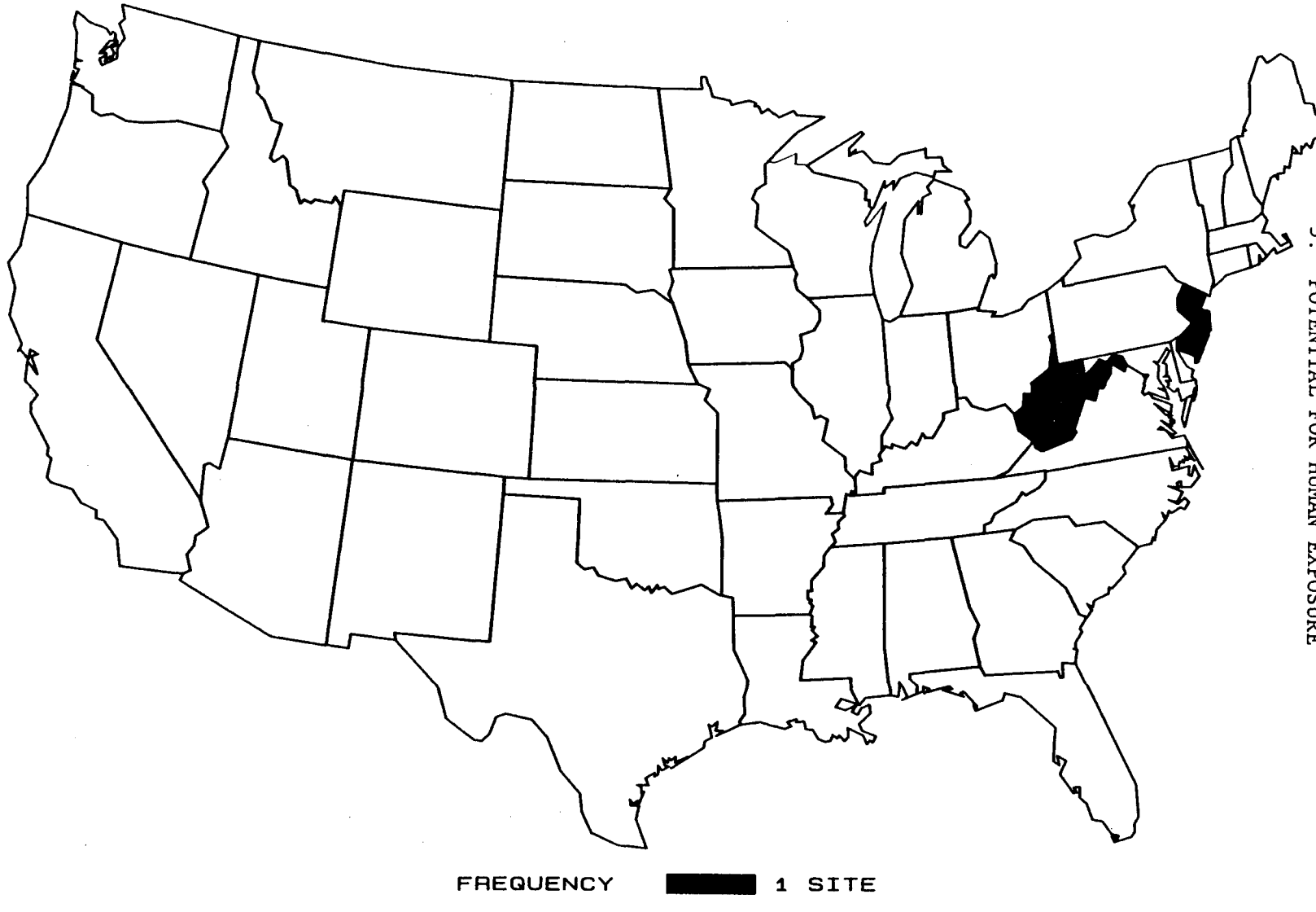
Releases of methyl mercaptan may occur from industrial sources. However, manufacturers, users, and processors of methyl mercaptan are not required to report quantities of this substance released to environmental media, since methyl mercaptan is not on the SARA Section 313 Toxic Chemical List. Therefore, releases of methyl mercaptan during normal operations are not reported in the Toxics Release Inventory (TRI 1989).

5.2.1 Air

Methyl mercaptan is released to the atmosphere from both natural and anthropogenic sources. Natural sources-include vegetation, animal wastes, microbial degradation, and natural gas (Adams et al. 1979; Farwell et al. 1979; Graedel 1978; Reid 1958). Estimation of average methyl mercaptan emission from a saline marsh in North Carolina was 6.56 g sulfur/m^2/year (Adams et al. 1979). No other quantitative data regarding emissions from natural sources were located.

Potential industrial emission sources include wood pulp, oil shale, and petroleum-processing plants and sewage treatment plants (EPA 1987b; Graedel 1978; Reid 1958; Sklarew et al. 1984). Releases may also occur from . hydrolysis or combustion of wool (Junk and Ford 1980; Reid 1958). A survey of about 2,950 industrial facilities in North Carolina reported fugitive and stack emissions of methyl mercaptan totalling 239,594 pounds/year (McCune 1990).

FIGURE 5-1. FREQUENCY OF NPL SITES WITH METHYL MERCAPTAN CONTAMINATION *



* Derived from View 1989

5. POTENTIAL FOR HUMAN EXPOSURE

5.2.2 Water

No data were located regarding the amount of methyl mercaptan released to water. However, this compound was identified in both the influent and the effluent of a wastewater treatment plant. It is likely that methyl mercaptan is formed in the water by chemical reaction or microbiological fermentation, rather than being released from industrial or municipal sources (Reid 1958; Van Langenhove et al. 1985). Data from the Contract Laboratory Program (CLP) Statistical Database indicate that methyl mercaptan was not detected in surface water or groundwater at about 400 hazardous waste sites (CLPSD 1986).

5.2.3 Soil

Methyl mercaptan occurs naturally in many soils and may be adsorbed to the soil from the atmosphere (Smith et al. 1973). No data were located regarding land releases of methyl mercaptan from industrial sources. Land disposal.restrictions have been proposed for methyl mercaptan (EPA 1989c).

Methyl mercaptan was detected in two soil samples at a geometric mean concentration in positive samples of 83 μg/kg, at 1 of 455 hazardous waste sites (CLPSD 1986). It is important to note that the CLP Statistical Database includes data from both NPL and non-NPL sites. Since methyl mercaptan may occur naturally in soils, occurrence at a hazardous waste site does not necessarily indicate a release to the environment from the site.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Methyl mercaptan is a gas with a vapor pressure of 1.97 atm at 25°C (EPA 1983). A small fraction of atmospheric methyl mercaptan may dissolve intowater vapor (such as clouds and rain drops). A Henry's law constant (H) estimates the tendency of a chemical to partition between its gas phase and water. A value for H has not been experimentally measured, but it may be estimated by dividing the vapor pressure of methyl mercaptan by its water solubility at the same temperature (Mabey et al. 1982). In this case, an estimated value for H is 3.85×10^{-3} atm-m^3/mole (EPA 1983). The magnitude of this value suggests that only a small fraction of gaseous methyl mercaptan would dissolve in water and that most would remain in the air.

Gaseous methyl mercaptan may also partition to soils. Sorption capacities of six-air-dry soil samples ranged from 2.4 to 32.1 mg CH_3,SH per g of soil (Smith et al. 1973). The range for most soils was 2.2-21.4 mg/g of soil. These authors concluded that soil may be a sink for gaseous organosulfur compounds. No information was located on the fate of sorbed methyl mercaptan.

5. POTENTIAL FOR HUMAN EXPOSURE

Methyl mercaptan is very soluble in water. Its solubility at 20°C is approximately 23.3 g/L (EPA 1983). The magnitude of the estimated Henry's law constant (3.85×10^{-3} atm-m^3/mole) indicates that a large fraction of the dissolved methyl mercaptan will volatilize from solution, depending on temperature, relative humidity, air currents, and the extent of mixing of the solution.

Methyl mercaptan may not be bioconcentrated significantly in water; however, no information was located on this topic. An octanol/water partition coefficient (K_{ow}) estimates the partitioning of a chemical between octanol and water. Octanol is believed to best imitate the fatty structures in plants and living animal tissues. Based on its solubility in water (Hassett et al. 1983), the K_{ow} of methyl mercaptan can be calculated as approximately 19. This low value suggests that methyl mercaptan will not partition to fat tissues significantly. A bioconcentration factor (BCF) relates the concentration of chemical in aquatic plants or animals to the concentration of the chemical in the medium in which they live. Based on the empirical regressions of Kenaga (1980) using soil sorption parameters, an estimated BCF for methyl mercaptan is about l-2. This low BCF indicates that bioconcentration is not a significant fate mechanism for volatile methyl mercaptan released into the environment. However, no experimentally-measured BCFs for methyl mercaptan were located to corroborate these predicted values.

Methyl mercaptan in water may have very little tendency to be adsorbed by soils and sediments. The extent of adsorption of sparingly water-soluble compounds is often highly correlated with the organic-carbon content of the adsorbent (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, and may be used to rank the relative mobility of the chemical in soil-water systems. Based on its solubility in water, an estimated K_{oc} for methyl mercaptan can be calculated as 17, using the empirical regression of Hassett et al. (1983). This low value indicates that methyl mercaptan is very highly mobile in soil as compared with other compounds listed by Roy and Griffin (1985). However, methyl mercaptan is not a sparingly soluble chemical in water. Methyl mercaptan is also a weak acid that dissociates in water, yielding an anion. The adsorption of ionic chemicals cannot be predicted by K_{oc} concepts. The dissociation constants (pKa) of mercaptans in general are on the order of 11.4 (Reid 1958; Yabroff 1940). Consequently, the relative proportion of methyl mercaptan as an ion is probably insignificant in environmentally-relevant waters where the pH is less than 9. Therefore, the estimated K_{oc} value of 17 may be a reasonable indicator of how this chemical partitions between water and soil. No corroborative information was located.

5. POTENTIAL FOR HUMAN EXPOSURE

5.3.2 Transformation and Degradation

5.3.2.1 Air

The major fate of atmospheric methyl mercaptan is photooxidation. Methyl mercaptan may be transformed by photon-photolytic oxidation, yielding hydrogen, sulfur dioxide, dimethyl disulfide, and other polysulfides (Haines et al. 1956; Sheraton and Murray 1981). Methyl mercaptan may also be oxidized by tropospheric oxygen radicals, yielding dimethyl disulfide and other sulfide compounds (Nip et al. 1981). The rate constant for this reaction at ambient temperatures (about 25°C) has been measured to be approximately $1.77\text{-}1.90 \times 10^{-12}$ cm^3/molecule-set (Nip et al. 1981; Slagle et al. 1976). If the mean concentration of ground-state oxygen radicals is about 5×10^{-4} molecules/cm3 (Cupitt 1980), then the atmospheric half-life of methyl mercaptan is on the order of 4 months.

Methyl mercaptan may be more rapidly transformed by interacting with atmospheric hydroxyl radicals. The measured rate constant for this reaction at ambient temperatures ranges from 2.1 to 9.04×10^{-11} cm3/molecule-see (Atkinson et al. 1977; Cox and Sheppard 1980; Hynes and Wine 1987; Mac Leod et al. 1984; Wine et al. 1984). Given that the concentration of tropospheric hydroxyl radicals varies from 3×10^5 to about 1×10^7 molecules/cm^3 (Mac Leod et al. 1984), it follows that the atmospheric half-life of methyl mercaptan is on the order of 0.2-30 hours. Consequently, it appears that gaseous methyl mercaptan is labile in the troposphere. Transformation products include sulfur dioxide, methylsulfenic acid (CH_3SOH), and methyl sulfide radicals (Hatakeyama and Akimoto 1983). Several other reaction products have been predicted but not confirmed.

Experimental data have also demonstrated that methyl mercaptan is labile in polluted air where nitrogen oxide (NO_x) concentrations are higher (Balla and Heicklen 1985; Sickles and Wright 1979). Nitrogen oxides catalyze the photooxidative transformations of methyl mercaptan. Reaction products underthese conditions include sulfur dioxide, nitric acid, formaldehyde, methylnitrate, methanesulfonic acid, inorganic sulfate (Grosjean 1984), dimethyldisulfide, and nitric oxide (Balla and Heicklen 1985).

Reaction with the nitrate radical (NO_3) may be the dominant atmospheric loss process for methyl mercaptan under certain conditions (Dlugokencky and Howard 1988; Mac Leod et al. 1986). The rate constant for the reaction of atmospheric methyl mercaptan with NO_3 was recently determined (Dlugokencky and Howard 1988; Mac Leod et al. 1986). Based on a rate constant of about 1×10^{-12} cm3/molecule-set and a NO_3 concentration of 2.4×10^8 molecule/cm^3, Mac Leod et al. (1986) calculated an atmospheric lifetime of 1.2 hours for methyl mercaptan, less than the estimated atmospheric lifetime (8.4 hours) based on reaction with the OH radical.

5.3.2.2 Water

Very little is known about nonbiologically-mediated transformations of methyl mercaptan in water. It seems likely that methyl mercaptan will photooxidize and oxidize in water, but no information was located.

5.3.2.3 soil

Methyl mercaptan may be degraded by methanogenic bacteria in soil, but there is little information available. Methyl mercaptan in solution was metabolized to methane and carbon dioxide when in contact with anaerobic freshwater sediments and sewage sludge (Zinder and Brock 1978). No other information on transformation or degradation in soil was located.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Methyl mercaptan was detected in ambient air at 4 ppb (8.2 μg/m^3> and in a primary school in Japan at 2.8 ppb (5.7 μg/m3) (Okita 1970). No other studies were located regarding atmospheric concentrations of methyl mercaptan.

5.4.2 Water

Groundwater and surface water monitoring studies do not generally include methyl mercaptan. This compound was not detected in a screen of about 1,800 community and private wells in Wisconsin (Krill and Sonzogni 1986). No other studies regarding water concentrations of methyl mercaptan were located.

5.4.3 Soil

Although methyl mercaptan is produced by microbial degradation in soils, is adsorbed from the atmosphere by soil, and is volatilized from soil (Adams et al. 1 979; Farwell et al. 1979; Reid 1958; Smith et al. 1973), no quantitative data on the concentration of methyl mercaptan in ambient soils were located.

5.4.4 Other Environmental Media

Methyl mercaptan has been identified as a volatile component of roasted filberts and Beaufort cheese (Dumont and Adda 1978; Kinlin et al. 1972). Trace amounts are present in the roots and leaves of some plants, in natural gas and, as a result of digestive and metabolic processes, in urine and feces (Reid 1958). Methyl mercaptan is also found in commercially extractable quantities in the "sour gas" of west Texas (Reid 1958).

5. POTENTIAL FOR HUMAN EXPOSURE

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Since methyl mercaptan is a naturally occurring substance present in foods and sometimes formed during digestive and metabolic processes, the general population will most likely be exposed to trace amounts of this compound. However, the available data are inadequate to estimate the extent of exposure of the general population to either natural or anthropogenic sources of methyl mercaptan.

Inhalation exposure in occupational settings is probably the most significant human exposure scenario for methyl mercaptan. Santodonato et al. (1985) estimated that about 19,000 workers were potentially exposed to methyl mercaptan in the 1970s. The estimate of workers potentially exposed to methyl mercaptan increased from 357 in the early 1970s to about 6,200 in the early 1980s (NOES 1989; NOHS 1989). Neither the NOHS nor the NOES databases contain information on the frequency, concentration, or duration of exposure of workers to any of the chemicals listed therein. These surveys provide only estimates of the number of workers potentially exposed to chemicals in the workplace. Most occupational exposures are likely to occur in sewage treatment plants and pulp mills, rather than in methyl mercaptan production or consumptive use facilities. Mean methyl mercaptan concentrations in workplace air ranged from 0.070 to 0.263 ppm in sewage plants and from 0.021 to 3.70 ppm in pulp mills in Finland (Kangas and Ryosa 1988; Kangas et al. 1984) and from 0.55 to 1.06 ppm at a lockgate on a Japanese river (Okita 1970). No other data on workplace air concentrations were located.

Since methyl mercaptan has a penetrating and extremely unpleasant odor and the odor threshold in air is quite low (1.6 ppb) (Amoore and Hautala 1983), it is unlikely that humans would willingly tolerate exposure to concentrations much above the odor threshold for any substantial time period. However, humans in occupational settings may rapidly succumb to extremely high levels of methyl mercaptan, as in the case of the worker who died after emptying tanks of methyl mercaptan (see Chapter 2).

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Workers in sewage treatment plants, pulp mills, chemical plants, and other industrial or agricultural settings where chemical or microbiological formation of methyl mercaptan is significant would have potentially high exposure to this compound. People living in the immediate vicinity of these facilities as well as in the vicinity of hazardous waste sites also have higher exposure potential than does the general population.

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 methyl mercaptan 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 methyl mercaptan.

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 Data Needs

Physical and Chemical Properties. The dissociation constant of methyl mercaptan in water is not known precisely (Reid et al. 1958; Yabroff 1940) and this measurement would be useful in predicting the environmental fate and transport of this compound. A laboratory verification of the estimated Henry's law constant for methyl mercaptan (Hassett et al. 1983) would provide a more accurate measurement of air-water partitioning.

Production, Import/Export, Use, and Disposal. No data were located with regard to past or present production, use, release, or disposal of methyl mercaptan. Since most human exposure to methyl mercaptan is not associated with production, use, or disposal, but rather with sewage treatment, wood pulping, or oil processing facilities (EPA 1987b; Graedel 1978; Reid 1958; Sklarew et al. 1984), additional data on its production and use will probably not significantly affect estimates of human exposure to this compound. However, data on methyl mercaptan releases from those facilities where the chemical is produced inadvertently (sewage treatment, wood pulping, etc.) would be useful in evaluating the potential for human exposures.

Environmental Fate. Small amounts of methyl mercaptan may partition from air to water or soil (EPA 1983; Smith et al. 1973). Based on measured physical properties, methyl mercaptan is likely to volatilize from water to air (EPA 1983), but has little tendency to adsorb to soils (Hassett et al. 1983). Methyl mercaptan is likely to be mobile in environmental media (Hassett et al. 1983). Additional research on the soil sorption of gaseous methyl mercaptan may be helpful in describing the transport of the gas phase in the vadose zone. The reaction mechanisms of methyl mercaptan transformations in the atmosphere are fairly-well understood (Atkinson et al. 1977; Balla and Heickler 1985; Cox and Sheppard 1980; Dlugokencky and Howard 1988; Haines et al. 1956; Hynes and Wine 1987; Mac Leod et al. 1986; Nip et al. 1981; Sheraton and Murray 1981; Slagle et al. 1976), but the environmental fates of some of the transformation products are not well known. Very little is known about the fate of methyl mercaptan in water. It would be helpful to collect data on oxidation, hydrolysis, photodegradation, and

biodegradation in surface water and groundwater. Research on the biodegradation and abiotic transformation of methyl mercaptan in soils would also be useful.

Bioavailability from Environmental Media. Methyl mercaptan is soluble in water and may have very little tendency to be adsorbed to soils or sediments (EPA 1983; Hassett et al. 1983). Therefore, it will be bioavailable from natural waters. However, there are no data on the potential absorption of methyl mercaptan via the oral or dermal routes. These data would be useful in assessing the potential effects of recreational use of natural waters contaminated with methyl mercaptan. Information on the absorption of inhaled methyl mercaptan released to air would also be useful in assessing its bioavailability from that medium.

Food Chain Bioaccumulation. There are no data on the bioconcentration of methyl mercaptan by aquatic organisms, or data on the bioaccumulation of methyl mercaptan in the food chain. However, this lack of data may not be amajor limitation, because the food chain bioaccumulation of methyl mercaptan is unlikely owing to its high volatility and water solubility (EPA 1983; Hassett et al. 1983).

Exposure Levels in Environmental Media. There are few studies measuring concentrations of methyl mercaptan in any environmental media (Krill andSonzogni 1986; Okitu 1970). Since levels in ambient air, water, and soil are unknown, monitoring studies would confirm the presence or absence of this compound in these media. Data on ambient air levels at hazardous waste sitesand estimates of human intake would be particularly useful.

Exposure Levels in Humans. Exposures of humans to natural sources of methyl mercaptan are difficult to estimate. Measurements of methyl mercaptan in workplace air would be useful in estimating occupational exposures. Because methyl mercaptan is always present in human tissue independent of exposure, these levels cannot be used as a measure or indication of exposure without confirmatory data on exogenous levels of methyl mercaptan.

Exposure Registries. No exposure registries for methyl mercaptan were located. This compound is not currently one of the compounds for which a subregistry has been established in the National Exposure Registry. The compound 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 the exposure to this compound.

5.7.2 On-going Studies

Remedial investigations and feasibility studies conducted at the 2 NPL sites known to be contaminated with methyl mercaptan will add more information to the available database on exposure levels in environmental media and exposure levels in humans. No other information was located on any on-going studies on the fate, transport, or potential for human exposure to methyl mercaptan.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring methyl mercaptan in'environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify methyl mercaptan. Rather, the intention is to identify well established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect methyl mercaptan in environmental samples are the methods approved by federal agencies such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

As a volatile material boiling at only 5.95°C (Windholz 1983), methyl mercaptan, CH_3SH, also called methanethiol, is readily determined by gas chromatographic analysis. The sensitivity and selectivity of detection are increased by the use of sulfur-selective detectors; in one study, substitution of a sulfur-selective flame photometric detector for a flame ionization detector reduced the detection limit from 20 to 2 μg/unit sample (Knarr andRappaport 1980). Hydrogen sulfide (H_2S), dimethyl sulfide ($[CH_3]_2S$), and dimethyl disulfide ($[CH_3]_2S_2$) are other reduced sulfur compounds that may occur along with methyl mercaptan and are commonly determined along with it. Normally, methyl mercaptan is collected from the gas phase or from vapor evolved from the sample matrix on a column of solid sorbent, such as Tenax@. Collection on molecular sieve is also possible (Kangas and Ryosa 1988), although problems are encountered from incomplete desorption of methyl mercaptan from molecular sieve. Cryogenic (low temperature) collection may also be possible and is less likely to lead to alterations of the analyte in the collection apparatus (Brettell and Grob 1985). The presence of water can result in reduced sorption capacity for methyl mercaptan as well as decomposition during thermal desorption. Sorption efficiency is improved markedly by removal of water from the air stream with calcium chloride (Tangerman 1986). Purge-and-trap techniques are used to collect methyl mercaptan from water (Badings et al. 1985). Headspace vapor in equilibrium with the sample in a closed container may also be subjected to gas chromatography.

6.1 BIOLOGICAL MATERIALS

Methods for detection of methyl mercaptan in biological materials are summarized in Table 6-l.

Methyl mercaptan has been determined in a variety of biological materials as shown in Table 6-l. Normally,'for determination in biological samples, methyl mercaptan is released from the sample matrix and collected on a column of solid sorbent, cryogenically or as headspace gas. As a result of

TABLE 6-1. Analytical Methods for Determining Methyl Mercaptan in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Accuracy	Reference
Bacterial cultures	Mix with potassium carbonate, collection of headspace vapor at 60°C	GC/MS	No data[a]	No data[a]	Hayward et al. 1977
Clostridium bacterial cultures	Collection of headspace vapor under vacuum	GC/MS	1-10 ppb[b]	No data	Rimbault et al. 1986
Blood, brain tissue	No data	GC/SSD	No data	No data	Al Mardini et al. 1984
Collagen	Collection of headspace vapor	GC	No data	No data	Johnson and Tonzetich 1985
Blood and serum	Release from metabolites, collection on Tenax®	GC/SSD	<0.3 µmol/L	92±7%-99±4%	Tangerman et al. 1985
Breath	Trapping from breath onto Tenax®, desorption	GC/SSD	0.2 ng/L (0.1 ppb)	97±5%	Tangerman et al. 1983

[a]Analytical results were reported as "peak areas", not concentrations.
[b]Level in headspace gas.

GC = gas chromatography; MS = mass spectrometry; SSD = sulfur-specific detector

6. ANALYTICAL METHODS

Phase II metabolic reactions in biological systems (Manahan 1989), methyl mercaptan may be bound as conjugates from which it must be released prior to analysis. Two such bound fractions of methyl mercaptan have been identified in human serum (Tangerman et al. 1985). In one fraction, from which the methyl mercaptan is released by acid, the methyl mercaptan is thought to be bound as methyl-beta-D-thioglucuronide. In another fraction methyl mercaptan is covalently bound to proteins in a disulfide linkage and is released by reaction with dithiothreitol.

6.2 ENVIRONMENTAL SAMPLES

For the determination of methyl mercaptan in air, the analyte is usually trapped and concentrated from a large volume of air on a solid sorbent such as Tenax®, activated carbon, or molecular sieve from which it is released thermally for subsequent measurement. It is advisable to dry the air sample with calcium chloride prior to collection of methyl mercaptan to preventanalyte decomposition on the collection medium (Kangas and Ryosa 1988; Tangerman 1986). For aqueous and solid waste samples, methyl mercaptan is purged with an inert gas and collected on a solid such as Tenax®, or cryogenically, followed by thermal desorption and measurement. Gas chromatography using sensitive and highly specific mass spectrometry (MS) or highly sensitive flame photometric detection (FPD) for detection is the analytical method of choice for the determination of methyl mercaptan in environmental samples.

Methods for the determination of methyl mercaptan in environmental samples are summarized in Table 6-2.

6.3 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 methyl mercaptan is available. Where adequate informationis not available, ATSDR, in conjunction with the NTP, is required to assurethe initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of methyl mercaptan.

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.

TABLE 6-2. Analytical Methods for Determining Methyl Mercaptan in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Accuracy	Reference
Ambient air	Removal of water by calcium chloride, adsorption on molecular sieve, thermal desorption	GC/FPD	<0.01 cm^3/m^3	No data	Kangas and Ryosa 1988
Air	Removal of water by calcium chloride, trap from air onto Tenax® at -196°C, desorption at 200°C	GC/FPD	<12 ppt	93±7%[a]	Tangerman 1986
Air[b]	Retention by activated carbon	GC	No data	No data	ASTM 1987
Air	Collection on a glass fiber filter impregnated with mercuric acetate	GC/FPD	17 $\mu g/m^3$	98.4±0.22%[c]	Knarr and Rappaport 1980
Flue gases	Collection on sample loop, direct injection	GC/FPD	<1 ppm	No data	De Souza 1987
Water	Purge, cryogenic trap	HRGC	No data	No data	Badings et al. 1985
Water[d]	Direct injection	GC	1 mg/L	No data	ASTM 1988
Waste water	Purge from water by helium, collect on Tenax®, thermal desorption	GC/MS	No data	No data	Van Langenhove et al. 1985
Soil[e]	Purge by helium; collection on solid, thermal desorption	GC/MS	5 µg/kg	No data	EPA 1986

[a]As recovery from Tenax®
[b]Absorption characteristics for sampling atmospheric vapor with activated carbon for subsequent analysis by GC.
[c]At 1 ppm
[d]General method for the determination of volatile organic matter in water using flame ionization detection. Selectivity and sensitivity for methyl mercaptan can be greatly enhanced with sulfur-selective detection.
[e]Also applicable to sediment and solid waste.

FPD = flame photometric detector; GC = gas chromatography; HRGC = high resolution gas chromatography; MS = mass spectrometry; ppt = parts per trillion

6. ANALYTICAL METHODS

6.3.1 Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Sensitive and selective methods are available for the qualitative and quantitative measurement of methyl mercaptan in biological materials, after it is separated from its sample matrix (Al Mardini et al. 1984; Hayward et al. 1977; Johnsonand Tonzetich 1985; Rimbault et al. 1986; Tangerman et al. 1983, 1985). However, there are currently no methods available to qualitatively or quantitatively correlate exposure to methyl mercaptan with biomarkers in tissue or fluid. As discussed previously (Section 2.5), tissue and fluid levels of methyl mercaptan can be independent of exogenous exposure to that compound.

In the analysis of methyl mercaptan in biological materials, capillary gas chromatography, also commonly known as high-resolution gas chromatography (HRGC), has greatly facilitated the analysis of compounds such as methyl mercaptan that can be measured by gas chromatography and has resulted in vast improvements in resolution and sensitivity. The instrumental capability to separate volatile analytes by HRGC is, for the most part, no longer the limiting factor in their analysis.

It would be useful to have the means to transfer analytes that have been isolated from a biological matrix, quantitatively and in a narrow band, to the HRGC, and to identify and accurately measure the quantity of compounds in the HRGC peaks. Mass spectrometric detection and Fourier transform infrared spectroscopy (FTIR) may prove to be the most useful methods for these functions.

There is a lack of standard methods for the measurement of metabolites of methyl mercaptan in biological materials and development of these methods would facilitate their determination in routine practice.

Specific methods for biomarkers that correlate levels of methyl mercaptan or its metabolites with toxic effects in exposed populations are not available. These methods would be helpful in defining the potential health risks of certain tissue or fluid levels of these compounds, independent of their source.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Methods for determining the parent compound, methyl mercaptan, in water, air and waste samples with excellent selectivity and sensitivity are well developed (ASTM 1987, 1988; Badings et al. 1985; De Souza 1987; EPA 1986; Kang as and Ryosa 1988; Knarr and Rappaport 1980; Tangerman 1986; Van Langenhove et al. 1985), so the database in this area is good andundergoing constant improvement. For example, research is on-going to develop a "Master Analytical Scheme" for organic compounds in water (Michael et al. 1988), which includes methyl mercaptan as an analyte. The overall goal is to detect and quantitatively measure organic compounds at 0.1 μg/L in drinking

water, 1 ug/L in surface waters, and 10 μg/L in effluent waters. Analytes are to include numerous nonvolatile compounds and some compounds that are only "semi-soluble" in water, as well as volatile compounds (bp<l50"C).

Improved methods are needed for the determination of methyl mercaptan in solid environmental samples, including soil and sediments. The standard EPA Method 8240 for gas chromatography/mass spectrometry of volatile organics in wastes, soils, and sediments (EPA 1986) could be tested thoroughly for methyl mercaptan analysis and optimized for this application.

Sampling methodologies for compounds such as methyl mercaptan continue to pose problems such as nonrepresentative samples, insufficient sample volumes, contamination, and labor-intensive, tedious extraction and purification procedures (Green and Le Pape 1987). It is desirable to have means to measure organic compounds such as methyl mercaptan in situ in water and other environmental media without the need for sampling and extraction procedures to isolate the analyte prior to analysis.

Degradation products of methyl mercaptan in environmental media are difficult to determine because these products may come from a number of sources other than methyl mercaptan.

6.3.2 On-going Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of methyl mercaptan and other volatile organic compounds in blood. These methods use high resolution gas chromatography and magnetic sector mass spectrometry which gives detection limits in the low parts per trillion range.

Examination of the literature suggests that other studies are underway to improve means for determining methyl mercaptan and other reduced sulfur compounds in biological samples and environmental media. Improvements continue to be made in chromatographic separation and detection, including supercritical fluid extraction and supercritical fluid chromatography (Smith 1988). Fourier transform infrared flow cell detectors are sensitive and selective for the detection of compounds such as methyl mercaptan that have been separated by fluid chromatography (Wieboldt et al. 1988). Immunoassay methods of analysis are very promising for the determination of various organic pollutants and toxicants, and it is reasonable to assume that methyl mercaptan, and particularly its metabolites such as methyl-beta-Dthioglucuronide are candidates for this type of analysis.

7. REGULATIONS AND ADVISORIES

Because of its potential to cause adverse health effects in exposed people, a number of regulations and guidelines have been established for methyl mercaptan by various national and state agencies. These values are summarized in Table 7-1.

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Methyl Mercaptan

Agency	Description	Information	Reference
NATIONAL			
Regulations:			
a. Air:			
OSHA	PEL TWA	0.5 ppm (1 mg/m^3)	OSHA 1989 (29 CFR 1910.1000) Table Z-1-A
b. Water:			
EPA OWRS	General permits under NPDES	Yes	40 CFR 122, Appendix D, Table V
	Hazardous substance		40 CFR 116
	Reportable quantity	100 lbs	40 CFR 117.3
c. Nonspecific media:			
EPA OERR	Reportable quantity	100 lbs	EPA 1989a (40 CFR 302.4)
	Extremely hazardous substance TPQ	500 lbs	EPA 1987a (40 CFR 355)
EPA OSW	Hazardous waste constituent (Appendix VIII)	Yes	40 CFR 261
	Land disposal restrictions (proposed)	Yes	EPA 1989c (40 CFR 264, 268)
FDA	Food additive - synthetic flavoring substance	Yes	21 CFR 172.515
Guidelines:			
a. Air:			
ACGIH	TLV TWA	0.5 ppm (1 mg/m^3)	ACGIH 1986
NIOSH	IDLH	400 ppm	NIOSH 1985
	CEILING (15 min)	0.5 ppm	
STATE			
Regulations:			
a. Air:	Acceptable ambient air concentration		NATICH 1989
New York		3.30 μg/m^3 (1 yr)	
Virginia		16.0 μg/m^3 (24 hr)	
North Dakota	Maximum Acceptable Ambient Level	10 μg/m^3	Rydell 1990

ACGIH = American Conference of Governmental Industrial Hygienists; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IDLH = Immediately Dangerous to Life or Health Level; NIOSH = National Institute for Occupational Safety and Health; NPDES = National Pollutant Discharge Elimination System; OERR = Office of Emergency and Remedial Response; OSHA = Occupational Safety and Health Administration; OSW = Office of Solid Wastes; OWRS = Office of Water Regulations and Standards; PEL = Permissible Exposure Limit; TLV = Threshold Limit Value; TPQ = Threshold Planning Quantity; TWA = Time-Weighted Average

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9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (K_{oc}) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (K_d) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling Value -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, *or* postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

9. GLOSSARY

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days as specified in the Toxicological Profiles.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In Vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.

Lethal Concentration($_{Lo}$)(LC_{Lo}) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration($_{50}$) (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose($_{Lo}$)j (LD_{Lo}) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose($_{50}$) (LD_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time($_{50}$) (LT_{50}) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

9. GLOSSARY

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution. Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-hour shift.

q1* -- The upper-bound estimate of the low-dose slope of the dose-response curve -as determined by the multistage procedure. The ql* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and μg/m3 for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of'a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit *(STEL)* -- The maximum concentration *to* which *workers* can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

9. GLOSSARY

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA) -- An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX A

USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in nontechnical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or substance release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the substance.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)
Tables (2-1, 2-2, and 2-3) and figures (2-l and 2-2) are used to summarize health effects by duration of exposure and endpoint and to illustrate graphically levels of exposure associated with those effects. All entries in these tables andfigures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse-Effect Levels (NOAELS), Lowest-Observed-Adverse-Effect Levels (LOAELs) for Less Serious and Serious health effects, or Cancer Effect Levels (CELs). In addition, these tables and figures illustrate differences in response by species, Minimal Risk Levels (MRLs) ***to*** humans for noncancer end points, and EPA'S estimated range associated with an upper-bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. The LSE tables and figures can be used for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text.

The legends presented below demonstrate the application of these tables and figures. A representative example of LSE Table 2-l and Figure 2-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-1

(1) **Route of Exposure** One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data exist,

three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-l)and oral (LSE Figure 2-2) routes.

(2) **Exposure Duration** Three exposure periods: acute (14 days or less); intermediate (15 to 364 days); and chronic (365 days or more) are presented within each route of exposure. In this example, an inhalation study of intermediate duration exposure is reported.

(3) **Health Effect** The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table.

(4) **Kev to Figure** Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to define a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in Figure 2-l).

(5) **Species** The test species, whether animal or human, are identified in this column.

(6) **Exposure Frequencv/Duration** The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to [substance x] via inhalation for 13 weeks, 5 days per week, for 6 hours per day.

(7) **System** This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, anddermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect respiratory) was investigated in this study.

(8) **NOAEL** A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.00s ppm (see footnote "c").

(9) **LOAEL** A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest exposure level used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to

quantify the adverse effect accompanies the LOAEL. The "Less Serious" respiratory effect reported in key number 18 (hyperplasia) occurred at a LOAEL of 10 ppm.

(10) **Reference** The complete reference citation is given in Chapter 8 of the profile.

(11) **CEL** A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiological studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses which did not cause a measurable increase in cancer.

(12) **Footnotes** Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "c" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See LSE Figure 2-l

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure levels for particular exposure duration.

(13) **Exposure Duration** The same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14) **Health Effects** These are the categories of health effects for which reliable quantitative data exist. The same health effects appear in the LSE table.

(15) **Levels of Exposure** Exposure levels for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure levels are reported on the log scale "y" axis. Inhalation exposure is reported in mg/m3 or ppm and oral exposure is reported in mg/kg/day.

(16) **NOAEL** In this example, 18r NOAEL is the critical end point for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates a NOAEL for the test species (rat). The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) **CEL** Key number 38r is one of three studies for which Cancer Effect Levels (CELs) were derived. The diamond symbol refers to a CEL for the test species (rat). The number 38 corresponds to the entry in the LSE table.

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(18). **Estimated Upper-Bound Human Cancer Risk Levels** This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1^*).

(19). **Key to LSE Figure** The Key explains the abbreviations and symbols used in the figure.

1 → TABLE 2-1. Levels of Significant Exposure to [Chemical x] - Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	LOAEL (effect) Serious (ppm)	Reference
2 → INTERMEDIATE EXPOSURE							
3 → Systemic		5 ↓	6 ↓	7 ↓	8 ↓	9 ↓	10 ↓
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
Cancer					11 ↓		
38	Rat	18 mo 5d/wk 7hr/d				20 (CEL, multiple organs)	Wong et al. 1982
39	Rat	89-104 wk 5d/wk 6hr/d				10 (CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79-103 wk 5d/wk 6hr/d				10 (CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

12 → [b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5×10^{-3} ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

CEL = cancer effect level; d = day(s); hr = hour(s); LOAEL = lowest-observed-adverse-effect level; mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s)

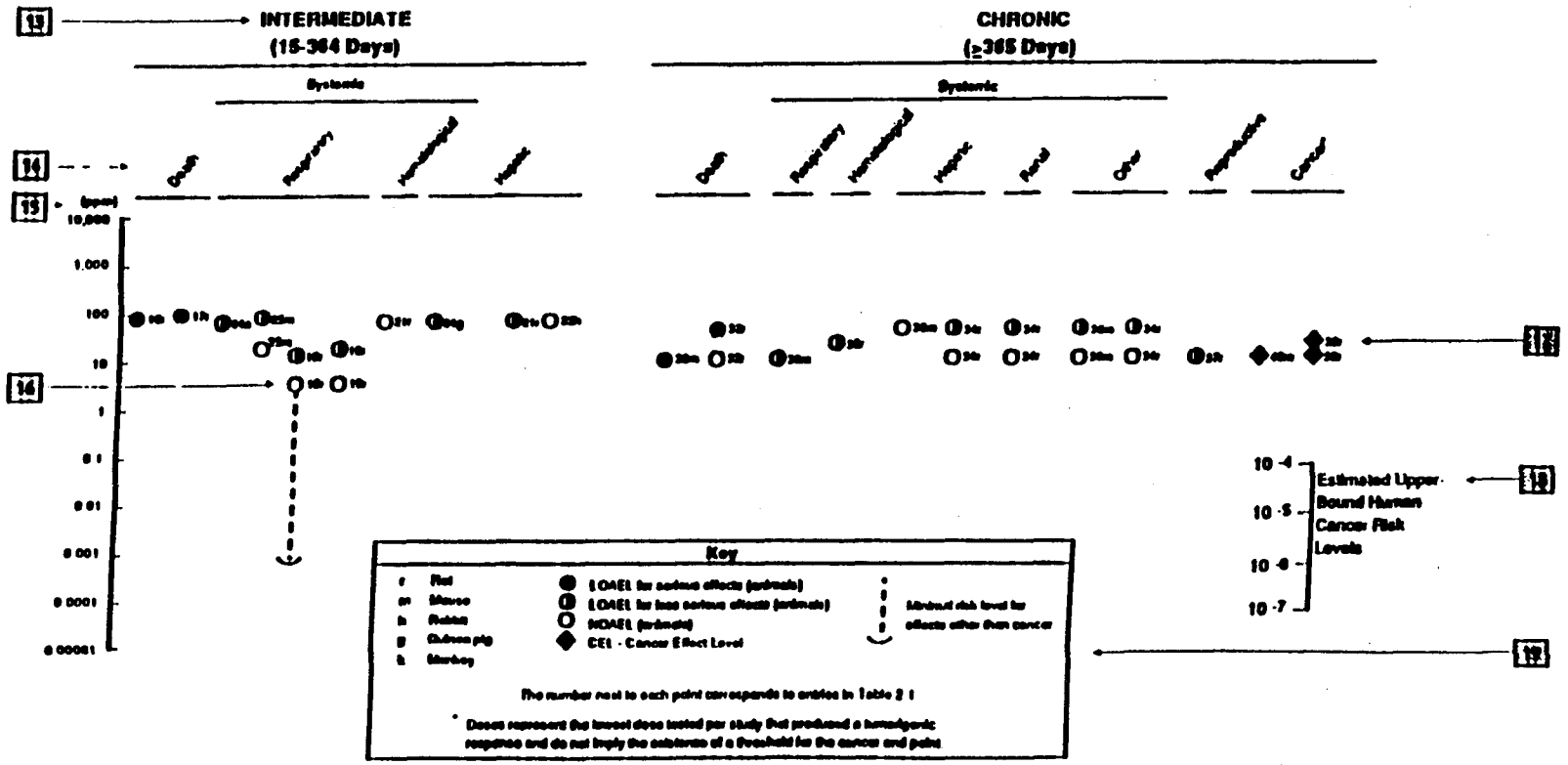

FIGURE 2-1. Levels of Significant Exposure to [Chemical X]-Inhalation

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Chapter 2 (Section 2.4)

Relevance to Public Health

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicological, epidemiological, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions.

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section discusses health effects by end point. Human data are presented first, then animal data. Both are organized by route of exposure (inhalation, oral, and dermal) and by duration (acute, intermediate, and chronic). In vitro data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. MRLs for noncancer end points if derived, and the end points from which they were derived are indicated and discussed in the appropriate section(s).

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Identification of Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information was available, MRLs were derived. MRLs are specific for route (inhalation or oral) and duration (acute, intermediate, or chronic) of exposure. Ideally, MRLs can be derived from all six exposure scenarios (e.g., Inhalation - acute, -intermediate, -chronic; Oral - acute, -intermediate, - chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a substance emission, given the concentration of a contaminant in air or the estimated daily dose received via food or water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

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MRL users should be familiar with the toxicological information on which the number is based. Section 2.4, "Relevance to Public Health," contains basic informationknown about the substance. Other sections such as 2.6, "Interactions with Other Chemicals" and 2.7, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology used by the Environmental Protection Agency (EPA) (Barnes and Dourson, 1988; EPA 1989a) to derive reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the end point which, in its best judgement, represents the most sensitive humanhealth effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential effects (e.g., systemic, neurological, and developmental). In order to compare NOAELs and LOAELs for specific end points, all inhalation exposure levels are adjusted for 24hr exposures and all intermittent exposures for inhalation and oral routes of intermediate and chronic duration are adjusted for continous exposure (i.e., 7 days/week). If the information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. The NOAEL is the most suitable end point for deriving an MRL. When a NOAEL is not available, a Less Serious LOAEL can be used to derive an MRL, and an uncertainty factor (UF) of 10 is employed. MRLs are not derived from Serious LOAELs. Additional uncertainty factors of 10 each are used for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the adjusted inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.

APPENDIX B

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BSC	Board of Scientific Counselors
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CLP	Contract Laboratory Program
cm	centimeter
CNS	central nervous system
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
f_1	first generation
fpm	feet per minute
ft	foot
FR	Federal Register
g	gram
GC	gas chromatography
HPLC	high performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health
IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio
kg	kilogram
Koc	octanol-soil partition coefficient
Kow	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration low
LC_{50}	lethal concentration 50 percent kill
LD_{Lo}	lethal dose low
LD_{50}	lethal dose 50 percent kill
LOAEL	lowest-observed-adverse-effect level

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LSE	Levels of Significant Exposure
m	meter
mg	milligram
min	minute
mL	milliliter
mm	millimeters
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectroscopy
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
nm	nanometer
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPL	National Priorities List
NRC	National Research Council
NTIS	National Technical Information Service
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
pg	picogram
pmol	picomole
PHS	Public Health Service
PMR	proportional mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure limit
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SCE	sister chromatid exchange
SIC	Standard Industrial Classification
SMR	standard mortality ratio
STEL	short-term exposure limit
STORE	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxic Release Inventory
TWA	time-weighted average
U.S.	United States
UF	uncertainty factor

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WHO	World Health Organization
>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
μm	micron
μg	microgram

APPENDIX C

PEER REVIEW

A peer review panel was assembled for methyl mercaptan. The panel consisted of the following members: Dr. Sharon Johnson, Visiting Scientist, Department of Biology, Johns Hopkins University; Dr. Derek Hodgson, Chairman, Department of Chemistry, University of Wyoming; Dr. Shane Que Hee, Associate Professor, School of Public Health, University of California. These experts collectively have knowledge of methyl mercaptan's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability, as amended.

A joint panel of scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.