TOXICOLOGICAL PROFILE FOR VANADIUM AND COMPOUNDS

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

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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.

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Disease Registry

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1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about vanadium and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,177 sites on its National Priorities List (NPL). Vanadium has been found at 23 of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for vanadium. As EPA evaluates more sites, the number of sites at which vanadium is found may change. The information is important for you because vanadium may cause harmful health effects and because these sites are potential or actual sources of human exposure to vanadium.

When a chemical is released from a large area, 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 substance such as vanadium, 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 VANADIUM?

Vanadium is a natural element in the earth. It is a white to gray metal, often found as crystals. It has no particular odor. Vanadium occurs naturally in fuel oils and coal. In the environment it is usually combined with other elements such as oxygen, sodium, sulfur, or chloride. The forms of vanadium most likely to be found at waste sites are not well known. One manmade form, vanadium oxide (vanadium bound to oxygen), is most often used by industry, mostly in making steel. Vanadium oxide can be a yellow-orange powder, dark-grey flakes, or yellow crystals. Much smaller amounts are used in making rubber, plastics, ceramics, and certain other chemicals. The most likely way for the chemical to get into the air is when fuel oil is burned. When rocks and soil containing vanadium are broken down into dusts by wind and rain, vanadium can get into the air, groundwater, surface water, or soil. It does not dissolve well in water, but it can be carried by the water, much as particles of sand might be carried. For more information on its forms and uses, see Chapters 3 and 4.

1.2 HOW MIGHT I BE EXPOSED TO VANADIUM?

Most people are exposed daily to very low levels of vanadium in food, drinking water, and air. Most of your intake is from food, and you eat about 10-20 micrograms daily. The vanadium in these sources is at least partially due to naturally occurring vanadium in rocks and soil. Vanadium is naturally found in soil and rocks at about 150 parts of vanadium per million parts of soil (150 ppm) in the earth's crust. Vanadium combined with oxygen (vanadium oxide) gets into the air when people burn fuel oil or coal. You can be exposed to vanadium if you breathe in this air. Vanadium pentoxide is in dusts in some factories that use it for making steel. Ash from burning fuel oil or the leftover products from processing vanadium-containing ore can be put into landfills following proper treatment procedures. If these products are crushed, it is possible that you might breathe in some dusts containing vanadium. Also, the action of rain and wind may cause some vanadium to move out of a landfill and onto nearby soil, food crops, and water supplies. Some foods contain either naturally occurring vanadium or vanadium from man-made sources; you can be exposed to vanadium when you eat these foods. Vanadium has been found in groundwater and at hazardous waste sites throughout the United States. The exposure routes most likely at hazardous waste sites are not well known. For more information on how you might be exposed to vanadium, see Chapter 5.

1.3 HOW CAN VANADIUM ENTER AND LEAVE MY BODY?

If vanadium is in the air, you can breathe it into your lungs. Most of it leaves your body in the air you breathe out, but some stays in your lungs. The part that isn't breathed out can go through your lungs and get into your bloodstream. You may eat or drink small amounts of vanadium in food and water. Most of this does not enter your bloodstream, but leaves your body in your feces. However, small amounts that you swallow can enter your bloodstream. Most of the vanadium that enters your bloodstream leaves your body quickly in the urine. If you get vanadium on your skin, it is unlikely that it will enter your body by passing through your skin. For more information about how vanadium enters and leaves your body, see Chapter 2.

1.4 HOW CAN VANADIUM AFFECT MY HEALTH?

If you breathe large amounts of vanadium dusts for short or long periods, you will have lung irritation that can make you cough, and you can also have a sore throat and red irritated eyes. These effects stop soon after you stop breathing it. People who breathed 0.1 milligram (mg) of vanadium per cubic meter (m^3) of air for 8 hours coughed for about 1 week and had irritated eyes. No studies designed to look for cancer in laboratory animals exposed to vanadium were found. In studies that looked for health effects other than cancer, rats and mice that drank water containing vanadium or breathed in air containing vanadium throughout their lives did not have more tumors than animals that were not exposed to vanadium. Some minor birth defects (such as

slightly smaller offspring, offspring with broken blood vessels on parts of their bodies or chemical changes in their lungs) occurred when female rats drank vanadium in water when they were pregnant. We do not know if vanadium would cause birth defects in people because these effects may occur only in animals. Monkeys and rats that breathed the dusts of vanadium compounds had changes in the cells in the lungs. Rats that drank sodium metavanadate in the water had minor kidney damage. Rabbits that breathed large amounts of vanadium dust died, as did rats and mice that drank large amounts. For more information on health effects in people and animals after breathing, eating, or touching vanadium, see Chapter 2.

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

Since vanadium is a natural element in the earth, we all have a small amounts in our bodies. There are some tests to show whether you have been exposed to larger than normal amounts of vanadium. Vanadium can be measured in the urine and blood. People exposed to larger than normal amounts will show larger than normal amounts in their urine and blood for a few days. Some workers who have been exposed to large amounts of vanadium may have a green color on the tongue. None of these tests can tell if you will become sick from the vanadium but they are specific for vanadium exposure. For more information on ways to tell whether you have been exposed to vanadium see Chapters 2 and 6.

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

Releases to the environment of more than 1,000 pounds of vanadium pentoxide must be reported to the National Response Center. EPA has decided that if you eat less than 9 micrograms (μg) of vanadium pentoxide per kilogram (kg) of your body weight, your health is protected. The Occupational Safety and Health Administration (OSHA) has set a legal limit of 0.05 mg of vanadium pentoxide respirable dust per m^3 of air (0.05 mg/m^3) for workers who are exposed to vanadium in workroom air during an 8-hour shift for a 40-hour workweek. Respirable dust is dust small enough to enter the lungs when breathed in. For more information on regulations and guidelines, see 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:

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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 vanadium 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 vanadium based on toxicological studies and epidemiological investigations.

Elemental vanadium does not occur in nature; however, vanadium compounds exist in over 50 different mineral ores and in association with fossil fuels. It has six oxidation states (l-, 0, 2+, 3+, 4+, and 5+) of which 3+, 4+, and 5+ are the most common. The toxicologically significant compounds are vanadium pentoxide (V_2O_5), sodium metavanadate ($NaVO_3$), sodium orthovanadate (Na_3VO_4), vanadyl sulfate ($VOSO_4$), and ammonium vanadate (NH_4VO_3). Vanadium pentoxide dust is usually encountered in occupational settings, and humans would be exposed via the inhalation route. Information for the other vanadium compounds comes from oral studies in animals.

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 noobserved-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.

Although methods have been established to derive these levels (Barnes et al. 1988; EPA 1989), 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

2.2.1.1 Death

No studies were located regarding death in humans after inhalation exposure to vanadium.

Only one study was located regarding death in animals after inhalation exposure to vanadium. In this study designed to determine the LD_{50}, two of four rabbits died following an acute exposure to 114 mg vanadium/m^3 as vanadium pentoxide (Sjoeberg 1950). The NOAEL and LOAEL values are recorded in Table 2-1 and plotted in Figure 2-1.

2.2.1.2 Systemic Effects

The highest NOAEL values and all reliable LOAEL values for each species and duration category are recorded in Table 2-1 and plotted in Figure 2-1.

Respiratory Effects. One experimental study utilizing two volunteers provided accurate exposure levels and showed that mucus formed and coughing occured following an acute exposure to 0.06 mg vanadium/m^3 as vanadium pentoxide (Zenz and Berg 1967). The onset of coughing and of mucus formation was delayed 7-24 hours. Pulmonary function tests were normal. This LOAEL was used to calculate the acute inhalation MRL of 0.0002 mg vanadium/m^3. Vanadium is used in making steel and is released from burning fuel oil, therefore, occupational exposure to vanadium pentoxide dusts stems mostly from metallurgy and boiler-cleaning. Workers exposed to a range of levels of vanadium pentoxide dusts for as little as 1 day (Levy et al. 1984; Musk and Tees 1982; Thomas and Stiebris 1956; Zenz et al. 1962), or as long as 6 or more years

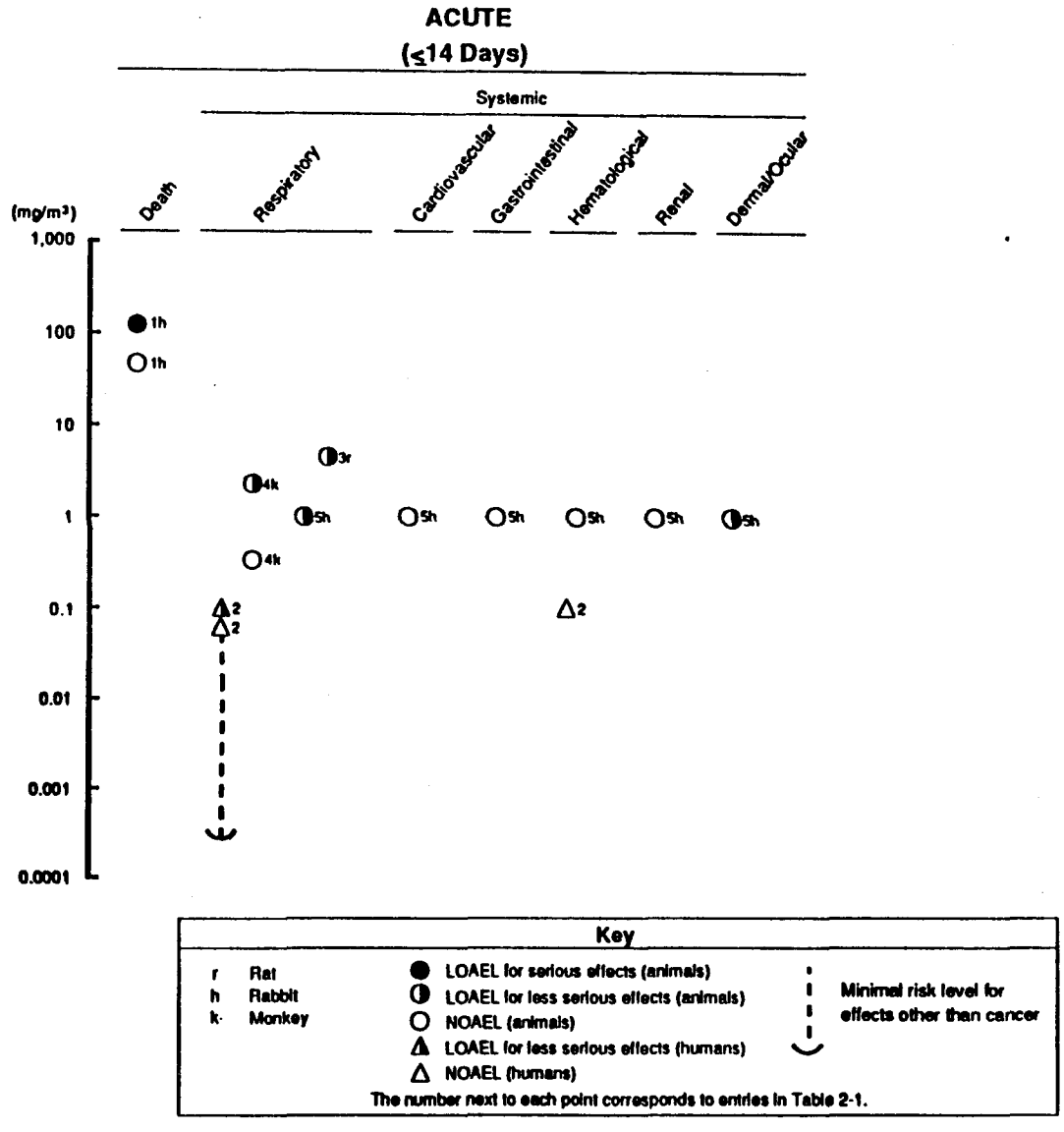
TABLE 2-1. Levels of Significant Exposure to Vanadium and Compounds - Inhalation

Key to figure[a]	Species	Exposure duration/ frequency	System	NOAEL (mgV/m^3)	LOAEL (effect) Less serious (mgV/m^3)	LOAEL (effect) Serious (mgV/m^3)	Reference	Form
ACUTE EXPOSURE								
Death								
1	Rabbit	1 d 7 hr/d		43		114 (2/4 died)	Sjoeberg 1950	V_2O_5
Systemic								
2	Human	8 hr	Resp Hemato	1	0.06[b] (bronchial irritation)		Zenz and Berg 1967	V_2O_5
3	Rat	2 wk 5 d/wk 6 hr/d	Resp		4.7 (alveolar proteinosis)		Lee and Gillies 1986	$BiVO_4$
4	Monkey	2 wk 1 d/wk 6 hr/d	Resp	0.34	2.5 (less lung function)		Knecht et al. 1985	V_2O_5
INTERMEDIATE EXPOSURE								
Systemic								
5	Rabbit	8 mo 1 hr/d	Resp Derm/oc Renal Gastro Cardio Hemato	0.8 0.8 0.8 0.8	0.8 (dyspnea) 0.8 (eye irritation)		Sjoeberg 1950	V_2O_5

[a]The number corresponds to entries in Figure 2-1.
[b]Used to derive an acute inhalation Minimal Risk Level (MRL) of 0.0002 mg vanadium/m^3. Concentration divided by uncertainty factor of 100 for human variability and use of a LOAEL and multiplied by 8/24 to extrapolate to a full day exposure.

$BiVO_4$ = bismuth orthovanadate; Cardio = cardiovascular; d = day(s); Derm/oc = Dermal/ocular; Gastro = gastrointestinal; Hemato = hematological; hr = hour(s); LOAEL = lowest-observed-adverse-effect level; mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory; V = vanadium; V_2O_5 = vanadium pentoxide; wk = week(s)

FIGURE 2-1. Levels of Significant Exposure To Vanadium and Compounds - Inhalation



(Lewis 1959; Orris et al. 1983; Sjoeberg 1956; Vintinner et al. 1955; Wyers 1946), show mild respiratory distress, such as cough, wheezing, chest pain, runny nose, or sore throat. One study of chronically-exposed workers showed increased neutrophils in the nasal mucosa (Kiviluoto et al. 1979, 1980, 1981. More severe pathology has not been reported. Symptoms are reversible within days or weeks after exposure ceases. Inhalation exposure is believed to predominate in occupational settings but oral (mucociliary clearance) could contribute to total exposure. Data were not located to assess the relationship of exposure level *or* duration to severity of response. Chest x-rays and pulmonary function tests were normal in most cases. Chronic effects were infrequently reported.

Animal data support the human findings and provide additional evidence that vanadium cornpounds are respiratory toxicants. Monkeys that breathed 2.8 mg vanadium/m^3 as vanadium pentoxide for 6 hours showed increased pulmonary resistance 1 day later which was not seen at 0.3 mg vanadium/m^3 (Knecht et al. 1985). They also had a dramatic increase in polymorphonuclear leucocytes in bronchioalveolar lavage, thus increasing total cell counts. Rats that breathed bismuth orthovanadate for 6 hours a day for 2 weeks showed increases in lung weight, and alveolar proteinosis as shown by an increased accumulation of alveolar macrophages, lung lipids, and type II pneumocytes (Lee and Gillies 1986). Rabbits that were exposed for one hour a day for 8 months had difficulty breathing (Sjoeberg 1950).

Cardiovascular Effects. Workers exposed chronically to vanadium pentoxide dusts at incompletely documented exposure levels had normal blood pressure values (Vintinner et al. 1955). No other cardiovascular parameters were investigated in this study, but another study revealed normal electrocardiograms in vanadium workers (Sjoeberg 1950).

Rabbits exposed one hour a day for 8 months to vanadium pentoxide did not show histopathological evidence of cardiovascular damage (Sjoeberg 1950), but this study does not provide a thorough investigation of cardiovascular function.

Gastrointestinal Effects. Volunteers exposed acutely to vanadium pentoxide dusts had no gastrointestinal complaints (Zenz and Berg 1967). People who were exposed to vanadium in oil-burner ashes also did not show gastrointestinal symptoms (Sjoeberg 1950). One study found that workers exposed chronically to vanadium dusts in factories sometimes complained of nausea and vomiting (Levy et al. 1984), but these symptoms can have a number of causes (such as exposure to other substances) and cannot be directly attributed to the vanadium. These people probably also swallowed *some* of the dusts.

Rabbits exposed for 8 months to high levels (200 mg/m^3) of vanadium pentoxide dusts showed little histopathological damage to the gastrointestinal system (Sjoeberg 1950).

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Hematological Effects. Volunteers exposed acutely (Zenz and Berg 1967),as well as workers exposed chronically to vanadium dusts, had normal hematological values (Kiviluoto et al. 1981a; Sjoeberg 1950; Vintinner et al. 1955).

Rabbits exposed acutely or chronically to vanadium pentoxide dusts showed no bone marrow changes upon histological examination (Sjoeberg 1950).

Musculoskeletal Effects. Muscular strength was not. altered in one study of workers exposed to vanadium pentoxide (Vintinner et al. 1955).

No studies were located regarding musculoskeletal effects in animals after inhalation exposure to vanadium.

Hepatic Effects. Workers exposed chronically to 0.01-0.5 mg/m^3 of vanadium dusts had normal-serum levels of four enzymes (serum alkaline phosphatase, alanine amino-transferase, aspartate aminotransferase, and lactate dehydrogenase) that are commonly used to detect possible liver damage (Kiviluoto et al. 1981a).

Rabbits exposed for 8 months to vanadium pentoxide dusts showed some fatty degeneration of the liver (Sjoeberg 1950). However, liver functidn was not tested, and the author stated, without explanation, that the liver changes were of no special significance.

Renal Effects. Workers exposed chronically to 0.01-0.5 mg/m^3 of vanadium dusts had normal serum levels of 18 enzymes and other substances commonly used to detect possible kidney damage (Kiviluoto et al. 1981b). Workers in other studies of chronic exposure to vanadium had normal urine levels of substances used to detect kidney disease (casts, protein levels, urea) (Sjoeberg 1950; Vintinner et al. 1955).

Rabbits exposed acutely or chronically to vanadium pentoxide dusts showed fatty degeneration of the kidney, but the author, without explanation, did not attribute this to the vanadium (Sjoeberg 1950). No other studies were located regarding hepatic effects in animals following inhalation exposure to vanadium.

Dermal/Ocular Effects. Workers chronically exposed to vanadium dusts in factories had slight to moderate eye irritation in addition to respiratory distress (Levy et al. 1984; Lewis 1959; Sjoeberg 1950; Thomas and Stiebris 1956; Vintinner et al. 1955). Brief exposure to vanadium dust can also cause conjunctivitis (Zenz et al. 1962). The other significant peripheral finding in some workers was a green discoloration of the tongue attributed to direct deposition of vanadium. Workers had no increases in dermatitis as compared to controls (Vintinner et al. 1955), but some workers had skin rashes (Orris et al. 1983).

Rabbits exposed to vanadium pentoxide dusts also showed conjunctivitis (severity not specified) from acute or chronic exposures (Sjoeberg 1950).

Other Systemic Effects. Workers exposed to vanadium ore dust also reported weight loss (Vintinner et al. 1955).

2.2.1.3 Immunological Effects

The only human data located found that workers chronically exposed to unspecified levels of vanadium dusts in factories showed no significant signs of allergic reactions on the skin or in the respiratory system (Sjoeberg 1950). .This, however, cannot be considered to be an adequate evaluation of immunological function.

Rabbits exposed acutely or chronically to vanadium pentoxide dusts did not show histopathological changes in the spleen (Sjoeberg 1950), but this is not a complete assessment of the immune system.

2.2.1.4 Neurological Effects

Volunteers exposed acutely had no neurological complaints (Zenz and Berg 1967). Most workers exposed to vanadium dusts did not report major adverse neurological signs (Sjoeberg 1956; Vintinner et al. 1955). However, some workers complained of dizziness, depression, headache, or tremors of the fingers and arms (Levy et al. 1984; Vintinner et al. 1955), which may or may not have been specifically due to vanadium exposure.

Rabbits exposed to vanadium pentoxide for 8 months did not show pathological changes in the brain (Sjoeberg 1950). No other animal studies were located which tested neurological function.

No studies were located regarding the following health effects in humans or animals after inhalation exposure to vanadium.

2.2.1.5 Developmental Effects

2.2.1.6 Reproductive Effects

2.2.1.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.4.

2.2.1.8 Cancer

No studies were located regarding cancer in humans or animals after inhalation exposure to vanadium.

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding death in humans after oral exposure to vanadium.

A gavage study has shown that 41 mg vanadium/kg as sodium metavanadate is the LD_{50} (14 days) for rats, and the value for mice is 31.2 mg/kg (Llobet and Domingo 1984). These values are recorded in Table 2-2 and plotted in Figure 2-2. Chronic exposures of up to 4.1 mg vanadium/kg as vanadyl sulfate in food or water did not affect mortality in rats or mice, respectively (Schroeder and Balassa 1967; Schroeder et al. 1970).

2.2.2.2 Systemic Effects

The highest NOAEL values and all reliable LOAEL values for body weight changes in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

No studies were located regarding musculoskeletal or dermal/ocular effects in humans or animals following oral exposure to vanadium.

Respiratory Effects. No studies were located regarding respiratory effects in humans after oral exposure to vanadium.

Rats receiving sodium metavanadate in the drinking water for 3 months had mononuclear cell infiltration, mostly perivascular, in the lungs (Domingo et al. 1985).

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans after oral exposure to vanadium.

Rats fed 15 mg vanadium/kg as ammonium vanadate for 2 months showed increased right ventricular pressure and pulmonary hypertension, but no changes in systemic circulation (Susie and Kentera 1986). This laboratory also showed that sodium orthovanadate in the food for 6 months did not alter heart rate or blood pressure, but did induce vasoconstriction (Susic and Kentera 1988). Rats that had one kidney removed had increased systolic blood pressure within 7 weeks of consuming 5 mg/kg/day of vanadium in the diet (Steffen et al. 1981).

Gastrointestinal Effects. Very few data are available regarding gastrointestinal effects. Human volunteers (assumed body weight, 70 kg) given 0.47-1.3 mg vanadium/kg as ammonium vanadyl tartrate in capsules for 45-68 days had intestinal cramping and diarrhea (Dimond et al. 1963). Since vehicle and compound controls were not used, it is difficult to determine whether this effect was caused by the vanadium. Workers exposed to vanadium

TABLE 2-2. Levels of Significant Exposure to Vanadium and Compounds - Oral

Key to figure[a]	Species	Route	Exposure duration/ frequency	System	NOAEL (mg V/kg/day)	LOAEL (effect) Less serious (mg V/kg/day)	LOAEL (effect) Serious (mg V/kg/day)	Reference	Form
ACUTE EXPOSURE									
Death									
1	Rat	(GW)	1 d 1 x/d		16		41 (LD_{50})	Llobet and Domingo 1984	$NaVO_3$
2	Mouse	(GW)	1 x		17		31 (LD_{50})	Llobet and Domingo 1984	$NaVO_3$
Developmental									
3	Rat	(G)	GD 6-14			8.4 (facial hemorrhage)		Paternain et al. 1987	$NaVO_3$
INTERMEDIATE EXPOSURE									
Systemic									
4	Human	(C)	45-68 d	Hepatic Hemato Renal	1.3 1.3 1.3			Dimond et al. 1963	
5	Rat	(W)	3 mo	Renal Resp Hepatic	0.3[b] 0.3 2.87	0.57 (hemorrhagic foci) 0.57 (vascular infiltration)	2.87 (effects increase)	Domingo et al. 1985	$NaVO_3$
6	Rat	(F)	100 d	Other	2	3.9 (decreased weight gain in females)		Franke and Moxon 1937	$NaVO_3$
7	Rat	(F)	75-103d	Hemato Other	6.6 6.6	30 (decreased weight) gain)		Mountain et al. 1953	V_2O_5
8	Rat	(F)	2 mo	Cardio		15 (increased ventricular pressure)		Susic and Kentera 1986	NH_4VO_3
Immunological									
9	Mouse	(W)	4-13 wk		6.5			Sharma et al. 1981	Na_3VO_4

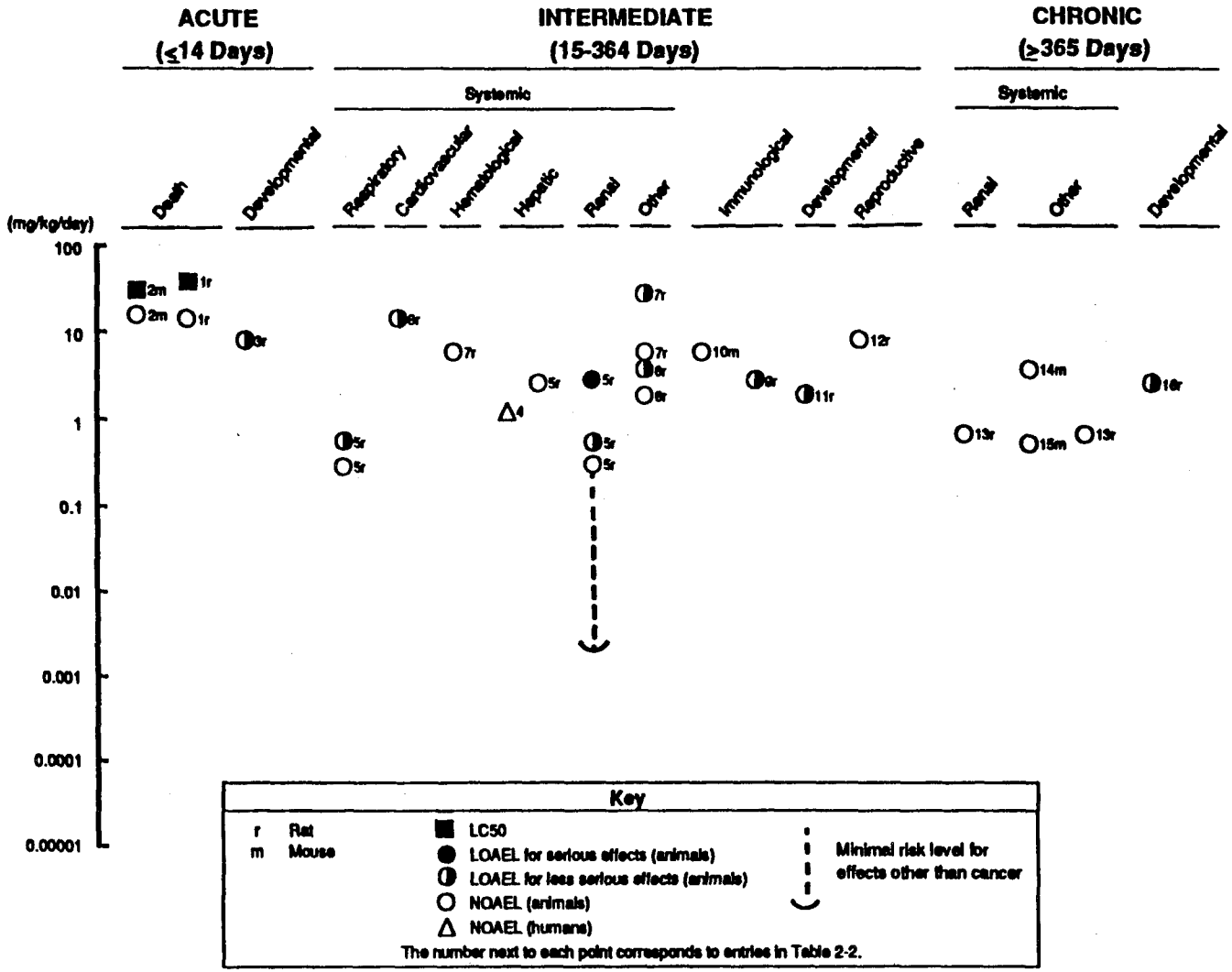
TABLE 2-2 (Continued)

Key to figure[a]	Species	Route	Exposure duration/ frequency	System	NOAEL (mg V/kg/day)	LOAEL (effect) Less serious (mg V/kg/day)	LOAEL (effect) Serious (mg V/kg/day)	Reference	Form
Developmental									
10	Rat	(G)	60 d			2.1 (reduced pup weigh and length)		Domingo et al. 1986	$NaVO_3$
Reproductive									
11	Rat	(GW)	60 d		8.4			Domingo et al. 1986	$NaVO_3$
CHRONIC EXPOSURE									
Systemic									
12	Rat	(W)	2.5 yr	Renal Other	0.7 0.7			Schroeder et al. 1970	$VOSO_4$
13	Mouse	(F)	2 yr	Other Cardio Renal Resp Hemato	4.1 4.1 4.1 4.1 4.1			Schroeder and Balassa 1967	$VOSO_4$
14	Mouse	(W)	2.5 yr	Other	0.54			Schroeder and Mitchner 1975	$VOSO_4$
Developmental									
15	Rat	(W)	2 gen ad lib			2.8 (altered lung collagen)		Kowalska et al. 1988	$NaVO_3$

[a]The number corresponds to entries in Figure 2-2.
[b]Used to derive an intermediate oral Minimal Risk Level (MRL) of 0.003 mg/kg/day. Dose divided by uncertainty factors of 10 for human variability and 10 for interspecies variability.

ad lib = ad libitum; AVT = ammonium vanadyl tartrate; (C) = capsule; Cardio = cardiovascular; d = day(s); (F) = food; (G) = gavage, vehicle not specified; (GW) = gavage in water; Gd = gestation day; gen = generation; Hemato = hematological; LD_{50} = lethal dose, 50% kill; LOAEL = lowest-observed-adverse-effect level; mo = month(s); $NaVO_3$ = sodium metavanadate; Na_3VO_4 = sodium orthovanadate; NH_4VO_3 = ammonium metavanadate; NOAEL = no-observed-adverse-effect level; Resp = respiratory; V = vanadium; V_2O_5 = vanadium pentoxide; $VOSO_4$ = vanadyl sulfate; (W) = drinking water; wk = week(s); x = time(s); yr = year(s)

FIGURE 2-2. Levels of Significant Exposure To Vanadium and Compounds - Oral



dusts may have swallowed some of the dusts. Some experienced nausea and vomiting (Levy et al. 1984). A study designed to look at hematological changes noted that the rats exposed to the highest dietary dose of 50 ppm exhibited diarrhea throughout the experiment (Franke and Moxon 1937).

Hematological Effects. Human volunteers (assumed body weight, 70 kg) given 0.47-1.3 mg vanadium/kg as ammonium vanadyl tartrate in capsules for 45-68 days had no hematological abnormalities as measured by white blood cell count, differential count, platelets and reticulocytes (Dimond et al. 1963). Sodium metavanadate in food for 100 days had no effect on hemoglobin levels in rats (Franke and Moxon 1937).

Hepatic Effects. The one human study located showed no changes in serum glutamic oxaloacetic transferase, cholesterol, triglyceride, or phospholipid levels following exposure to 0.47-1.3 mg vanadium/kg as ammonium vanadyl tartrate in capsules for 45-68 days (Dimond et al. 1963). Rats given sodium metavanadate in the drinking water for 3 months also did not show enzyme activity levels, bilirubin levels, or cholesterol levels indicative of liver damage (Domingo et al. 1985).

Renal Effects. Humans given 0.47-1.3 mg vanadium/kg as ammonium vanadyl tartrate capsules for 45-68 days did not show any changes in urinalysis for albumin, hemoglobin, or formed elements. Blood urea nitrogen levels were also unchanged (Dimond et al. 1963).

Minor renal effects (altered renal function, as indicated by increased plasma urea, and mild histological changes) were seen in rats after oral exposure to sodium metavanadate for 3 months at levels up to 10% of the oral LD_{50} (Domingo et al. 1985). The author reported a dose-related trend, but quantitative histopathological data were not provided. This study was used to calculate an oral MRL for intermediate exposure as indicated in the footnote in Table 2-2.

Other Systemic Effects. No studies were located regarding other systemic effects in humans after oral exposure to vanadium.

Rats given sodium metavanadate in the food for an intermediate period of time showed a slight decrease in body weight (Franke and Moxon 1937; Mountain et al. 1953). Mice chronically exposed to vanadyl sulfate in the drinking water showed a slight, but not statistically significant, weight increase as compared to controls (Schroeder and Mitchener 1975), while experiments from the same laboratory under comparable exposure conditions showed no weight changes in other mice or rats (Schroeder and Balassa 1967; Schroeder et al. 1970), respectively.

2.2.2.3 Immunological Effects

No studies were located regarding immunological effects in humans after oral exposure to vanadium.

Minimal information on immunological effects in animals was located. Mice exposed to vanadium in the drinking water for 1-3 months showed a dose-related but nonsignificant decrease in the antibody-forming cells in the spleen when challenged with sheep erythrocytes (Sharma et al. 1981). Mild spleen hypertrophy and hyperplasia were seen in rats treated with vanadium in the drinking water for 3 months (Domingo et al. 1985), but further immunological tests were not performed. The human NOAEL and rat LOAEL are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.4 Neurological Effects

No studies were located regarding neurological effects in humans or animals after oral exposure to vanadium.

2.2.2.5 Developmental Effects

No studies were located regarding developmental effects in humans after oral exposure to vanadium.

Oral exposure to sodium metavanadate had only very slight effects in the development of rats. One study showed no embryolethality, teratogenicity, or significant skeletal or visceral abnormalities in pups exposed during gestation (Paternain et al. 1987). There was an increase (but,not doserelated) in facial and dorsal hemorrhages. The toxicological significance of this finding is not known. Maternal toxicity was not described. A two-generation, one-dose study in rats showed altered lung collagen metabolism in fetuses of adults with life-time exposure (Kowalska 1988). The toxicological significance of this finding is also not known. When rat dams were given high doses of sodium metavanadate in a reproduction study, pup size (weight and length) was only slightly (but statistically significantly) reduced at birth and throughout lactation (Domingo et al. 1986). More severe developmental effects were not seen. The rat dams did not show toxicity. Reliable LOAEL values from these studies are recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.6 Reproductive Effects

No studies were located regarding reproductive effects in humans after oral exposure to vanadium.

Gavage doses of sodium metavanadate given to male and female rats before mating and to female rats during gestation and lactation did not affect fertility, reproduction, or parturition (Domingo et al. 1986). This NOAEL value is recorded in Table 2-2 and plotted in Figure 2-2.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals after oral exposure to vanadium. Genotoxicity studies are discussed in Section 2.4.

2.2.2.8 Cancer

No studies were located that specifically studied cancer in humans or animals after oral exposure to vanadium. However, some studies designed to test other end points noted no increase in tumor frequency in rats and mice chronically exposed to 0.5-4.1 mg vanadium/kg as vanadyl sulfate in drinking water (Schroeder and Balassa 1967; Schroeder and Mitchener 1975; Schroeder et al. 1970).

Although results of these oral studies were negative for carcinogenicity, they were inadequate for evaluating carcinogenic effects because insufficient numbers of animals were used, it was not determined whether or not a maximum tolerated dose was achieved, a complete histological examination was not performed, and only one exposure dose per study was evaluated.

2.2.3 Dermal Exposure

No studies were located regarding the following health effects in humans or animals after dermal exposure to vanadium.

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

Genotoxicity studies are discussed in Section 2.4.

2.2.3.8 Cancer

No studies were located regarding cancer in humans or animals after dermal exposure to vanadium.

2.3 TOXICOKINETICS

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

Several occupational studies indicate that absorption can occur in humans following inhalation exposure. An increase in urinary vanadium levels was found in workers exposed to less than 1 ppm of vanadium (Gylseth et al. 1979; Kiviluoto et al. 1981b; Lewis 1959; Orris et al. 1983). The vanadium concentration in serum was also reported to be higher than the nonoccupationally exposed controls following exposure to vanadium pentoxide dust (Kiviluoto et al. 1981b). There is a possibility that oral exposure (mucociliary clearance) contributed to vanadium levels in the serum. The rate and extent of vanadium absorption in humans is not known.

Indirect evidence of absorption after inhalation of vanadium in animals is indicated in studies in which vanadium was administered intratracheally. Soluble vanadium compounds that are inhaled and deposited are readily absorbed. Initial pulmonary clearance is rapid in rats. There was rapid 100% absorption of vanadium in rats receiving radiolabeled vanadyl chloride (Conklin et al. 1982). The greatest absorption of a radioactive dose, ^{48}V, was found to occur 5 minutes after administration (Roshchin et al. 1980). Most of the vanadium, 80% and 85% of the tetravalent (V4+) and pentavalent (V5+) forms of vanadium, respectively, cleared from the lungs 3 hours after intratracheal exposure (Edel and Sabbioni 1988). After 24 hours, more than 50% of vanadyl oxychloride was cleared from the lungs of male rats (Oberg et al. 1978), and at 3 days, 90% of vanadium pentoxide was eliminated from the lungs of female rats (Conklin et al. 1982). In another study 50% was cleared in 18 minutes, and the rest within a few days (Rhoads and Sanders 1985).

Intratracheal administration of vanadium in rats indicates that rapid absorption of vanadium in humans may occur following acute exposure. Indirect evidence from occupational studies suggests that absorption of vanadium after chronic exposure to vanadium pentoxide may also occur.

2.3.1.2 Oral Exposure

No studies were located regarding the rate and extent of absorption in humans after oral exposure to vanadium. No systemic toxic effects were observed in volunteers who consumed vanadium as ammonium vanadyl tartrate in capsules, suggesting that it may be poorly absorbed (Dimond et al. 1963).

The absorption of vanadium through the gastrointestinal tract of animals is low. Less than 0.1% of an intragastric dose was detectable in the blood of rats at 15 minutes postexposure, and less than 1% at 1 hour (Roshchin et al. 1980). Similarly, only 2.6% of an orally administered radiolabeled dose of vanadium pentoxide was absorbed 3 days after exposure in rats (Conklin et al.

1982). Indirect evidence is also given from animal studies indicating that a portion of vanadium is absorbed following oral administration. Vanadium was reported in tissues and urine within hours after a single (Edel and Sabbioni 1988) and repeated oral exposure in rats (Bogden et al. 1982; Parker and Sharma 1978). Young rats that consumed vanadium in the drinking water and feed were found to have higher tissue vanadium levels 21 days after birth than they did 115 days after birth (Edel et al. 1984). The data suggest that there is a higher absorption of vanadium in these young animals due to a greater nonselective permeability of the undeveloped intestinal barrier.

2.3.1.3 Dermal Exposure

No specific studies were located regarding absorption in humans or animals after dermal exposure to vanadium, although absorption by this route is generally considered to be very low (WHO 1988). Because vanadium is a metal, absorption through the skin is thought to be quite minimal due to its low solubility.

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

No data have been located regarding the distribution of vanadium in humans immediately following exposure. At autopsy, vanadium has been detected in the lungs (in 52% of the cases) and intestines (in 16% of the cases) of humans with no known occupational exposure (Schroeder et al. 1963). This is probably accumulation from chronic breathing of vanadium from naturally occurring dusts or air contaminated with fuel oil combustion waste products. The amount detected in the intestines is probably from swallowing the dusts. The heart, aorta, brain, kidney, muscle, ovary, and testes were found to have no detectable vanadium concentrations. Bone was not tested. The study was limited because exposure levels were not determined and insensitive detection methods were used. Serum vanadium levels in occupationally exposed workers were highest within a day after exposure followed by a rapid decline in levels upon cessation of exposure (Gylseth et al. 1979; Kiviluoto et al. 1981b). Analytical studies have shown low levels of vanadium in human kidneys and liver, with even less in brain, heart, and milk. Higher levels were detected in hair, bone, and teeth (Byrne and Kosta 1978).

Vanadium is rapidly distributed in tissues of rats after acute intratracheal administration. Within 15 minutes after exposure to 0.36 mg/kg vanadium oxychloride, radiolabeled vanadium was detectable in all organs except the brain. The highest concentration was in the lungs, followed by the heart and kidney. The other organs had low levels. Maximum concentrations were reached in most tissues between 4 and 24 hours (Oberg et al. 1978). Vanadium is found to have a two-phase lung clearance after a single acute exposure (Oberg et al. 1978; Rhoads and Sanders 1985). The initial phase is rapid with a large percentage of the absorbed dose distributed to most organs

and blood 24 hours postexposure, followed by a slower clearance phase. Vanadium is transported mainly in the plasma. It is found in appreciable amounts in the blood initially and only at trace levels 2 days after exposure (Roshchin et al. 1980). The pentavalent and tetravalent forms of vanadium compounds were found to have similar distribution patterns (Edel and Sabbioni 1988). Three hours after exposure to the pentavalent or tetravalent form, 15%-17% of the absorbed dose was found in the lung, 2.8% in the liver, and 2% in the kidney (Edel and Sabbioni 1988). Although levels in the kidney are high after exposure, the bone had greater retention of vanadium.

Skeletal levels of vanadium peaked 1-3 days postexposure (Conklin et al. 1982; Rhoads and Sanders 1985; Roshchin et al. 1980) and have been reported to persist after 63 days (Oberg et al. 1978). This indicates that the retention site of vanadium is the bones.

Limited information was located regarding the distribution of vanadium in humans following inhalation exposure. Acute animal studies suggest that there is an initial accumulation of vanadium in the lungs, kidneys, and liver of rats, as well as high levels in the blood. However, retention of vanadium occurs primarily in the bone. Though there were no animal data on longer exposure to vanadium via the inhalation route, it seems likely that experimental studies would show distribution patterns similar to these seen with chronic human exposures.

2.3.2.2 Oral Exposure

No studies were located regarding distribution in humans after oral exposure to vanadium.

Acute studies with rats showed the highest vanadium concentration to be located in the skeleton. Male rats had approximately 0.05% of the administered ^{48}V in bones, 0.01% in the liver, and less than 0.01% in the kidney, blood, testis, or spleen after 24 hours (Edel and Sabbioni 1988). Similar findings were noted by other authors who found that the bone had the greatest concentration of radiolabeled vanadium, followed by the kidney (Roshchin et al. 1980). Conklin et al. (1982) reported that after 3 days, 25% of the absorbed vanadium pentoxide was detectable in the skeleton and blood of female rats.

Oral exposure for an intermediate duration produced the highest accumulation of vanadium in the kidney. In young male rats at 3 weeks of age, the kidneys, heart, and lungs had the highest levels immediately following exposure (Edel et al. 1984). Vanadium in the kidney, liver, and lung decreased significantly at 115 days of age. There was an accumulation in muscle and fat, related to the growing mass of the tissues with age. The higher levels of vanadium in the young rat tissues may be due to the higher retention capacity of the undeveloped tissues, or a greater permeability of the intestinal wall. Adult rats exposed to 5 or 50 ppm vanadium in the

drinking water for 3 months had the highest vanadium levels in the kidney, followed by bone, liver, and muscle (Parker and Sharma 1978). The retention in bone may have been due to phosphate displacement. All tissue levels plateaued at the 3rd week of exposure. A possible explanation for the initially higher levels in the kidney during intermediate-duration exposure is the daily excretion of vanadium in the urine. When the treatment is stopped, levels decrease in the kidney.

At the cessation of treatment, vanadium mobilized rapidly from the liver and slowly from the bones. Other tissue levels decreased rapidly after oral exposure was discontinued. Thus, retention of vanadium was much longer in the bones (Edel et al. 1984; Parker and Sharma 1978).

The distribution of vanadium in humans following oral exposure may be assessed from animal studies. In acute-duration exposures, vanadium is rapidly distributed, primarily in the bones. Following intermediate-duration exposure, it is apparent that vanadium concentrations reaching the tissues are low, with the kidney, bones, liver, and lungs showing the highest levels initially. Prolonged retention of vanadium occurs only in the skeleton. Placental transfer of vanadium is suggested by the increased incidence of fetal abnormalities from dams receiving sodium metavanadate (Paternain et al. 1987).

2.3.2.3 Dermal Exposure

No studies were located regarding distribution in humans and animals after dermal exposure to vanadium.

2.3.2.4 Other Routes of Exposure

After intraperitoneal administration to rats, vanadium is distributed to all organs. After 24 hours, the highest concentrations are in the bones and kidney, though initial levels are highest in the kidney (Roshchin et al. 1980; Sharma et al. 1980). This is similar to the distribution seen following inhalation and oral exposure.

2.3.3 Metabolism

Vanadium is an element, and as such, is not metabolized. However, in the body, there is an interconversion of two oxidation states of vanadium, the tetravalent form, vanadyl (V+4), and the pentavalent form, vanadate (V+5). Vanadium can reversibly bind to transferrin protein in the blood and then be taken up into erythrocytes. These two factors may affect the biphasic clearance of vanadium that occurs in the blood. Vanadate is considered more toxic than vanadyl, because vanadate is reactive with a number of enzymes and is a potent inhibitor of the Na+K+-ATPase of plasma membranes (Harris et al. 1984; Patterson et al. 1986). There is a slower uptake of vanadyl into erythrocytes compared to the vanadate form. Five minutes after an intravenous

administration of radiolabeled vanadate or vanadyl in dogs, 30% of the vanadate dose and 12% of the vanadyl dose is found in erythrocytes (Harris et al. 1984). It is suggested that this difference in uptake is due to the time required for the vanadyl form to be oxidized to vanadate. When V+4 or V+5 is administered intravenously, a balance is reached in which vanadium moves in and out of the cells at a rate that is comparable to the rate of vanadium removal from the blood (Harris et al. 1984). Initially, vanadyl leaves the blood more rapidly than vanadate, possibly due to the slower uptake of vanadyl into cells (Harris et al. 1984). Five hours after administration, blood clearance is essentially identical for the two forms. A decrease in glutathione, NADPH, and NADH occurs within an hour after intraperitoneal injection of sodium vanadate in mice (Bruech et al. 1984). It is believed that vanadate requires these cytochrome P-450 components for oxidation to the vanadyl form. A consequence of this action is the diversion of electrons from the monooxygenase system resulting in the inhibition of drug dealkylation (Bruech et al. 1984).

Vanadium in the plasma can exist in a bound or unbound form (Bruech et al. 1984). Vanadium as vanadyl (Patterson et al. 1986) or vanadate (Harris and Carrano 1984) reversibly binds to human serum transferrin at two metalbinding sites on the protein. With intravenous administration of vanadate or vanadyl, there is a short lag time for vanadate binding to transferrin, but, at 30 hours, the association is identical for the two vanadium forms (Harris et al. 1984). The vanadium-transferrin binding is most likely to occur with the vanadyl form as this complex is more stable (Harris et al. 1984). The transferrin-bound vanadium is cleared from the blood at a slower rate than unbound vanadium in rats, which explains a biphasic clearance pattern (Sabbioni and Marafante 1978). The metabolic pathway appears to be independent of route of exposure (Edel and Sabbioni 1988).

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Occupational studies showed that urinary vanadium levels significantly increased in exposed workers (Gylseth et al. 1979; Kiviluoto et al. 1981b; Lewis 1959; Orris et al. 1983; Zenz et al. 1962). Male and female workers exposed to 0.1-0.19 mg/m^3 vanadium in a manufacturing company, had significantly higher urinary levels (20.6 μg/L) than the nonoccupationally exposed control subjects (2.7 μg/L) (Orris et al. 1983). The correlation between ambient vanadium levels and urinary levels of vanadium is difficult to determine from these epidemiological studies (Kiviluoto et al. 1981b). In most instances, no other excretion routes were monitored. Analytical studies have shown very low levels in human milk (Byrne and Kosta 1978). Evidence from animal studies supports the occupational findings. Vanadium administered intratracheally to rats was reported to be excreted predominantly in the urine (Oberg et al. 1978) at levels twice that found in the feces (Khoads and Sanders 1985). Three days after exposure to vanadium pentoxide, 40% of the

recovered ^{48}V dose was cleared in the urine while 30% remained in the skeleton, and 2%-7% was in the lungs, liver, kidneys, or blood (Conklin et al. 1982).

Epidemiological studies and animal studies suggest that elimination of vanadium following inhalation exposure is primarily in the urine.

2.3.4.2 Oral Exposure

No studies were located regarding excretion in humans after oral exposure to vanadium.

Since vanadium is poorly absorbed in the gastrointestinal tract, a large percentage of vanadium is excreted unabsorbed in the feces in rats following oral exposure. More than 80% of the administered dose of ammonium metavanadate accumulated in the feces after 6 days (Patterson et al. 1986). After 2 weeks of exposure, 59.1+18.8% of sodium metavanadate was found in the feces (Bogden et al. 1982). However, the principal route of excretion of the small absorbed portion of vanadium is through the kidney in animals.

2.3.4.3 Dermal Exposure

No studies were located regarding excretion in humans or animals after dermal exposure to vanadium.

2.4 RELEVANCE TO PUBLIC HEALTH

An acute-duration inhalation MRL of 0.0002 mg/m^3 was derived. Zenz and Berg (1967) exposed volunteers to vanadium pentoxide dust at levels of 0.06, 0.1, and 0.6 mg vanadium/m^3 for 8 hours. Subjects exposed at 0.06 mg vanadium/m^3 had increased mucus formation and slight coughing 1 day after exposure. These effects ceased within 4 days. At 0.1 mg vanadium/m^3, coughing was more persistent. Effects were more pronounced at higher concentration levels. There were no reports of fever, increased pulse, or other signs of irritation at any dose level. Pulmonary function tests were normal. The 0.06 mg vanadium/m^3 level was considered a LOAEL for coughing, which was regarded as a sign of respiratory irritation. The MRL value was calculated by dividing the actual administered dose of vanadium (0.06 mg/m^3) by an uncertainty factor of 100 (for human variability and the use of a LOAEL) and corrected for less than 24 hours of exposure (8/24), thus obtaining an MRL value of 0.0002 mg vanadium/m^3. The use of this study for the derivation of an MRL is supported by numerous epidemiological studies (Levey et al. 1984; Lewis 1959; Musk and Tees 1982; Orris et al. 1983; Sjoeberg 1956; Thomas and Stiebris 1956; Vintinner et al. 1955; Wyers 1946; Zenz et al. 1962) as well as animal studies (Knecht et al. 1985; Lee and Gillies 1986) that demonstrate that the target organ for inhaled vanadium compounds is the respiratory system.

Neither intermediate-duration nor chronic-duration inhalation MRLs were derived for vanadium because of a lack of quantitative exposure data.

An acute-duration oral MRL was not derived for vanadium because of a lack of quantitative exposure data. One acute-duration oral study reported an increase in facial and dorsal hemorrhages in rats exposed to sodium metavanadate, but these developmental effects were not dose related (Paternain et al. 1987), and the toxicological significance of this finding is unknown.

An intermediate-duration oral MRL value of 0.003 mg vanadium/kg/day was derived. Domingo et al. (1985) administered 0, 5, 10, or 50 ppm of sodium metavanadate in the drinking water of rats for 3 months. All treated groups showed mild histological changes in kidneys, lungs, and spleen, and the changes became progressively more severe with increased dosages. Serum cholesterol and glucose levels, liver function, organ weights, weight gain, and water consumption were unaffected at all exposure levels. Vanadium was not detected in organs of animals receiving 5 ppm but was found in the kidneys and spleen of animals exposed at 10 ppm and in all organs of animals exposed at 50 ppm. Based on these findings, a NOAEL at the 5-ppm exposure level was used for the derivation of an intermediate-duration oral MRL. The administered dose (5 ppm) was converted from ppm in water to a mg vanadium/kg weight dose as follows (assuming an intake of 0.14 L/kg/day): 5 ppm in water = 5 mg vanadium/L; 5 mg vanadium/L x 0.14 L/kg/day x 41% vanadium in sodium metavanadate = 0.287 mg vanadium/kg/day, which is rounded to 0.3 mg vanadium/kg/day

Since the study used animals and a NOAKL was used as the MRL end point, the MRL value is calculated by dividing the adjusted administered dose (0.3 mg vanadium/kg/day) by an uncertainty factor of 100 (10 for extrapolation from animals to humans, and 10 for human variability); thus obtaining an MRL value of 0.003 mg vanadium/kg/day. The use of this NOAEL for the derivation of an MRL is supported by other studies that reported adverse developmental effects (Domingo et al. 1986), cardiovascular effects (Susic and Kentera 1986, 1988), and gastrointestinal effects (Dimond et al. 1963; Franke and Moxon 1937) at levels greater than the NOAEL used for the MRL.

A chronic-duration oral MRL was not derived for vanadium because of a lack of quantitative exposure data. Several chronic-duration oral studies using mice and rats exposed to vanadyl sulfate reported no significant changes in body weight (Schroeder and Balassa 1967; Schroeder and Mitchener 1975; Schroeder et al. 1970). However, these were not used because data was not available to determine the most sensitive end point for the derivation of a chronic-duration oral MRL. A two-generation, one-dose study of rats exposed to sodium metavanadate reported altered lung collagen metabolism in fetuses of adults with life-time exposure (Kowalska 1988). However, the toxicological significance of this finding is unknown.

Acute-duration, intermediate-duration, and chronic-duration dermal MRLs were not derived for vanadium because of the lack of an appropriate methodology for the development of dermal MRLs.

The major adverse health effect in humans from vanadium has been seen in workers exposed to large amounts of vanadium pentoxide dusts. These people have coughs, chest pains, sore throats, and irritated eyes, but the symptoms disappear soon after exposure ceases. The response is similar to that of an upper respiratory tract infection. Data were not located to assess the relationship of exposure levels or duration to severity of response. No other significant health effects of vanadium have been found. Large amounts of vanadium dusts would need to occur near hazardous waste sites for most people to be at risk. People could also be exposed to vanadium in fly ash when coalburning boilers are used, cleaned or destroyed. It is possible that vanadium might leach into water supplies near hazardous waste sites, but since the gastrointestinal absorption is so low, the health implications for people drinking the water are not readily apparent. Likewise, dermal absorption is low, and the relevance of exposure to vanadium in soil surrounding waste sites would need to be evaluated on a case by case basis.

Death. There are no reports of death in humans following inhalation, oral, or dermal exposure to vanadium. Humans are unlikely to be in contact with large enough amounts of vanadium to cause death. Rabbits have died from breathing 60 mg vanadium/m^3 as vanadium pentoxide. The LD_{50} value for gavage administration of sodium vanadate in rats is 41 mg vanadium/kg. This is much higher than the LD_{50} values for intraperitoneal injections of sodium metavanadate, which are 11 mg vanadium/kg in rats and 13 mg vanadium/kg in mice (Chanh 1965).

Systemic Effects

Respiratory Effects. The only significant, clearly documented, effect in humans is mild to moderate respiratory distress and mucosal irritation from exposure to vanadium dusts. Vanadium workers may have coughs, wheezing, chest pain, sore throats, or eye irritation, which can last for several days after exposure. These effects are common to many types of dust exposures. The effects are no more severe than those experienced during a routine upper respiratory tract infection and can sometimes be delayed for several hours after exposure. Chronic effects are not reported with regularity. Chest xrays and urine and blood analyses in these people are normal. These workers often develop a green color on their tongues from direct accumulation of vanadium.

Studies in animals support the findings that vanadium primarily effects the respiratory system. The respiratory system responds to the particulate matter by increasing the number of leukocytes which are used to clear away the foreign matter. Respiratory distress lead to death in rats following intraperitoneal injections of sodium metavanadate (Donaldson et al. 1985).

The mechanism of vanadium's effect on the respiratory system is similar to that of other metals. In vitro tests show that vanadium damages alveolar macrophages (Castranova et al. 1984; Sheridan et al. 1978; Waters et al. 1974; Wei and Misra 1982). It does this by decreasing the macrophage membrane integrity, thus impairing the cells' phagocytotic ability and viability. Without macrophages, the respiratory system's ability to clear itself of many other particles normally found in the air is diminished.

Renal Effects. Minor renal effects (altered renal function, as indicated by increased plasma urea, and mild histological changes) were seen in rats after oral exposure to sodium metavanadate for 3 months at levels up to 10% of the oral LD_{50} (Domingo et al. 1985). A few animal studies have shown renal effects from parenteral injections of vanadium. These include increased lipid peroxidation (Donaldson et al. 1985) and decreased tubular reabsorption (Westenfelder et al. 1981). Vanadium, like most metals, has also been shown to accumulate transiently in the kidneys following parenteral injections (Roshchin et al. 1980), or oral exposure (Bogden et al. 1982; Conklin et al. 1982; Edel and Sabbioni 1988; Parker and Sharma 1978). However, it is difficult to determine the potential for toxicity in humans. However, renal effects have not been observed upon urinalysis in occupationally exposed workers (Kiviluoto et al. 1981b; Sjoeberg 1950; Vintinner et al. 1955).

Other Systemic Effects. Other minor systemic effects (weight loss) have been seen in animals, but there are not enough collaborative data to indicate that vanadium poses significant risks to any other organ system. A study in mice fed vanadium chronically showed a lack of histopathological effects in unspecified tissues (Schroeder and Balassa 1967).

In vitro experiments have shown that vanadium as vanadate inhibits sodium-potassium ATPase activity and thus inhibits the sodium potassium pump (Nechay and Saunders 1978). This pump is necessary for proper transport of materials across cell membranes. The kidney (Higashino et al. 1983; Phillips et al. 1983), heart (Aiton and Cramb 1985; Akera et al. 1983), red blood cells (Beauge et al. 1980; Siemon et al. 1982), and brain (Keller and Sharma 1985) are affected in vitro.

Immunological Effects. Very few data are available on the immunological effects of vanadium in humans or animals. One intermediate-duration oral mouse study of sodium orthovanadate showed no immunological damage as measured by a response to sheep erythrocytes (Sharma et al. 1981). Intraperitoneal injections of ammonia metavanadate into mice have caused impairment in response to bacterial challenges also decreased peritoneal macrophage phagocytic ability (Cohen et al. 1986). These authors have suggested that the decreased macrophage response may explain why vanadium workers have increased susceptibility to respiratory disease.

Neurological Effects. Humans who have been exposed to vanadium dusts in the workplace have generally not reported significant effects related to the nervous system. Nonspecific effects such as dizziness or headaches have been reported by some workers. It is possible that the effects that vanadium has in inhibiting the sodium-potassium pump would adversely affect the nervous system, but this has not been tested and/or reported. Rats given intraperitoneal injections of vanadium showed lethargy and ataxia (Haider and Kashyap 1989), but the relevance of this to humans exposed by expected routes is not known. Vanadium does not accumulate in the brain of humans or animals. In the absence of animal data via relevant routes, the neurotoxicity of vanadium could not be fully assessed.

Developmental Effects. No direct information is available on developmental effects of vanadium in humans. Offspring of animals that have had oral exposure to vanadium have shown slight defects, including increases in visible hemorrhages (Paternain et al. 1987), altered lung collagen metabolism (Kowalska 1988), and slight decreases in fetal length and weight (Domingo et al. 1986). Minor skeletal abnormalities have been noted in the offspring of animals that have been injected with vanadium (Carlton et al. 1982; Wide 1984). These included supernumary ribs and delayed skeletal ossification. Maternal toxicity was not observed at the doses producing these developmental effects in these two studies. Because these effects were so minor and do have correlations to human development, the relevance of these animal findings to developmental effects in humans is not known.

Reproductive Effects. Autopsy data have not provided detectable levels of vanadium in human reproductive organs. It is unlikely that the reproductive system is a sensitive indicator for vanadium toxicity in humans. Only one animal study was located that specifically tests the effects of vanadium on reproduction. In this well-conducted rat study, no adverse effects on fertility, reproduction, or parturition were noted when male and female rats were exposed to sodium metavanadate and then mated.

Genotoxic Effects. The only information on genotoxicity of vanadium is from in vitro studies, as shown in Table 2-3. The majority of these studies show positive effects in test systems using bacteria, yeast, and mouse cells in culture for end points such as recombination repair, gene mutation, or DNA synthesis. None of these studies showed any indication of a cytotoxic effect. Human leukocytes have been shown to have DNA strand breaks from exposure to vanadate (Birnboim 1988). These in vitro data indicate that vanadium has the potential for genotoxicity in humans. The application of vanadium salts at low concentrations (<0.1 pM) stimulated colony formation in fresh human tumor cells, but high concentrations (>0.1 pM) inhibited growth (Hanauske et al. 1987). The mechanism for this action is not clear. The authors suggest that vanadium be further tested for its antitumor activity in animals.

TABLE 2-3. Genotoxicity of Vanadium and Compounds In Vitro

Species	End point	Results: With activation	Results: Without activation	Reference	Form
Bacillus subtilis	Recombination repair	+	+	Kada et al. 1980	V_2O_5
Escherichia coli	Gene mutation	No data	+	Kanematsu et al. 1980	V_2O_5
Salmonella typhimurium	Gene mutation	No data	-	Kanematsu et al. 1980	V_2O_5
Saccharomyces cerevisiae	Induction of diploid spores	No data	+	Sora et al. 1986	$VOSO_4$
Mouse 3T3 and 3T6 cells	DNA synthesis	No data	+	Smith 1983	Na_3VO_4, $VOSO_4$
Human tumor cells	Colony formation	No data	+	Hanauske et al. 1987	<0.1 pM V
Human tumor cells	Colony formation	No data	-	Hanauske et al. 1987	>0.1 pM V
Human leukocytes	DNA strand break	No data	+	Birnboim 1988	Na_3VO_4

+ = positive; - = negative; Na_3VO_4 = sodium metavanadate; pM = picomol; V_2O_5 = vanadium pentoxide; V = vanadium; $VOSO_4$ = vanadyl sulfate

Cancer. No studies regarding the carcinogenicity of vanadium in humans were located. Workers who have been exposed to vanadium dusts did not show an increased number of cancer deaths (Orris et al. 1983; Sjoeberg 1950; Vintinner et al. 1955), although detailed studies were not performed. Studies designed to test effects other than cancer in animals have not noted any increases in tumors resulting from inhalation (Sjoeberg 1950) or oral (Schroeder and Balassa 1967) exposure to vanadium. Although results of these oral studies were negative for carcinogenicity, they were inadequate for evaluating carcinogenic effects because insufficient numbers of animals were used, it was not determined whether or not a maximum tolerated dose was achieved, a complete histological examination was not performed, and only one exposure dose per study was evaluated. Therefore an acceptable assessment of carcinogenic potential in humans cannot be made.

2.5 BIOMARKERS 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 vanadium 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 as 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 vanadium 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 Vanadium

Several biomarkers of exposure have been identified for vanadium but none of them can be used to quantitatively determine exposure levels. Vanadium is found in the urine of exposed workers. This measurement is specific for vanadium. Some vanadium workers develop a characteristic green tongue, as a result of direct accumulation of the vanadium dusts on the tongue (Lewis 1959). One report from the 1950s states that vanadium exposure was associated with decreased cystine content in the fingernails of vanadium workers (Mountain 1955). However, alterations in cystine levels can also be associated with dietary changes and with other disease states, so this is not specific for vanadium exposure. No other commonly measured cellular changes have been identified with vanadium exposure.

2.5.2 Biomarkers Used to Characterize Effects Caused by Vanadium

The primary effects of exposure to vanadium dusts are coughing, wheezing, and other respiratory difficulties. These effects, however, are not specific to vanadium and can be found following inhalation of many types of dusts.

2.6 INTERACTIONS WITH OTHER CHEMICALS

Vanadium in the drinking water of mice had no influence on tumor induction by the known carcinogen 1,2-dimethylhydrazine given by subcutaneous injection (Kingsnorth et al. 1986), but dietary vanadium did decrease mammary tumors in mice caused by l-methyl-1-nitrosourea administered concurrently (Thompson et al. 1984). The latter effect may have been due to interaction with DNA.

The combination of manganese and vanadium or of nickel and vanadium administered to pregnant mice caused some alterations in behavioral development of the pups as compared to either element administered alone (Hoshishima et al. 1983). Oral administration of vanadium in rats interfered with copper metabolism, probably by inhibiting the intestinal absorption of copper (Witkowska et al. 1988).

2.7 POPULATIONS THAT ABE UNUSUALLY SUSCEPTIBLE

No unusually susceptible populations have been identified, but persons with pre-existing respiratory disorders such as asthma may be expected to have increased adverse effects from breathing vanadium dusts.

2.8 MITIGATION OF EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to vanadium. 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 vanadium. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

There are two main objectives for treating internal vanadium exposure: decreasing absorption and increasing excretion. There is no known treatment to decrease absorption or increase elimination after inhaling vanadium and/or its compounds. Following oral exposure, dilution with water or milk is one way to decrease overall absorption (Stutz and Janus.2 1988). To decrease gastrointestinal absorption, especially for organic vanadium compounds, it has been suggested that activated charcoal be given to the patient. Emesis induced immediately after an acute oral exposure may remove part of the ingested dose from the stomach. Gastric lavage has been suggested as being effective if performed soon after ingestion or in patients who are unconscious or at risk of convulsing (HSDB 1992). Two methods have been discussed in the literature for increasing excretion of the chemical after it has been ingested. One method is to administer calcium disodium edentate as a chelating agent (Haddad and Winchester 1990; Stutz and Janusz 1988). The other method is to give cathartic medication such as magnesium sulfate (Stutz and Janusz 1988). If vanadium gets onto the skin, washing the contaminated area with soapy water has been advised. For ocular exposure, it is suggested that the eyes be flushed with large amounts of saline or water (Stutz and Janusz 1988).

After acute inhalation exposure to high concentrations of vanadium and/or compounds, pulmonary edema may result. If so, oxygen administration may be necessary. Experimental evidence suggests that the administration of steroids such as prednisolone succinate or phthalate may prevent the development of a chemical lung edema (Stutz and Janusz 1988).

Enhanced excretion of vanadium was achieved with chelation therapy provided by deferoxamine mesylate (DFOA) (Gomez et al. 1988). Humans or animals with vanadium poisoning have not been helped by the chelating agent dimercaprol (BAL), which is often effective in lessening the toxicity of other metals (Lusky et al. 1949). Intraperitoneal injections of ascorbic acid and

of ethylene diamine tetraacetate (EDTA) reduced vanadium-induced morbidity in mice and rats (Jones and Basinger 1983; Mitchell and Floyd 1954).

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 vanadium 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 vanadium.

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.

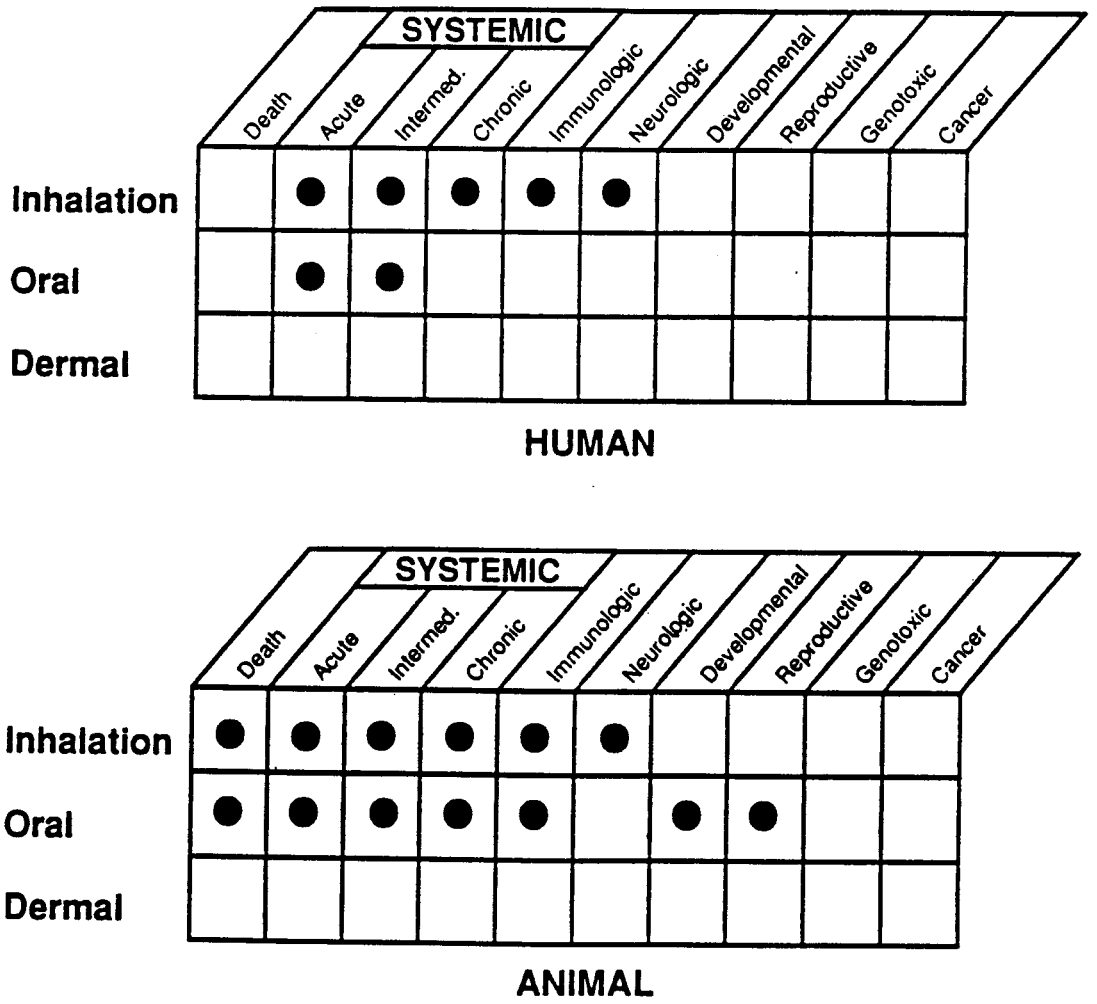
2.9.1 Existing Information on Health Effects of Vanadium

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to vanadium are summarized in Figure 2-3. The purpose of this figure is to illustrate the existing information concerning the health effects of vanadium. 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).

Data are available from humans regarding acute, intermediate, and chronic inhalation exposure to vanadium pentoxide and on immunologic and neurologic effects, primarily from case studies of factory workers. Data regarding acute effects are available from volunteers who ingested ammonium vanadyl tartrate in capsules for intermediate periods. No human dermal data were located.

Data are available regarding the effects of inhalation of bismuth orthovanadate in rats and vanadium pentoxide in monkeys following acute and intermediate exposures. Data are available following acute, intermediate, and chronic oral exposures in animals, including information on death (from sodium metavanadate or vanadyl sulfate), immunological (from sodium orthovanadate), neurological (from vanadium pentoxide), developmental, and reproductive effects (from sodium metavanadate). No animal dermal data were located.

FIGURE 2-3. Existing Information on Health Effects of Vanadium and Compounds



● Existing Studies

2.9.2 Data Needs

Acute-Duration Exposure. Sufficient information is available from occupationally exposed humans to identify the respiratory system as a target organ following acute inhalation exposure (Levy et al. 1984; Musk and Tees 1982; Thomas and Stiebris 1956; Zenz and Berg 1967; Zenz et al. 1962). The mechanism is known to be interference with alveolar macrophages (Castranova et al. 1984; Sheridan et al. 1978; Waters et al. 1974; Wei and Misra 1982). Data are not available to determine target organs in humans from acute oral or dermal exposure. Vanadium is very poorly absorbed from the gastrointestinal system (Conklin et al. 1982; Roschin et al. 1980) or skin (WHO 1988), so it is unlikely to result in a significant internal dose by these routes. However, since children are known to absorb some metals (such as lead) more readily than adults, they may be more susceptible to vanadium poisoning. Data were sufficient to derive an MRL for inhalation exposure (Zenz and Berg 1967). Further, animal studies designed to determine the level of vanadium in the air that would cause respiratory distress would be helpful in determining the relationship between the exposure level or duration and the severity of the response. This would be useful to determine possible toxic effects on humans exposed for an acute period near a hazardous waste site.

Intermediate-Duration Exposure. Sufficient information is available from intermediate-duration studies in animals to identify the respiratory system as a target organ following inhalation exposure (Domingo et al. 1985; Sjoeberg 1950). An intermediate MRL could not be derived for inhalation exposure due to a lack of quantitative exposure data. An intermediate MRL was derived for oral exposure from an animal study showing slight toxic effects in kidneys, lungs, and spleen (Domingo et al. 1985). Lethality data are not available for intermediate-duration inhalation or dermal exposure, but these data are unlikely to help in assessing effects from low-level exposure. Animal studies using a number of concentration levels designed to test the level of vanadium in the air that would cause respiratory distress would be helpful in determining an intermediate MRL. These studies should include tests that could be used to predict the relationship between the exposure level or duration and the severity of the response which may be seen in people exposed for an intermediate duration near a hazardous was site.

Chronic-Duration Exposure and Cancer. Sufficient information is available in occupationally exposed humans to identify the respiratory system as a target organ following chronic inhalation exposure (Lewis 1959; Orris et al. 1983; Sjoeberg 1956; Vintinner et al. 1955; Wyers 1946). Data are not available to determine target organs in humans from chronic oral or dermal exposure. Vanadium is very poorly absorbed from the gastrointestinal system (Conklin et al. 1982; Roschin et al. 1980) or skin (WHO 1988), so it is unlikely to result in a significant internal dose by these routes. Quantitative exposure data were not sufficient to derive a chronic MRL for any exposure route. Lethality data are not available for chronic inhalation,

oral, or dermal exposure, but these data would be unlikely to help in assessing effects from low-level exposure. Animal studies designed to test the level of vanadium in the air that would cause respiratory distress would be helpful in determining a chronic MRL. These studies should include tests that could be used to predict the relationship between the exposure level or duration and the severity of the response for people exposed near hazardous waste sites.

Specific tests for carcinogenicity have not been performed in humans or animals by any route. Available occupational data using the inhalation route and chronic animal studies in two species using the oral route have not indicated any tumor increases. Although vanadium is not suspected of being a carcinogen, a definitive cancer assay would be necessary to show this.

Genotoxicity. There are no in vivo studies in humans or animals by any route investigating the genotoxicity of vanadium. The few in vitro studies located generally show positive effects in cultured bacteria (Kada et al. 1980; Kanematsu et al. 1980), yeast (Sora et al. 1986), and mouse cells (Smith 1983). The results of one study showing DNA strand breaks in human leukocytes suggest that further studies using human cells would be helpful in determining if vanadium is genotoxic in people (Birnboim 1988).

Reproductive Toxicity. No data exist on reproductive effects on humans from exposure to vanadium by any exposure route. One animal study shows that vanadium did not affect reproductive parameters in rats following oral exposure (Domingo et al. 1986). Since vanadium is poorly.absorbed from the gastrointestinal tract (Conklin et al. 1982; Roschin et al. 1980) and skin (WHO 1988), exposure by these routes is unlikely to be a health risk in humans. Toxicokinetic studies in humans (Schroeder et al. 1963) and reliable studies in animals (Edel and Sabbioni 1988) do not indicate that the reproductive system accumulates vanadium. Humans are most likely to be exposed to vanadium in the air, but the reproductive system does not appear to be a sensitive target of vanadium toxicity. Further studies would not appear to be particularly useful.

Developmental Toxicity. No human data were located on developmental effects of vanadium exposure by any exposure route. Since vanadium is poorly absorbed by the gastrointestinal tract (Conklin et al. 1982; Roschin et al. 1980) or skin (WHO 1988), exposure by these routes would be unlikely to result in a significant internal dose. Animal toxicokinetic studies do not indicate that the fetus accumulates vanadium. The lack of developmental studies decreases the confidence in the MRL.

Some animal studies have shown slight developmental effects following oral exposure to vanadium (Paternain et al. 1987). These studies were flawed since results from the same laboratory were not consistent across the studies. The likelihood of adverse effects occurring in humans if they were exposed to

sufficient quantities of vanadium is not known. Further animal studies would be unlikely to reveal human risk from vanadium.

Immunotoxicity. Effects on lymphoid tissue or peripheral lymphocytes have not been noted in the occupational studies in humans (Sjoeberg 1950) or in the animal studies (Sharma et al. 1981; Sjoeberg 1950). However, this system may still be affected since vanadium has been shown to have adverse effects on macrophages in vivo and in vitro (Cohen et al. 1986). Few workers have shown allergic responses or contact dermatitis from vanadium exposure (Sjoeberg 1950), so further work in this area is probably not critical.

Neurotoxicity. Very little information exists on the neurotoxicity of vanadium to humans or animals. Since numerous workers have been exposed to vanadium dusts and fumes in the workplace and have not reported or shown significant adverse neurological signs, it is unlikely that the neurological system is a sensitive target of vanadium exposure (Sjoeberg 1956; Vintinner et al. 1955; Zenz and Berg 1967). However, it is possible that modern tests of subtle neurological effects in humans and animals may be more sensitive in revealing neurotoxicity caused by vanadium.

Epidemiological and Human Dosimetry Studies. Studies of health effects on people who have inhaled vanadium in the workplace clearly show that the target organ is the respiratory system (Domingo et al. 1985; Levy et al. 1984; Lewis 1959; Musk and Tees 1982; Orris et al. 1983; Sjoeberg 1950, 1956; Thomas and Stiebris 1956; Vintinner et al. 1955; Wyers 1946; Zenz and Berg 1967; Zenz et al. 1962). The dose-response relationship is not known, because exposure levels are not well quantified. Further information on exposure levels associated with respiratory effects would be useful. However, people living near hazardous waste sites are unlikely to come in contact with amounts of vanadium dusts large enough to cause adverse health effects. Further epidemiological studies may be useful in revealing adverse health effects in people living near boiler ash dumps. Additional information on potentially susceptible populations, such as those people with asthma or other respiratory problems, would be useful. Although vanadium can be found in foods, it is very poorly absorbed through the gastrointestinal tract (Conklin et al. 1982; Roshchin et al. 1980) or skin (WHO 1988) and is unlikely to pose a significant health threat by these routes. It is possible however, that children may absorb vanadium better than adults do.

Biomarkers of Exposure and Effect. Biomarkers specific for exposure to vanadium include the presence of vanadium in the urine (Gylseth et al. 1979; Kiviluoto et al. 1981b; Lewis 1959; Orris et al. 1983; Zenze et al. 1962) and a green discoloration of the tongue (Lewis 1959), the latter resulting from the direct accumulation of vanadium pentoxide. Further studies would be helpful in correlating urinary vanadium levels with exposure levels. Vanadium can also be measured in the hair (Stokinger et al. 1953), and studies could be performed to determine if a correlation exists between levels of vanadium in hair and exposure levels. In the 1950s, decreased cystine content of the hair

or fingernails was described as a possible biomarker of exposure (Mountain 1955). However, this is not specific for vanadium since other factors, such as diet or disease, can also affect cystine content.

There are no specific biomarkers of effects. It is possible that further biochemical studies might show specific effects. For example, it is possible that specific effects may be seen on lung cells, which can be examined by lavage.

Absorption, Distribution, Metabolism, and Excretion. Data are available from human and animal studies regarding the kinetics of vanadium following inhalation and oral exposure. Specific data from dermal exposure are lacking, although significant absorption of vanadium by this route in humans is unlikely (WHO 1988). No animal studies were located that test absorption after inhalation exposure, although information is available from intratracheal exposures (Conklin et al. 1982; Edel and Sabbioni 1988; Oberg et al. 1978; Rhoads and Sanders 1985) Since inhalation is most likely to result in a significant exposure for humans, more data on the rate and extent of absorption may be useful. More data on kinetics following oral or dermal exposure would not be helpful, since it is believed that absorption in humans and animals is low by these routes. It is possible however, that children may absorb vanadium better than adults do.

Comparative Toxicokinetics. Animal data (Conklin et al. 1982; Oberg et al. 1978; Rhoads and Sanders 1985; Roshchin et al. 1980) and limited human (Dimond et al. 1963; Gylseth et al. 1979; Schroeder et al. 1963) data are available on the kinetics of vanadium. There is little reason to believe that vanadium toxicokinetics would differ between animals and humans. The data indicate that the kinetics are similar in both. However, as with any particulate substance, extrapolations on inhalation absorption rates from animals to humans would be difficult. Studies are available in humans, rats, mice, and dogs. No particular data needs are apparent.

Mitigation of Effects. Information is available regarding treatment of cases of acute oral exposure to vanadium, including traditional methods of decreasing absorption and increasing elimination (Stutz and Janusz 1988). Washing the skin or eyes following acute dermal exposure has also been recommended (Stutz and Janusz 1988). Treatment for acute inhalation exposure is limited to supportive treatment for pulmonary edema (Stutz and Janusz 1988). One chelation method has been suggested for mitigating the actions of vanadium once it has entered the bloodstream (Haddad and Winchester 1990; Stutz and Janusz 1988). Information regarding treatment or mitigation following intermediate or chronic exposures is lacking. Such information would be useful in the treatment of persons who may have been exposed to vanadium and/or its compounds near hazardous waste sites.

2.9.3 On-going Studies

Vanadium pentoxide is cited for mutagenicity, genetic, and pulmonary sensitization testing by the NTP as of April 9, 1990. The NTP Chemical Manager is William J. Moorman. This will include a repeated dose inhalation study in rats and mice, and a test in Salmonella. Vanadium is not cited for on-going research by the International Agency for Research on Cancer (IARC) as of 1987.

Current federal research in progress includes the following studies:

Investigator	Affiliation	Research Description
Knect, E.	NIOSH	Inhalation studies
Mittag, T.W.	Mt. Sinai School of medecine	Effects on enzymes and intraocular pressure in animals
Reid, J.	SRI International	Prechronic toxicity of vanadium pentoxide
Wei, C.I.	University of Florida	Immunotoxicity in mouse peritoneal macrophages

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical identities of various vanadium compounds are shown in Table 3-1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties of various vanadium compounds are shown in Table 3-2.

TABLE 3-1. Chemical Identity of Vanadium and Compounds[a]

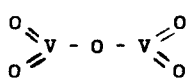
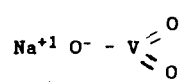
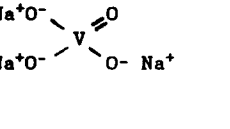
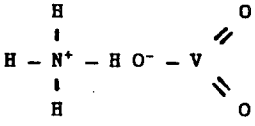
Characteristic	Vanadium	Vanadium pentoxide	Vanadyl sulfate	Sodium metavanadate
Synonyms	Vanadium-51	Vanadic anhydride; divanadium pentaoxide; divanadium pentoxide; vanadium oxide; vanadic acid; vanadic acid anhydride[b,c]	Vanadium oxysulfate; oxysulfato vanadium; vanadium oxide sulfate; vanadium oxosulfate; oxo (sulfat (2-)-0)-vanadium[e,d]	Vanadic acid; monosodium salt[d]
Trade names	No data	CI 77938	CI 77940	No data
Chemical formula	V	V_2O_5[c]	$VOSO_4$[d]	$NaVO_3$[d]
Chemical structure	V[f]		$O{=}V^{+2}\ (SO_4)^{-2}$	
Identification numbers:				
CAS registry	7440-62-2[g]	1314-62-1[h]	27774-13-3[b]	13718-26-8[d]
NIOSH RTECS	YW1355000[d]	YW2450000	YW1925000[d]	YW1050000[d]
EPA hazardous waste	No data	P120	No data	No data
OHM/TADS	No data	7217394	7216945[d]	No data
DOT/UN/NA/IMCO shipping	No data	DOT/UN2862[b]	NA 9152; UN2931[d]	No data
HSDB	1022	1024	1026	No data
NCI	No data	No data	No data	No data

TABLE 3-1 (Continued)

Characteristic	Sodium orthovanadate	Ammonium metavanadate
Synonyms	Vanadic (II) acid; trisodium salt; sodium vanadate; sodium vanadate oxide; trisodium orthovandate[d]	Ammonium vanadate; vanadic acid; ammonium salt
Trade names	No data	No data
Chemical formula	Na_3VO_4[d]	NH_4VO_3
Chemical structure		
Identification numbers:		
CAS registry	13721-39-6[d]	7803-55-6
NIOSH RTECS	YW1120000[d]	YW0875000[d]
EPA hazardous waste	No data	P119
OHM/TADS	No data	No data
DOT/UN/NA/IMCO shipping	No data	UN 2859[d]
HSDB	No data	6310
NCI	No data	No data

[a]All information obtained from HSDB 1990 except where noted
[b]Sax 1988
[c]Windholz 1989
[d]RTECS 1989
[e]Hawley 1977
[f]Possible valence states: 1-, 0, 2+, 3+, 4+, 5+
[g]Grayson 1989
[h]NIOSH 1985

CAS = Chemical Abstracts Services; 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

TABLE 3-2. Physical and Chemical Properties of Vanadium and Compounds[a]

Property	Vanadium	Vanadium pentoxide	Vanadyl sulfate	Sodium metavanadate
Molecular weight	50.942[b]	181.9[c]	163.0[c]	121.93[b]
Color	Light grey or white lustrous[c]	Yellow to rust brown crystals[c]	Blue[c]	Colorless[b]
Physical state	Powder or crystal[c]	Crystals[c]	Crystalline powder[c]	Crystals[b]
Melting point	1,890 ± 10°C; 1,917°C[b,c]	690°C[c]	No data	630°C[b]
Boiling point	3380°C[b]	1,750°C (decomposes)[d]	No data	No data
Density	6.11g/cm^3 at 18.7°C[c]	3.357 g/cm at 18°C	No data	No data
Odor	No data	Odorless[e]	Odorless[d]	No data
Odor threshold:				
Water	No data	No data	No data	No data
Air	No data	No data	No data	No data
Solubility:				
Water at 20°C	Insoluble[c]	1 g/125 mL[c]	Soluble[c]	211 g/L at 25°C; 388 g/L at 75°C[f]
Organic solvents	No data	Soluble in acetone; insoluble in alcohol[c]	No data	No data
Partition coefficients:				
Log octanol/water K_{ow}	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data
Vapor pressure	No data	0 mmHg[e]	No data	No data
Henry's law constant	No data	No data	No data	No data
Autoignition temperature	No data	Not flammable	No data	No data
Flashpoint	No data	Not flammable	Not flammable[d]	No data
Flammability limits	No data	Not flammable	Not flammable[d]	No data
Conversion factors	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data

TABLE 3-2 (Continued)

Property	Sodium orthovanadate	Ammonium metavanadate
Molecular weight	183.91; 183.94[b,i]	116.98[b]
Color	Colorless[b]	White-yellowish or colorless[b]
Physical state	Hexagonal prisms[g]	Crystals[b]
Melting point	850°C-856°C[b]	200°C (decomposes)[b]
Boiling point	No data	No data
Density	No data	2.326 g/cm^3 at 20°C[b]
Odor	No data	No data
Odor threshold:		
Water	No data	No data
Air	No data	No data
Solubility:		
Water	Soluble in water[b]	Slightly soluble[b]
Organic solvent	Insoluble in alcohol[h]	Insoluble in alcohol, ether[f]
Partition coefficients:		
Log octanol/water K_{ow}	No data	No data
Log K_{oc}	No data	No data
Vapor pressure	No data	No data
Henry's law constant	No data	No data
Autoignition temperature	No data	Not flammable
Flashpoint	No data	Not flammable
Flammability limits	No data	Not flammable
Conversion factors	No data	No data
Explosive limits	No data	No data

[a]All information obtained from HSDB 1990 unless otherwise noted.
[b]Grayson 1983
[c]Windholz 1983
[d]Weiss 1986
[e]NIOSH 1985
[f]Stokinger 1981
[g]Sax 1988
[h]Weast 1983
[i]RTECS 1989

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Vanadium is widely, but sparsely, distributed in the earth's crust (Byerrum et al. 1974; Windholz 1983). It may be found at levels as great as 0.07% in the lithosphere and exists in the form of over 50 different mineral' ores (Grayson 1983). The principal ores are carnotite, patronite, roscoelite, and vanadinite (Grayson 1983; Byerrum et al. 1974; Weast 1969; Windholz 1983). Vanadium is also found in phosphate rock, some iron ores, and crude petroleum deposits. Flue-gas deposits from oil-fired furnaces have been found to contain up to 50% vanadium pentoxide (Brooks 1986; Grayson 1983; Symanski 1983; Weast 1969).

Vanadium occurs primarily as a by-product or coproduct during the extraction of other compounds such as iron, titanium, phosphate, or petroleum. Within the United States it is extracted from carnotite, phosphate-rock deposits, titaniferous magnetites, and vanadiferous clays. A process called salt roasting during the initial stage of extraction produces the oxide concentrate. The ores, petroleum residues, iodide thermal decomposition products, and slags formed during ferrovanadate production are crushed, dried, finely ground, mixed with a sodium salt, and roasted. The product, sodium metavanadate, is then mixed with sulfuric acid, and the resultant precipitate dried to form vanadium pentoxide (Brooks 1986; Browning 1969; Byerrum et al. 1974; Grayson 1983). The vanadium pentoxide can then be processed further to form the required vanadium compound. Pure vanadium is difficult to obtain as it tends to be readily contaminated by other elements. Methods to extract pure vanadium include calcium reduction, solvent extraction, thermal decomposition, and electrolytic refining (Grayson 1983; Weast 1969).

World production of vanadium from ores, petroleum concentrates, and slags has remained fairly constant over the last few years and is presently around 34,300 tons (Hilliard 1987). The levels of vanadium recovered from petroleum residues, ashes, and spent catalysts throughout the world are not available; however, within the United States and Japan, recovery of vanadium and its compounds, in particular vanadium pentoxide and ferrovanadium, increased between 1983 and 1987.

Unfortunately, precise data on domestic production of vanadium from ores, concentrates, and slags from 1985 to the present are unavailable in order to avoid disclosing company proprietary data. However, the amount of vanadium recovered from ores and concentrates decreased from 2,171 tons in 1983 to 1,617 tons in 1984, and production levels from these sources are reported to have continued to decline between 1985 and 1987. This decline was partially compensated for by increased production from low-cost petroleum residues, utility ash, and spent catalysis. Production volumes from these sources increased from 893 tons in 1983 to 2,695 tons in 1985, an increase of approximately 281%; volumes remained reasonably constant through 1987 (Hilliard 1987).

TABLE 4-1. Facilities that Manufacture or Process Vanadium and Compounds[a]

Facility	Location	Maximum Amount on site (lbs)	Use
Harvey Engineering & Manufacturing Company	Hot Springs, AK	1,000-9,999	For sale/distribution; as an article component
Vulcraft Division Of Nucor Corp.	Fort Payne, AL	10,000-99,999	As an article component
Nibco, Inc. Blytheville Division	Blytheville, AR	1,000-9,999	As an article component
Aerochem, Inc.	Orange, CA	100-999	As an impurity; as a formulation component
Union Pacific Resources Company	Wilmington, CA	1,000-9,999	As a processing aid
Kloppenberg & Company	Englewood, CO	1,000-9,999	In ancillary or other uses
Laclede Steel Company .	Alton, IL	10,000-99,999	Import; as a byproduct; as a reactant; as a formulation component; as an article component
Caterpillar Inc. Seal Ring	Peoria, IL	10,000-99,999	As an article component; in ancillary or other uses
Ltv Steel Company Inc.	East Chicago, IN	1,000-9,999	As a formulation component
New York Blower Company	La Porte, IN	10,000-99,999	In re-packaging
Syndicate Store Fixtures, Inc.	Middlebury, IN	10,000-99,999	As an article component
Dana Corporation	Syracuse, IN	10,000-99,999	As a formulation component
Total Petroleum, Inc.	Arkansas City, KS	100,000-999,999	As a processing aid
Koch Sulfur Products Company	Desoto, KS	10,000-99,999	As a processing aid
National-Southwire Aluminum	Hawesville, KY	1,000-9,999	As a reactant
Browning Manufacturing Division	Maysville, KY	100,000-999,999	Import; for sale/distribution
Baltimore Specialty Steels Corporation	Baltimore, MD	10,000-99,999	Produce; as a byproduct; as a formulation component
Koch Refining Company	Saint Paul, MN	10,000-99,999	As an impurity
Koch Sulfur Products Company	Wilmington, NC	100,000-999,999	As a processing aid
Shieldalloy Metallurgical Corporation	Newfield, NJ	1,000,000-9,999,999	Produce; import; for sale/distribution; as an impurity; as a formulation component; in re-packaging
Shieldalloy Metallurgical Corporation	Cambridge, OH	1,000,000-9,999,999	For on-site use/processing; as a byproduct; as a reactant
Canton Drop Forge	Canton, OH	No Data	As an article component
Buckeye Steel Castings	Columbus, OH	1,000-9,999	As an article component
Sohio Oil Company Toledo Refinery	Oregon, OH	1,000-9,999	As an impurity; as a processing aid
Titanium Business Operation	Milwaukie, OR	1,000-9,999	As an article component
Oregon Steel Mills, Inc.	Portland, OR	1,000-9,999	As a reactant
Blaw Knox Corporation Blaw Knox Equipment Division	Blawnox, PA	100,000-999,999	As an article component
Lukens Steel Company	Coatesville, PA	10,000-99,999	As an article component
Ajusta Buckets, Inc.	Erie, PA	1,000-9,999	For on-site use/processing; as an article component; as a manufacturing aid

TABLE 4-1 (Continued)

Facility	Location	Maximum Amount on site (lbs)	Use
Sharon Steel Corporation	Farrell, PA	1,000-9,999	Import; as a byproduct; as a formulation component; as an article component
BP Oil Company - Marcus Hook Refinery	Marcus Hook, PA	1,000-9,999	As a processing aid
Lockheed Aeromod Center, Inc.	Greenville, SC	0-99	As an article component
Phillips 66 Company Sweeny Refinery and Petrochemical	Sweeny, TX	100,000-999,999	As a processing aid
Du Pont Victoria Site	Victoria, TX	10,000-99,999	As a processing aid
Roanoke Electric Steel Corporation	Roanoke, VA	1,000-9,999	As a formulation component
Harnischfeger Corporation	Milwaukee, WI	1,000-9,999	Produce; as a byproduct
Blaw Knox Rolls	Wheeling, WV	10,000-99,999	As a formulation component

[a]Derived from TRI87 (1989)

The major facilities within the United States that manufacture or process vanadium and vanadium-containing compounds are listed in Table 4-1.

4.2 IMPORT/EXPORT

The import of vanadium by the United States can be split into three different products: vanadium-containing materials such as ores, slags, and residues from which the vanadium must still be recovered; ferrovanadium; and manufactured vanadium compounds (principally vanadium pentoxide). Due to shortages of domestic ore and petroleum residues, imports of the former increased substantially from 1983 to 1987, rising from 58 to 2,264 tons. On the other hand, imports of ferrovanadium have declined from 1,461 tons in 1984 to 422 tons in 1987. Imports of vanadium pentoxide were approximately 400 tons in both 1984 and 1987, despite falling to as low as 63 tons in 1985. In 1986, the top four exporters of vanadium to the United States were Austria, Canada, the Federal Republic of Germany, and the Republic of South Africa (Hilliard 1987).

Despite being a net importer of raw vanadium materials, the United States has remained an exporter of processed vanadium products. The United States exports vanadium principally in the form of vanadium pentoxide, which is the primary source for the production of chemicals, catalysts, alloys, and other vanadium compounds. Vanadium pentoxide and catalysts containing vanadium pentoxide have accounted for between 61% (1987) and 82% (1984) of all domestic exports. In 1984, the United States exported a total of 4,498 tons of vanadium. Since then, exports have declined, reaching a level of 2,486 tons in 1986 and remaining fairly constant through 1987. The major importers of vanadium from the United States are Canada, the Federal Republic of Germany, Japan, and Mexico. These are followed by Taiwan and the Republic of Korea (Hilliard 1987).

4.3 USE

Vanadium and its compounds are currently used for a wide variety of purposes. The annual consumption of vanadium within the United States increased from 3,277 tons in 1983 to 4,883 tons by 1985 and remained around this level through 1987. Approximately 83% of the vanadium consumed in the United States is utilized as an alloying agent in the steel industry (Hilliard 1987). These steels are used in a variety of products, such as automobile parts, springs, and ball bearings. Fourteen percent of domestic vanadium consumption is used in the production of ferrovanadium alloys. These are invaluable in the manufacture of jet aircraft engines. Likewise, the nonferrous titanium alloys are essential in the manufacture of supersonic aircrafts. Despite accounting for around 0.3% of domestic consumption, vanadium compounds also have an important role as industrial catalysts. Vanadium-containing catalysts are used in several oxidation reactions such as the manufacture of phthalic anhydride and sulfuric acid, as well as in the

production of pesticides and black dyes, inks, and pigments, that are used by the textile, printing, and ceramics industries. Other minor functions of vanadium compounds include their use as color modifiers in mercury-vapor lamps, driers in paints and varnishes, corrosion inhibitors in flue-gas scrubbers, and as components in photographic developers.

In the past, vanadium compounds were also used in refractories as a green colorant for glass and as a depolarizer in ultraviolet screening glass. Future applications of vanadium compounds may include an increased number of uses as a catalyst, a potential role in superconductors, thermal or lightactivated resistor-conductors, vanadate glasses, electro-optical switches, and the production of high magnetic fields (Brooks 1986; Browning 1969; Grayson 1983; Hilliard 1987; Mackinson et al. 1978; Symanski 1983; Weast 1969).

4.4 DISPOSAL

Where possible, vanadium compounds are recycled rather than disposed. Vanadium-containing products, such as vanadium pentoxide dust, that are spilled or are not being recycled may be disposed following treatment under current federal and state regulations. In the case of released vanadium pentoxide fumes, cleanup of the area through ventilation is recommended. For vanadium spills, ventilation and absorption of the liquid by sand or another similarly noncombustible absorbent material is required. The contaminated absorbent material should then be removed to a safe place away from potential human exposure before being placed in a secured sanitary landfill. Consultation with a hazardous material disposal expert is also suggested (Dutch Safety Institute 1980; Grayson 1983; Hilliard 1987; HSDB 1990).

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Vanadium is a white to gray metal with compounds widely distributed at low concentrations in the earth's crust. The average concentration of vanadium compounds in the earth's crust is 150 mg/kg. Elemental vanadium does not occur in nature, but its compounds exist in over 50 different mineral ores and in association with fossil fuels, It has six oxidation states (1-, 0, 2+, 3+, 4+, and 5+) of which 3+, 4+, and 5+ are the most common. The ion is generally bound to oxygen.

Vanadium is released naturally to air through the formation of continental dust, marine aerosols, and volcanic emissions. Anthropogenic sources include the combustion of fossil fuels, particularly residual fuel oils, which constitute the single largest overall release of vanadium to the atmosphere. These releases are generally in the form of vanadium oxides and contribute approximately two-thirds of atmospheric vanadium. The natural release of vanadium to water and soils occurs primarily as a result of weathering of rocks and soil erosion. This process usually involves the conversion of the less-soluble trivalent form to the more soluble pentavalent form. Deposition of atmospheric vanadium is also an important source both near and far from industrial plants burning residual fuel oils rich in vanadium. Other anthropogenic sources include leachates from mining tailings, vanadium-enriched slag heaps, municipal sewage sludge, and certain fertilizers. Natural releases to water and soil are far greater overall than anthropogenic releases to the atmosphere.

The general population is exposed to background levels of vanadium primarily through ingestion of food. Workers in industries processing or using vanadium compounds are commonly exposed to higher than background levels via the inhalation pathway. The most recent estimate by NIOSH indicates that in 1980 about 5,319 people were exposed to vanadium pentoxide in their workplace. Exposure through inhalation may also be of importance in urban areas where large amounts of residual fuel oil are burned. Other populations possibly exposed to higher than background levels include those ingesting foodstuffs contaminated by vanadium-enriched soil, fertilizers, or sludge. Populations in the vicinity of vanadium-containing hazardous waste sites may also be exposed to higher than background levels, however, there is little information regarding relevant or significant exposure pathways under these circumstances.

EPA has identified 1,177 NPL sites; vanadium has been found at 23 of the sites. 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 EPA, this number may change (View 1989). The frequency of these sites within the United States can be seen in Figure 5-1.

5.2 RELEASES TO THE ENVIRONMENT

According to the SARA Section 313 Toxics Release Inventory (TRI87), an estimated total of 78,588 pounds of vanadium were released to the environment (air, water, and land from manufacturing and processing facilities in the United States in 1987 (TRI 1989). The TRI87 data must be viewed with caution since these data represent first-time, incomplete reporting of estimated releases by these facilities. Only certain types of facilities were required to report. This is not an exhaustive list.

Releases to the environment from U.S. facilities that manufactured or processed vanadium and its compounds in 1987 are listed in Table 5-1.

5.2.1 Air

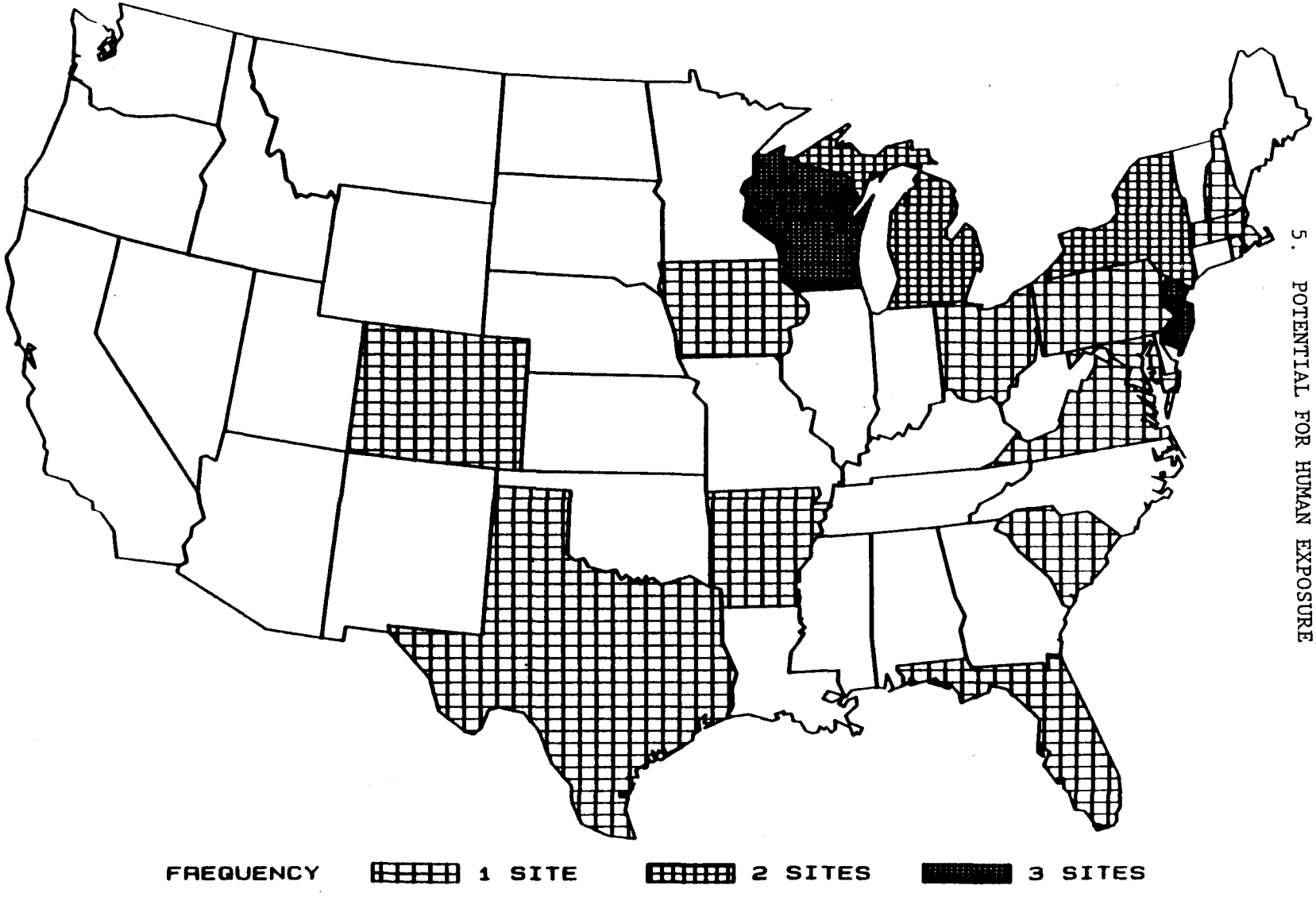
Natural sources of atmospheric vanadium include continental dust, marine aerosol, and volcanic emissions (Byerrum et al. 1974; Van Zinderen Bakker and Jaworski 1980; Zoller et al. 1973). The quantities entering the atmosphere from each of these sources are uncertain; however continental dust is believed to account for the largest portion of naturally emitted atmospheric vanadium followed by marine aerosols. Contributions from volcanic emissions are believed to be negligible when compared with the other two sources (Zoller et al. 1973).

Anthropogenic releases of vanadium to the air account for approximately two-thirds of all vanadium emissions (Zoller et al. 1973). According to TRI87, an estimated total of 20,702 pounds of vanadium were released to the atmosphere from manufacturing and processing facilities in the United States in 1987 (TRI 1989). The limitations of the estimate generated by this database, as discussed in Section 5.2, must be kept in mind, particularly as the largest anthropogenic releases of vanadium to the atmosphere are attributed to the combustion of residual fuel oils and coal, which are probably not included in the TRI87 database. These limitations are further emphasized by the fact that in 1968, the United States combustion of coal alone released an estimated 1,750 tons of vanadium oxides into the atmosphere. Other estimates for 1968 have attributed as much as 3,760 tons to this source (Byerrum et al. 1974). Furthermore, estimates of emissions from the combustion of residual fuel oils in 1969 ranged from 12,400 to 19,000 tons, while in 1970 this estimate rose to 14,000-22,000 tons (Byerrum et al. 1974). Additional unquantified sources within the United States include the burning of nearly 300 coal waste piles and the burning of wood, vegetable matter, and solid wastes, although contributions from the latter three sources may be minimal (Byerrum et al. 1974).

5.2.2 Water

EPA's Contract Laboratory Program Statistical Database (CLPSD) indicates that vanadium has been detected in surface water at 6% and in groundwater at

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



* Derived from View 1989

TABLE 5-1. Releases to the Environment from Facilities that Manufacture or Process Vanadium and Compounds[a]

Facility	Location	Total (lbs)						
		Air	Underground injection	Water	Land	Environment	POTW[b] transfer	Off-site transfer
Harvey Engineering & Manufacturing Company	Hot Springs, AK	180	0	0	0	180	0	0
Vulcraft Division Of Nucor Corp.	Fort Payne, AL	0	0	0	0	0	0	4,449
Nibco, Inc. Blytheville Division	Blytheville, AR	365	0	0	0	365	0	0
Aerochem, Inc.	Orange, CA	0	0	0	714	714	0	17
Union Pacific Resources Company	Wilmington, CA	300	0	0	0	300	0	6,900
Kloppenberg & Company	Englewood, CO	250	No Data	0	250	500	0	0
Laclede Steel Company	Alton, IL	94	0	0	0	94	0	241
Caterpillar Inc. Seal Ring	Peoria, IL	No Data	No Data	No Data	0	No Data	0	No Data
Ltv Steel Company Inc.	East Chicago, IN	250	0	1	750	1,001	0	0
New York Blower Company	La Porte, IN	0	No Data	0	0	0	0	0
Syndicate Store Fixtures, Inc.	Middlebury, IN	0	0	0	0	0	0	0
Dana Corporation	Syracuse, IN	0	0	0	0	0	0	No Data
Total Petroleum, Inc.	Arkansas City, KS	0	0	0	300	300	0	14,300
Koch Sulfur Products Company	Desoto, KS	1	No Data	0	0	1	0	0
National-Southwire Aluminum	Hawesville, KY	1,566	0	91	0	1,657	0	0
Browning Manufacturing Division	Maysville, KY	500	0	0	0	500	0	0
Baltimore Specialty Steels Corporation	Baltimore, MD	500	0	500	0	1,000	0	0
Koch Refining Company	Saint Paul, MN	140	0	0	580	720	No Data	2
Koch Sulfur Products Company	Wilmington, NC	250	0	0	0	250	0	0
Shieldalloy Metallurgical Corporation	Newfield, NJ	1,450	0	0	45,000	46,450	0	0
Shieldalloy Metallurgical Corporation	Cambridge, OH	9,750	0	0	7,100	16,850	0	20,000
Canton Drop Forge	Canton, OH	0	0	0	1,600	1,600	0	0
Buckeye Steel Castings	Columbus, OH	500	0	0	250	750	0	1,000
Sohio Oil Company Toledo Refinery	Oregon, OH	750	0	0	250	1,000	0	250

TABLE 5-1 (Continued)

Facility	Location	Total (lbs) Air	Underground injection	Water	Land	Environment	POTW[b] transfer	Off-site transfer
Titanium Business Operation	Milwaukie, OR	43	0	0	0	43	0	8,087
Oregon Steel Mills, Inc.	Portland, OR	250	0	0	0	250	0	0
Blaw Knox Corporation Blaw Knox Equipment Division	Blawnox, PA	0	0	0	0	0	0	0
Lukens Steel Company	Coatesville, PA	500	0	250	0	750	0	2,730
Ajusta Buckets, Inc.	Erie, PA	250	0	0	0	250	0	0
Sharon Steel Corporation	Farrell, PA	63	0	0	0	63	0	4,511
BP Oil Company - Marcus Hook Refinery	Marcus Hook, PA	250	0	250	0	500	0	1,916
Lockheed Aeromod Center, Inc.	Greenville, SC	0	0	0	0	0	0	0
Phillips 66 Company Sweeny Refinery and Petrochemical	Sweeny, TX	2,000	0	0	0	2,000	0	50,081
Du Pont Victoria Site	Victoria, TX	0	0	0	0	0	0	0
Roanoke Electric Steel Corporation	Roanoke, VA	0	0	0	0	0	0	0
Harnischfeger Corporation	Milwaukee, WI	250	0	0	0	250	0	0
Blaw Knox Rolls	Wheeling, WV	250	0	0	0	250	0	41,000
Totals		20702	0	1092	56794	78588	0	155484

[a]Derived from TRI87 (1989)
[b]POTW -- publicly owned treatment works

30% of 2,783 Superfund hazardous waste sites that have had samples of all media analyzed by the CLP. The geometric mean concentration of vanadium for all sites testing positive is 18 ppm and 31 ppm for surface water and groundwater, respectively (CLPSD 1989). Note that the CLPSD includes data from NPL sites only.

Natural sources of vanadium release to water include wet and dry deposition, soil erosion, and leaching from rocks and soils. The largest amount of vanadium release occurs naturally through water erosion of land surfaces. It has been estimated that approximately 32,300 tons of vanadium are dissolved and transported to the oceans by water, and an additional 308,650 tons are thought to be transported in the form of particulate and suspended sediment (Van Zinderen Bakker and Jaworski 1980).

Anthropogenic releases to water and sediments are far smaller than natural sources (Van Zinderen Bakker and Jaworski 1980). Such sources of vanadium in water may include leaching from the residue of ores and clays, vanadium-enriched slags, urban sewage sludge, and certain fertilizers, all of which are subjected to rain and groundwater drainage, as well as leachate from ash ponds and coal preparation wastes (Byerrum et al. 1974; Van Zinderen Bakker and Jaworski 1980). Leaching may potentially occur from landfills and from the airborne particulate matter that is deposited in areas with high residual fuel oil combustion, although neither of these release sources is documented.

According to TRI87, an estimated total of 1,092 pounds of vanadium were released to surface water from manufacturing and processing facilities in the United States in 1987 (TRI 1989). However, as detailed in Section 5.2, this estimate must be viewed with caution.

5.2.3 Soil

The CLPSD indicates that vanadium has been detected in the soil at 48% of 2,783 Superfund hazardous waste sites that have had samples of all media analyzed by the CLP. The geometric mean concentration of vanadium for all sites testing positive is 21 ppm (CLPSD 1989). Note that the CLPSD includes data from NPL sites only.

Natural releases of vanadium to soil result from weathering of rockbearing vanadium minerals, precipitation of vanadium particulate from the atmosphere, deposition of suspended particulate from water, and plant and animal wastes. The largest amount of vanadium released to soil occurs through the natural weathering of geological formations (Byerrum et al. 1974; Van Zinderen Bakker and Jaworski 1980).

Anthropogenic releases of vanadium to soil are less widespread than natural releases and occur on a smaller scale. These include the use of certain fertilizers containing materials with a high vanadium content such as

rock phosphate (10-1,000 mg/kg vanadium), superphosphate (50-2,000 mg/kg vanadium), and basic slag (1,000-5,000 mg/kg vanadium) (Van Zinderen Bakker and Jaworski 1980) as well as disposal of industrial wastes such as slag heaps and mine tailings. Additional release to the environment may also result from the disposal of vanadium-containing wastes in landfills, although this has not been specifically documented, and from wet and dry deposition of airborne particulate, particularly in areas with high levels of residual fuel oil combustion (Byerrum et al. 1974).

According to TRI87, an estimated total of 56,794 pounds of vanadium were released to soil from manufacturing and processing facilities in the United States in 1987 (TRI 1989). However, as detailed in section 5.2, this estimate must be viewed with caution.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

The global biogeochemical cycling of vanadium is characterized by releases to the atmosphere, water, and land by natural and anthropogenic sources, long-range transportation of particles in both air and water, wet and dry deposition, adsorption, and complexing. Vanadium generally enters the atmosphere as an aerosol. From natural sources, vanadium is probably in the form of mineral particles; it has been suggested that these may frequently be in the less-soluble trivalent form (Byerrum et al. 1974; Zoller et al. 1973). From man-made sources almost all the vanadium released to the atmosphere is in the form of simple or complex vanadium oxides (Byerrum et al. 1974).

The size distribution of vanadium-bearing particles in the atmosphere is substantially altered during long-range transportation (Zoller et al. 1973). Natural sources of vanadium, as well as man-made sources such as oreprocessing dust, tend to release large particles that are more likely to settle near the source. Smaller particles, such as those emitted from oil-fueled power plants, have a longer residence time in the atmosphere and are more likely to be transported farther away from the site of release (Zoller et al. 1973). Vanadium transported within the atmosphere is eventually transferred to soil and water on the earth's surface by wet and dry deposition and dissolution in sea water (Duce and Hoffman 1976; Van Zinderen Bakker and Jaworski 1980). Eventually, in the course of biogeochemical movement between soil and water, these particulates are adsorbed to hydroxides or associated with organic compounds and are deposited on the sea bed (WHO 1988).

The transport and partitioning of vanadium in water and soil is influenced by pH, redox potential, and the presence of particulate. In fresh water, vanadium generally exists in solution as the vanadyl ion (V^{4+}) under reducing conditions and the vanadate ion (V^{5+}) under oxidizing conditions, or as an integral part of, or adsorbed onto, particulate matter (Wehrli and Stumm

1989). The chemical formulas of the vanadyl species most commonly reported in fresh water are VO^{2+} and $VO(OH)^{+}$, and the vanadate species are $H_2VO_4^-$ and HVO_4^{2-} (Wehrli and Stumm 1989). The partitioning of vanadium between water and sediment is strongly influenced by the presence of particulate in the water. Both vanadate and vanadyl species are known to bind strongly to mineral or biogenic surfaces by adsorption or complexing (Wehrli and Stumm 1989). Thus, vanadium is transported in water in one of two ways: solution or suspension. It has been estimated that only 13% is transported in solution, while the remaining 87% is in suspension (WHO 1988).

Upon entering the ocean, vanadium in suspension or sorbed onto particulate is deposited upon the sea bed (WHO 1988). The fate of the remaining dissolved vanadium is more complex. Only about 0.001% of vanadium entering the oceans is estimated to persist in soluble form (Byerrum et al. 1974). Sorption and biochemical processes are thought to contribute to the extraction of vanadium from sea water (WHO 1988). Adsorption to organic matter as well as to manganese oxide and ferric hydroxide, demonstrated by the high particle-water partition coefficient of $5.7X10^5$ L/kg for the adsorption of manganese oxide in sea water, results in the precipitation of the dissolved vanadium (Wehrli and Stumm 1989; WHO 1988). Biochemical processes are also of importance in the partitioning from sea water to sediment (WHO 1988). Some marine organisms, in particular the ascidians (sea squirts), bioconcentrate vanadium very efficiently, attaining body concentrations approximately 10,000 times greater than the ambient sea water (Byerrum et al. 1974). Upon the death of the organism, the body burden adds to the accumulation of vanadium-in silt (WHO 1988). The extent to which either bioconcentration or adsorption dominates is uncertain (WHO 1988).

In general, marine plants and invertebrates contain higher levels of vanadium than terrestrial plants and animals. In the terrestrial environment bioconcentration is more commonly observed amongst the lower plant phyla than in the higher, seed-producing phyla. The vanadium levels in terrestrial plants are dependent upon the amount of water-soluble vanadium available in the soil, pH, and growing conditions. It has been found that the uptake of vanadium into the above-ground parts of many plants is low, although root concentrations have shown some correlation with levels in the soil (Byerrum et al. 1974). Certain legumes, such as Astralagus preussi, have been shown to be vanadium accumulators. Vanadium is believed to replace molybdenum as a specific catalyst in nitrogen fixation (Cannon 1963), and the root nodules of these plants may contain vanadium levels three times greater than those of the surrounding soil (Byerrum et al. 1974). Of the few plants known to actively accumulate vanadium, Amanita muscaria, a poisonous mushroom, has been demonstrated to contain levels up to 112 ppm (dry weight). Vanadium appears to be present in all terrestrial animals, but, in vertebrates, tissue concentrations are often so low that detection is difficult. The highest levels of vanadium in terrestrial mammals are generally found in the liver and skeletal tissues (Van Zinderen Bakker and Jaworski 1980; WHO 1988). No data are available regarding biomagnification of vanadium within the food chain,

but human studies suggest that it is unlikely; most of the l%-2% vanadium that appears to be absorbed by humans following ingestion is rapidly excreted in the urine with no evidence of long-term accumulation (Fox 1987).

The form of vanadium present in the soil is determined largely by the parent rock. Ferric hydroxides and solid bitumens (organic) constitute the main carriers of vanadium in the sedimentation process. Iron acts as a carrier for trivalent vanadium due to the great affinity between trivalent vanadium and trivalent iron, and is responsible for its diffusion through molten rocks where it becomes trapped during crystallization. The mobility of vanadium in soils is affected by the pH of the soil. Relative to other metals, vanadium is fairly mobile in neutral or alkaline soils, but its mobility decreases in acidic soils (Van Zinderen Bakker and Jaworski 1980). Similarly, under oxidizing, unsaturated conditions some mobility is observed, but under reducing, saturated conditions vanadium is immobile (Van Zinderen Bakker and Jaworski 1980).

5.3.2 Transformation and Degradation

Vanadium is a metallic element. Despite forming complexes with organic matter, it is generally not incorporated into organic compounds. Thus transformation occurs primarily between various inorganic compounds during its movement through the environment, and biotransformation is not considered to be an important environmental fate process.

5.3.2.1 Air

Vanadium-containing particulates emitted to the atmosphere from anthropogenic sources are frequently simple or complex oxides (Byerrum et al. 1974) or may be associated with sulfates (Zoller et al. 1973). Generally, lower oxides formed during combustion of coal and residual fuel oils, such as vanadium trioxide, undergo further oxidation to the pentoxide form, often before leaving the stacks (EPA 1985a). The average residence time for vanadium in the atmosphere is unknown as the particle size varies considerably. An estimated residence time of about 1 day has been proposed for the settling of fly ash vanadium pentoxide when associated with hydrogen sulfate (EPA 1985a)

5.3.2.2 Water

Vanadium entering water is generally converted from the less-soluble trivalent state to the more-soluble pentavalent state (Byerrum et al. 1974). The species of vanadium most likely to be found in sea water are $(H_2V_4O_{13})^{4-}$, HVO_4^{2-}, and VO^{3-} (Van Zinderen Bakker and Jaworski 1980). Vanadium is continuously precipitated from sea water by ferric hydroxides and organic matter (WHO 1988) and forms sediments on the seabed.

5.3.2.3 Soil

Weathering of rocks and minerals during soil formation may extract vanadium in the form of a complex anion that may remain in the soil or enter the hydrosphere. Vanadium remains in the soil after being precipitated from the weathering solution. This can be brought about by precipitation with polyvalent cations such as divalent calcium and divalent copper, by binding with organic complexing agents, adsorbing onto anion exchangers such as clay particles in the soil, and coprecipitating and adsorbing to hydrous ferric oxide in the soil (Van Zinderen Bakker and Jaworski 1980). In the presence of humic acids, mobile metavanadate anions can be converted to the immobile vanadyl cations resulting in local accumulation of vanadium (Van Zinderen Bakker and Jaworski 1980.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Levels of vanadium measured in ambient air vary widely between rural and urban locations. Concentrations measured over the South Pole ranged from 0.001 to 0.002 nanograms (ng) of vanadium per cubic meter (m^3) (WHO 1988) and are frequently two orders of magnitude smaller than those over the ocean at middle latitudes (WHO 1988). For example, measurements taken at nine rural sites located in the Eastern Pacific averaged 0.1 ng vanadium/m^3 (range 0.02-0.8 ng vanadium/m^3). Similar measurements taken at five different rural sites in northwestern Canada were found to average 0.72 ng vanadium/m^3 (range 0.21-1.9 ng vanadium/m^3) (Zoller et al. 1973). Between the years 1965 and 1969, average ambient concentrations in rural air in the United States ranged from less than 1 to 40 ng vanadium/m^3 (Byerrum et al. 1974), although some rural areas may have levels as high as 64 ng vanadium/m^3 due to localized burning of fuel oils with a high vanadium content (WHO 1988).

Vanadium levels in ambient urban air vary extensively with the season (WHO 1987; Zoller et al. 1973). U.S. cities can be divided into two groups based on the levels of vanadium present. The first group of cities is widely distributed throughout the United States and is characterized by ambient air concentrations that range from 3 to 22 ng vanadium/m^3 with an average of 11 ng vanadium/m^3 (approximately 20 times that of remote areas). Cities in the second group, primarily located in the northeastern United States, have concentrations that range from 150 to 1,400 ng vanadium/m^3 with an average of 620 ng vanadium/m^3 (Zoller et al. 1973). The variation is attributed to the use of large quantities of residual fuel oil by cities in the second group for the generation of heat and electricity, particularly during winter months (Zoller et al. 1973).

5.4.2 Water

Levels of vanadium in fresh water illustrate geographic variations produced by differences in effluents and leachates, from both anthropogenic and natural sources, entering the water table. Measurements of vanadium in such natural fresh waters as the Animas, Colorado, Green, Sacramento, San Joaquin, and San Juan Rivers, as well as some fresh water supplies in Wyoming, range from 0.3 to 200 μg vanadium/L (Byerrum et al. 1974; Van Zinderen Bakker and Jaworski 1980). The presence of naturally occurring uranium ores resulted in rivers in the Colorado Plateau containing vanadium levels of up to 70 μg/L, and in Wyoming levels were found to range from 30 to 220 μg/L (Byerrum et al. 1974). Some municipal waters have been found to contain levels of between 1 and 6 μg vanadium/L (Van Zinderen Bakker and Jaworski 1980), although levels of 19 μg vanadium/L have been reported in nine New Mexico municipalities (Byerrum et al. 1974).

Levels in sea water are considerably lower than those in freshwater because much of the vanadium is precipitated (Byerrum et al. 1974; Van Zinderen Bakker and Jaworski 1980). The concentrations measured usually average l-3 μg vanadium/L (Van Zinderen Bakker and Jaworski 1980) although levels as high as 29 μg/L have been reported (Byerrum et al. 1974). The total content of vanadium in sea water has been estimated to be 7.5×10^{12} kg (7.5×10^{9} metric tons) (Byerrum et al. 1974).

5.4.3 Soil

Vanadium is found throughout the earth's crust at an average level of 150 mg/kg. The level of vanadium measured in soil is closely related to the parent rock type (Van Zinderen Bakker and Jaworski 1980; Waters 1977). A range of 3-310 mg/kg has been observed, with tundra podsols and clays exhibiting the highest concentration, 100 mg/kg and 300 mg/kg, respectively (Byerrum et al. 1974). The average vanadium content of soils in the United States is 200 mg/kg (Byerrum et al. 1974) and seems to be most abundant in the western United States, especially the Colorado Plateau (Cannon 1963; Grayson 1983).

5.4.4 Other Environmental Media

The majority of foods have naturally occurring low concentrations of vanadium, many of them 1 mg/g or less (Byrne and Kosta 1978). Food items containing the highest levels of vanadium include ground parsley (1,800 ng/g dry weight), freeze-dried spinach (533-840 ng/g), wild mushrooms (50-2,000 ng/g dry weight), and oysters (455 ng/g wet weight) (Byrne and Kosta 1978). Intermediate levels are found in food types such as certain cereals (ranging from 0.7 ng/g in maize to 30 ng/g in Macedonian rice), fish (ranging from 3.5 ng/g in mackerel to 28 ng/g in freeze-dried tuna), and liver (ranging from 7.3 ng/g in beef to 38 ng/g in chicken) (Byrne and Kosta 1978). In

general, seafoods have been found to be higher in vanadium than terrestrial animal tissues (WHO 1988).

Fossil fuels frequently contain vanadium. Vanadium is found in almost all coals used in the United States, with levels ranging from extremely low to 10 g/kg (Byerrum et al. 1974; WHO 1988). Eastern U.S. coal has an average content of 30 ppm, western coal has an average content of 15 ppm, and coal from the interior contains an average of)34 ppm (Byerrum et al. 1974). The average vanadium content of bituminous and anthracite coal is 30 ppm and 125 ppm, respectively (Byerrum et al. 1974). Vanadium is also found in crude petroleum oils; levels range from 1 to 400 g/metric ton (Byerrum et al. 1974). Content in domestic oils range from 0.1 ppm in New Mexico to 78 ppm in Montana. Venezuelan crude oils are thought to have the highest vanadium content, ranging from 0.6 ppm in San Joaquin to 1,400 ppm in Boscan (Byerrum et al. 1974).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Although vanadium concentrations in foodstuffs are generally not higher than 1 ng/g (Byrne and Kosta 1978), food is the major source of exposure to vanadium for the general population (Vouk 1979). This route of exposure is particularly relevant when the food is contaminated with soil because soil contains an average of about 10,000 times as much vanadium as is found in many biological materials (Byrne and Kosta 1978). Since young children tend to ingest soil and dust during daily activities, this type of exposure is of particular importance for them. For the general population as a whole, daily dietary intake has been estimated to be on the order of a few tens of micrograms (Byrne and Kosta 1978) although other estimates from earlier studies utilizing different and possibly less sensitive analytical methods have been as high as 2 mg (Schroeder et al. 1963). In a study by Byrne and Kosta (1979), the mean vanadium levels in total dietary samples obtained in a nutrition survey in five Italian towns ranged from 8 to 12 μg (WHO 1988). Higher dietary intake levels are possible when food is grown in soil contaminated with greater than background levels of vanadium.

Drinking water is not considered to be an important source of vanadium exposure for the general population. Although concentrations may range from 0.2 to greater than 100 μg/L (Vouk 1979), depending upon the specific geographical location, 91% of samples from the United States had values below 10 μg/L with an average of 4.3 μg/L, and most values appear to be around 1 μg/L (Vouk 1979).

The general population may also be exposed to airborne vanadium through inhalation, particularly in areas where use of residual fuel oils for energy production is high (Zoller et al. 1973). Assuming air concentrations of approximately 50 ng/m^3, Byrne and Kosta (1978) estimated a daily intake of 1 μg vanadium by the inhalation route.

The total body pool of vanadium in the general population is estimated to be around 100 μg (Byrne and Kosta 1978). This estimate is based upon body burden levels of 3 ng/g in bone, up to 0.2 μg/g in blood, 0.5 ng/g in muscle, 0.7 ng/g in fat, 10 ng/g in liver, 0.7 ng/g in brain, 30 ng/g in lung, and 5 ng/g in kidney (ICRP 1975).

The National Occupational Hazard Survey (NOHS), conducted by NIOSH in 1972-1974, estimated that 2,562 workers in 333 plants were potentially exposed to vanadium pentoxide in 1970. The largest number of exposed employees worked in the stone, clay, and glass products industry, and the second largest group was involved with electric, gas, and sanitary services (NIOSH 1976).

Preliminary data from a second workplace study, the National Occupational Exposure Survey (NOES) also conducted by NIOSH in 1980-1983, indicated that 5,319 workers in 151 plants were potentially exposed to vanadium in the workplace in 1980. Of the 5,319 workers 84% were exposed specifically to vanadium pentoxide. The largest number of workers were exposed in the chemicals and allied products industry (NIOSH 1984a).

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.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

The most likely pathway of vanadium exposure for the general population is the ingestion of food bearing soil residue. Thus, populations consuming foods grown in soils supplemented with fertilizers or sludge containing vanadium may be exposed to concentrations higher than background levels. This is due primarily to surface deposition. Because infants and toddlers have a tendency to ingest soil and dust during everyday activities, soil containing background or higher levels of vanadium may result in young children being exposed to greater amounts than the general population.

Populations in areas with high levels of residual fuel oil consumption may also be exposed to above background levels of vanadium, both from increased particulate deposition upon food crops and soil in the vicinity of power plants and higher ambient air levels (Zoller et al. 1973). Cities in the northeastern United States frequently fall into this category, where ambient air levels often range from 150 to 1,400 ng/m^3 (Zoller et al. 1973).

Populations living near the 23 NPL sites known to be contaminated with vanadium also may be exposed to high levels of vanadium compounds through contact with contaminated media.

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 vanadium 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 vanadium.

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 physical and chemical properties of vanadium and its compounds are reasonably well documented (see Tables 3-1 and 3-2). Further information, such as partition coefficients, would be helpful in understanding the transport and transformation of vanadium in the environment.

Production, Import/Export, Use, and Disposal. Companies involved in the vanadium production industry (see Table 4-1), methods used in extraction and processing (Brooks 1986; Browning 1969; Byerrum et al. 1974; Grayson 1983; Weast 1969), uses of various vanadium compounds (Brooks 1986; Browning 1969; Grayson 1983; Hilliard 1987; Mackinson et al. 1978; Symanski 1983; Weast 1969), and various sources of release arewell documented (see Table 5-1). Information on recent domestic production volumes, particularly since 1985; is unavailable because the information is proprietary. In addition, there is little information available describing the amounts of vanadium consumed in each use category or the quantities recycled and disposed of within the United States. Few details were found regarding the specific disposal methods used (Dutch Safety Institute 1980; Grayson 1983; Hilliard 1987; HSDB 1990). Information in each of these areas would provide an indication of the potential for human exposure as a result of disposal practices, and a broader picture of the vanadium industry as a whole in both domestic and global contexts.

According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxics Release Inventory (TRI), which contains this information for 1987, became available in May of 1989. This database will be updated yearly and should provide a list of industrial production facilities and emissions.

5. POTENTIAL FOR HUMAN EXPOSURE

Environmental Fate. The relative contributions of natural (Byerrum et al. 1974; Zuller et al. 1973) and anthropogenic sources (Byerrum et al. 1974) of vanadium to the different environmental media are well documented. Partitioning between the various media is described, in particular from soil to water and from water to sediment (Wehrli and Stumm 1989; WHO 1988), but specific coefficients are not available. Information on the transport of vanadium within each media is documented (Duce and Hoffman 1976; Wehrli and Stumm 1989; WHO 1988; Zoller et al. 1973), however, more details regarding the transformation between the different forms of vanadium would be useful in expanding the understanding of the biogeochemical cycling of this element. Further information on the transport and transformation of vanadium in the environment would also be helpful in identifying media relevant to human exposure pathways.

Bioavailability from Environmental Media. Occupational studies on the uptake of vanadium via the inhalation route exist; however, data suggesting that this route is relevant with regard to hazardous waste sites are lacking. Dermal absorption data are limited, however it is likely that absorption via this route is low since vanadium, like other metals, has low solubility in lipids (WHO 1988). The primary concern regarding uptake of vanadium in the vicinity of contaminated waste sites is ingestion, particularly of contaminated food, soil, or water by children playing in the area (Byrne and Kosta 1978; Vouk 1979). However, sufficient animal data exist to indicate that absorption of vanadium via this route is limited (Conklin et al. 1982; Roshchin et al. 1980). Confirmation of this conclusion by human data would be helpful, especially since children may absorb more than adults.

Food Chain Bioaccumulation. The uptake of vanadium in aquatic plants and animals is reasonably well documented; levels of vanadium present in different species have been established (Byerrum et al. 1974; WHO 1988). Levels present in terrestrial plants (Byerrum et al. 19741; Cannon 1963) and animals (Van Zinderen Bakker and Jaworski 1980; WHO 1988) have been established for several species. Uptake of vanadium by terrestrial plants grown on sludge-amended, or vanadium-containing fertilized fields has been studied. Vanadium does not appear to concentrate in above-ground portions of terrestrial plants (Byerrum et al. 1974); however, more information on accumulation in root crops might be useful in identifying populations with dietary intake that exceeds background. In general, bioconcentration and biomagnification data are limited. Further information would be useful in defining dietary pathways for general population exposure, and in estimating exposures at NPL sites.

Exposure Levels in Environmental Media. Vanadium levels in environmental media are reasonably well documented although more recent information would enable a more accurate assessment of potential exposure levels (Byerrum et al. 1974; Byrne and Kosta 1978; Van Zinderen Bakker and Jaworski 1980; Waters 1977; WHO 1988; Zoller et al. 1973). Current information on emission levels from the combustion of residual fuel oil would

enable a more complete picture of populations potentially exposed to higher than background ambient air levels. Further studies on the levels and forms of vanadium found in food would be helpful in narrowing the range of values observed. This would allow a better estimation of dietary exposure. Moreover, information concerning levels found in environmental media in the vicinity of hazardous waste sites would be particularly useful.

Exposure Levels in Humans. Information was located describing levels of vanadium present in human tissues for the general population (Byrne and Kosta 1978). Improved sensitivity of analytical techniques would enable a more accurate estimation of exposure levels. Little information is available on tissue levels found in populations near hazardous waste sites. Further investigations of this nature would be useful in identifying risks attached to higher than background exposures, particularly for the ingestion pathway. Although vanadium can be detected in urine samples, this does not appear to have been correlated with exposure levels such as might be found near hazardous waste sites.

Exposure Registries. No exposure registries for vanadium 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

No long-term research studies on the environmental fate of vanadium were identified. Environmental monitoring is being conducted in conjunction with remedial investigations and feasibility studies at 23 NPL sites known to be contaminated with vanadium. This will add to the available database on exposure levels in environmental media, chemical species, fate, and transport of the compounds.

No on-going studies or long-term research concerning occupational or general population exposures to vanadium were identified.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring vanadium 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 vanadium. 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 vanadium in environmental samples are the methods approved by federal agencies such as EPA and 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.

6.1 BIOLOGICAL MATERIALS

A number of analytical techniques have been used to determine ppm to ppt levels of vanadium in biological materials. These include neutron activation analysis (NAA), graphite furnace atomic absorption spectrometry (GFAAS), spectrophotometry, isotope dilution thermal ionization-mass spectrometry (IDMS), and inductively coupled plasma atomic emission spectrometry (ICP-AES). Table 6-l summarizes the analytical methods for determining vanadium in biological materials.

In general, biological and environmental samples may be prepared prior to quantification of vanadium by acid digestion with nitric acid. Sample dilution with nitric acid or other agents to solubilize vanadium from the sample matrix can also be employed. If the concentration of vanadium in the dissolved sample is very low, preconcentration techniques such as chelation or extraction may be used. Chelation and extraction efficiency will vary with the technique used.

Owing to its high sensitivity, the NAA technique has been widely used to measure trace elements (including vanadium) in biological samples (Allen and Steinnes 1978; Lavi and Alfassi 1988; Mortin and Chasteen 1988; Mousty et al. 1984). The NAA technique is based on the interaction of the nuclei of vanadium atoms in the sample with thermal neutrons, resulting in the emission of photons (gamma rays). The resultant gamma ray is detected with a highresolution lithium-drifter germanium detector. The concentration of vanadium is determined through its short-lived (half-life = 3.75 minutes) radionuclide 52V. Detection limits of low- to sub-ppb (μg/L) levels of vanadium in blood and urine samples were obtained (Allen and Steinnes 1978; Lavi and Alfassi 1988; Mousty et al. 1984). The advantages of the NAA technique are its sensitivity and multi-elemental capability. The disadvantages of this technique include its high cost and the limited availability of nuclear facilities for NAA analysis.

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Blood and urine	Digest sample and evaporate; redissolve in acid; extract with MIBK; evaporate; redissolve in acid	NAA	~1 µg/L (blood); 2-4 µg/L (urine)	No data	Allen and Steinnes 1978
	Digest sample and evaporate; extract and concentrate with BTA, evaporate in benzene; dissolve in acid	GFAAS	0.08 µg/L (serum); 0.06 µg/L (urine)	90.3% (serum); 90.8% (urine)	Ishida et al. 1989
	Digest sample, evaporate; redissolve in water; extract with CPCHA in chloroform	Spectrophotometry	0.8 mg/L	No data	Paul and Gupta 1982
	Digest sample	ICP-AES	µg/L levels	No data	Kawai et al. 1989
Serum	Coprecipitate sample with lead nitrate or bismuth nitrate; dry and irradiate	NAA	0.7 µg/L	No data	Lavi and Alfassi 1988
Serum and liver	Digest sample and evaporate; redissolve in acid, concentrate on cation exchange column evaporate; redissolve in ammonium acetate	IDMS	2.6 µg/L (serum); 0.0987 µg/g (liver)	No data	Fassett and Kingston 1985

BTA = benzoyl-N-(o-tolyl)hydroxyl amine; CPCHA = chlorophenylcinnamohydroxamic acid; GFAAS = graphite furnace atomic absorption spectrometry; ICP-AES = inductively coupled plasma atomic emission spectrometry; IDMS = isotope mass spectrometry; MIBK = methyl isobutyl ketone; NAA = neutron activation analysis

GFAAS has also been used for measuring trace levels of vanadium in the serum and urine of humans and animals (Ishida et al. 1989; Mousty et al. 1984). Detection limits of 0.08 μg/L in serum and 0.06 μg/L in urine were achieved (Ishida et al. 1989). The GFAAS technique is as sensitive as NAA, and is also rapid, simple, relatively free from interference, and relatively inexpensive (Ishida et al. 1989; Krishnan et al. 1976).

Spectrophotometry has been extensively used to measure vanadium in environmental and biological samples (Abbasi 1981 and 1987; Agrawal 1975; Gupta and Tandon 1973; Jha 1979; Paul and Gupta 1982). The method typically involves dry or wet ashing of the sample, followed by preconcentration via an extraction procedure using chloroform and a chelating agent specific for vanadium. The spectrophotometric technique is convenient, rapid, selective, and sensitive for measuring ppm (mg/L) levels of vanadium in blood and urine samples (Paul and Gupta 1982).

A procedure has been developed for the determination of vanadium in biological materials using IDMS. In this procedure, the vanadium isotope 5% in the sample was increased by adding a ^{50}V-enriched spike solution, and ion counting detection was employed (Fassett and Kingston 1985). Isobaric interferences caused by chromium and titanium in the matrix require efficient dissolution and clean-up procedures prior to mass spectrometric measurements. These include wet digestion and dry-ashing of the sample matrix, followed by separation of vanadium from the matrix by chelation on an ion-exchange chromatography column. Detection limits of 2.6 μg of vanadium/L of serum and 0.0987 μg of vanadium/g of liver were obtained (Fassett and Kingston 1985). Although the sensitivity for measuring vanadium by the IDMS technique is in the ppb range in biological and environmental samples, it is a time-consuming and expensive technique.

6.2 ENVIRONMENTAL SAMPLES

Many of the analytical methods for detecting vanadium in biological samples have also been used to measure vanadium in environmental samples. They are detailed in Table 6-2. These include GFAAS, spectrophotometry, IDMS, and ICP-AES. Other techniques employed for measuring vanadium in environmental samples are flame atomic absorption spectrometry (FAAS) and direct current plasma-atomic emission spectrometry (DCP-AES). The most widely used methods utilize some modification of atomic adsorption spectrometry (AAS). In general, similar methods are employed for preparation and clean up of environmental and biological samples prior to quantification of vanadium (see Section 6.1).

Both AAS and AES methods are commonly used to detect vanadium in air. Trace levels of vanadium (as vanadium pentoxide) have been detected in air samples by GFAAS (Quickert et al. 1974). A detection limit of 0.25 ng of vanadium/m^3 of sample for an air sample of 2,000 m^3 was achieved. A method

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Collect air sample on acetyl-cellulose filter; digest and evaporate; redissolve in acid	ICP-AES	Working range of 5.0-2,000 $\mu g/m^3$ for a 500-L air sample	No data	NIOSH 1984b (Method 7300)
	Collect sample on filter; extract with trichloro-ethylene; digest; evaporate; redissolve in acid	DCP-AES	4 $\mu g/m^3$ for a 25-L sample	100%	Pyy et al. 1983
	Collect sample on glass fibre filter; digest; evaporate; redissolve in acid	GFAAS	0.25 ng/m^3 for an air sample of 2,000 m^3	No data	Quickert et al. 1974
Water	Acidify sample; extract and concentrate with HC PMC PTH in chloroform	Spectrophotometry	0.07 µg/sample	No data	Jha 1979
Water and waste water	Digest sample; evaporate; redissolve in acid	GFAAS and FAAS	4 µg/L (GFAAS); 200 µg/L (FAAS)	No data	EPA 1986a (Methods 7911 and 7910)
Water, plants, soils, and rocks	Acidify sample; oxidize with potassium permanganate; extract with DAMNHA in chloroform	Spectrophotometry	0.05 µg/sample	No data	Abbasi 1981
Citrus leaves and oyster tissue	Digest sample; evaporate; redissolve in acid; concentrate cation on exchange column; elute with HCl/H_2O_2; evaporate; redissolve in ammonium acetate	IDTI-MS	2.316 µg/g (oyster tissue); 0.245 µg/g (citrus leaves)	No data	Fassett and Kingston 1985
Soil and cabbage leaves	Digest sample; evaporate; redissolve in water; extract with N-o-CPCHA in chloroform	Spectrophotometry	0.8 µg/g	No data	Paul and Gupta 1982

DAMNHA = N-(p-N, N-dimethylanilino-3-methoxy-2-napho)hydroxamic acid; DCP-AES = direct current plasma atomic emission spectrometry; FAAS = flame atomic absorption spectrometry; GFAAS = graphite furnace atomic absorption spectrometry; HCl = hydrochloric acid; H_2O_2 = hydrogen peroxide; HC PMC PTH = N-hydroxy-N-p-chlorophenyl-N-(2-methyl-S-chloro)phenyl-p-toluamide hydrochloride; ICP-AES = inductively coupled plasma atomic emission spectrometry; IDTI-MS = isotope dilution thermal ionization-mass spectrometry; N-o-CPCHA = N-o-chlorophenylcinnamohydroxamic acid

for the determination of vanadium in workplace air using DCP-AES was reported by Pyy et al. (1983). A detection limit of 4 μg of vanadium/m^3 of sample and a practical working range of 0.01-100 μg of vanadium/m^3 of sample were obtained. DCP-AES was shown to have a sensitivity and precision equal to or greater than commonly used AAS techniques. No limitations of this method were noted by the authors. NIOSH has recommended,ICP-AES (Method 7300) for detecting vanadium and other elements in air. A working range of 5-2,000 μg of vanadium/m^3 of sample in a 500-L air sample was obtained (NIOSH 1984b).

GFAAS and FAAS are the techniques (Methods 7911 and 7910) recommended by EPA's Office of Solid Waste and Emergency Response for measuring low levels of vanadium in water and waste water (EPA 1986a). Detection limits of 4 μg of vanadium/L of sample and 200 μg of vanadium/L of sample were achieved using GFAAS and FAAS techniques, respectively. Spectrophotometry has also been employed to measure ppm levels of vanadium in aqueous media (Abbasi 1981; Jha 1979).

Spectrophotometry is the method commonly employed to analyze for the presence of vanadium in soil. Detection of low ppm concentrations in the soil have been reported (Abassi 1981; Paul and Gupta 1982). IDMS and spectrophotometry have been used for measuring low ppm (μg/g) levels of vanadium in plant and marine animal tissues (Abbasi 1981; Fassett and Kingston 1985; Paul and Gupta 1982).

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 vanadium 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 vanadium.

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.

6.3.1 Data Needs

Methods for Determining Biomarkers of Exposure and Effect. AAS methods are the most widely used to measure low- to sub-ppb (μg/L) levels of vanadium in blood, urine, tissues, and other biological media (Ishida et al. 1989; Krishnan et al. 1976; Mousty et al. 1984). Other methods include NAA (Allen and Steinnes 1978; Lavi and Alfassi 1988; Morten and Chasteen 1988; Mousty et al. 1984), AES (Kawai et al. 1989), and ITDI-MS (Fassett and Kingston 1985). These methods have all been demonstrated to be sensitive, precise, and reliable methods to measure metals as long as sample preparation procedures are rigidly followed and cleanliness and purity of all vessels and reagents are maintained. Background levels of vanadium have been reported with these techniques, but discrepancies and problems have occurred because of the extremely low levels of vanadium found in many samples. Contamination from reagents and containers used in analyses can approach background levels and interfere with results. All of these techniques provide sensitive and reliable measures of exposure with the capability of correlating environmental levels with tissue and urinary levels of vanadium. Improvements in sample preparation techniques that simplify sample preparation while maintaining or increasing reliability of analyses would be advantageous. Since there are no well-documented biomarkers of effect specific for vanadium, it is difficult to assess the sensitivity and reliability of these methods for measuring levels associated with health effects.

A decreased level of cystine (or cysteine) in hair and fingernails has been historically linked to vanadium exposure and suggested as a monitor of exposure (Mountain 1955). Accurate and precise methods exist for measuring these amino acids, but their depletion in hair and fingernails is not specific for vanadium exposure. More recent research did not indicate a correlation between cystine (or cysteine) depletion and vanadium exposure. There does not appear to be a need for additional research on this topic.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. AAS methods are the most widely used to measure levels of vanadium in environmental media (EPA 1986a; Quickert et al. 1974). In addition, AES techniques (NIOSH 1984b; Pyy et al. 198j), IDTI-MS (Fassett and Kingston 1985), and spectrophotometry (Abbasi 1981; Jha 1979) are available to measure vanadium in air, water, wastewater, soil, plants, and marine tissues. As with biological material, these methods are sensitive and reliable as long as sample preparation and cleanup are carefully done.

Since the most significant exposure to vanadium occurs in workers occupationally exposed to airborne vanadium, and significant absorption occurs by the inhalation route, air is the media of concern for potential human exposure. The GFAAS technique has sufficient accuracy and precision to measure background levels of vanadium in air as well as levels at which health effects might occur (Quickert et al. 1974). At hazardous waste sites, exposure is mostly likely to occur by ingestion of contaminated water, soil,

or plants, although absorption via this route is small. The techniques recommended by EPA, GFAAS and FAAS (Methods 7910 and 7911), provide sensitive and reliable measures of ppb levels of vanadium in water and waste water (EPA 1986a). Spectrophotometry is commonly used to detect vanadium in soil accurately (Abbasi 1981; Paul and Gupta 1982). IDTI-MS and spectrophotometry are used to measure low-ppm levels of vanadium in plants as well as marine tissues (Abbasi 1981; Fassett and Kingston 1985; Paul and Gupta 1982). No additional methods for detecting vanadium in environmental media appear to be necessary at this time; however, improvements in sample preparation could increase sensitivity and reliability.

6.3.2 On-going Studies

No on-going studies regarding methods for measuring vanadium in biological and environmental samples were located.

7. REGULATIONS AND ADVISORIES

Vanadium is on the list of chemicals appearing in "Toxic Chemicals Subject to Section 313 of the Emergency Planning and Community Right-to-Know Act of 1986" (EPA 1987c).

The international, national, and state regulations and guidelines regarding vanadium and its compounds in air, water, and other media are summarized in Table 7-l.

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Vanadium and Compounds

Agency	Description	Information	References
INTERNATIONAL			
WHO	TWA air quality guideline for vanadium (24-hr)	1 $\mu g/m^3$	WHO 1987
NATIONAL			
Regulations:			
a. Air:			
OSHA	PEL ceiling (transitional limits)		OSHA 1974 (29 CFR 1910.1000)
	Vanadium pentoxide (respirable dust)	0.5 mg/m^3	
	Vanadium pentoxide (fume)	0.1 mg/m^3	
	PEL TWA--8-hr (final rule limits)		OSHA 1989
	Vanadium pentoxide (respirable dust)	0.05 mg/m^3	
	Vanadium pentoxide (fume)	0.05 mg/m^3	
b. Water:			
EPA OWRS	NPDES Permit Testing Requirements; toxic pollutants and hazardous substances required to be identified by existing dischargers if expected to be present: vanadium[a]	Yes	EPA 1983 (40 CFR 122, Appendix D, Table V)
c. Other:			
DOT	DOT-IMO: Poison B; label: Poison		DOT 1980 (49 CFR 172.102)
	Ammonium metavanadate	Yes	
	Vanadium trioxide (dust)	Yes	
	Vanadium pentoxide (dust)	Yes	
	Vanadyl sulfate	Yes	
	DOT-Hazard: Corrosive material		DOT 1980 (49 CFR 172.101)
	Vanadium oxytrichloride	Yes	
	Vanadium tetrachloride	Yes	
EPA OERR	CERCLA reportable quantity		EPA 1985b (40 CFR 302.4); EPA 1986b (40 CFR 117.3)
	Ammonium metavanadate	1,000 pounds (454 kg)	
	Vanadium pentoxide	1,000 pounds (454 kg)	
	Vanadyl sulfate	1,000 pounds (454 kg)	
	Extremely hazardous substance TPQ		EPA 1987a (40 CFR 355, Appendix A)
	Vanadium pentoxide	100/10,000 pounds	
EPA OSW	Designation of (CERCLA) hazardous substances		EPA 1978 (40 CFR 116.4); EPA 1985b (40 CFR 302.4)
	Ammonium metavanadate	Yes	
	Vanadium pentoxide	Yes	
	Vanadyl sulfate	Yes	
	Listing as hazardous waste: Discarded commercial chemical products off-specifications species container residues, and spill residues thereof		EPA 1980 (40 CFR 261.33[e])
	Ammonium metavanadate	Yes	
	Vanadium pentoxide	Yes	
	Listing as hazardous waste constituents		EPA 1988 (40 CFR 261, Appendix VIII)
	Ammonium metavanadate	Yes	
	Vanadium pentoxide	Yes	
	Groundwater monitoring requirement		EPA 1987b (40 CFR 264, Appendix IX)
	Vanadium (total)	Yes	
	Toxic chemical release reporting; Community Right-to-Know (Proposed)		EPA 1987c
	vanadium (fume or dust)	Yes	

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (Continued)

Agency	Description	Information	References
NATIONAL (cont'd)			
OSHA	Meets criteria for proposed OSHA medical records rule		OSHA 1982
	Ammonium metavanadate	Yes	
	Isobutyl orthovanadate	Yes	
	Sodium metavanadate	Yes	
	Sodium tetravanadate	Yes	
	Vanadium[a]	Yes	
	Vanadium tetrachloride	Yes	
	Vanadium oxytrichloride	Yes	
	Vanadium pentoxide (dust)	Yes	
Guidelines:			
a. Air:			
ACGIH	TLV TWA		ACGIH 1986
	Vanadium pentoxide (dust and fume)	0.05 mg/m^3	
	REL Ceiling (15 min)		NIOSH 1985
	Vanadium compounds[b]	0.05 mg Vanadium/m^3	
	Vanadium pentoxide (dust and fume)	0.05 mg/m^3	
NIOSH	IDLH		NIOSH 1985
	Vanadium pentoxide (dust and fume)	70 mg/m^3	
b. Other:			
EPA	RfD (oral)		
	Vanadium pentoxide	$9x10^{-3}$ mg/kg/day	IRIS 1989
STATE			
Regulations and Guidelines:			
a. Air:	Acceptable ambient air concentrations		NATICH 1988
	Vanadium		
Connecticut	(8-hr)	1.0000 $\mu g/m^3$	
Massachussetts	(24-hr)	0.1400 $\mu g/m^3$	
Nevada	(8-hr)	0.0010 mg/m^3	
	Vanadium pentoxide		
Massachussetts	(24-hr)	0.1400 $\mu g/m^3$	
North Dakota	(8-hr)	0.0005 mg/m^3	
Virginia	(24-hr)	0.8000 $\mu g/m^3$	

[a]The forms of vanadium regulated are not specified.
[b]The ceiling and time-weighted average values given for vanadium compounds by NIOSH (1977) reflect the equivalent vanadium concentrations, not concentrations for the compounds themselves.

ACGIH = American Conference of Governmental Industrial Hygienists; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DOT = Department of Transportation; DOT-IMO = Department of Transportation/International Maritime Organisation; EPA = Environmental Protection Agency; IDLH = Immediately Dangerous to Life or Health Level; IRIS = Integrated Risk Information System; NATICH = National Air Toxics Information Clearinghouse; NIOSH = National Institute for Occupational Safety and Health; NPDES = National Pollutant Discharge Elimination System; ODW = Office of Drinking Water; 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; REL = Recommended Exposure Limit; RfD = Reference dose; STEL = Short Term Exposure Limit; TLV = Threshold Limit Value; TPQ = Threshold Planning Quantity; TWA = Time-Weighted Average; WHO = World Health Organization

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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 (Kd) -- 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$_{(LO)}$ (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.

q_1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually pg/L for water, mg/kg/day for food, and $\mu g/m^3$ 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 (2-1 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 and figures 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 2-1 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 2-1) 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 cate.gories 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. Key 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 2-1).

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

6. Exposure Frequency/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, and dermal/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 MKL of 0.005 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 2-1

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 Effect 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/m^3 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.

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.

SAMPLE

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
INTERMEDIATE EXPOSURE							
Systemic							
18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
Cancer							
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.

[b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5 x 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)

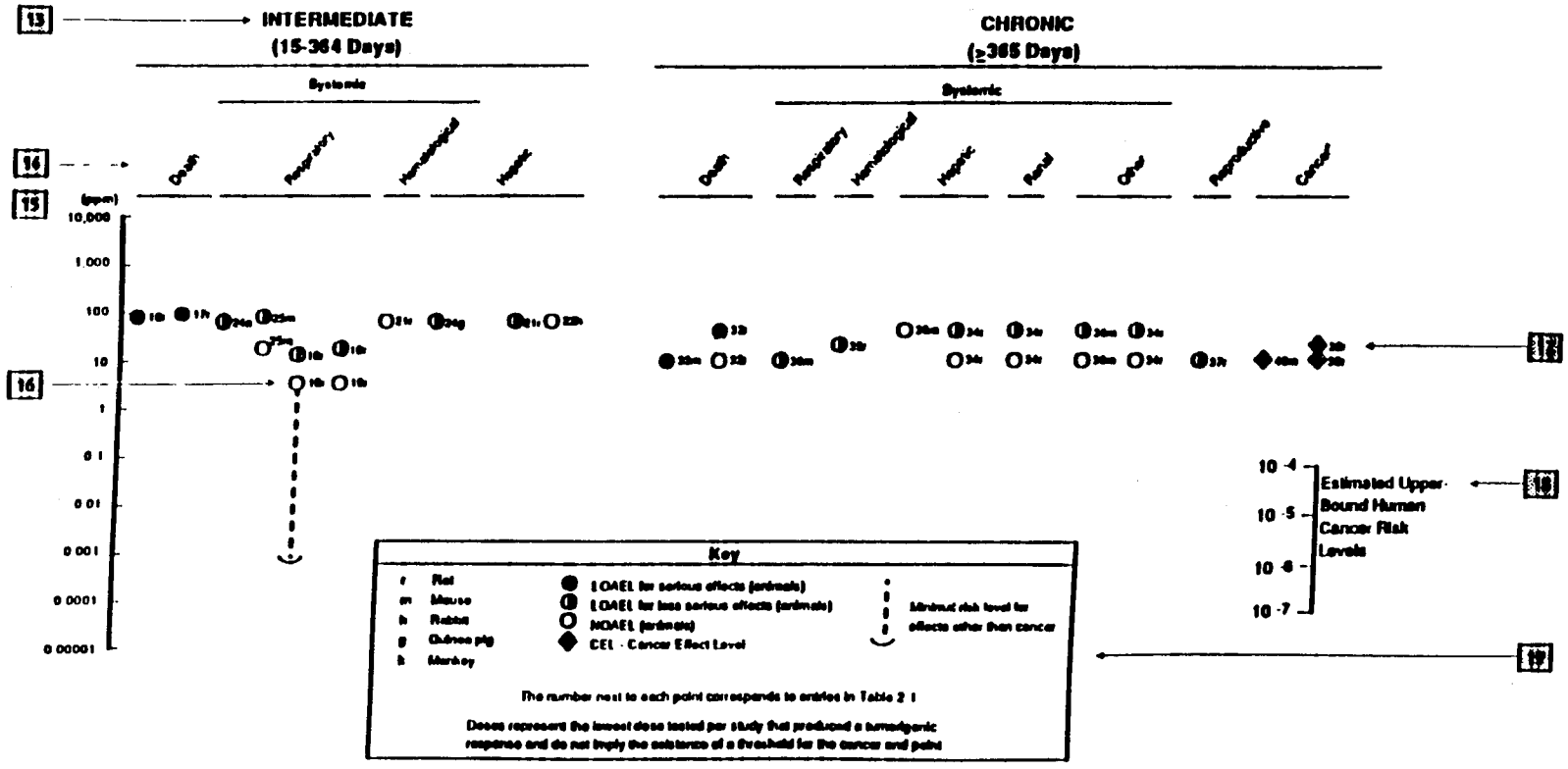

FIGURE 2-1. Levels of Significant Exposure to [Chemical X]-Inhalation

APPENDIX A

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 aquaint 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 information known 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

APPENDIX B

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
STORET	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 vanadium. The panel consisted of the following members: Dr. Leo Newland, Professor and Director, Environmental Sciences Program, Texas Christian University, Fort Worth Texas; Dr. Paul Mushak, Consultant in Health and Chemical Sciences, Durham, North Carolina; Dr. Andrew L. Reeves, Department of Occupational and Environmental Health, Wayne State University, Detroit, Michigan. These experts collectively have knowledge of vanadium'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 the Comprehensive Environmental Response, Compensation, and Liability Act of 1986, Section 104.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have 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.

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