TOXICOLOGICAL PROFILE FOR JET FUELS JP-4 AND JP-7

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

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UPDATE STATEMENT

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles contact ATSDR at:

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Atlanta, Georgia 30333

FOREWORD

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and the Environmental Protection Agency (EPA) and in support of Department of Defense information needs. 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 succinctly characterizes the toxicologic 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 toxicologic 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.

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, when 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 significant to protect public health will be identified by ATSDR and the EPA. The focus of the profiles is on health and toxicologic information; therefore, we have included this information in the beginning of the document.

Each profile must include the following:

(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a 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 that present a significant risk to human health of acute, subacute, and chronic health effects.

(C) When appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that might present significant risk of adverse health effects in humans.

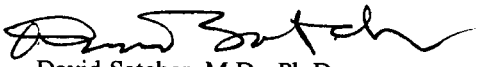
The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). Section 211 of SARA also amended Title 10 of the U. S. Code, creating the Defense Environmental Restoration Program. Section 2704(a) of Title 10 of the U. S. Code directs the Secretary of Defense to notify the Secretary of Health and Human Services of not less than 25 of the most commonly found unregulated hazardous substances at defense facilities.

Section 2704(b) of Title 10 of the U. S. Code directs the Administrator of the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare a toxicological profile for each substance on the list provided by the Secretary of Defense under subsection (b).

Foreword

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



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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Green Border Review. Green Border review assures consistency with ATSDR policy.

2. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

3. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

4. Quality Assurance Review. The Quality Assurance Branch assures that consistency across profiles is maintained, identifies any significant problems in format or content, and establishes that Guidance has been followed.

PEER REVIEW

A peer review panel was assembled for JP-4 and JP-7. The panel consisted of the following members:

1. Dr. William Nick Norton, Professor, Biology Department, Southeastern Louisiana University, Hammond, Louisiana;

2. Dr. Laurence Martin Holland, Private Consultant, 215 Rio Bravo, Los Alamos, New Mexico;

3. Dr. Arthur Gregory, Private Consultant, Techto Enterprises, Sterling, Virginia;

4. Dr. Tim Borges, Technical Information Analyst, Oak Ridge National Laboratory, Oak Ridge, Tennessee; and

5. Dr. Bruce Jacobs, Environmental Health Engineering Services Manager, General Physics Corporation, Edgewood, Maryland.

These experts collectively have knowledge of JP-4's and JP-7's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

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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1. PUBLIC HEALTH STATEMENT

This statement was prepared to give you information about jet fuels JP-4 and JP-7 and to emphasize the human health effects that may result from exposure to them. The Environmental Protection Agency (EPA) has identified 1,397 hazardous waste sites as the most serious in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal clean-up activities. JP-4 has been found in at least 4 of these sites. JP-7 has not been found in any NPL site. However, the number of NPL sites evaluated for JP-4 and JP-7 is not known. As EPA evaluates more sites, the number of sites at which JP-4 and JP-7 are found may increase. This information is important for you to know because JP-4 and JP-7 may cause harmful health effects and because these sites are potential or actual sources of human exposure to JP-4 and JP-7.

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 chemical such as JP-4 or JP-7, 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, lifestyle, and state of health.

1.1 WHAT ARE JET FUELS JP-4 AND JP-7?

JP-4 and JP-7 (jet propellant-4 and jet propellant-7) are substances that are used by the U.S. Air Force as aircraft fuels. They are also called jet fuel-4 and jet fuel-7. JP-4 is a colorless

to straw-colored liquid. It smells like gasoline and/or kerosene. JP-7 is also a liquid, usually colorless. It smells like kerosene. Both JP-4 and JP-7 are flammable. JP-4 can be made by refining either crude petroleum oil or shale oil. JP-7 is made by refining kerosene, a product of refined crude petroleum. Both JP-4 and JP-7 are blends of other chemicals made according to standards specified by the U.S. Air Force for each fuel. Both JP-4 and JP-7 are liquids at room temperature, but they can also change into vapor.

In this profile, JP-4 and JP-7 are discussed together. See Chapter 3 for more information on the chemical and physical properties of JP-4 and JP-7. More information on the production and use of JP-4 and JP-7 is found in Chapter 4.

1.2 WHAT HAPPENS TO JET FUELS JP-4 AND JP-7 WHEN THEY ENTER THE ENVIRONMENT?

We have information about what happens to JP-4 or its components in the environment. Although JP-7 is similar, there is not much information about what happens to it in the environment. JP-4 enters the environment when it spills or leaks into water or soil. It can enter the air during manufacturing, by evaporation of spills, and when it is discarded or jettisoned from jets during flight. JP-4 is a mixture of many chemicals. After it is released, the mixture spreads out in the atmosphere, and the component chemicals behave differently than they did in the liquid mixture. The behavior of each component in the environment depends on its individual chemical and physical properties. When JP-4 enters the air from flying jets as unburned fuel, some of the constituent chemicals fall back to the earth and land on water or soil. Other chemicals stay in the air and may change to different compounds when they react with light or other chemicals. Most of the chemicals in JP-4 evaporate when JP-4 spills into water. Some of the chemicals that do not evaporate as fast may dissolve in the water. If the water is very rough when the spill occurs, more JP-4 components will dissolve in the water. The chemicals that dissolve in the water are broken down further by microorganisms or become attached to the solid materials, called sediment, in the water. The chemicals that bind to this sediment may settle to the bottom of the water and stay there for a

long time. When JP-4 spills or leaks to soil, some of the chemicals evaporate, but many of them are broken down by microorganisms. Some of them may also stick to the soil. Components that do not break down easily and components that stick to soil particles may stay in the soil for a long time. Currently, no information is available about what happens to JP-7 or its components in the environment, but it is similar in composition to JP-4 so it would probably act like JP-4 when it enters the environment.

We know that many chemicals found in JP-4 can break down in the atmosphere to other chemicals, but we do not know what many of these breakdown products are. We have some information on several chemicals found in jet fuel (for example, benzene, toluene, hexane, xylene, and lead). We know more about what happens to them when they enter the environment as individual chemicals. When they enter the environment as part of jet fuel, they may behave the same way as when they are released alone. You can find more information on several individual components of jet fuel in the ATSDR toxicological profiles for these chemicals. See Chapters 4 and 5 for more information on what happens to JP-4 when it enters the environment.

1.3 HOW MIGHT I BE EXPOSED TO JET FUELS JP-4 AND JP-7?

It is unlikely that you would be exposed to JP-4 unless you work with jet fuel or live very close to where it is used or spilled. Exposure to JP-4 can occur if you touch soil or water contaminated from a spill or leak. If you drink water contaminated with JP-4 you will be exposed to the chemicals in the mixture. You might breathe in some of the chemicals evaporating from a spill or leak site if you stay in the area where an accident has occurred. Exposure to some components might occur from air releases if the components settle to the ground near populated areas.

Workers involved in making or transporting JP-4 or in refueling military aircraft that use JP-4 might breathe air containing it. They might also spill some on their skin. Occupational data from 1981 to 1983 show that about 4,866 workers employed in 633 plants might have been exposed to JP-4. See Chapter 5 for more information on how exposure to JP-4 might occur.

1. PUBLIC HEALTH STATEMENT

No information is available specifically on exposure of individuals to JP-7. However, it is similar in composition to JP-4 and it is reasonable to assume that you could be exposed to it in the same way as described above for JP-4.

1.4 HOW CAN JET FUELS JP-4 AND JP-7 ENTER AND LEAVE MY BODY?

JP-4 and JP-7 can enter your bloodstream when you breathe them in, when you drink water containing them, or when your skin comes in contact with them. This can occur in the workplace or if you live near a manufacturing facility or an Air Force base. We do not know how much of the compounds your body might take up if you breathe them, drink them, or get them on your skin. We have no information on what happens to these chemical mixtures once they enter your body. We do not know if they remain in any tissues in the body. We also do not know whether these compounds leave the body in the urine or feces. See Chapter 2 for further discussion.

1.5 HOW CAN JET FUELS JP-4 AND JP-7 AFFECT MY HEALTH?

We know very little about the human health effects caused by JP-4 and JP-7. Breathing in large amounts of JP-4 would cause you to feel suffocated and breathing would be painful. Animal studies showed that breathing in extremely high levels of JP-4 and JP-7 does not cause death. We do not know if breathing in large amounts could cause death in people. Breathing in high levels of JP-4 has caused harmful effects on the nervous system. Some of the nervous system effects in people include headache, dizziness, nausea, depression, anxiety, memory loss, and irritability. Nervous system effects have occurred in people exposed to vapor from jet fuels like JP-4 for short and long periods in their jobs. Laboratory animals that breathed very high levels of JP-4 vapor for a short time developed nervous system effects, including poor coordination and convulsions. In lower doses, JP-4 vapor has caused animals to have a depressed level of activity compared with animals that were not exposed. Experimental animals have also had decreased numbers of white blood cells after breathing JP-4 vapor. Changes in liver cells have also been seen in animals exposed to either JP-4 or JP-7 vapor. Studies in animals show that both JP-4 and JP-7 can cause skin and eye

irritation. JP-4 may cause skin cancer in mice or rats after exposure by skin contact. The data about cancer effects from breathing in JP-4 or JP-7 are not clear-cut. No data about cancer effects exist for exposure to JP-4 or JP-7 by eating or drinking. We do not know if JP-4 or JP-7 causes cancer in people. We do not have any information on whether JP-4 or JP-7 can cause birth defects or if they affect reproduction. For more information on the health effects of JP-4 and JP-7, see Chapter 2.

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO JET FUELS JP-4 AND JP-7?

There is no medical test that shows if you have been exposed to JP-4 or JP-7. For information on tests for measuring exposure to some individual components of jet fuels, see the ATSDR toxicological profiles on benzene, toluene, xylene, and polycyclic aromatic hydrocarbons. See Chapters 2 and 6 for more information on medical tests.

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

The government has developed regulations and guidelines for JP-4 and JP-7 and the chemicals in them. These are designed to protect the public from the possible harmful health effects of the chemicals. The Occupational Safety and Health Administration (OSHA) and the Air Force Office of Safety and Health (AFOSH) regulate levels of petroleum products in the workplace. The maximum allowable amount of petroleum distillates in workroom air during an 8-hour workday, 40-hour workweek, is 500 parts per million (ppm). For more information on regulations and guidelines, see Chapter 7.

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1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, GA 30333
Phone 404-639-6000

This agency can also provide you with information on the location of the nearest occupational and environmental health clinic. These clinics specialize in the recognition, evaluation, and treatment of illnesses resulting 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 jet fuels JP-4 and JP-7 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 JP-4 and JP-7 based on toxicological studies and epidemiological investigations.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

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 (14 days or less), intermediate (15-364 days), and chronic (365 days or more).

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

The significance of the exposure levels shown in the tables and figures may differ depending on the user’s perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons may be interested in levels of exposure associated with “serious” effects. Public health officials and project managers concerned with appropriate actions to take at hazardous waste

sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) may be of interest to health professionals and citizens alike.

The jet fuels JP-4 and JP-7 are liquid military aviation turbine fuels whose composition varies slightly with the nature of the crude petroleum from which they were derived (Dukek 1978). Jet fuels derived from crude oil, the common name for liquid petroleum, are referred to as petroleum-derived jet fuels. Jet fuels derived from an organic material found in shale that can be converted by heat to shale oil are called shale-derived jet fuels. JP-4 is a wide-cut fuel; this is a refinery term indicating that it is distilled from crude oil using a broad temperature range and consists of hydrocarbons in a wide range of chain-lengths (4 to 16 carbons long) (Air Force 1989b; CONCAWE 1985). It was developed by the U.S. Air Force in order to ensure fuel availability in times of war (Dukek 1978; ITC 1985). JP-7 is a kerosene with a high flash point and is used in advanced supersonic aircraft. The jet fuels are blends of various hydrocarbons, including alkanes (paraffins) and cycloalkanes (naphthenes), aromatics, and olefins, as well as small amounts of compounds such as benzene, n-hexane, and polycyclic aromatic hydrocarbons.

The purpose of this chapter is to consider the toxicological effects of exposure to the mixture JP-4 or JP-7. Exposure to jet fuel components, exhaust, or combustion products will not be discussed. For information concerning the possible toxicity associated with exposure to some of the individual components of jet fuels, the reader is referred to the ATSDR toxicological profiles for benzene (ATSDR 1991a), toluene (ATSDR 1990), total xylenes (ATSDR 1991c), and polycyclic aromatic hydrocarbons (ATSDR 1991b). In addition, because of the variable composition of the jet fuels, the molecular weights are unknown (Kinkead et al. 1974).

2.2.1 Inhalation Exposure

2.2.1 .I Death

No studies were located regarding death in humans after inhalation exposure to JP-4 or JP-7.

2. HEALTH EFFECTS

Exposure of Sprague-Dawley rats to concentrations as high as 5,000 mg/m^3 shale- or petroleum derived JP-4 for 4 hours did not result in any mortality or apparent toxic signs during the 2-week post exposure holding period (Clark et al. 1989).

Intermediate-duration exposure of rats and mice to concentrations of JP-4 as high as 5,000 mg/m^3 resulted in death in 1 of 40 exposed mice and 1 of 50 exposed rats, between 4 and 6 months after the exposure was begun (Air Force 1974). It was concluded that exposure to the test substance was probably not responsible for the deaths of these animals since two unexposed mice and one unexposed rat also died and because there were no abnormal histological findings in the rat. No deaths occurred when dogs or monkeys were exposed to similar JP-4 concentrations for 8 or 6 months, respectively (Air Force 1974).

No increase in mortality was seen in chronic studies in which mice and rats were exposed intermittently (6 hours/day, 5 days/week) to as much as 5,000 mg/m^3 JP-4 (Air Force 1981i; Bruner et al. 1993) or in studies where rats were exposed to 750 mg/m^3 JP-7 (Air Force 19828, 1983e, 1991). Additionally, no increase in mortality was observed in rats or mice 12 months after chronic intermittent exposure (6 hours/day, 5 days/week) to 5,000 mg/m^3 JP-4 (Bruner et al. 1993).

2.2.1.2 Systemic Effects

No studies were located regarding cardiovascular, gastrointestinal, musculoskeletal, dermal or ocular effects in humans or animals after inhalation exposure to JP-7. No studies were located regarding gastrointestinal, musculoskeletal, dermal or ocular effects in humans after inhalation exposure to JP-4. No studies were located regarding musculoskeletal or dermal effects in animals after inhalation exposure to JP-4.

The highest NOAEL values and all reliable LOAEL values for systemic effects for each study and end point are recorded in Table 2-l and plotted in Figure 2-l.

Respiratory Effects. No studies were located regarding respiratory effects in humans after inhalation exposure to JP-7.

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
INTERMEDIATE EXPOSURE							
Systemic							
1	Monkey (Rhesus)	6 mo 5 d/wk 6 hr/d	Hemato	5000			Air Force 1974 JP-4
			Hepatic	5000			
			Bd Wt	5000			
2	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Hemato	1000			Air Force 1980 JP-4 (PET)
			Hepatic	1000 F	500 M (9% decreased liver weight)		
			Renal	500 M	1000 M (22% increased kidney weight)		
				1000 F			
			Bd Wt	500			
3	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Resp	1000			Air Force 1984b JP-4 (PET)
			Hemato	1000			
			Hepatic	1000			
			Renal	1000 F	500 M (hyaline degeneration of renal tubular epithelium, renal tubular casts related to alpha-2μ-globulin nephropathy)		
			Bd Wt		500 (unspecified decreased body weight)		

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
4	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Hemato	1000			Air Force 1984c JP-4 (SH)
			Hepatic	500 F	1000 F (5% increased liver weight) 500 M (11% increased liver weight)		
			Renal	1000 F	500 M (19% increased kidney weight, 26% decreased urine osmolality)		
			Bd Wt	1000			
5	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Resp	1000 M			Newton et al. 1991 JP-4 (SH)
6	Mouse (C57BL/6)	90 d 7 d/wk 24 hr/d	Resp	1000 F			Air Force 1984b JP-4 (PET)
			Hepatic		500[b] F (fatty degeneration)		
			Renal	1000 F			
7	Dog (Beagle)	8 mo 5 d/wk 6 hr/d	Resp	5000			Air Force 1974 JP-4
			Gastro	2500	5000 (emesis)		
			Hemato	5000 M 2500 F	5000 F (unspecified increased red blood cell fragility)		
			Bd Wt	5000			
8	Dog (Beagle)	90 d 7 d/wk 24 hr/d	Resp	1000			Air Force 1984b JP-4 (PET)
			Cardio	1000			
			Renal	1000			
			Other	1000			

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL			Reference Chemical Form
					Less serious (mg/m3)		Serious (mg/m3)	
	Neurological							
9	Monkey (Rhesus)	6 mo 5 d/wk 6 hr/d			2500	(unspecified depressed activity)		Air Force 1974 JP-4
10	Dog (Beagle)	8 mo 5 d/wk 6 hr/d			2500	(unspecified depressed activity)		Air Force 1974 JP-4
	Reproductive							
11	Rat (F-344, S-D, Wistar, O-M)	90 d 7 d/wk 24 hr/d			1000 M	(at day 90: 3% increased testis weight for Fischer 344 rats)		Air Force 1984d JP-4 (SH)

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
CHRONIC EXPOSURE							
Systemic							
12	Rat (Fischer 344)	1 yr 5 d/wk 6 hr/d	Resp	750			Air Force 1991 JP-7
			Hemato	750 F	150 M (16% decreased WBC count)		
			Hepatic		150[c] (21and 29% increased alkaline phosphatase in males and females respectively, 9% increased absolute liver weight in females)		
			Renal	750 F	150 M (hyaline droplet formation, hydronephrosis,tubular mineralization and 13% increased BUN)		
			Ocular	750			
			Bd Wt		150 (unspecified decrease "throughout the study period")		
13	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hemato		1000 (23 and 24% reduced mean WBC in females and males, respectively)		
			Hepatic	5000			
			Renal	1000 M	5000 M (mild progressive nephropathies, medullary mineral deposits)		
				5000 F			
			Bd Wt	5000			

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
14	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hepatic	5000 F	1000 M (11% decreased liver weight - 12 months post-exposure)		
			Renal		1000 (4 and 10%decreased kidney weight in males and females respectively, increased medullary mineral deposits in 14% of males - 12 months post-exposure)		
			Bd Wt	1000			
15	Mouse (C57BL/6)	1 yr 5 d/wk 6 hr/d	Hepatic	750 M	150 F (inflammation after 12-month post-exposure period)		Air Force 1991 JP-7
16	Mouse (C57BL/6)	1 yr 5 d/wk 6 hr/d	Endocr	750 M	150 F (43% increased incidence of adrenal capsular cell hyperplasia)		Air Force 1991 JP-7
17	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d	Resp		1000 (M: 38% increased nasolacrimal duct hyperplasia. F: 27% increased mild pulmonary inflammation)		Bruner et al. 1993 JP-4
			Hepatic	5000 M 1000 F	5000 F (37% increased lymphocytic inflammatory infiltrates)		
			Renal	5000			
			Bd Wt	5000			

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
18	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hepatic	5000			
			Renal	5000			
			Bd Wt	5000			
Immuno./Lymphor							
19	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d		5000 M	1000 F (24% increased spleen weight)		Bruner et al. 1993 JP-4
Reproductive							
20	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d			5000 (increased cystic degeneration of the prostate in 52% of males; increased cystic hyperplasia of the mammary glands in 35% of females - 12 months post-exposure)		Bruner et al. 1993 JP-4
21	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d		5000			Bruner et al. 1993 JP-4

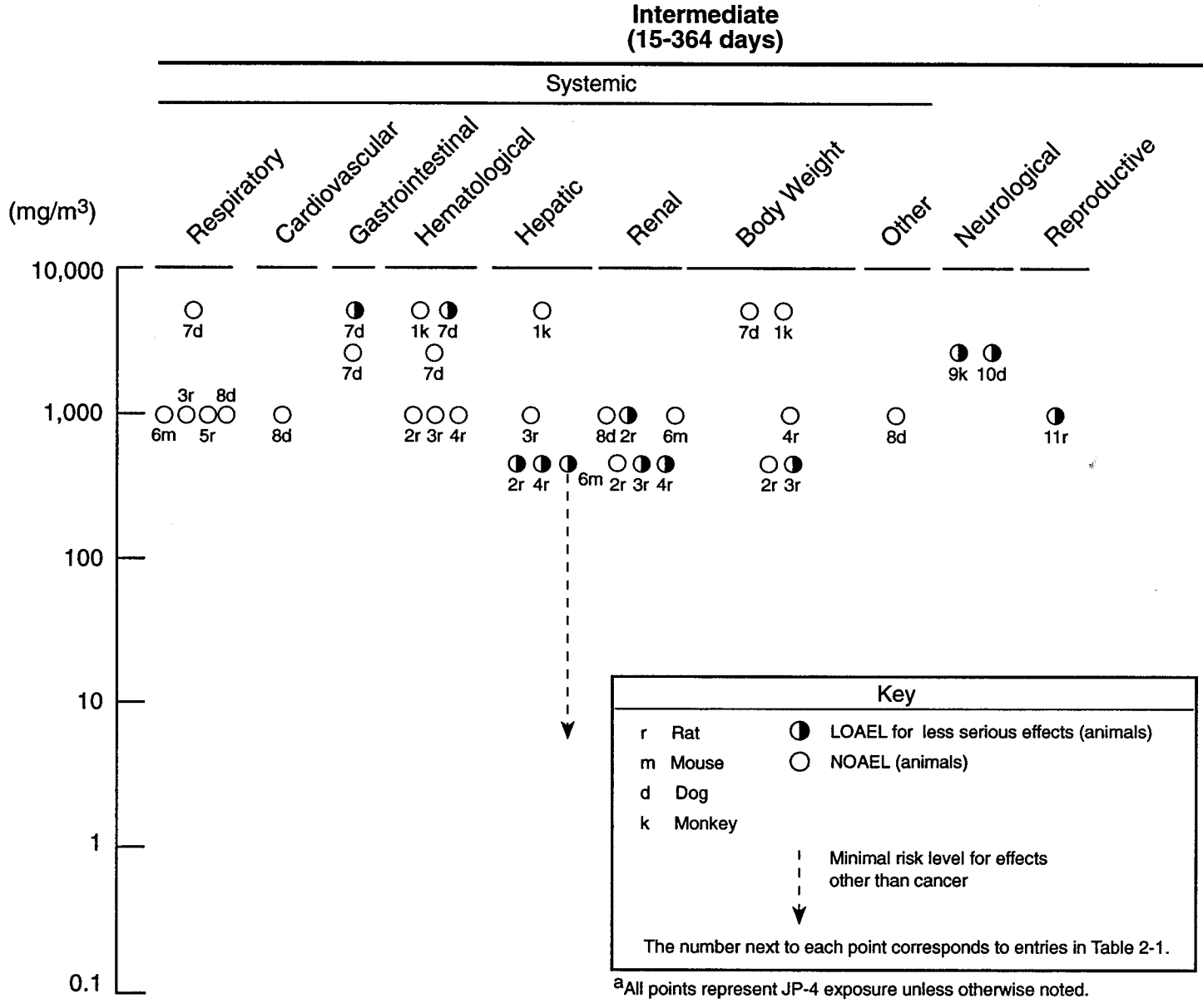
TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL			Reference Chemical Form
					Less serious (mg/m3)		Serious (mg/m3)	
22	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d		5000 F	1000 M	(increased testicular atrophy in 47% of males - 12 months post-exposure)		Bruner et al. 1993 JP-4

[a]The number corresponds to entries in Figure 2-1.
[b]Used to derive an intermediate inhalation minimal risk level (MRL) of 9 mg/m^3, concentration divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) and multiplied by a factor of 5.7 for converting from animal to human exposure.
[c]Used to derive a chronic inhalation MRL of 0.3 mg/m^3, concentration adjusted from intermittent to continuous dosing (150 mg/m^3 x 5 d/7 d x 6 hr/24 hr); adjusted concentration divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) and multiplied by a factor of 3.3 for converting from animal to human exposure.

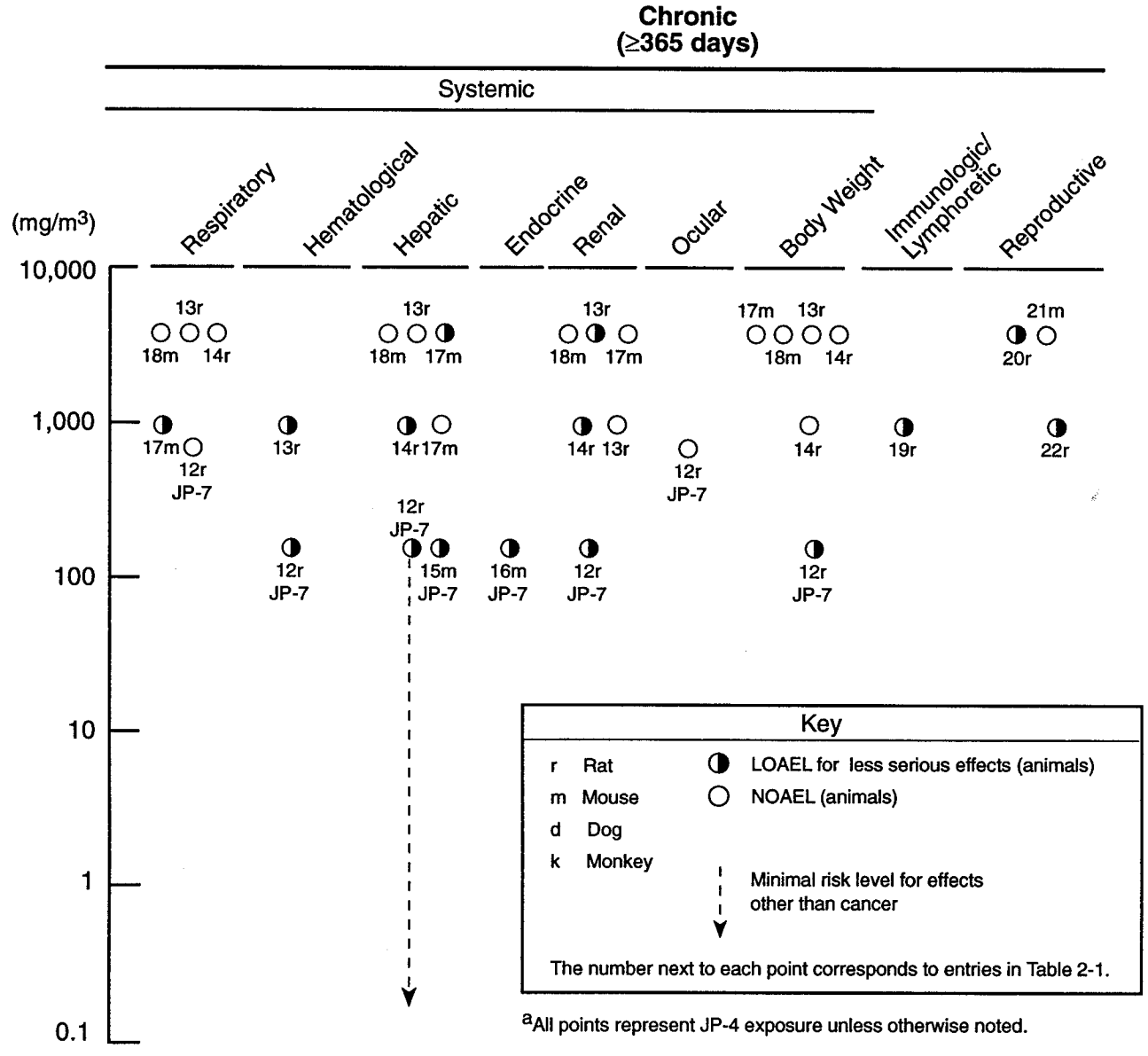
Bd Wt = body weight; BUN = blood urea nitrogen; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); F = female; F-344 = Fischer 344; Gastro = gastrointestinal; HCT = hematocrit; Hemato = hematological; HGB = hemoglobin; hr = hour(s); Immuno./Lymphor = immunological/lymphoreticular; JP-4 = jet propellant-4; JP-7 = jet propellant-7; LOAEL = lowest-observable-adverse-effect level; LT50 = time to 50% kill; O-M = Osborne-Mendel; M = male; MCH = mean corpuscular hemoglobin; mo = month(s); NOAEL = no-observable-adverse-effect level; PET = petroleum-derived; Resp = respiratory; SH = shale-derived; S-D = Sprague-Dawley; WBC = white blood cell; wk = week(s).

Figure 2-1. Levels of Significant Exposure to Jet Fuels[a] – Inhalation



[a]All points represent JP-4 exposure unless otherwise noted.

Figure 2-1. Levels of Significant Exposure to Jet Fuels[a] – Inhalation (continued)



[a]All points represent JP-4 exposure unless otherwise noted.

2. HEALTH EFFECTS

A pilot who was exposed to high levels of JP-4 vapor had symptoms of intoxication, but pulmonary function appeared normal upon clinical examination. Lungs were clear to percussion and auscultation, and respirations were normal (Davies 1964). The authors estimated that the exposure levels were between 3,000 and 7,000 ppm, based on the degree of the pilot's neurological impairment.

Intermediate-duration studies in rats revealed normal pulmonary mechanics (lung volume, pressurevolume relationships), pulmonary dynamics (airway resistance, lung compliance), and gas distribution and transfer in anesthetized rats exposed to 1,000 mg/m3 shale-derived JP-4 (Air Force 1985c; Newton et al. 1991). The effects of intermittent exposure to 1,000 or 5,000 mg/m^3 JP-4 were determined in dogs, rats, and mice with up to a 12-month postexposure period (Air Force 1974, 1976, 1984b) indicated that JP-4 did not cause adverse respiratory clinical signs or lung histopathology.

Chronic exposure (12 months) to 1,000 or 5,000 mg/m^3 JP-4 did not cause respiratory tract irritation or pulmonary lesions in rats at the end of the exposure period or 12 months postexposure (Bruner et al. 1993). Differing effects were observed in mice exposed to JP-4 under an identical study design (Bruner et al. 1993). At the end of the 12-month exposure period, mild pulmonary inflammation was seen only in treated females, and hyperplasia of the nasolacrimal duct epithelium was detected only in treated males. However, those effects had disappeared by the end of the 12-month postexposure period.

Cardiovascular Effects. A pilot who was exposed to estimated concentrations of 3,000-7,000 ppm JP-4 did not show any adverse effects on blood pressure or heart sounds (Davies 1964).

Dogs exposed for 90 days to 1,000 mg/m3 JP-4 did not experience cardiac histopathological changes (Air Force 1984b).

Gastrointestinal Effects. Exposure to 5,000 mg/m^3 JP-4 for 8 months caused emesis in male and female dogs (Air Force 1974), but no emesis was seen at 2,500 mg/m^3 JP-4.

2. HEALTH EFFECTS

Hematological Effects. No studies were located regarding hematological effects in humans after inhalation exposure to JP-7.

Accidental exposure of a pilot to a high concentration of JP-4 during a leak in the jet's fuel system did not result in any abnormalities in hematological or clinical chemistry tests during a physical examination performed after an unspecified period of time had passed since the exposure (Davies 1964).

Hematological parameters have been measured on a routine basis during exposure of animals to JP-4 and JP-7 in intermediate- and chronic-duration studies. Such measurements have included red and white blood cell counts, methemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hematocrit, and hemoglobin concentration. Exposure for 90 days to 1,000 mg/m^3 JP-4 caused increased white blood cell counts and increased the mean corpuscular hemoglobin in Fischer 344 rats (Air Force 1984d). In the same study, increased white blood cell counts and decreased hematocrit and hemoglobin concentrations were observed in Osborne-Mendel rats. In contrast, continuous exposure (24 hours/day) of rats to 1,000 mg/m^3 JP-4 vapor for 90 days did not affect white blood cell and red blood cell counts in males or females (Air Force 1980).

Treatment for 12 months, 5 days/week, 6 hours/day with 0, 1,000, or 5,000 mg/m^3 JP-4 revealed a treatment-related decrease in white blood cell count and blood glucose levels in exposed male and female rats at the conclusion of the exposure period (Bruner et al. 1993). Histopathological evaluation of various tissues in the exposed rats did not reveal a definitive cause for the decreases in white blood cells. However, bone marrow cytopenia was reported to be of borderline statistical significance (significance level not specified) in the treated animals. The incidence in males of this finding was 0%, 1%, and 4% for the control, low, and high concentrations, respectively. Incidence in females was 0%, 0%, and 2%, respectively. These findings may have contributed to the decreases in white blood cell count. The LOAEL for this effect was 1,000 mg/m^3.

The results of hematological tests conducted in monkeys and dogs following intermediate-duration (Air Force 1974, 1984c) or chronic-duration exposures (Air Force 1981i) revealed no significant effects that were dose dependent or out of the range of normal biological variation.

2. HEALTH EFFECTS

Intermediate-duration exposure of animals to 2,500 or 5,000 mg/m^3 JP-4 was tested in combination with 12.5 or 25 ppm benzene, respectively (Air Force 1974). Benzene was administered in combination with the jet fuel because benzene is sometimes a contaminant of jet fuels and exposure to benzene is associated with hematological effects. Both air-exposed controls and a positive control group were used for comparison. Three species of animals were exposed to 25 ppm benzene so that the level would not exceed that equivalent to a 6-hour time-weighted average concentration of 10 ppm (Air Force 1974, 1976). For further information on the hematological effects of benzene, refer to the ATSDR toxicological profile for benzene (ATSDR 1991a). In this study, the myeloid/erythroid ratio in rats and the hematocrit, hemoglobin, and red blood cell counts in monkeys were not different from those of the air-exposed control group after 6 months of exposure to JP-4 (Air Force 1974). However, between weeks 12 and 24 of this study, red blood cell fragility was abnormally high in female dogs exposed to 5,000 mg/m^3 JP-4 (Air Force 1974). This effect was transient, since red blood cell fragility was normal at the end of the exposure. No concomitant hemolytic changes occurred in these animals, and the mechanisms and significance, if any, of these findings are unclear. In a 90-day continuous exposure (24 hours/day) of male and female dogs (3 per group) to 500 or 1,000 mg/m^3, there was no increase in red blood cell fragility (Air Force 1980).

Rats chronically exposed to 750 mg/m^3 JP-4 did not exhibit any abnormal hematology, but alkaline phosphatase and blood urea nitrogen were elevated at 150 mg/m^3 (Air Force 1991).

Hepatic Effects. No studies were located regarding hepatic effects in humans after inhalation exposure to JP-4 or JP-7.

Hepatocellular fatty change occurred in the livers of 88-89% of JP-4-exposed C57BL/6 mice (50 females/group) after 90 days of continuous exposure (24 hours/day) to 500 or 1,000 mg/m^3 (Air Force 1984b). The lesions in mice were described as multiple, discrete vacuoles of varying sizes within the hepatocytes. They occurred primarily in the centrilobular region of the liver and were regarded as reversible degenerative processes. The incidence of these lesions immediately after the exposure period was 3/49 for controls, 42/48 (87%) for 500 mg/m^3, and 40145 (88%) for 1,000 mg/m^3 JP-4. A LOAEL of 500 mg/m^3 was identified for fatty changes in the liver. The incidence of sinusoidal hematopoiesis also increased with increasing exposure concentration; however, statistical significance was only achieved in the 1,000-mg/m^3 group. Rats and dogs, also included in that study, did not develop histopathological liver changes. In contrast, intermediate exposure to 500 or 1,000 mg/m^3

2. HEALTH EFFECTS

JP-4 has been shown to increase (Air Force 1980, 1984c, 1984d) male rat liver weight, but doses as high as 1,000 mg/m^3 JP-4 apparently have no effect on female rat liver weight (Air Force 1980, 1984c).

Chronic (12 months), intermittent exposure (5 days/week, 6 hours/day) to 1,000 or 5,000 mg/m^3 JP-4 caused no liver toxicity in rats that were examined at the end of the 12-month exposure period (Bruner et al. 1993). However, in a subset of the exposed animals examined 12 months after the end of the exposure period, the same doses caused non-dose-related decreases in male, but not female, rat liver weight (Bruner et al. 1993). In mice exposed to JP-4 under an identical study design, there was an increase in lymphocytic inflammatory infiltrates in the livers of high-dose female mice, but not males, at the end of the 12-month exposure period (Bruner et al. 1993). However, that effect was no longer evident 12 months after the end of the exposure period.

Chronic exposure of C57BW6 mice to 0 (control), 150, or 750 mg/m^3 JP-7 resulted in an increased incidence of hepatic inflammation in female mice exposed to 750 mg/^{3} after a l-year postexposure period (Air Force 1991). One year after the end of the exposure period, hepatic inflammation was discovered in females from both the 150 and 750 mg/m^3 groups. Hepatic inflammation was not observed in the exposed males. A LOAEL of 150 mg/m^3 was identified for hepatic inflammation in female mice.

Renal Effects. No studies were located regarding renal effects in humans after inhalation exposure to JP-4 or JP-7.

Blood urea nitrogen was elevated, but considered to be within normal limits, in Fischer 344 rats exposed continuously (24 hours/day) for 90 days to 500 or 1,000 mg/m^3 shale- or petroleum-derived JP-4 (Air Force 1980, 1984c). In a subsequent l-year study using an intermittent exposure protocol (6 hours/day, 5 days/week) and a higher concentration of JP-4 (5,000 mg/m^3), blood urea nitrogen was increased only in female rats (Air Force 1981i). Thus, no consistent effect was seen in this parameter with JP-4 exposure.

The effects of intermediate (24 hours/day for 90 days) exposure to 500 or 1,000 mg/m^3 shale-derived JP-4 was determined in rats (Air Force 1984c). Increased kidney weight was observed in male rats at 500 mg/m^3, but no effect on kidney weight was seen in females at either dose of JP-4. Urinalysis

conducted in the male rats revealed a 50-70% decrease in osmolality at termination of exposure and 2 weeks postexposure. Urine pH was not affected. The decreased osmolality was also found when comparing the renal effects in four strains of male rats (Fischer 344, Sprague-Dawley, Wistar, and Osborne-Mendel) after 90 days of continuous exposure (24 hours/day) to 1,000 mg/m^3 JP-4 (Air Force 1984d). In this study, rats from all four strains were killed midway through the exposure period (45 days) and at the end of the exposure period. No effect on urine osmolality was observed at the 45-day interim kill. But after 90 days, urine osmolality.was statistically decreased in all except the Wistar strain of rats. Urine osmolality was decreased in the Wistar rats, but the variability in the treated group prevented statistical significance from being reached. Blood urea nitrogen was transiently elevated in the Fischer 344 and Sprague-Dawley strains at 45 days of exposure. That effect was not detected in any strain at the end of the dosing period. Similarly, blood creatinine levels were elevated after 45 days of exposure in the Fischer 344 and Wistar rats, but that effect was also transient as no differences were found in blood creatinine in any strain after 90 days of exposure. Kidney weight was increased in all strains at the end of the 90-day exposure period. The methods section in the report states that additional animals were allowed to live for 6 or 12 months postexposure, but there is no mention of those animals in any other section of the report. Consequently, it is not known if the renal effects persisted after dosing had concluded.

Absolute kidney weight was increased in male Fischer 344 rats exposed continuously (24 hours/day) for 90 days (Air Force 1980) to 500 or 1,000 mg/kg JP-4 and Sprague-Dawley rats exposed intermittently (6 hours/day, 5 days/week) for 8 months (Air Force 1976) to 5,000 mg/m^3 JP-4. Chronic (12 months) intermittent exposure to 1,000 or 5,000 mg/m^3 JP-4 decreased kidney weight in male and female rats 12 months after the end of the exposure period (Bruner et al. 1993).

Histopathological changes have also been observed following intermediate- and chronic-duration exposure to JP-4 treatment (Air Force 1984b; Bruner et al. 1993) or chronic JP-7 treatment (Air Force 1991). Microscopic examination of the kidneys revealed hyaline droplet formation in renal proximal tubular epithelium in both dose groups; this effect was more severe in high dose animals, indicating a dose-response relationship in male rats exposed to 1,000 or 5,000 mg/m^3 JP-4 (Air Force 1984b). In addition, there were intratubular casts of necrotic debris in the outer renal medulla. Mild progressive kidney neuropathies and medullary mineral deposits were observed in male, but not female, rats exposed to 5,000 mg/m^3 JP-4 for 12 months, 6 hours/day, 5 days/week (Bruner et al. 1993). Twelve months after the conclusion of the exposure period, medullary mineral deposits were still present in the

5,000 mg/m^3 group. Moreover, those changes were also seen in the kidneys of rats exposed to 1,000 mg/m^3 JP-4 (Bruner et al. 1993). Similar effects were observed in rats after 1 year of intermittent exposure to 150 or 750 mg/m^3 JP-7 (Air Force 1991). No nephrotoxicity was observed in mice following chronic (12 months), intermittent exposure to 1,000 or 5,000 mg/m^3 JP-4 (Bruner et al.1993).

The histopathological changes described above are characteristic of a syndrome of nephropathy unique to male rats following intermediate- or chronic-duration inhalation exposure to hydrocarbons (Bruner et al. 1993). These changes have also been found to increase with age (Air Force 1991). This syndrome was not induced in female rats (Air Force 1976, 1984b, 1991; Bruner et al. 1993), mice of either sex (Air Force 1976, 1980, 1984b; Bruner et al. 1993), or dogs of either sex (Air Force 1984b) when exposed to JP-4 or JP-7. This type of nephropathy appears to be unique to male rats and is most likely not relevant to humans (EPA 1991) (see Section 2.4); therefore, this end point was not used for MRL derivation.

Endocrine Effects. Chronic (12 months) intermittent exposure to 5,000 mg/m^3 JP-4 in rats caused an increase in cystic degeneration of the prostate 12 months postexposure (Bruner et al. 1993). No effects were observed in female rats, or in mice of both sexes, under identical exposure conditions (Bruner et al. 1993).

Ocular Effects. Chronic (1 year, 5 days/week) exposure to 750 mg/m^3 did not cause any histopathological changes in the eyes of male or female rats (Air Force 1991).

Body Weight Effects. The effects of intermediate exposure to between 500 and 1,000 mg/m^3 JP-4 on body weight has not been consistent. Intermediate-duration exposure of rats to JP-4 decreased the body weight of male (Air Force 1980, 1984b) and female (Air Force 1980, 1984b, 1984c) rats. However, similar doses and dosing models produced no effect on rat body weight (Air Force 1984d). Additionally, doses of JP-4 as high as 5,000 mg/m^3 did not affect the body weight of dogs (Air Force 1974) or monkeys (Air Force 1974).

Chronic (1 year, 5 days/week, 6 hours/day) exposure to 750 mg/m^3 JP-4 had no effect on rat body weight (Air Force 1991). Similarly, chronic exposure to 1,000 or 5,000 mg/m^3 JP-4 did not adversely affect body weight in rats immediately after a 12-month exposure period (Bruner et al. 1993).

However, 1,000 mglm^3 caused minor body weight reductions (3-4%) in both female and male rats 12 months postexposure (Bruner et al. 1993). This statistically significant decrease in body weight is not considered to be biologically significant. Mice exposed to 1,000 or 5,000 mg/m^3 JP-4 for 1 year did not exhibit adverse body weight effects either at the end of the exposure period or 12 months postexposure (Bruner et al. 1993).

Other Systemic Effects. Histological exammation of rat lymph nodes after the intermediate exposure to 1,000 mg/m^3 JP-4 did not reveal any abnormalities (Air Force 1984b). Chronic exposure to 5,000 mg/m^3 JP-4 in rats increased the incidence of cystic hyperplasia of the mammary glands 12 months after a l-year intermittent exposure period (Bruner et al. 1993).

2.2.1.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological and lymphoreticular effects in humans after inhalation exposure to JP-4 or JP-7. Additionally, no studies were found regarding immunological and lymphoreticular effects in animals after inhalation exposure to JP-7.

Chronic (12 months) intermittent exposure to 1,000 mg/m^3 JP-4 was found to increase spleen weight in female rats at the end of the dosing period (Bruner et al. 1993). However, no effect on spleen weight was observed at the higher dose of 5,000 mg/m^3 or at either dose 12 months after the end of the exposure period.

2.2.1.4 Neurological Effects

No studies were located regarding neurological effects in humans or animals after inhalation exposure to JP-7.

Acute exposure to a high level of JP-4 (3,000-7,000 ppm) from a fuel leak on a routine flight produced a groggy, weak, intoxicated state in the pilot (Davies 1964). Neurological examination revealed that the mild intoxication was accompanied by normal cardiovascular and respiratory function. The pilot had a staggering gait, mild muscular weakness, decreased sensitivity to painful stimuli, slight slurring of speech, and a positive Romberg; these effects were no longer evident 36 hours postexposure.

2. HEALTH EFFECTS

Animals acutely exposed by inhalation to very high concentrations of JP-4 (38,000 mg/m^3) exhibited neurotoxic effects including poor coordination and convulsions (Air Force 1974). Dogs (4 males, 2 females/exposure level), monkeys (1 male, 3 females/exposure level), rats (50 males/exposure level), and mice (40 females/exposure level) were exposed to 0, 2,500, or 5,000 mg/m^3 JP-4, 6 hours/day, 5 days/week for 6 months (rats, mice, and monkeys) or 8 months (dogs) (Air Force 1974). During the initial 3 weeks of exposure, dogs were reported to have decreased activity compared to control animals. When the animals were not sleeping, they were reported to be "quiescent and prostrate" during exposure periods. Monkeys in both JP-4 groups also demonstrated decreased activity, but to a lesser extent than the dogs. Rats and mice did not exhibit neurological signs at either dose of JP-4.

No long-term epidemiological studies were located regarding exposure to JP-4.

No NOAEL values for neurological effects of JP-4 were recorded in Table 2-l or plotted in Figure 2-l. The case study (Davies 1964) has inadequately characterized exposure conditions and the intermediate animal exposure studies lacked presentation of important experimental details.

2.2.1.5 Reproductive Effects

No studies were located regarding reproductive effects in humans after inhalation exposure to JP-4 or JP-7. Additionally, no studies were found regarding reproductive effects in animals after inhalation exposure to JP-7.

Chronic (12 months) exposure to 1,000 or 5,000 mg/m^3 of JP-4 did not adversely affect the testis in rats, but did cause testicular atrophy in mice 12 months after the end of exposure period (Bruner et al. 1993).

2.2.1.6 Developmental Effects

No studies were located regarding developmental effects in humans or animals after inhalation exposure to JP-4 or JP-7.

2.2.1.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals after *in vivo* inhalation exposure to JP-4 or JP-7. Genotoxicity studies are discussed in Section 2.4.

2.2.1.8 Cancer

No studies were located regarding carcinogenic effects in humans after inhalation exposure to JP-4 or JP-7.

Long-term animal studies were conducted to investigate the potential of JP-4 or JP-7 to induce cancer in laboratory animals. Groups of 50 male Sprague-Dawley rats and 40 female CF-1 mice were exposed to JP-4 intermittently (6 hours/day, 5 days/week) for 8 months. Interim sacrifices were performed immediately after exposure and at 12 months postexposure (Air Force 1976). No increase in the incidence of tumors was seen in any group following gross and histopathologic examination of tissues from either rats or mice.

Fischer-344 rats exposed chronically to JP-4 for 12 months at 5,000 mg/m^3 had an increased incidence of interstitial cell tumors in the testis 12 months after the termination of the exposure period (Bruner et al. 1993). Under an identical exposure regimen, no effect on the incidence of neoplastic lesions was seen in mice (Bruner et al. 1993). A l-year JP-7 exposure produced no toxicologically significant treatment-related neoplastic lesions in mice or rats except for a small increase in the incidence of C-cell adenomas and kidney adenomas in male rats exposed to 750 mg/m^3 of JP-7 (Air Force 1991).

The exposure period in the above carcinogenicity studies was only 1 year compared to the 2 years (lifetime) of exposure normally included in standard carcinogenicity assays. This less-than-lifetime exposure was chosen because the authors believed it is more typical of military occupational exposure to jet fuels. Nevertheless, the results from the above studies suggest that jet fuels JP-4 and JP-7 are not carcinogenic to humans.

2. HEALTH EFFECTS

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding death in humans after oral exposure to JP-4 or JP-7, or in animals after oral exposure to JP-7.

The acute oral administration of 5,000 mg/kg (Clark et al. 1989) or 8,000 mg/kg (Air Force 1974) shale-derived JP-4 to rats did not result in treatment-related mortality. Two of three mice died after administration of 500 mg/kg JP-4; one of three mice died after administration of 1,000 mg/kg (Air Force 1974). However, no histopathology was performed on these animals and the numbers of mice dosed in this study were so small that the reported deaths are not necessarily relevant.

2.2.2.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, or body weight effects in humans or animals after oral exposure to JP-4 or JP-7.

No studies were located regarding the following health effects in humans or animals after oral exposure to JP-4 or JP-7:

2.2.2.3 Immunological and Lymphoreticular Effects

2.2.2.4 Neurological Effects

2.2.2.5 Reproductive Effects

2.2.2.6 Developmental Effects

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans after oral exposure to JP-4 or JP-7, or in animals after oral exposure to JP-7.

Two dominant lethal studies were found in the literature where mice or rats were orally exposed to JP-4. Ten random-bred, male CD-l mice received the compound in their food for 5 consecutive days at concentrations of 7.6, 22.8, and 68.4 mg/kg (0.01, 0.03, and 0.09 mL/kg, respectively). Two days after the last treatment, each male was caged with two untreated virgin females for 7 days. At the end of 1 week, the females were replaced with two new untreated females; this process was repeated for 7 weeks. The females were killed 14 days after the midweek of mating, and their uteri were examined for live, dead, and total implantation. When the negative controls were compared to the treated females, no significant differences were noted for dominant lethal effects. This finding suggests that JP-4 was not clastogenic in the germinal cells of male mice (Air Force 1978a). However, the results cannot be considered conclusive because of the small number of pregnant females used in the study. The interpretation of the results is further confounded by the fact that the highest dose used in the study was probably too low to cause significant cellular toxicity.

Ten random-bred male rats were exposed to JP-4 by gavage for 5 consecutive days (Air Force 1978a). The concentrations tested were 68.4, 228, and 684 mg/kg (0.09, 0.3, and 0.9 mL/kg, respectively). The mating protocol was the same as that used in the mouse dominant lethal experiment. The administration of JP-4 did not decrease the average number of implantations per litter except after the fourth week of mating, when a transient decrease of 31-50% was noted for the low through high doses of JP-4, respectively. Individually significant reductions in the number of implants per litter were detected only for the 0.3 mL/kg group at that time. There was no increase in the average number of resorptions per litter or in the average number of late fetal deaths. Thus, the effects appeared to be confined to the pre-implantation phase. Except for the effects noted for week 4, indices of reproductive function were comparable to controls. Since there were no significant dominant lethal effects corresponding to the pre-implantation effects, the researchers considered the results to be negative (Air Force 1978a). As in the mouse study, the sample size of pregnant female rats per group was small, which renders the study inconclusive.

Other genotoxicity studies are discussed in Section 2.4.

2.2.2.8 Cancer

No studies were located regarding cancer in humans or animals after oral exposure to JP-4 or JP-7.

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding death in humans after dermal exposure to JP-4 or JP-7, or in animals after dermal exposure to JP-7.

Acute (24 hours) dermal application of 2,000 mg/kg shale-derived JP-4 (Clark et al. 1989; Dennis 1982a) or petroleum-derived JP-4 (Clark et al. 1989) to rabbits did not result in mortality after a 24-hour or 14-day time period, respectively. No rabbits died after dermal application of 0.5 mL undiluted JP-7 to the skin (Air Force 1984a).

Application of shale-derived JP-4 to the skin of C3H mice on a chronic basis resulted in a greater survival rate compared to those treated with petroleum-derived JP-4 (Clark et al. 1988). At week 52 of a 105-week study in which animals were treated with shale-derived JP-4, the survival rate was ≈90% compared to ≈72% in animals treated with petroleum-derived JP-4. By the end of the 2-year study, both groups had similar survival rates (≈15%). However, petroleum-derived JP-4 appeared to have greater toxicity than shale-derived JP-4 by virtue of the higher mortality that occurred in the first year of exposure, and both groups had a lower survival rate than controls (≈50%). More information regarding the differences between shale- and petroleum-derived jet fuels is provided in the introduction to Chapter 4. Both groups appeared to have a higher mortality than did control animals, although no statistics were shown. Mortality resulted from inflammatory lesions at the site of the test material application and subsequent septicemia. The mortality data from those studies were not included in Table 2-2 because of the lack of statistical testing.

2.2.3.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, or musculoskeletal effects in humans or animals after dermal exposure to JP-4 or JP-7. The highest NOAEL values and all reliable LOAEL values for systemic effects for each study and end point are recorded in Table 2-2.

Hepatic Effects. No studies were located regarding hepatic effects in humans after dermal exposure to JP-4 or JP-7 or in animals after dermal exposure to JP-7.

Application of 2,000 mg/kg shale-derived JP-4 to the skin of rabbits for 24 hours did not result in hepatic lesions after a 14-day postexposure period (Dennis 1982a).

Renal Effects. No studies were located regarding renal effects in humans after dermal exposure to JP-4 or JP-7 or in animals after dermal exposure to JP-7.

Dermal application of 2,000 mg/kg shale-derived JP-4 in five male and five female rabbits for 24 hours did not result in pathological renal effects related to the test material after a 14-day postexposure period (Dennis 1982a). In one animal, a pathological lesion was noted on one kidney but was not believed to be related to the test material.

Dermal Effects. No studies were located regarding dermal effects in humans after dermal exposure to JP-4 or JP-7.

Experiments in rabbits show that acute exposure to JP-4 or JP-7 is irritating to the skin. Application of 0.5 mL undiluted JP-4 (both shale- and petroleum-derived) produced severe irritation that was characterized by edema and erythema 24 hours post-application (Air Force 1984a; Clark et al. 1989; Dennis 1982b; Walter 1982c), whereas the application of the same amount of JP-7 was shown to produce slightly greater irritation that persisted for a longer period of time (Air Force 1984a). Chronic application of 25 mg undiluted petroleum- or shale-derived (from hydrotreated crude shale) JP-4 to the skin of mice resulted in initial dermal irritation that progressed to necrosis and visible separation and sloughing of skin (Clark et al. 1988).

TABLE 2-2. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Dermal

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL		Reference Chemical Form
				Less Serious	Serious	
ACUTE EXPOSURE						
Systemic						
Rabbit (New Zealand)	24 hr	Dermal		0.5 mL	(no skin irritation at 24 hours but moderate erythema at 72 hours)	Air Force 1984a JP-4 (PET)
Rabbit (New Zealand)	24 hr	Dermal		0.5 mL	(severe primary dermal irritation; moderate erythema, mild edema at 72 hours)	Air Force 1984a JP-4 (SH)
Rabbit (New Zealand)	24 hr	Dermal		0.5 mL	(severe primary irritation, slight edema, moderate erythema at 72 hours)	Air Force 1984a JP-7
Rabbit (New Zealand)	once	Ocular	0.1 mL			Air Force 1984a JP-4 (PET)
Rabbit (New Zealand)	once	Ocular	0.1 mL			Air Force 1984a JP-4 (SH)
Rabbit (New Zealand)	24 hr	Hepatic	2000 mg			Dennis 1982a JP-4 (SH)
		Renal	2000 mg			
		Dermal		2000 mg	(mild inflammation discoloration of skin)	
Rabbit (New Zealand)	24 hr	Dermal		0.5 mL	(severe dermal irritation)	Dennis 1982b JP-4 (SH)

TABLE 2-2. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL Less Serious		LOAEL Serious		Reference Chemical Form
Gn pig (Hartley)	4 x	Dermal	0.1 mL					Air Force 1984a JP-4 (PET)
Gn pig (Hartley)	4 x	Dermal		0.1 mL	(weak to mild dermal sensitization potential)			Air Force 1984a JP-7
Gn pig (Hartley)	2 d	Dermal		0.1 mL	(mild to moderate dermal sensitization)			Air Force 1984a JP-4 (SH)
Gn pig (HLA Hartley)	3 wk 1 x/wk 6 hr	Dermal	0.25 M mL					Clark et al. 1989 JP-4 (PET)
Gn pig (HLA Hartley)	3 wk 1 x/wk 6 hr	Dermal	0.25 M mL					Clark et al. 1989 JP-4 (SH)
INTERMEDIATE EXPOSURE								
Systemic								
Gn pig (Hartley)	3 wks 1 x/wk 6 hr/day	Dermal	0.25 M mL					Walter 1982c JP-4 (PET)
CHRONIC EXPOSURE								
Cancer								
Mouse (C3H/Hen)	105 wk 3 x/wk					25 mg	(24 and 17% increased incidence of squamous cell carcinoma and fibrosarcoma, respectively)	Clark et al. 1988 JP-4 (SH)

TABLE 2-2. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Dermal (continued)

Species/ (Strain)	Exposure/ Duration/ Frequency/ (Specific Route)	System	NOAEL	LOAEL			Reference Chemical Form
				Less Serious	Serious		
Mouse (C3H/Hen)	105 wk 3 x/wk				25 mg	(increased incidence of squamous cell carcinoma and fibrosarcoma)	Clark et al. 1988 JP-4 (PET)

d = day(s); Derm = dermal; Gn Pig = guinea pig; hr = hour(s); JP-4 = jet propellant-4; JP-7 = jet propellant-7; LOAEL = lowest-observable-adverse-effect level; M = male; NOAEL = no-observable-adverse-effect level; NS = sex not specified; PET = petroleum-derived; SH = shale-derived; wk = week(s); x = times.

2. HEALTH EFFECTS

Ocular Effects. No studies were located regarding ocular effects in humans after dermal exposure to JP-4 or JP-7.

There was no evidence of primary ocular irritation after application of undiluted shale-derived JP-4, undiluted petroleum-derived JP-4, or JP-7 to the eyes of rabbits (Air Force 1984a; Clark et al. 1989; Dennis 1982c; Walter 1982a). Some studies (Walter 1982a) noted that when shale-derived JP-4 was applied and not rinsed from the rabbits' eyes, minimal irritation (0.3 out of a maximum 2.0 score) resulted 24 hours after instillation of test material. The irritation cleared by the 7th day postexposure.

2.2.3.3 Immunological and Lymphoreticular Effects

No information is available on the immunological effects of JP-4 or JP-7 in humans or animals following dermal exposure.

JP-4 (shale-derived or petroleum-derived) did not cause dermal sensitization in guinea pigs when applied to the skin in a 50% dilution in mineral oil (Clark et al. 1989; Walter 1982c). However, JP-7 and shale-derived JP-4 have sensitization potential (Air Force 1984a). Data regarding the immunological effects of JP-4 are limited to the dermal sensitization tests conducted in guinea pigs (Air Force 1984a; Clark et al. 1989; Walter 1982c). In these studies petroleum-derived JP-4 was not found to be a dermal sensitizer. However, JP-7 and shale-derived JP-4 have weak-to-mild and mildto-moderate sensitization potential, respectively (Air Force 1984a).

No studies were located regarding the following health effects in humans or animals after dermal exposure to JP-4 or JP-7:

2.2.3.4 Neurological Effects

2.2.3.5 Reproductive Effects

2.2.3.6 Developmental 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 carcinogenic effects after dermal exposure to JP-4 or JP-7 in humans, or in animals after dermal exposure to JP-7.

The effects of intermittent (3 times/week) dermal administration of 25 mg of shale- or petroleumderived JP-4 to the skin of mice for 105 weeks on the incidence of neoplasms was studied (Clark et al. 1988). Squamous cell carcinoma and fibrosarcoma formation was increased in the mice exposed to shale-derived (50% incidence) and petroleum-derived JP-4 (26% incidence) compared to the appropriate control groups (2% and 0%, respectively). In general, shale-derived JP-4 (derived from hydrotreated crude shale oil) had greater irritant and carcinogenic potency than did petroleum-derived JP-4. The positive control substances, crude shale-derived and petroleum-derived oils (not hydrotreated), had skin cancer incidences of 54% and 84%, respectively. Other histopathological diagnoses were judged by the authors to be secondary to the long-term irritation at the test site. The most noteworthy of these diagnoses was reactive hyperplasia of the spleen and bone marrow that probably resulted from septicemia that developed from the attendant inflammation, necrosis, and infection at the application site. The incidence of these findings was not reported.

2.3 TOXICOKINETICS

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

No studies were located that examined the absorption of JP-4 or JP-7 in humans or animals after inhalation exposure. However, indirect evidence from the case report of a pilot exposed to a JP-4 fuel leak indicates that JP-4 can be absorbed following inhalation exposure in humans (Davies 1964). Animals exposed to JP-4 on an acute, intermediate, or chronic basis, or exposed chronically to JP-7,

also exhibited effects that provide evidence for inhalation absorption in animals (Air Force 1974, 1976, 1980, 1983, 1984b, 1985b, 1991; Bruner et al. 1993).

2.3.1.2 Oral Exposure

There is no quantitative information on the absorption of JP-4 or JP-7 following oral exposure in humans or animals.

2.3.1.3 Dermal Exposure

There is no quantitative information on the absorption of JP-4 or JP-7 following dermal exposure in humans or animals. Animal studies have shown that both JP-4 and JP-7 are irritating to the skin (Air Force 1984b; Clark et al. 1988, 1989; Dennis 1982b; Walter 1982a, 1982c), and long-term studies have demonstrated the carcinogenic potential of JP-4 at the site of application (Clark et al. 1988). However, no effects have been reported in these studies in organs or tissues distant from the site of application of the test material.

2.3.2 Distribution

There is no quantitative information on the distribution of JP-4 or JP-7 following inhalation, oral, or dermal exposure in humans or animals. However, liver effects after treatment of mice with JP-4 suggest distribution to that organ (Air Force 1984b; Bruner et al. 1991).

2.3.3 Metabolism

There is no quantitative information on the metabolism of JP-4 or JP-7 following inhalation, oral, or dermal exposure in humans or animals.

2.3.4 Excretion

There is no quantitative information on the excretion of JP-4 or JP-7 following inhalation, oral, or dermal exposure in humans or animals.

2.3.5 Mechanisms of Action

It is apparent from animal studies described in the earlier sections that exposure to JP-4 or JP-7 causes toxicity, but data have been descriptive (e.g., decreased liver weight) instead of mechanistic (e.g., slows nerve conduction). Additionally, the absorption and distribution of the jet fuels is not understood. Thus, insufficient data exist for postulating a mechanism of action. Moreover, since both fuels are complex mixtures, it seems likely that elucidating a mechanism of action would be difficult.

2.4 RELEVANCE TO PUBLIC HEALTH

Exposure to JP-4 and JP-7 may occur via the inhalation, oral, or dermal routes, but exposure by inhalation is most likely because of the high volatility of many of the jet fuel components. Military personnel and those involved in the manufacture of the jet fuels are at the greatest risk for exposure because the fuels are produced only for military use. Thus, apart from those individuals involved in the manufacturing process, persons living or working near or on a military base would constitute the greatest population at risk for JP-4 and JP-7 exposure. Additionally, military personnel stationed on aircraft carriers or submarines would also be at increased risk.

JP-4 and JP-7 are also found in waste sites, so exposure of the general public to the fuels in those areas is possible, but not likely. Moreover, because the jet fuels are complex mixtures of components with differing volatilities, solubilities, and biodegradation potentials, it is probable that people will be exposed to only a subset of the components from the original mixture. However, because of the large number of components in JP-4 and JP-7, it is impractical, if not impossible, to predict what components of the original mixture will be present at a waste site. Therefore, the inhalation exposure MRLs described below are based on the concentration of the original complex mixture. Additionally, the concentrations of JP-4 or JP-7 reported in the studies used to derive the MRLs are based on the concentration of total hydrocarbons present in the vapors after the original mixture was heated to 50 °C.

2. HEALTH EFFECTS

Minimal Risk Levels for Jet Fuels JP-4 and JP-7.

Inhalation MRLs.

Only one controlled acute-duration inhalation exposure study for JP-4 was found (Clark et al. 1989), and it was limited by a low number of animals per group. No acute-duration exposure studies were located for JP-7. Thus, no acute inhalation MRLs'"were calculated for JP-4 and JP-7. However, sufficient information exists for the calculation of intermediate and chronic exposure MRLs for JP-4 and JP-7, respectively. The MRLs are based on hepatic toxicity because the liver appears to be a target organ for JP-4- and JP-7-related toxicity (Air Force 1974, 1984b, 1984c, 1991; Bruner et al. 1993).

- An MRL of 9 mg/m^3 has been derived for intermediate-duration inhalation exposure (15-364 days) to JP-4.

The intermediate inhalation exposure MRL of 9 mg/m^3 was based on an increase in hepatic toxicity observed in mice at 500 mg/m^3 (Air Force 1984b). In that study, female C57BL/6 mice (150/group) were exposed to 0, 500, or 1,000 mg/m^3 of petroleum-derived JP-4 continuously for 90 days. The variation in the day-to-day concentration of JP-4 was reported to be less that 1%. Hepatocellular fatty changes were seen in both dose groups. The changes were described as multiple, discrete vacuoles of varying sizes within the cytoplasm of hepatocytes, especially in the centrilobular region of the liver. The incidence of the hepatic fatty degenerative changes was 6%, 15%, and 25% in the control, 500 mg/m^3, and 1,000 mg/m^3 groups, respectively. Renal tubular dilatation was also increased at 500 mg/m^3, but not at 1,000 mg/m^3. This was thought to be an incidental finding resulting from mild glomerulonephritis, common in aging mice. Inflammation and lymphocytic inflammatory infiltrate was found in females exposed to 500 mg/m^3 and was frequently accompanied by hyaline degeneration. These findings are common in older C57BW6 mice, and because the effects were not dose-dependent, they were not considered to be treatment-related. Based on the increased incidence of hepatic toxicity at 500 mg/m^3 JP-4 and an uncertainty factor of 300 (10 for the use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) and a human equivalent dose conversion factor of 5.7, an MRL of 9 mg/m^3 was calculated. However, this MRL may be overly conservative for intermittent exposure and should probably used for screening purposes.

2. HEALTH EFFECTS

- An MRL of 0.3 mg/m^3 has been derived for chronic-duration inhalation exposure (365 days or more) to JP-7.

The chronic inhalation exposure MRL of 0.3 mg/m^3 was based on an increase in hepatic toxicity observed in rats at 150 mg/m^3 (Air Force 1991). The average variability of chamber JP-7 concentrations during the experiment was 5%. In that study, the tumorigenic effect of JP-7 was studied in a year-long exposure (6 hours/day, 5 days/week) of Fischer 344 rats (100/sex/group) to 0 (air), 150, or 750 mg/m^3 JP-7. Following the exposure period, 10 animals/sex/group were killed and examined while the remaining animals were killed after a l-year postexposure period. Liver, kidney, and spleen weights were determined at sacrifice, and portal blood samples were taken for clinical chemistry and hematologic determinations. Additionally, gross and microscopic histopathological examination of the collected tissues was performed. One year after the end of the exposure period, hepatic inflammation was discovered in females from both the 150 and 750 mg/m^3 groups. Hepatic inflammation was not observed in the exposed males. A LOAEL of 150 mg/m^3 was identified for hepatic inflammation in female mice. Exposure to JP-7 did not result in any change in mortality when exposed rats were compared to controls. Based on the increased incidence of hepatic toxicity at 150 mg/m^3 JP-7, an uncertainty factor of 300 (10 for the use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability), a human equivalency dose factor of 3.3 (0.36 m3/day/0.38 kg x 70 kg/20 m^3/day), and a continuous exposure adjustment of 0.18 (6 hours/24 hours x 5 days/7 days), an MRL of 0.3 mg/m^3 was calculated.

Oral MRLs.

No MRLs for acute-, intermediate-, or chronic-duration exposure to JP-4 or JP-7 were calculated because insufficient toxicological data exist for those fuels. The data on the potential toxicity of orally administered JP-4 were limited to acute exposure studies (Air Force 1974; Clark et al. 1989). No studies designed to determine the toxic effects of oral exposure to JP-7 were found.

No acute-, intermediate-, or chronic-duration dermal MRLs were derived for JP-4 or JP-7 because of the lack of an appropriate methodology for the development of dermal MRLs.

2. HEALTH EFFECTS

Death. No studies were located that reported human deaths resulting from JP-4 or JP-7 exposure by any route. The LD_{50} has not been determined in laboratory animals. However, data indicate that the lethal inhalation concentration for JP-4 in monkeys, dogs, rats, and mice exceeds 5,000 mg/m^3 (Air Force 1974, 1976, 1980, 1984b, 1985b; Clark et al. 1989; Newton et al. 1991). Inhalation exposure of rats or mice to up to 750 mg/m^3 JP-7 did not result in any deaths (Air Force 1982f, 1991). Oral administration of up to 8,000 mg/kg JP-4 in rats was not lethal. Some mortality was found in mice given 500 or 1,000 mg/kg JP-4 (Air Force 1974), but the small number of animals used in the study makes interpretation of the results difficult. No studies were located that reported death from oral JP-7 exposure. Death did not occur after acute dermal application of up to 2,000 mg (Dennis 1982a) or chronic application of 25 mg of JP-4 to the skin of animals (Clark et al 1988). In rabbits, the acute-duration dermal exposure to 0.5 mL JP-7 did not result in any deaths (Air Force 1984a). Although environmental data are limited, based on the high doses of JP-4 and JP-7 that are necessary to cause death, it is unlikely that JP-4 or JP-7 levels near hazardous waste sites are sufficient to cause death in exposed populations.

Systemic Effects.

Respiratory Effects. It is uncertain whether exposure to JP-4 causes respiratory effects in humans. In fact, there are no reports of chronic human occupational exposure to JP-4. No respiratory effects were reported after an acute accidental inhalation exposure to high levels of JP-4 (Davies 1964). In animal studies, inhalation exposure to up to 5,000 mg/m^3 JP-4 (Air Force 1974, 1976, 1984b; Bruner et al. 1993) or up to 750 mg/m^3 JP-7 (Air Force 1982g, 1983e) did not result in any reported alterations in respiratory clinical signs. Pulmonary mechanics and function did not change after intermediate-duration inhalation exposure to 1,000 mg/m^3 JP-4 (Air Force 1985c; Newton et al. 1991). The data regarding respiratory effects of JP-4 and JP-7 are insufficient to draw conclusions about the effects that may be seen in the workplace or near waste disposal sites.

Hematological Effects. No information is available on the hematological effects of JP-4 or JP-7 exposure in humans. In animals, routine hematological testing revealed occasional differences in various hematological tests; however, the values were within the normal range of biological variation (Air Force 1974, 1980, 1982f, 1984b, 1985b, 1991; Bruner et al. 1993). Additionally, the hematological effects were not dose-dependent or found in both sexes. Thus, they were not regarded as physiologically significant.

2. HEALTH EFFECTS

Hepatic Effects The effect of JP-4 or JP-7 on the human liver is unknown. Female mice exposed to 500 mg/m^3 JP-4 continuously for 90 days had degenerative fatty changes in liver cells (Air Force 1984b) that were likely reversible (Bruner et al. 1993). The fatty changes were not seen in a 12-month intermittent (6 hours/day, 5 days/week) exposure. Inflammation of the liver occurred in female mice exposed intermittently for 12 months to 150 mg/m^3 JP-7. In general, there were no changes in blood chemistry that would indicate abnormal liver function in animals exposed by inhalation. It is unknown if liver effects would occur in humans exposed to JP-4 or JP-7 at hazardous waste sites. There are no data regarding liver effects after oral or dermal administration of JP-4 or JP-7 in animals.

Renal Effects. There are no data regarding the effect of JP-4 or JP-7 on renal function in humans. In animal experiments, male rat nephropathy is a common finding after inhalation exposure to either JP-4 or JP-7 (Air Force 1976, 1984b, 1991; Bruner et al. 1993). However, the evidence is overwhelming that the male rat nephropathy is unique to male rats, and is related to the binding of xenobiotic compounds to $\alpha_{2\mu}$-globulin, a low molecular weight serum protein synthesized in the liver of male rats. Subsequent accumulation of this complex is thought to trigger pathological responses within the kidney (Bruner et al. 1993). This syndrome is characterized by the following progression of lesions (Alden 1986; Bruner 1984; Bruner et al. 1993; EPA 1991; Short et al. 1987):

- Excessive accumulation of hyaline droplets in the P2 segment of the proximal tubule region of the kidney. This accumulation is evident after 1 or 2 days of exposure and is reversible within 3 days to 2 weeks after termination of exposure. The hyaline droplets are associated with the protein $\alpha_{2\mu}$-globulin.

- .Evidence of single cell necrosis in the P2 segment epithelium and exfoliation of these degenerated cells and cell fragments filled with crystalloid phagolysosomes into the tubule lumen after 5 days of continuous exposure. This can also be seen with longer exposure.

- Sustained regenerative tubule cell proliferation with continued exposure. After the initial cytotoxic injury, evidence of regeneration of the tubular epithelium can be seen as an increase in cell proliferation within the P2 segment in response to cell damage and loss. The cell proliferation can be seen following 3 weeks of continuous exposure and is also

obvious after 48 weeks of exposure. Tubular dilation and tubular epithelial necrosis are often associated with the regenerative changes.

- Accumulation of granular casts, formed from the cellular debris and subsequent tubule dilation, is seen at the junction of the P3 segment and the thin loop of Henle. This can be seen as early as 2-3 weeks after exposure begins. These casts are not always seen in male rat nephropathy and may reflect a more severe response.

- Linear mineralization of the renal papillar tubules with hyperplasia of the renal pelvic urothelium. These lesions are thought to be the result of mineralized remnants of debris from disintegrating granular casts that lodge in the prebend segments of Henle's loop.

Several mechanisms have been proposed to account for this unique sequence of events in male rats following exposure to certain hydrocarbons, including the jet fuels. Currently, the most likely mechanism is that a metabolite of jet fuel or one of its constituents (especially isoparaffinic hydrocarbons) binds to $\alpha_{2\mu}$globulin. The complex is then reabsorbed in the proximal tubule and phagocytized by lysosomes within the tubule cells. This protein complex is difficult to catabolize and accumulates in the lysosomes. Eventually, the lysosomes burst, and digestive enzymes contained within the lysosomes induce cytotoxicity and cell death, which in turn leads to the accumulation of casts and the hyperplastic events described above (Swenberg et al. 1989).

The available data indicate that the nephrotoxic syndrome is induced by hydrocarbons such as jet fuels and is unique to male rats. The hepatic synthesis of $\alpha_{2\mu}$-globulin protein is under androgenic control and is found at concentrations 100-300 times higher in male rat urine than in female rat urine (Shapiro and Sachchidananda 1982; Van Doren et al. 1983). Human urine contains only 1% of the total concentration of this protein present in mature male rat urine (Olson et al. 1990). $\alpha_{2\mu}$-Globulin and associated hyaline droplet accumulation and the associated constellation of nephrotoxic effects that are observed in male rats have not been observed in female rats, or in mice or monkeys of either sex (Air Force 1976, 1980, 1984b, 1991; Brnner et al. 1993). In addition, this syndrome could not be induced in male NCI-Black-Reiter rats, an inbred strain of rats that does not synthesize $\alpha_{2\mu}$-globulin (Dietrich and Swenberg 1991). In light of this evidence, EPA's Risk Assessment Forum in its document entitled *Alpha-$_{2\mu}$p-Globulin: Association with Chemically-Induced Renal Toxicity and Neoplasia in the Male Rat* (EPA 1991), made the following conclusions:

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> "If a compound induces $\alpha_{2\mu}$g accumulation in hyaline droplets, the associated nephropathy in male rats is not used as an endpoint to determine noncancer (systemic) effects potentially occurring in humans. Likewise, quantitative estimates of noncancer risk (e.g., reference doses and margin-of-exposure determinations) are based on other endpoints wherever possible."
>
> "...If the sequence of lesions characteristic-of the $\alpha_{2\mu}$g syndrome are present, the associated nephropathy in the male rat does not contribute to determinations of noncarcinogenic hazard of risk."

Thus, it does not appear that the nephrotoxicity observed in male rats after exposure to JP-4 or JP-7 is relevant to humans exposed to JP-4 or JP-7 in the workplace or at hazardous waste sites.

Dermal Effects. There is no information regarding the dermal effects of JP-4 or JP-7 in humans after acute, intermediate, or chronic exposure to JP-4 or JP-7. Experiments in rabbits show that acute application of JP-4 or JP-7 is irritating to the skin. Application of 0.5 mL undiluted JP-4 (both shaleand petroleum-derived) produced severe irritation that was characterized by edema and erythema 24 hours post-application (Air Force 1984a; Clark et al. 1989; Dennis 1982b; Walter 1982c), whereas the application of the same amount of JP-7 was shown to produce slightly greater irritation that persisted for a longer period of time (Air Force 1984a). Skin sensitization assays in guinea pigs have shown that petroleum-derived JP-4 is not a dermal sensitizer (Clark et al. 1989; Walter 1982c). However, JP-7 and shale-derived JP-4 appear to have weak-to-mild and mild-to-moderate sensitization potential, respectively (Air Force 1984a).

Ocular Effects. There is no information regarding the ocular effects of JP-4 or JP-7 in humans after acute, intermediate, or chronic exposure to JP-4 or JP-7. Petroleum-derived JP-4, shale-derived JP-4, and JP-7 caused no irritation when applied to the eyes of rabbits (Air Force 1984a; Clark et al. 1989; Dennis 1982c; Walter 1982a).

Body Weight Effects. Decreases in body weight were observed in some, but not all, rats exposed to JP-4 in intermediate- or chronic-duration experiments (Air Force 1980, 1981i, 1985b; Bruner et al. 1993). The decrease in weight gain was found to occur primarily in male rats and may be related to altered protein metabolism in male rats, which was related to the synthesis, excretion, and conservation

of $\alpha 2\mu$,-globulin by the kidney (Bruner et al. 1993). The significance of body weight depression for humans cannot be determined from these findings.

Immunological and Lymphoreticular Effects. Data regarding the immunological effects of JP-4 are limited to the dermal sensitization tests conducted in guinea pigs (Air Force 1984a; Clark et al. 1989; Walter 1982c). In these studies petroleum-derived JP-4 was not found to be a dermal sensitizer. However, JP-7 and shale-derived JP-4 have weak-to-mild and mild-to-moderate sensitization potential, respectively (Air Force 1984a). No studies were located regarding the immunological effects in humans after inhalation, oral, or dermal exposure to JP-7. It is not possible to determine the likelihood of immunological effects occurring in humans because of the paucity of data.

Neurological Effects. The only information found regarding human exposure to JP-4 is a case study in which a pilot was accidentally exposed to a very high level of the jet fuel from a fuel leak (Davies 1964). The exposure concentration was estimated to be approximately 3,000-7,000 ppm. In this case report, the overwhelming finding was neurological impairment, specifically described as "intoxication." Other cardiovascular and respiratory functions appeared normal on physical exam. Therefore, it is likely that under very high exposure conditions, the nervous system is the target organ for JP-4 toxicity. Supportive evidence is found in an acute exposure of rats (number unspecified) to a very high concentration of JP-4 (38,000 mg/m^3) that resulted in poor coordination and convulsions (Air Force 1974). Those studies are both flawed by poor characterization of exposure concentrations. No studies were located regarding neurological effects in animals or humans after oral or dermal exposure to JP-4. There is no information regarding the neurological effect of JP-7 exposure in humans or animals after inhalation, oral, or dermal exposure.

Reproductive Effects. No studies were located regarding reproductive effects in humans or animals after inhalation, oral, or dermal exposure to JP-4 or JP-7. Since no information is available, the likelihood of reproductive effects occurring in humans cannot be determined.

Developmental Effects. No studies were located regarding developmental effects in humans or animals after inhalation, oral, or dermal exposure to JP-4 or JP-7. Since no information is available, the likelihood of developmental effects occurring in humans cannot be determined.

2. HEALTH EFFECTS

Genotoxic Effects. No studies involving human exposure to jet fuels were located, and only two animal in viva studies were found. Male mice and rats were exposed to JP-4 and then allowed to mate with unexposed females in dominant lethal experiments. Statistically significant dominant lethal effects were not observed for either mice or rats (Air Force 1978a). However, because of the small sample size of pregnant females, the results cannot be considered conclusive. Refer to Table 2-3 for a further summary of these results.

Most of the genotoxicity data concerning jet fuels comes from *in vitro* studies. Human diploid WI-38 cells (cells derived from embryonic lung) were treated with JP-4 and examined for unscheduled deoxyribonucleic acid (DNA) synthesis (Air Force 1978a). Unscheduled DNA synthesis (UDS) is a repair process that occurs when DNA has been damaged. Therefore, UDS activity is an indirect measurement of DNA damage. The cells were treated with 0.1, 0.5, 1.0, and 5.0 µL/mL (in water) in both activation and nonactivation systems. A dose-dependent increase in UDS activity was observed, indicating that JP-4 can produce repairable damage in the DNA of human WI-38 cells. The cells that were cultured in the presence of metabolic activators exhibited greater UDS activity suggesting that toxic metabolites may be involved. The remaining *in vitro* investigations were negative for chromosome aberrations in Chinese hamster ovary cells (EPA 1982a, 1982b; Galloway 1982a, 1982b), gene mutations in mouse L5178Y lymphoma cells (Air Force 1978a; Cifone 1982a, 1982b; EPA 1982a, 1982b), and gene mutations in *Saccharomyces cerevisiae* (Air Force 1978a) and *Salmonella typhimurium* (Air Force 1978a; EPA 1982a, 1982b; Jagannath 1982; Rabenold 1982). Refer to Table 2-4 for a further summary of these results. One of the series of studies compared the effects of two types of JP-4: shale-derived JP-4 (Cifone 1982b; EPA 1982b; Galloway 1982b; Rabenold 1982) and petroleum-derived JP-4 (Cifone 1982a; EPA 1982a; Galloway 1982a; Jagannath 1982). The difference in origin did not produce a difference in effect; the results were negative in all tests for both types of JP-4.

The only positive response to JP-4 was observed in human WI-38 cells tested for UDS; but the nature of the DNA damage was not necessarily mutagenic (Air Force 1978a). The negative data for gene mutations and chromosome aberrations suggest that JP-4 is not a mutagenic or clastogenic mixture. The negative results observed in the dominant lethal experiments and the micronuclei study may not be reliable because of low sample size and poor experimental protocol. Results from Ames testing indicated that JP-4 was not mutagenic. Additionally, the solubility and volatility of hydrocarbon mixtures such as JP-4 or JP-7 is a confounding factor in experiments involving exposure of cultured

TABLE 2-3. Genotoxicity of JP-4[a] *In Vivo*

Species (test system)	End point	Results	Reference
Mammalian cells:			
Mouse (germinal cells)	Dominant lethal mutation	+/–	Air Force 1978a
Rat (germinal cells)	Dominant lethal mutation	+/–	Air Force 1978a

[a]No information regarding the genotoxicity of JP-7 was located.

+/– = inconclusive result; JP-4 = jet propellant-4; JP-7 = jet propellant-7

Table 2-4. Genotoxicity of JP-4[a] *In Vitro*

Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms				
Salmonella typhimurium (TA1535, TA1537, TA1538, TA98, TA100)	Gene mutation	–	–	Air Force 1978a
S. typhimurium (TA1535, TA1537, TA1538, TA98, TA100)	Gene mutation	–	–	Galloway 1982b; Dennis 1982b[b]
S. typhimurium (TA1535, TA1537, TA1538, TA98, TA100)	Gene mutation	–	–	Cifone 1982b
Eukaryotic organisms:				
Fungi:				
Saccharomyces cerevisiae (D_4)	Gene mutation	–	–	Air Force 1978a
Mammalian cells:				
Mouse L5178Y lymphoma cells (TK +/– locus)	Gene mutation	–	–	Air Force 1978a
Mouse L5178Y lymphoma cells (TK +/– locus)	Gene mutation	–	–	Cifone 1982a; Dennis 1982b[b]
Mouse L5178Y lymphoma cells (TK +/– locus)	Gene mutation	–	–	EPA 1982a
Chinese hamster (ovary cells)	Chromosome aberrations	–	–	Jagannath 1982; Dennis 1982b[b]
Chinese hamster (ovary cells)	Chromosome aberrations	–	–	Rabenold 1982
Dog (peripheral lymphocytes)	Micronuclei induction	No data	–[c]	Air Force 1979b
Human (WI-38 cells)	Unscheduled DNA synthesis	+	+[d]	Air Force 1978a

[a]No information regarding the genotoxicity of JP-7 was located.
[b]Petroleum derived JP-4 tested
[c]Result is not meaningful because of unquantifiable testing protocol.
[d]Metabolic activation produced results of greater magnitude.

– = negative result; + = positive result; DNA = deoxyribonucleic acid; JP-4 = jet propellant-4; JP-7 = jet propellant-7; TK = thymidine kinase; WI-38 cells derived from human embryonic lung

cells to mixtures of such hydrocarbons. Negative data may, therefore, be misinterpreted in such a system. No genotoxicity data were obtained for JP-7.

Cancer. No studies were located regarding cancer in humans after inhalation, oral, or dermal exposure to JP-4 or JP-7. In inhalation animal studies, there does not appear to be any carcinogenic potential of chronic JP-7 exposure (Air Force 1991). A l-year JP-4 exposure in rats and mice resulted in increased alveolar/bronchiolar tumors in female rats and mice (Bruner et al. 1993). Renal tumor increases that were seen in male rats were attributable to $\alpha 2\mu$-globulin nephropathy syndrome (see the discussion of renal effects above) and are not likely to be relevant to other animals or to humans. Finally, an increased hepatocellular tumor incidence occurred in treated female mice (9/80) versus controls (2/83). In males, this trend was reversed (l/38 treated versus 14/71 controls). There are currently widely divergent views regarding the validity of mouse liver tumors as an indication of human carcinogenicity for a compound (EPA 1986b). Squamous cell carcinoma and fibrosarcoma formation was increased in the mice exposed to shale-derived (50% incidence) and petroleum-derived JP-4 (26% incidence) compared to the appropriate control groups (2% and 0%, respectively) (Clark et al. 1988). The current animal data regarding the carcinogenicity of JP-4 are equivocal, and the evidence is insufficient to draw conclusions regarding the carcinogenic potential of JP-4 or JP-7 in humans exposed at hazardous waste sites.

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 JP-4 and JP-7 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 JP-4 and JP-7 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 or Quantify Exposure to Jet Fuels JP-4 and JP-7

No biomarkers of exposure were identified for JP-4 or JP-7. No standard procedures exist for identifying or quantifying exposure to JP-4 or JP-7. For information on biomarkers of exposure for the individual components in JP-4 and JP-7, the ATSDR profiles on benzene (ATSDR 1991a), toluene (ATSDR 1990), total xylenes (ATSDR 1991c) and polycyclic aromatic hydrocarbons (ATSDR 1991b) can be consulted. However, the biomarkers of exposure for these chemicals are not specific for JP-4 or JP-7 exposure.

2.5.2 Biomarkers Used to Characterize Effects Caused by Jet Fuels JP-4 and JP-7

No biomarkers of effect were found for JP-7. Potential biomarkers for neurological effects of JP-4 are mild muscular weakness, staggering gait, and decreased sensitivity to painful stimuli (Davies 1964). Those effects are not specific enough to be useful as biomarkers for JP-4 exposure since they are a component of the clinical signs associated with the exposure to most volatile organic compounds. For more information on biomarkers for renal and hepatic effects of chemicals see ATSDR/CDC Subcommittee Report on Biological Indicators of Organ Damage (1990) and for information on biomarkers for neurological effects see OTA (1990).

2.6 INTERACTIONS WITH OTHER CHEMICALS

When benzene was added to a JP-4 inhalation mixture, experimental animals did not demonstrate any difference in hematological, blood chemistry, or histopathological results when compared to airexposed controls (Air Force 1974, 1976). No other information was located regarding the influence of other chemicals on the toxicity of JP-4 or JP-7.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to JP-4 and JP-7 than will most persons exposed to the same level of JP-4 and JP-7 in the environment. Reasons include genetic make-up, developmental stage, health and nutritional status, and chemical exposure history. These parameters result in decreased function of the detoxification and excretory processes (mainly hepatic and renal) or the pre-existing compromised function of target organs. For these reasons we expect the elderly with declining organ function and the youngest of the population with immature and developing organs will generally be more vulnerable to toxic substances than healthy adults. Populations who are at greater risk due to their unusually high exposure are discussed in Section 5.6, Populations With Potentially High Exposure.

Review of the literature regarding the effects of exposure to JP-4 or JP-7 does not indicate susceptibility of specific populations to these chemicals. There are very limited data on exposure of humans to JP-4 or JP-7; however, the results from animal studies do not indicate sensitivity in specific groups to the toxicity of these mixtures.

2. HEALTH EFFECTS

2.8 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to JP-4 or JP-7. 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 JP-4 or JP-7. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

2.8.1 Reducing Peak Absorption Following Exposure

Following dermal contact with JP-4 or JP-7, the skin should be wiped off and washed with soap and warm water. After washing, hand cream may be applied to the exposed skin to restore lost oils. If the eyes have been exposed, it is recommended that they be flushed with copious amounts of cool, clean water for at least 15 minutes. Common treatments of the eyes include application of antibiotic creams to prevent secondary infection and a soothing or anesthetic agent. Following ingestion, it is recommended that the victim drink water or milk. Vomiting should not be induced because of the risk of aspiration of jet fuel hydrocarbons. Following inhalation of jet fuel vapors, it has been suggested that the victim be administered oxygen (Tupper 1989; Weiss 1986).

2.8.2 Reducing Body Burden

There is no specific method for enhancing the elimination of JP-4 or JP-7 because the metabolic pathways and excretion pathways for these jet fuels is essentially unknown. Interventions designed to increase elimination may be of limited effectiveness because many of the components of JP-4 and JP-7 are lipophilic. However, it may be possible to increase the elimination of the highly volatile components of the fuels by increasing the respiratory frequency,

2.8.3 Interfering with the Mechanism of Action for Toxic Effects

No information on interfering with the mechanism of action for toxic effects of either JP-4 or JP-7 is provided because the metabolic pathways and excretion pathways for these jet fuels is essentially unknown.

2. HEALTH EFFECTS

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 JP-4 and JP-7 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 JP-4 and JP-7.

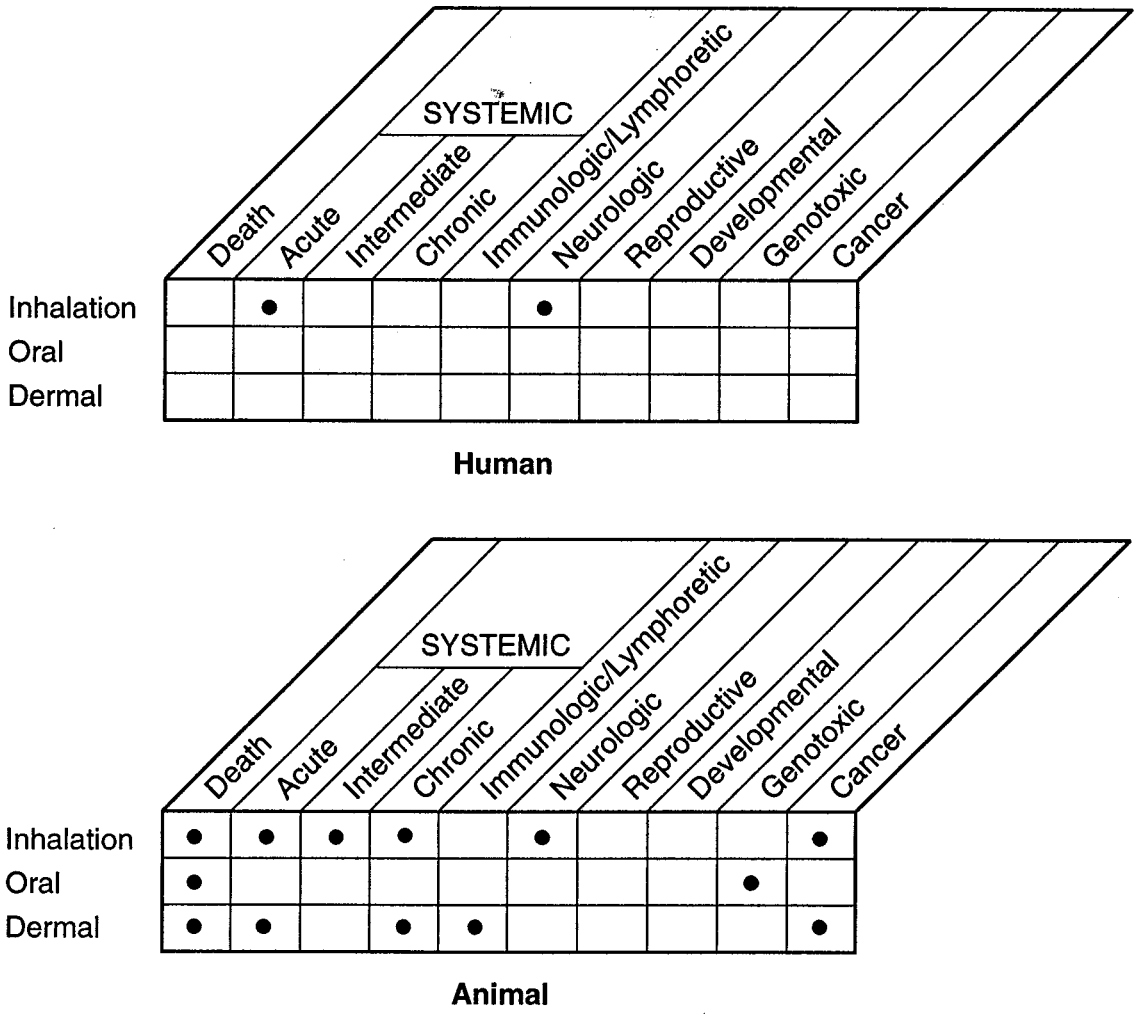
The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. This definition should not be interpreted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

2.9.1 EXISTING INFORMATION ON HEALTH EFFECTS OF JET FUELS JP-4 AND JP-7

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to JP-4 and JP-7 are summarized in Figures 2-2 and 2-3. The purpose of the figures is to illustrate the existing information concerning the health'effects of JP-4 and JP-7. Each dot in the figures 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 the figures should not be interpreted as "data needs" information (i.e., data gaps that must necessarily be filled).

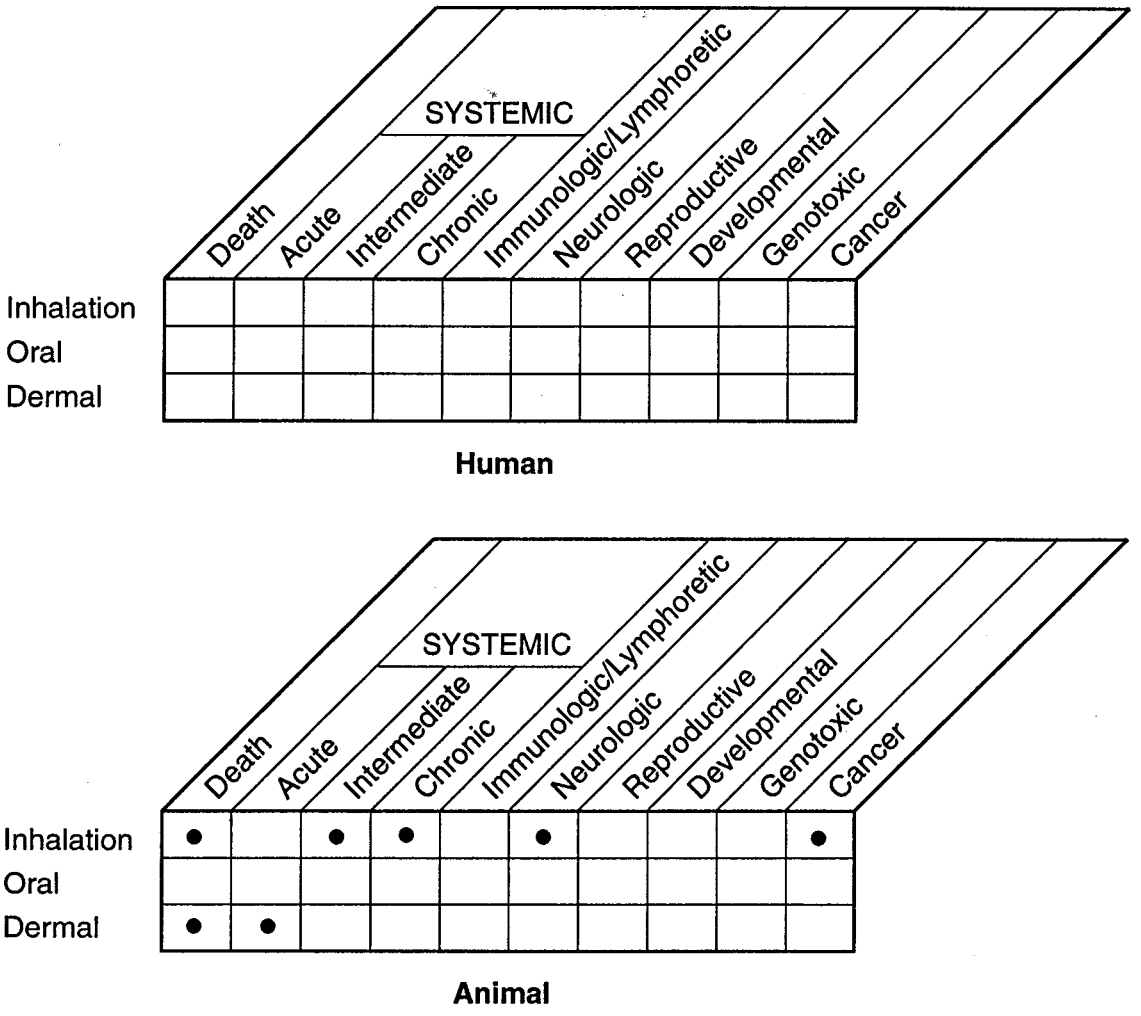
One case study was located detailing the acute neurological effects of accidental JP-4 exposure (Davies 1964). No other data were found on the health effects of inhalation exposure to JP-4 or JP-7 in humans. Animal data exist for death and for intermediate and chronic neurological, and cancer effects following inhalation exposure to JP-4; for death and genotoxic effects following oral exposure to JP-4; and for death and acute and chronic cancer effects following dermal exposure to JP-4. Therefore, as can be seen in Figure 2-2, the majority of the available information for JP-4 is on the health effects of inhalation and dermal exposure in animals. Very limited information exists on the effects of oral exposure in animals. No data were found on the health effects of oral and dermal exposure in

FIGURE 2-2. Existing Information on Health Effects of JP-4



● Existing Studies

FIGURE 2-3. Existing Information on Health Effects of JP-7



● Existing Studies

humans. The only available information for JP-7 was on death and intermediate, chronic, and cancer effects following inhalation exposure in animals. As can be seen in Figure 2-3, limited data were found on the health effects of inhalation exposure in animals to JP-7. Data on dermal exposure to JP-7 exist for death and acute effects. No other health effects data were found for either humans or animals.

2.9.2 Identification of Data Needs

Acute-Duration Exposure. The central nervous system appears to be the target of JP-4 toxicity following acute-duration inhalation exposure in humans. Acute inhalation exposure to JP-4 is characterized by a groggy, weak, intoxicated state including staggering gait, mild muscular weakness, and decreased sensitivity to painful stimuli (Davies 1964). Accidental inhalation exposure of a pilot to a high concentration of JP-4 from a fuel leak did not result in any abnormalities in hematological or clinical chemistry tests (Davies 1964). No information was available on acute-duration oral or dermal exposure of humans to JP-4 or JP-7, or on acute-duration inhalation, oral, or dermal exposure of humans to JP-7. Animals acutely exposed by inhalation to very high concentrations of JP-4 (38,000 mg/m^3) exhibited neurotoxic effects including poor coordination and convulsions (Air Force 1974). Acute dermal exposures to JP-4 and JP-7 indicate that both substances are skin irritants (Air Force 1984a; Clark et al. 1989; Dennis 1982a, 1982b; Walter 1982c). No pharmacokinetic data were available for either substance to support the identification of target organs across routes of exposure for animals or humans. No evidence was seen of primary ocular irritation following acute exposure to JP-4 or JP-7 (Air Force 1984a; Clark et al. 1989; Dennis 1982c; Walter 1982a). Petroleum-derived JP-4 was not a dermal sensitizer in guinea pigs (Clark et al. 1989; Walter 1982c). However, JP-7 and shale-derived JP-4 have sensitizing potential (Air Force 1984a). Acute exposure to high levels of JP-4, by all three routes, did not result in any mortality (Clark et al. 1989; Dennis 1982a). No quantitative information was available on acute-duration inhalation or oral exposure of animals to JP-7. No acute MRLs have been developed because of the absence of quantitative information regarding acuteduration inhalation or oral exposure to JP-4 or JP-7. More quantitative information on the levels of exposure that elicit various acute-duration oral, inhalation, or dermal exposure effects in humans and animals would be helpful, as would information on what the thresholds are for these effects.

2. HEALTH EFFECTS

Intermediate-Duration Exposure. No information is available on the effects of intermediate-duration exposure to JP-4 or JP-7 in humans. No pharmacokinetic data were available to support the identification of target organs across routes of exposure for either humans or animals. Intermediateduration inhalation exposure to JP-4 or JP-7 did not result in any dose-dependent pathophysiological responses in routine hematological tests in monkeys, dogs, or rats (Air Force 1974, 1980, 1984b, 1984c) with the exception of a decrease in white blood cell count after intermediate- or chronicduration exposure in rats (Air Force 1980). Increased blood urea nitrogen was measured in rats exposed continuously by inhalation for 90 days to 500 or 1,000 mg/m^3 JP-4 (Air Force 1980, 1984c). That effect was not repeated in later studies using intermittent exposure to 5,000 mg/m^3 JP-4 (Air Force 1981i). In that study, blood urea nitrogen was found to be decreased after exposure. Kidney weight was increased in male rats exposed by inhalation to JP-4 for an intermediate duration (Air Force 1976, 1980). Histopathological changes related to $\alpha_{2\mu}$-globulin nephropathy were seen in these male rats. The results of dominant lethal studies in rats and mice orally exposed to JP-4 were negative (Air Force 1978a). More information is needed on the effects of intermediate-duration inhalation, oral, and dermal exposures to JP-4 and JP-7 in humans and animals in order to adequately identify target organs. This is especially true for neurological effects, one of the most sensitive end points for JP-4 (Air Force 1974; Davies 1964) and, most likely, JP-7 exposures. Sufficient inhalation data exist to calculate an intermediate-duration inhalation exposure MRL of 9 mg/m^3.

Chronic-Duration Exposure and Cancer. No chronic-duration exposure studies were found in humans for exposure to JP-4 or JP-7 following inhalation exposure. No chronic-duration exposure studies in humans were found for exposure to JP-4 or JP-7 by the oral or dermal routes.

No chronic-duration exposure studies were found that identified the central nervous system as the target of JP-4 or JP-7 toxicity in animals. Chronic-duration inhalation exposure studies using JP-4 or JP-7 in rats and mice showed no increase in mortality during the exposure period or 12 months postexposure (Air Force 1981i, 1982f, 1982g, 1983e, 1991; Bruner et al. 1993). Chronic inhalation of JP-4 did not result in statistically significant respiratory tract irritation or pulmonary lesions in rats or mice (Bruner et al. 1993). Chronic inhalation exposure to JP-4 resulted in decreased white blood cell count in rats (Bruner et al. 1993). Hepatic inflammation of female mice was seen after inhalation exposure to JP-7 (Air Force 1991).

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No information is available on the carcinogenicity of JP-4 or JP-7 in humans following chronic inhalation, oral, or dermal exposure. Chronic inhalation exposure to JP-4 or JP-7 did not result in an increased incidence of cancer in animals except for an increase in hepatocellular adenomas in female mice exposed high doses of JP-4 (Bruner et al. 1993). The incidence of this cancer is of unknown significance in mice (EPA 1986b). There was equivocal evidence for alveolar/bronchiolar tumors after inhalation exposure of rats (Bruner et al. 1993). JP-7 inhalation exposure did not result in significant increases in the incidence of cancer in rats (Air Force 1991). However, there were slight increases in the incidence of C-cell adenomas and kidney adenomas in the groups of male rats exposed to 750 mg/m^3 of JP-7 (Air Force 1991). Dermal application of undiluted JP-4 to the skin on a chronic basis resulted in increased incidence of squamous cell carcinoma and fibrosarcoma formation in mice at the site of application. There were no oncogenic effects in other organs (Clark et al. 1988). No information is available on the carcinogenicity of JP-4 or JP-7 in animals following chronic oral exposure. Further chronic inhalation or oral studies are recommended to help elucidate the carcinogenic potential of JP-4 and JP-7. Sufficient inhalation data exist to calculate a chronic exposure MRL of 0.3 mg/m^3.

Genotoxicity. JP-4 does not appear to be highly genotoxic in in vitro studies; however, there are no human data to indicate whether this substance acts by a genotoxic mechanism. Consistently negative results were gathered for gene mutations in both microbial species (Air Force 1978a; EPA 1982a, 1982b; Jagannath 1982; Rabenold 1982) and mammals (Air Force 1978a, 1979b; Cifone 1982a, 1982b; EPA 1982b; Galloway 1982a, 1982b). In addition, JP-4 was not clastogenic in Chinese hamster ovary cells (Jagannath 1982; Rabenold 1982). Although significant UDS was observed in human WI-38 cells (Air Force 1978a), more research is needed in order to determine the nature of the DNA damage. The only two *in vivo* (oral) studies obtained were inconclusive for JP-4's effects on the germinal cells of rats and mice due to small sample size of test animals (Air Force 1978a). Testing for sister chromatid exchange chromosome aberrations, UDS, and gene mutations in animals exposed to JP-4 *in vivo* would be helpful in determining whether or not this jet fuel poses a genotoxic threat to humans. Epidemiology studies of exposed workers, pilots, military personnel, or Air Force personnel would help even further in evaluating JP-4 as a potential human genotoxin. No studies were found in which JP-7 was used as a test chemical in genotoxicity experiments. Therefore, research is needed in order to evaluate the toxicity of this particular jet fuel.

2.HEALTH EFFECTS

Reproductive Toxicity. No information is available on the reproductive effects of-JP-4 or JP-7 in humans or animals following inhalation, oral, or dermal exposure. No pharmacokinetic data were located to support the potential of JP-4 or JP-7 to affect reproduction across routes of exposure. Reproductive organ toxicity data from studies of acute, intermediate (90-day), and chronic duration are needed for all three routes of exposure in order to establish whether JP-4 or JP-7 has the potential to induce reproductive effects.

Developmental Toxicity. No information is available on the developmental effects of JP-4 or JP-7 in humans or animals following inhalation, oral, or dermal exposure. No pharmacokinetic data were located to support the potential of JP-4 or JP-7 to affect development across routes of exposure. Developmental toxicity data are needed for all three routes of exposure in order to establish whether JP-4 or JP-7 has the potential to induce developmental effects in humans.

lmmunotoxicity and Lymphoreticular Effects. Data regarding the immunological effects of JP-4 are limited to the dermal sensitization tests conducted in guinea pigs (Air Force 1984a; Clark et al. 1989; Walter 1982c). In these studies petroleum-derived JP-4 was not found to be a dermal sensitizer. However, JP-7 and shale-derived JP-4 have weak-to-mild and mild-to-moderate sensitization potential, respectively (Air Force 1984a). No studies were located regarding the immunological effects in humans after inhalation, oral, or dermal exposure to JP-7. It is not possible to determine the likelihood of immunological effects occurring in humans because of the paucity of data. These results suggest that JP-4 may affect immune function. Thus, assessing the effects of oral or inhaled JP-4 on immune function in laboratory animals would be helpful.

Neurotoxicity. No information is available on the neurotoxic effects of JP-4 or JP-7 following oral or dermal exposure in humans and animals, or of JP-7 following inhalation exposure in humans. The central nervous system appears to be the target of JP-4 toxicity following acute inhalation exposure in humans. Acute exposure to a very high concentration of JP-4 produced a groggy, weak, intoxicated state in a pilot exposed to a fuel leak (Davies 1964). The pilot had a staggering gait, mild muscular weakness, and decreased sensitivity to pain; these effects were no longer evident by 36 hours postexposure (Davies 1964). No information was found on neurotoxic effects of JP-4 or JP-7 in humans following intermediate-duration or chronic-duration exposure. Long-term exposure of experimental animals to JP-7 does not result in overt signs of neurotoxicity or any gross pathological

responses (Air Force 1991). Acute exposure of rats to very high concentrations of JP-4 by inhalation produced poor coordination and convulsions (Air Force 1974).

Additional studies in humans and animals using all modes of exposure that examine sensitive neuropathological end points specifically for JP-4 or JP-7 would be useful to definitely determine the symptoms associated with both fuels.

Epidemiological and Human Dosimetry Studies. Limited epidemiological information exists from an early study regarding acute-duration exposure to JP-4 (Davies 1964). Exposure levels in this study were only grossly approximated. No chronic-duration epidemiological studies were located regarding exposure to JP-4 or JP-7. Exposure to JP-4 or JP-7 is thought to occur primarily in a small segment of the population, namely Air Force personnel. Thus, collecting sufficient numbers of exposed persons for meaningful epidemiological studies is difficult. However, because the population most likely to be exposed consists mainly of Air Force personnel, follow-up studies may be more easily performed. Thus, studies examining chronic-duration neurological, immunological, developmental, and systemic effects would be valuable if a sufficient number of exposed persons are identified. In the absence of studies on persons exposed to JP-4 or JP-7, epidemiological studies on persons exposed to the individual components of JP-4 or JP-7 are not a priority because the results of the genetic toxicology tests with JP-4 were negative.

Biomarkers of Exposure and Effect.

Exposure. No biomarkers of exposure were identified for JP-4 or JP-7. No standard procedures exist for identifying or quantifying exposure to JP-4 or JP-7. Studies delineating the metabolism and excretion of JP-4 or JP-7 are needed in order to identify potential biomarkers of exposure following acute, intermediate, and chronic exposures to these chemicals.

Effect. No biomarkers of effect were found for JP-7. Potential biomarkers for neurological effects of JP-4 are mild muscular weakness, staggering gait, and decreased sensitivity to painful stimuli (Davies 1964). Studies of acute, intermediate, and chronic exposures are needed in order to identify biomarkers of effects for specific target organs following exposure to JP-4 or JP-7.

2. HEALTH EFFECTS

Absorption, Distribution, Metabolism, and Excretion. No quantitative data were located regarding the absorption, distribution, metabolism, or excretion of JP-4 or JP-7 following inhalation, oral, or dermal exposure in humans or animals. Therefore, acute, intermediate, and chronic data are needed in order to assess the relative rates and extent of absorption, distribution, metabolism, and excretion with respect to all three routes of exposure, as well as with respect to time or dose.

Comparative Toxicokinetics. No studies were located regarding comparative toxicokinetics of JP-4 or JP-7. Human and animal data are needed in order to examine toxicokinetics across species (i.e., in humans and animals and in multiple species). This information is needed in order to identify similar target organs and to adequately assess which animals can serve as the best models for humans.

Mitigation of Effects. All of the treatment methods currently available for use in jet fuel exposure are supportive in nature (Tupper 1989; Weiss 1986). Since the mechanism(s) of jet fuel toxicity are not known, there are currently no methods specifically tailored to mitigating the effects of jet fuels by interfering with the mode of action. Additional information on the ultimate mechanism of jet fuel toxicity is needed before insights can be gained regarding treatment of exposure victims.

2.9.3 Ongoing Studies

No ongoing studies evaluating either the health effects or toxicokinetics of JP-4 or JP-7 were located.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The composition of aviation fuels has been established by the U.S. Air Force (Air Force 1977, 1981g, 1982d, 1988a, 1989c, 1990) using specifications that are based primarily on the characteristics that give the maximum performance of the aircraft for which the fuel is used (CRC 1984). JP-4 and JP-7 were developed for use by the U.S. Air Force. JP-4 is called a wide-cut fuel because it is produced from a broad distillation temperature range and contains a wide array of carbon chain-lengths, from 4 to 16 carbons long. It was initially developed for broad availability in times of need. The composition of JP-4 is approximately 13% (v/v) aromatic hydrocarbons, 1.0% olefin hydrocarbons, and 86% saturated hydrocarbons (ITC 1985). It has a distillation temperature range of 60 to 270 °C (MacNaughton and Uddin 1984). JP-7 was developed for use in advanced supersonic aircraft because of its thermal stability and high flashpoint (CRC 1984; Dukek 1978). It has a distillation temperature range of 182 to 288 °C and contains a maximum of 5% (by volume) aromatic compounds (see Table 3-7).

Aviation fuels consist primarily of hydrocarbon compounds (paraffins, cycloparaffins or naphthenes, aromatics, and olefins) and contains additives that are determined by the specific uses of the fuel (CRC 1984; Dukek 1978; IARC 1989). Paraffins and cycloparaffins are the major components. Paraffins have a high hydrogen-to-carbon ratio, with a high heat release per unit of weight and a cleaner burn than other hydrocarbons. Cycloparaffins have a lower hydrogen-to-carbon ratio, which results in less heat released per unit of weight but increases the fuel's density. These components reduce the freezing point of the fuel. Aromatic hydrocarbons are a good energy source but produce smoke when burned; therefore, the maximum levels are restricted (20-25% by volume in JP-4, 5% by volume in JP-7). Finally, olefins are similar to the paraffins but are unsaturated with lower hydrogento- carbon ratios. They are the most reactive of the hydrocarbons and are permitted at only 5% by volume in JP-4 (CRC 1984). Benzene, present in wide-cut fuels such as JP-4, is an ineffectual contaminant usually present below 0.5% (CONCAWE 1985; IARC 1989). Nonhydrocarbon compounds such as sulfur and sulfur compounds are also found. Additives such as antioxidants, metal deactivators, fuel system icing inhibitors, corrosion inhibitors, and static dissipator additives are all present in limited quantities in jet fuels in order to improve performance (CRC 1984).

3. CHEMICAL AND PHYSICAL INFORMATION

Information regarding the chemical identity of JP-4 and JP-7 is located in Tables 3-l and 3-2, respectively.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Information regarding the physical and chemical properties of JP-4 and JP-7 is located in Tables 3-3 and 3-4, respectively. Information regarding the major components of JP-4 derived from petroleum and shale oil is presented in Table 3-5. Depending on the origin of the crude and the production method, there could be considerable compositional variability between fuel oils of the same grade (Air Force 1988b). This variation is reflected in the allowed military specifications (mil spec) for JP-4 and JP-7 fuel oils as shown in Tables 3-6 and 3-7, respectively, and in the compositional variability of JP-4 fuels as shown in Tables 3-5 and 3-8.

TABLE 3-1. Chemical Identity of JP-4[a]

Characteristic	Information	Reference
Chemical name	JP-4	OHM/TADS 1985
Synonym(s)	Jet fuel-4	OHM/TADS 1985
Registered trade name(s)	MIL-T-5624-L-Amd. 1 wide cut; JP-4 military (gasoline type)	Air Force 1990; Dickson and Woodward 1987; Dukek 1978; IARC 1989
Chemical formula	NA[a]	
Chemical structure[a]	NA[a]	
Identification numbers:		
CAS Registry	50815-00-4	OHM/TADS 1985
NIOSH RTECS	NY9340000	RTECS 1994a
EPA Hazardous Waste	No data	
OHM/TADS	7217071	OHM/TADS 1985
DOT/UN/NA/IMCO Shipping	1863	CHRIS 1986
HSDB	No data	
NCI	No data	

[a] JP-4 is a mixed compound composed primarily of hydrocarbons (i.e., alkanes, cycloalkanes, alkybenzenes, indan/tetralins, and naphthalenes).

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 Substance Data Bank; JP-4 = jet propellant-4; NA = Not Applicable; 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. Chemical Identity of JP-7[a]

Characteristic	Information	Reference
Chemical name	JP-7	RTECS 1994b
Synonym(s)	Jet fuel-7	RTECS 1994b
Registered trade name(s)	MIL-T-38219A-Amd. 2, kerosene, low volatility	IARC 1989
Chemical formula	NA[a]	
Chemical structure[a]	NA[a]	
Identification numbers:		
CAS Registry	No data	
NIOSH RTECS	SE7548500	RTECS 1994b
EPA Hazardous Waste	No data	
OHM/TADS	No data	
DOT/UN/NA/IMCO Shipping	No data	
HSDB	No data	
NCI	No data	

[a] JP-7 is a mixed compound composed primarily of hydrocarbons (i.e., alkanes, cycloalkanes, alkybenzenes, indan/tetralins, and naphthalenes).

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 Substance Data Bank; JP-7 = jet propellant-7; NA = Not Applicable; 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 3-3. Physical and Chemical Properties of JP-4[a]

Property	Information	Reference
Molecular weight	Not applicable[b]	
Color	Colorless to straw colored	CHRIS 1986; Martel 1992
Physical state	Liquid	CHRIS 1986
Melting point	-46 °C	OHM/TADS 1985
	-40–72 °C	ITC 1985
Boiling point (1 atm)	50–270 °C	Air Force 1989b
	90–300 °C	ITC 1985
	45–280 °C	Dickson and Woodward 1987
Density:		
at 15 °C	751–802 kg/m^3 (specification)	
Odor	Like gasoline and/or kerosene	
Odor threshold:		
Water	No data	
Air	1 ppm	CHRIS 1986
Solubility:		
Water at 20 °C	57 mg/L	CRC 1984
Organic solvent(s)	Since many of the components are organic solvents, the fuel is generally miscible with organic solvents	ITC 1985
Partition coefficients:		
Log K_{ow}	Major components range from 3 to 4.5	ITC 1985
Log K_{oc}	No data	
Vapor pressure at 20 °C	91 mm Hg	Air Force 1989b
Henry's law constant	$1.00x10^{-4}$-$1.00x10^{+1}$ atm-m^3/mol	Air Force 1989b
Autoignition temperature	246 °C	CRC 1984
Flashpoint	-23–1 °C	NFPA 1986
Flammability limits	1.3% lower; 8.0% upper	NFPA 1986
Explosive limits	No data	

[a]JP-4, or jet propellant-4, is a mixed compound composed primarily of hydrocarbons (i.e., alkanes, cycloalkanes, alky-benzenes, indan/tetralins, and naphthalenes).
[b]Jet fuels are blends prepared to meet certain gross property specifications. Most characteristic data only reflect gross properties covered in the specifications. Proportions and values vary with the type of crude oil from which the final fuel is derived and the refining process used.

TABLE 3-4. Physical and Chemical Properties of JP-7[a]

Property	Information	Reference
Molecular weight	Not applicable[b]	
Color	Colorless	Martel 1992
Physical state	Liquid	CHRIS 1986
Melting point	-30 °C	ITC 1985
Boiling point (1 atm)	182–288 °C (specification)	Air Force 1977; CRC 1984
	205–300 °C	ITC 1985
	150–200 °C	Dickson and Woodward 1987
Density:		
at 15 °C	779–806 kg/m^3 (specification)	Air Force 1977; CRC 1984; Dukek 1978
Odor	Like kerosene	Martel 1992
Odor threshold:		
Water	No data	
Air	No data	
Solubility:		
Water at 20 °C	38.4 mg/L	CRC 1984
Organic solvent(s)	Generally miscible with organic solvents (e.g., benzene, Freon® 113, cyclohexane)	ASTM 1982; IARC 1989
Partition coefficients:		
Log K_{ow}	No data	
Log K_{oc}	No data	
Vapor pressure;		
at 149 °C	1.55x10^2 mm Hg	Air Force 1977
at 260 °C	2.48x10^3 mm Hg	Air Force 1977
Henry's law constant	No data	
Autoignition temperature	241 °C	CRC 1984
Flashpoint	43–66 °C	NFPA 1986
	60 °C (specification)	Air Force 1977; CRC 1984
Flammability limits	0.6% lower; 4.6% upper	Dukek 1978
Explosive limits	No data	

[a]JP-7, or jet propellant-7, is a mixed compound composed primarily of hydrocarbons (i.e., alkanes, cycloalkanes, alky-benzenes, indan/tetralins, and naphthalenes).
[b]Jet fuels are blends prepared to meet certain gross property specifications. Most characteristic data only reflect gross properties covered in the specifications. Proportions and values vary with the type of crude oil from which the final fuel is derived and the refining process used.

TABLE 3-5. Composition (weight %) of Shale-Derived and Petroleum-Derived JP-4

Constituents	Shale-derived	Petroleum-derived
N-alkanes		
Heptane	4.73	15.76
Octane	7.48	6.60
Nonane	7.24	2.54
Decane	11.25	2.24
Indane	0.42	0.17
Undecane	16.62	4.17
Dodecane	11.49	5.25
Tridecane	6.07	4.71
Tetradecane	3.19	1.02
Pentadecane	0.96	1.35
Total	69.45	43.81
Monosubstituted alkanes		
3-Methyl hexane	3.05	14.39
2-Methyl heptane	3.08	6.14
3-Methyl heptane	1.64	7.19
Total	7.77	27.72
Disubstituted alkane		
2,3-Dimethyl pentane	—	—
2,5-Dimethyl pentane	0.18	1.48
2,4-Dimethyl pentane	0.63	2.52
Total	0.81	4.00
Cyclohexanes		
Cyclohexane	1.52	2.13
Methyl cyclohexane	5.68	2.17
Ethyl cyclohexane	—	—
Total	7.20	4.30
Monosubstituted aromatics		
Methyl benzene	3.77	3.41
Disubstituted aromatics (xylenes)		
m-Xylene	2.60	2.71
p-Xylene	1.70	1.63
o-Xylene	2.00	1.89
Total	6.30	6.23
Multisubstituted aromatics		
1,3,5-Trimethylbenzene	1.52	1.09
1,2,4-Trimethylbenzene	2.00	3.52
1,2,3-Trimethylbenzene	0.30	1.04
Total	3.82	5.65
Overall total	99.12	95.12

Source: Air Force 1988b

TABLE 3-6. U.S. Military Specifications for JP-4 Fuel

	Issuing agency:		USAF	
	Specification:		MIL-T-5624-N	
	Revision date:		22 March 1990	
	Grade designation:		JP-4	Test method
	Fuel type:		Wide-cut	ASTM FTMS 791
Composition	Acidity, total (mg KOH/g)	Max.	0.015	D 3242
	Aromatics (vol%)	Max.	25.0	D 1319
	Olefins (vol%)	Max.	5.0	D 1319
	Sulfur, mercaptan (wt%) (1)	Max.	0.00	D 3227
	Sulfur, total (wt%)	Max.	0.4	D 1266/D 2622/ D 3120
	Color, saybolt	Max.	Report	D 156
Volatility	Distillation			
	Temp. Init. BP (°C)	Max.	Report	D 86/D 2887
(D 2887 limits in parentheses)	Temp. 10% Rec (°C)	Max.	Report	
	20% Rec (°C)	Max.	145 (130)	
	50% Rec (°C)	Max.	190 (185)	
	90% Rec (°C)	Max.	245 (250)	
	Final BP (°C)	Max.	270 (320)	
	Residue (vol%) (for D 86)	Max.	1.5	
	Loss (vol%) (for D 86)	Max.	1.5	
	Explosiveness (%)	Max.		
	Flash point (°C)	Max.		D 93
	Gravity, °API (15 °C)	Max.	45–57	D 1298
	Density, 15 °C (kg/m^3)	Max.	751–802	D 1298
	Vapor pressure (37.8 °C) kPa (psi)		14–21 (2.03–3.0)	D 323/D 2551
Fluidity	Freezing point, °C (F)	Max.	-58 (-72)	D 2336
	Viscosity @ -20 °C (cSt)	Max.	—	D 445
Combustion	Aniline-gravity product or	Min.	5250	D 1405
	Net heat of comb., MJ/kg (Btu/lb)	Min.	42.8 (18,400)	D 2382/D 3328/ D 240
	Smoke point or	Min.	20.0	D 1322
	Hydrogen content (wt%)	Min.	13.5	D 1018/D 3343/ D 3701
Corrosion	Copper strip (2 hr @ 100 °C)	Max.	1	D 130
Stability	JFTOT ΔP (mm Hg)	Max.	25	D 3241 (5)
	JFTOT tube color code	Max.	<3	
Contaminants	Existent gum (mg/100 mL)	Max.	7	D 381
	Particulates (mg/L)	Max.	1	D 2276 (2)
	Water reaction interface	Max.	1b	D 1094
	Water separation index modified	Min.	70 (3)	D 2550
	Flitration time (minutes)	Max.	10	(2)
Additives	Anti-icing (vol%)		0.10–0.15	5330, 5340,
	Antioxidant		Required (4)	3527 FED STD 791
	Corrosion inhibitor		Required	
	Metal deactivator		Option	
	Antistatic		Required	
Other	Conductivity (pS/m) at <29.4 °C		150–600	D 2624/D 4308
	Service		All	
	NATO code No.		F-40	

Notes: (1) The mercaptan sulfur determination may be waived if fuel "Doctor Sweet."
(2) Minimum one-gallon sample. Filtration time in accordance with D 2276 particulate.
(3) With all additives except electrical conductivity additive.
(4) If hydrogen treated blend stocks used—optional if no hydrotreating used.
(5) Test at 260 °C tube temperature.

Source: Air Force 1990; CRC 1984.

TABLE 3-7. U.S. Military Specifications for JP-7 Fuel

	Issuing agency:		USAF	
	Specification:		MILT-38219A - Amd. 2	
	Revision date:		26 January 1981	
	Grade designation:		JP-7	Test method
	Fuel type:		Low volatility	ASTM
Composition	Acidity, total (mg KOH/g)	Max.		D 3242
	Aromatics (vol%)	Max.	5	D 1319
	Olefins (vol%)	Max.		D 1319
	Sulfur, mercaptan (wt%)	Max.	0.001	D 3227
	or			
	Doctor test, N = negative	Max.	N	D 1266, D 2622 or
	Sulfur, total (wt%)		0.1	D 3120
Volatility	Distillation			
	Temp. Init. BP (°C)		182 min.	D 86 or D 2887
	10% Rec (°C)		196 min.	
	20% Rec (°C)		206 min.	
	50% Rec (°C)		Report	
	90% Rec (°C)		260 max.	
	Final BP (°C)		288 max.	
	Residue (vol%)		1.5 max.	D 86
	Loss (vol%)		1.5 max.	D 86
	Flash point (°C)		60 min.	D 56 or D 93
	Gravity, °API (15 °C)		44–50	D 1298
	Density, 15 °C (kg/m^3)		779–806	D 1298
	Vapor pressure @ 149° (kPa)	Max.	20.7 (1)	
	Vapor pressure @ 260° (kPa)	Max.	331 (1)	
Fluidity	Freezing point, (°C)	Max.	-43.5	D 2386
	Viscosity @ -40 °C (cSt)	Max.		D 445
	Viscosity @ -34.5 °C (cSt)	Max.	15.0	
Combustion	Net heat of comb., MJ/kg	Min.	43.5	D 240, D 2382, or D 3338
	Luminometer No.	Min.	75 (2)	D 1740
	Smoke point	Min.		D 1322
	Hydrogen content (wt%)	Min.	(2)	D 3343
Corrosion	Copper strip (2hrs @ 100 °C)	Max.	1b	D 130
Thermal stability	(JFTOT or coker)			
	JFTOT TDR	Max.	12 (3)	D 3241
	JFTOT (mm Hg pressure diff.)	Max.	25 (3)	D 3241
	Coker, tube deposit		<3 (4)	D 1660 (TS only)
	Coker (mm Hg pressure diff.)	Max.	76 (4)	D 1660 (TS only)
Contaminants	Existent gum (mg/100 mL)	Max.	5.0	D 381
	Particulate matter (mg/L)			D 2776
	FOB origin deliveries	Max.	.3	(5)
	FOB destination deliveries	Max.	.5	
	WSIM	Min.	85	D 2550 or D 3948
Additives	JFA-5 (mg/L)			
	Anti-icing (vol%)		0.10 to 0.15	FTMS 791, 5327, or
	Antioxidant		Option	5340
	Metal deactivator		Option	
	Lubricity (ppm)		200–250	
Other	Thermal precipitation rating	Max.	B-2 (6)	

Notes: (1) Vapor pressure test in accordance with Appendix C, MIL-T-38219A.
(2) If luminometer No. between 70 and 75, fuel acceptable—if hydrogen content is not less than 14.4 wt% as calculated by ASTM D 3343.
(3) Test by D 3241—conditions as specified in MIL-T-38219A Amd. 2 and tube rating in Appendix D.
(4) Research fuel coker—conditions as specified in MIL-T-38219A Amd. 2
(5) Minimum sample size of 3.785 L (1 gal) shall be filtered.
(6) Test by Appendix B. MIL-T-38219A.

Source: CRC 1984.

TABLE 3-8. Typical Hydrocarbon Composition of JP-4 Fuel[a]

Compound	JP-4[b]
N-alkanes	
Butane	0.12
Pentane	1.06
Hexane	2.21
Heptane	3.67
Octane	3.80
Nonane	2.25
Decane	2.16
Undecane	2.32
Dodecane	2.00
Tridecane	1.52
Tetradecane	0.73
Pentadecane	—
Hexadecane	—
Heptadecane	—
Octadecane	—
Isoalkanes	
Isobutane	0.66
2,2-Dimethylbutane	0.10
2-Methylpentane	1.28
3-Methylpentane	0.89
2,2-Dimethylpentane	0.25
2-Methylhexane	2.35
3-Methylhexane	1.97
2,2,3,3-Tetramethylbutane	0.24
2,5-Dimethylhexane	0.37
2,4-Dimethylhexane	0.58
3,3-Dimethylhexane	0.26
2,2-Dimethylhexane	0.71
2-Methylheptane	2.70
4-Methylheptane	0.92
3-Methylheptane	3.04
2,5-Dimethylheptane	0.52
2,4-Dimethylheptane	0.43
4-Ethylheptane	0.18
4-Methyloctane	0.86
2-Methyloctane	0.88
3-Methyloctane	0.79

TABLE 3-8. Typical Hydrocarbon Composition of JP-4 Jet Fuel[a] *(continued)*

Compound	JP-4[b]
2-Methylundecane	0.64
2,6-Dimethylundecane	0.71
2,4,6-Trimethylheptane	—
4-Methyldecane	—
2-Methyldecane	—
2,6-Dimethyldecane	—
2-Methylundecane	—
2,6-Dimethylundecane	—
Cycloparaffins	
Methylcyclopentane	1.16
Cyclohexane	1.24
t-1,3,-Dimethylcyclopentane	0.36
c-1,3,-Dimethylcyclopentane	0.34
c-1,2-Dimethylcyclopentane	0.54
Methylcyclohexane	2.27
Ethylcyclopentane	0.26
1,2,4-Trimethylcyclopentane	0.25
1,2,3-Trimethylcyclopentane	0.25
c-1,3-Dimethylcyclohexane	0.42
1-Methyl-3-ethylcyclohexane	0.17
1-Methyl-2-ethylcyclohexane	0.39
Dimethylcyclohexane	0.43
1,3,5-Trimethylcyclohexane	0.99
1,1,3-Trimethylcyclohexane	0.48
1-Methyl-4-ethylcyclohexane	0.48
n-Butylcyclohexane	0.70
Propylcyclohexane	—
Hexylcyclohexane	—
Heptylcyclohexane	—
Aromatic hydrocarbons	
Benzene	0.50
Toluene	1.33
Ethylbenzene	0.37
m-Xylene	0.96
p-Xylene	0.35
o-Xylene	1.01
Isopropylbenzene	0.30

TABLE 3-8. Typical Hydrocarbon Composition of JP-4 Jet Fuel[a] *(continued)*

Compound	JP-4[b]
n-Propylbenzene	0.71
1-Methyl-3-ethylbenzene	0.49
1-Methyl-4-ethylbenzene	0.43
1,3,5-Trimethylbenzene	0.42
1-Methyl-2-ethylbenzene	0.23
1,2,4-Trimethylbenzene	1.01
1,3-Diethylbenzene	0.46
1,4-Diethylbenzene	—
1-Methyl-4-propylbenzene	0.40
1,3-Dimethyl-5-ethylbenzene	0.61
1-Methyl-2-isopropylbenzene	0.29
1,4-Dimethyl-2-ethylbenzene	0.70
1,2-Dimethyl-4-ethylbenzene	0.77
1,2,3,4-Titramethylbenzene	0.75
1-Ethylpropylbenzene	—
1,2,4-Triethylbenzene	—
1,3,5-Triethylbenzene	—
Phenylcyclohexane	—
1-t-Butyl-3,4,5-trimethylbenzene	—
n-Heptylbenzene	—
Naphthalene	0.50
2-Methylnaphthalene	0.56
1-Methylnaphthalene	0.78
2,6-Dimethylnaphthalene	0.25
Biphenyl	—
1-Ethylnaphthalene	—
2,3-Dimethylnaphthalene	—
n-Octylbenzene	—

[a]Smith et al. 1981
[b]Concentrations in weight percent

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Jet fuels are primarily derived from crude oil, the common name for liquid petroleum. These jet fuels can be referred to as petroleum-derived jet fuels. Jet fuels can also originate from an organic material found in shale, called kerogen or petroleum solids: that can be converted by heat to shale oil. Jet fuels from this source are called shale-derived jet fuels (Hoffman 1983). Jet fuels are typically made by blending and refining various crude oil petroleum distillation products such as naphtha, gasoline, or kerosene in order to meet specific military or commercial specifications (Air Force 1989b). Since there is great variability in the concentrations of major components of crude oil, there is also a great variation in the final jet fuel product (Air Force 1989b). Therefore, there are many types of each jet fuel, and each jet fuel is not specified by chemical composition (Air Force 1989b; CRC 1984). JP-4 is a naphtha-type fuel made by blending straight-run kerosene streams with lower boiling distillates to fit the specifications given in Table 3-6 (Air Force 1989b; IARC 1989). JP-4 is known as a wide-cut fuel; it is made from the distillation products obtained over a wide range of temperatures and has a broad spectrum of hydrocarbon chain lengths varying from C_4 to C_{16} (Air Force 1989b; CONCAWE 1985). JP-4 is also made by blending and refining shale oil distillate streams (Stallard and Krautter 1984). JP-7 is made by blending kerosene distillates in order to achieve a product containing a maximum of 5% aromatics by volume and a maximum total weight of 0.1% sulfur (CRC 1984; IARC 1989). Once jet fuels are made, they are often transported through pipelines to terminals where additional substances such as metal deactivators, electrical conductivity additives, and fuel system icing inhibitors are added to the mixture (IARC 1989).

In 1970, total U.S. production of military and commercial jet fuels was approximately 38 million metric tons (IARC 1989). Production in the United States steadily increased over the next 15 years to about 57 million metric tons in 1985. Data on amounts of JP-4 and JP-7 produced during this 15-year period, as well as data on current production volumes of JP-4 and JP-7, are not available.

Data on specific manufacturers of JP-4 and JP-7 are not available. In 1978, the Standard Oil Company (SOHIO, Cleveland, Ohio) refined 87,000 barrels of crude shale oil to produce different fuel oils including jet fuels (Stallard and Krautter 1984). However, no report was located in the literature

that would indicate shale has been mined or retorted on a commercial scale for the production of jet fuels in recent years.

Since JP-4 and JP-7 are not required to be reported under SARA Section 313, there are no data for JP-4 and JP-7 in the Toxics Release Inventory (TRI 1993).

4.2 IMPORT/EXPORT

Import volumes of naphtha-type jet fuels such as JP-4 decreased considerably between 1981 and 1983 (ITC 1985). Total amounts of naphtha-type jet fuels imported into the United States were ≈2.7 million barrels in 1981, ≈1.9 million barrels in 1982, and 322,000 barrels in 1983. Current import data for JP-4 and JP-7 are not available. No export data were located for JP-4 or JP-7.

4.3 USE

Aviation turbine fuels such as JP-4 and JP-7 were not used until the 1930s when the first turbojet engine was developed (IARC 1989). Jet-powered aircraft had only limited use in World War II, but further military and commercial developments brought jet engines to the forefront as power sources for aircraft in the 1960s. The Air Force has used turbine-powered aircraft, which require the use of aviation turbine fuels such as JP-4 and JP-7, for over 25 years (Gleason and Martone 1979).

Both JP-4 and JP-7 are used exclusively as military aviation fuels by the U.S. military, especially the U.S. Air Force (Air Force 1989b; IARC 1989). However, there are indications that JP-4 has been used and stored at one U.S. Coast Guard Facility (Grand Traverse County, Michigan) (Twenter et al. 1985). JP-4 is a wide-cut fuel that meets operational requirements and offers a broad availability in the event of a war (CRC 1984; Dukek 1978). JP-4 is used in military aircraft such as the F-4 (Air Force 1981h). JP-7 is a kerosene fuel used by the Air Force for specific applications that require high thermal stability. Since JP-7 has a high flashpoint, it is used in supersonic Air Force aircraft (CRC 1984; Dukek 1978).

At one time, the U.S. Department of Defense consumed approximately 2.7% of the total petroleum products made in the United States (Gleason and Martone 1979). Approximately 50%, or 250,000

barrels per day, has been used as JP-4. JP-4 has constituted 85% of the turbine fuels used by the Department of Defense (Air Force 1989b).

4.4 DISPOSAL

Since JP-4 and JP-7 have been widely used by the U.S. Air Force, disposal information for JP-4 and JP-7 involves mostly the disposal of JP-4 released into the air, water, or soil in the case of accidental spills and normal aircraft operations.

Vapors generated in tank truck loading of JP-4 can be disposed of by the installation of a vapor recovery system (NIOSH 1989). Runoff of jet fuels from loading and unloading aircraft operations can be separated by an on-site oil/water separation system.

Several methods have been investigated for the disposal of JP-4 spilled onto soil from normal aircraft operations or from accidental spills. One method, in situ soil venting, involves using vacuum blowers to pull large amounts of air through soil contaminated with JP-4 (Elliot and DePaoli 1990). The air pulls out the soil gas, and the JP-4 contaminants volatilize as a result of disrupted equilibrium. Freeproduct extraction of JP-4 from soil and subsequent off-site cement kiln incineration have also been investigated as a means of disposal of JP-4 spills in soil and groundwater (EPA 1990b). Another process called in-situ bioventing, whereby oxygen is delivered by forced air movement through the contaminated unsaturated soils to stimulate in-situ biodegradation in an otherwise oxygen-limited zone, has been successfully applied to a contaminated test site (Air Force 1992). Thermophilic cornposting in the presence of horse manure and chicken manure has shown considerable promise for treating JP-4 contaminated soil (McMullen and Regan 1992). Excavation of soil contaminated with JP-4 and subsequent incineration at an approved EPA hazardous waste incineration site is another means of disposal that has been investigated for JP-4 (EPA 1990b). Additional information on the EPA hazardous waste regulations that apply to JP-4, JP-7 and incineration practices is available in Chapter 7.

Biodegradation of JP-4 in groundwater has also been investigated as a means to treat contaminated groundwater (EPA 1990b). This process involves the extraction of JP-4 from contaminated groundwater, addition of nutrients for subsequent reinjection, and *in situ* biodegradation of the volatile organic compounds found in JP-4. Carbon adsorption is another suggested method of treatment of

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

JP-4 in which activated carbon is injected into JP-4 contaminated groundwater. The activated carbon is later removed along with the JP-4.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

JP-4 and JP-7 are complex mixtures of hydrocarbons whose environmental fate depends primarily on the specific chemical and physical properties of their individual components. The individual components can be categorized into basic groups (paraffins, cycloparaffins, aromatics, and olefins), and these groups are common to both jet fuels. No information on the environmental fate of JP-7 was located. However, since the hydrocarbon groups making up the two compounds are similar, JP-7 can be expected to behave similarly to JP-4.

Jet fuel may be released to the environment by in-flight jettisoning of fuel and from spills or leaks to soil or water. Jet fuel jettisoned from planes can be transported by the wind. Some of it is transformed photochemically to ozone and other components of smog. It has been shown to form aerosols as a result of reactions with atmospheric chemicals, but the specific composition of the particulate material is not known. Most of the jet fuel released to water evaporates to the air. The components with the lowest boiling points volatilize most rapidly (e.g., short-chain alkanes, aromatics). Those with higher boiling points (e.g., branched alkanes, long-chain alkanes) persist longer in the water. Some of the hydrocarbons making up jet fuel are soluble in water (e.g., the aromaticsbenzene, toluene, and xylene). Under turbulent water conditions, the more soluble hydrocarbons remain dissolved longer and may partition to sediment or be biodegraded. The primary degradative fate process for jet fuel components in soil is biodegradation. While volatilization is expected to be the dominant fate process for these fuels from soil surfaces, biodegradation will become increasingly dominant as the soil depth increases. Some components of these fuels also migrate through the soil to groundwater.

Hydrocarbons associated with JP-4 and JP-7 have been detected in air in closed buildings where the fuels were being used or burned. Organic compounds found in JP-4 have been detected in groundwater following JP-4 leaks and spills. Hydrocarbons associated with JP-4 have also been found in soil surrounding fuel spill and leak sites. No data were located on the contamination of food, fish, shellfish, or terrestrial plants or animals.

5. POTENTIAL FOR HUMAN EXPOSURE

The National Occupational Exposure Survey conducted by NIOSH between 1980 and 1983 estimated that 4,866 employees had the potential to be exposed to JP-4 in the workplace (NOES 1990). Populations most likely to be exposed to JP-4 and JP-7 include those involved in jet fuel manufacturing or refueling operations, populations working or living on Air Force bases where the fuels are used and stored (and where leaks or spills are likely to occur), and those living or working near waste sites where the fuels are dumped.

JP-4 has been found in at least 4 of the 1,397 NPL hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (HazDat 1994). JP-7 has not been found in any NPL site. However, the number of NPL sites evaluated for JP-4 and JP-7 is not known. The frequency of these sites within the United States can be seen in Figure 5-1.

5.2 RELEASES TO THE ENVIRONMENT

JP-4 and JP-7 are fuel mixtures used by the U.S. military as aviation fuels. As a result of normal aircraft operations and fuel storage, JP-4 and JP-7 can be released into the environment. Under some conditions, it is common practice for aircraft to jettison excess fuel, releasing it into the environment (IARC 1989).

Since JP-4 and JP-7 releases are not required to be reported under SARA Section 313, there are no data for JP-4 and JP-7 in the Toxics Release Inventory (TRI 1993).

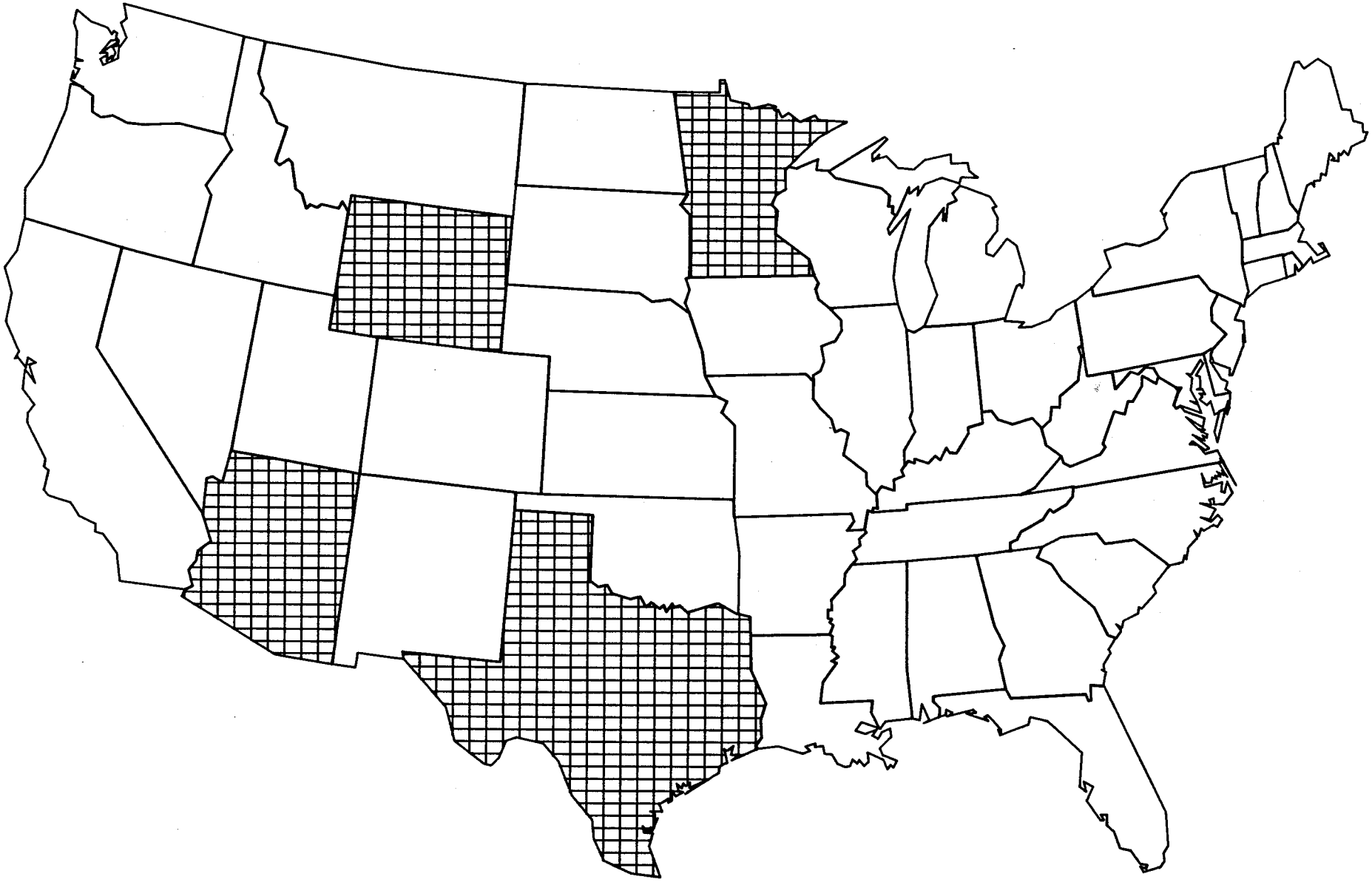
5.2.1 Air

JP-4 may be released into the atmosphere as vapors in loading and unloading operations in closed aircraft shelters (Air Force 1981h; NIOSH 1989). Releases into the air may also occur as a result of evaporation of JP-4 from contaminated soils or other spill sites (Air Force 1984b).

5.2.2 Water

JP-4 and JP-7 may be released into groundwaters as a result of seepage from contaminated soils during storage, aircraft maintenance, and fuel storage and dispensing operations (Twenter et al. 1985). A fuel layer of approximately 2 feet was identified in groundwater from shallow wells at Robins Air Force

FIGURE 5–1. FREQUENCY OF NPL SITES WITH JET FUEL (JP–4) CONTAMINATION *



*Derived from HazDat 1994

Base (Georgia) on a site where an undetermined amount of JP-4 was released into the soil from an underground fuel supply line in the 1960s (Air Force 1985a).

Groundwater intrusions of JP-4 were reported to have occurred as a result of cracks in the gunnite lining of the diked area surrounding three aboveground storage. tanks at the Niagara Falls Air Force Reserve Facility in New York (Air Force 1983a). Additional JP-4 was found in storm water drainings at the facility from underground inlet pipe, and in&t and outlet pipe leaks discovered in 1979 and 1982, respectively. Hydrocarbon groundwater contamination from leaking pipes in a JP-4 fuel farm occurred in a residential area surrounding the U.S. Navy air station in Traverse City, Michigan (Sammons and Armstrong 1986).

5.2.3 Soil

JP-4 and JP-7 may be released into soil as a result of leaks in underground or aboveground storage tank systems. In October 1975, approximately 83,000 gallons of JP-4 were lost from the bottom of a newly cleaned, aboveground storage tank at the Defense Fuel Supply Center in Charleston, South Carolina (Talts et al. 1977). Investigation of the soil revealed that JP-4 had moved through porous soil to a depth of approximately 7-14 feet. In 1972, approximately 42,000 gallons of JP-4 were released into the soil as a result of an external pipe leak at O'Hare Air Reserve Forces Facility, Illinois (Air Force 1983b). The dike had accumulated excess water as a result of heavy rains, and a drop in temperature caused the water to freeze and crush external piping to the tank. An undetermined amount of JP-4 was released into the soil from a leak in a 4-inch diameter pipe in 1965 at Robins Air Force Base (Air Force 1985a). Approximately 27,000 gallons of JP-4 were released into the soil in January 1985 as a result of an automatic filling system malfunction which caused underground storage tanks to overfill at Hill Air Force Base in Utah (Elliot and DePaoli 1990).

5.3 ENVIRONMENTAL FATE

5.3.1. Transport and Partitioning

Since JP-4 and JP-7 are mixtures of hydrocarbons, their movement in the environment is actually a function of the chemical and physical properties of the component hydrocarbons. Following release of jet fuel to air, water, or soil, the component hydrocarbons partition relatively independently of each

other based on their respective vapor pressures, solubilities, and Henry's law and sorption constants. For JP-4 and JP-7 mixtures, these values are ranges based on the component hydrocarbons. Information on the specific physical and chemical properties of several of the component hydrocarbons (e.g., benzene, toluene, xylene, naphthalene, etc.) can be found in the ATSDR toxicological profiles for these chemicals. The hundreds of hydrocarbons making up JP-4 and JP-7 fuel mixtures can be divided into a few groups of hydrocarbon classes with similar properties (Air Force 1989b; CRC 1984). These include paraffins (saturated straight-chain hydrocarbons), cycloparaffins (saturated cyclic hydrocarbons), aromatics (fully unsaturated six-carbon ring compounds), and olefins (unsaturated straight-chain and cyclic hydrocarbons). Paraffins and cycloparaffins are the major components and comprise about 90% of JP-4 by volume (79% by weight) (Air Force 1989b). Aromatics make up about 10-25% by volume of JP-4 but only about 5% of JP-7 (Air Force 1989b; IARC 1989); however, the specific composition of these fuels varies among manufacturers and probably between batches (Cooper et al. 1982). Jet fuel may also contain low and variable levels of nonhydrocarbon contaminants and additives such as sulfur compounds, gums, alcohols, naphthenic acids, antioxidants, metal deactivators, and icing and corrosion inhibitors (CRC 1984; IARC 1989). The variability in the composition contributes to the difficulty in making general conclusions about the fate and transport processes of these fuels in the environment.

Most of the principal JP-4 component hydrocarbons rapidly evaporate from water following a spill. Tests with both petroleum- and shale-derived JP-4 under various environmental conditions all showed volatilization of JP-4 component hydrocarbons to be the dominant fate process (Air Force 1987b, 1988b; EPA 1985). Complete evaporation of benzene, toluene, and *p*-xylene occurred within 24 hours in shake-flask experiments using water from three natural sources (EPA 1985). Ninety percent of the JP-4 evaporated within 6 days under the laboratory conditions used (Air Force 1988b). As expected, the hydrocarbons with the lowest boiling points evaporated most rapidly. Simulated spills of JP-4 to water suggested that most JP-4 component hydrocarbons evaporated within l-2 weeks following release (Air Force 1981f). In a model petroleum-derived JP-4 fuel spill into a natural freshwater sample, initial concentrations of total dissolved hydrocarbons were about 1 mg/L. At 1 and 2 weeks following the simulated spill, concentrations did not exceed 0.005 mg/L for any of the measured fuel components. This was attributed to the high volatility of the fuel. Shake-flask experiments have shown that increased dissolved organic carbon decreases the rate of hydrocarbon evaporation (Air Force 1988b). Laboratory experiments have shown that the evaporation rate of jet fuel and its components increases with wind velocity and, to a lesser extent, with temperature and fuel-layer

thickness (Air Force 1988d). Comparisons of dissolution and evaporation rates under several windspeed and mixing conditions showed that evaporation was the dominant fate process for jet fuel components in water.

JP-4 also evaporates from soil, although evaporation is not as important a fate process in soil as it is in water. A model soil core ecosystem was treated with JP-4 to simulate a spill (Air Force 1981e, 1982c). Headspace above the soil core revealed hydrocarbons from the JP-4 indicating that evaporation of component hydrocarbons had occurred. In model soil core ecosystems, volatilization accounted for 7% of the hydrocarbon loss compared to 93% for biodegradation (Coho 1990).

Some downward migration of JP-4 component hydrocarbons occurred in model soil core ecosystems treated with JP-4 to mimic a spill and watered to simulate rainfall (Air Force 1982c). Of nine hydrocarbons monitored for vertical migration through the core, only *n*-pentadecane and *n*-heptane migrated the 50 cm to the bottom of the core. They were first found at this depth 197 days following initiation of the experiment. These two compounds also persisted in the soil longer than the other hydrocarbons monitored. *n*-Decane, *n*-undecane, dodecane, *n*-tridecane, and *n*-tetradecane were found only at 10 cm below the surface. They were observed for 50-134 days following onset of the experiment and were not detected again. Additional data obtained by leachate collection indicated that the migration of hydrocarbons was best explained by channeling effects caused by biota and/or physical stresses since there was no direct correlation between leachate collection and hydrocarbon transport. Additional evidence for vertical migration of jet fuel hydrocarbons through soil comes from their detection in groundwater following leaks and spills to surface soil (EPA 1990b; Talts et al. 1977). Horizontal and vertical migration through soil has been confirmed by detection of JP-4 hydrocarbons in soil several meters from the spill site (EPA 1988a, 1990b).

The difficulties of determining the fate of JP-4 and its components are epitomized by the problems in determining the composition of its water-soluble fraction. Various results are likely to be obtained by different investigators even when the fuel tested and the methods used appear to be similar. Seventeen hydrocarbons were detected in an analysis of the water-soluble fractions of shale-derived and petroleum-derived JP-4, with the most abundant hydrocarbons being benzene, methylbenzene, and 3-methylhexane (Air Force 1988b). In contrast, only benzene, toluene, and p-xylene were found in significant concentrations in the water-soluble fraction of JP-4 (origin not specified) in laboratory simulations of field conditions, although other hydrocarbons could be detected (EPA 1985). The

aqueous concentration of JP-4 components under spill conditions was found to depend on the solubility of the individual components, the mixing of the mixture due to wind speed, the thickness of the fuel layer, the ionic strength of the aqueous solution, and the rate of evaporation of components (Air Force 198%). Laboratory experiments simulating a JP-4 spill to water measured both evaporation and dissolution of components under slow and fast wind speeds and under conditions that enhanced complete mixing. Under both conditions, only the component aromatics (benzene, toluene, ethylbenzene, and xylene) were soluble enough to-be detected in the aqueous phase before evaporative processes reduced their concentrations below detectable limits. Concentration measurements of these components in both the fuel and water suggested that, in general, the concentration of the lighter aromatics decreased in the fuel layer and increased in the water phase until evaporation began to substantially affect their concentration in the aqueous phase. Heavier aromatics initially decreased in the fuel but then increased as the lighter aromatics decreased. Aqueous concentrations increased over time and generally reached higher levels, and their evaporation was not as rapid. Increased wind speed increased both dissolution and evaporation of JP-4 components, but evaporation was increased substantially more than dissolution (a 5fold increase for evaporation compared to a 2-3-fold increase for dissolution). At both wind speeds, evaporation was dominant with rates on the order of mg/minute compared to dissolution rates in the pg/minute range. When sea water was used as the test medium, results were similar; however, the concentrations of the hydrocarbons dissolved in sea water were considerably less than when distilled water was used. This was attributed to the effect of high ionic strength on the solubility of the hydrocarbons. Increased thickness of the fuel layer increased the concentration of the dissolved hydrocarbons because evaporation was reduced. This increased the contact time between fuel components and the water. Solubility has also been found to increase with increasing concentrations of dissolved organic carbon (Air Force 1988b).

Movement of JP-4 on and in water was found to affect the important processes of evaporation and dissolution of JP-4 components. Variations in wind speed, the force responsible for mixing of fuel, created eddies in the aqueous medium that caused non-uniform variations in concentration of fuel components with water depth and increased evaporation. Experiments that examined spreading rate of a fuel film on water indicated that spreading was very rapid (Air Force 1988d). Tests showed that spreading was initially uniform, but as evaporative effects became noticeable, spreading became less uniform and the film eventually disintegrated. Rapid spreading reduced dissolution of the fuel by increasing evaporation and decreasing contact time.

5. POTENTIAL FOR HUMAN EXPOSURE

The data on the role of sediments in the fate of JP-4 and its components are contradictory. However, partitioning of jet fuel hydrocarbons to sediment does not seem to be an important fate process (Air Force 1981f; EPA 1985). Some data suggest that, under certain conditions, JP-4 hydrocarbons may adsorb to sediment and reduce volatilization (Air Force 1988b; EPA 1985). Quiescent bottle tests using natural water from a salt water marsh, a brackish polluted bay, and a freshwater river showed that volatility was reduced in sterile controls containing water and sediment compared to sterile controls containing only water (Air Force 1988b). "In contrast, when undisturbed or shaken gently, flasks containing water and sediment, or water only, and sterile control flasks containing water from the same sources exhibited no difference in the rate of disappearance of components (EPA 1985). When the flasks were shaken vigorously to imitate turbulent water conditions, volatilization of some components was reduced in the flasks with sediment and water compared to the flasks containing water only. Field and laboratory data on sediment that was dosed with JP-4 and then either returned to the pond or introduced to model laboratory systems indicate that sediment interaction of JP-4 components occurs and affects the volatility of JP-4. Sediment interactions increased persistence of JP-4 components to as much as 20 days in the field tests. Differences between laboratory and field data indicated that laboratory data were not good predictors of what would occur in the field. Evidence acquired using simulated petroleum- and shale-derived jet fuels indicates that neither the major representative components nor the JP-4 mixture have strong adsorption to standard clays or to sediments from natural fresh, brackish, or salt water sources (Air Force 1981f). The data also indicated that the magnitude of the adsorption constant on a particular sediment was dependent on the size and complexity of the dissolved hydrocarbon, the nature of the sediment, and the salinity of the water and inversely correlated with the water solubility of the dissolved hydrocarbon. Temperature and pH did not appear to have an effect on adsorption.

There are no bioconcentration data on JP-4 or JP-7; however, JP-8 was found to accumulate in flagfish exposed to concentrations ranging from 1.0 to 6.8 mg/L in the surrounding water from the egg stage to 128 days after hatching (Klein and Jenkins 1983). Similar results would be expected for JP-4 because of the similarity in composition and chemical and physical properties of these two fuels. The mean concentration of JP-8 in the whole-body tissue samples increased with increasing concentration of the water-soluble fraction (WSF) of the fuel. The bioconcentration factor (BCF), expressed as the ratio of the concentration in fish tissue to the concentration of the WSF of JP-8 in the aqueous environment, was found to be 159 (log value = 2.2). An additional experiment in adult flagfish exposed to 2.54 mg/L for a 14-day period yielded a BCF of 130 (log value = 2.1). The concentrations in liver,

muscle, and whole-body tissue following the 14-day exposure were 448, 165, and 329 mglkg wet weight of tissue. Placement of the fish in uncontaminated water showed a depuration rate similar to the accumulation rate. In 14 days, whole-body tissue levels of JP-8 were reduced by about 10%. Similar experiments in rainbow trout did not show a relationship between concentrations of JP-8 in the surrounding water and the whole-body concentration in the fish. The calculated BCF for trout was only 63-112 (log value of 1.8-2.1) indicating that the WSF of JP-8 does not concentrate as readily in this species.

5.3.2 Transformation and Degradation

5.3.2.1 Air

JP-4 has been found to react photochemically in air in the presence of nitrogen oxide compounds to form ozone (Air Force 1981b, 1982e; Carter et al. 1984). The formation of ozone decreased with increasing altitude, decreasing temperature, and decreasing ultraviolet light intensity. Initial experiments suggested that the nitrous oxide oxidation rates decreased with increasing pressure and decreasing temperature. However, further tests indicated that the temperature effect may have been an artifact of the radical source used in the simulation and that the nitrous oxide oxidation rate caused by JP-4 may actually increase with altitude. Therefore, the effect of temperature on the nitrous oxide oxidation rate is uncertain. Reactions of JP-4 in the air resulted in the formation of large amounts of aerosol material (Air Force 1981b).

5.3.2.2 Water

Data on the biodegradation of JP-4 components are mixed. Evidence from experiments using the WSF of JP-4 and water from three different natural sources (a pristine salt water marsh, a polluted brackish bay, and a pristine freshwater river) did not show any biodegradation (Air Force 1983f; EPA 1985). The authors of these studies attributed this to the rapid evaporation of the components from the water. In quiescent tests on the WSF of JP-4, biodegradation was observed in several flasks, but different results were obtained with water and/or sediment from different sources. In most tests, ethylbenzene, trimethylbenzene, and 1,4-dimethylethylbenzene were degraded. Benzene, cyclohexane, and toluene seemed to be more resistant to biodegradation. When the sample flasks were vigorously shaken to enhance hydrocarbon-sediment interactions, evidence of biodegradation of some of the component

hydrocarbons was observed. In general, the more substituted benzenes (e.g., p-xylene, ethylbenzene, methylethylbenzene, trimethylbenzene) and less volatile hydrocarbons seemed to be biodegraded. Some components were also biodegraded in similarly shaken, water-only flasks. There were some differences in biodegradation among the three water samples used, and biodegradation could not be detected in the polluted bay water. The variable results obtained with the three water sources, varying conditions, and inclusion or exclusion of sediment make it difficult to assess the relative importance of biodegradation of jet fuel in water. It is apparent, 'however, that biodegradation of at least some of the JP-4 hydrocarbons does occur. Sediment appeared to decrease biodegradation. Similar experiments using water from the same three sources supported evidence that biodegradation of JP-4 component hydrocarbons did occur (Air Force 1988b). Disappearance of hydrocarbons from the experimental flasks was compared to sterile flasks containing the same type of water or water/sediment. Measurement of biodegradation rates was difficult to determine because evaporation rates were so rapid. However, some differences between experimental and control flasks were observed and inclusion of selected radiolabeled hydrocarbons supported the assertion that biodegradation did occur and could play a role in removal of JP-4 hydrocarbons from aquatic systems, particularly under conditions that reduce volatility.

A comparison of field and laboratory data obtained from experiments on natural sediment dosed with JP-4 suggested that biodegradation did not occur in the field (Air Force 1987b). This was in contrast to laboratory data with the same sediment in which biodegradation was observed. The study authors determined that the conflicting results indicated that laboratory tests (quiescent bottles and plexiglass trays) were not good predictors of field behavior of JP-4 and its components. Studies of shallow water aquifers contaminated with JP-4 indicate that the mixture does not inhibit microbial activity and that selective aerobic biodegradation of component hydrocarbons may occur (Aelion and Bradley 1991). Results indicated that biodegradation might be limited by the available nitrogen in the ecosystem. Samples from a contaminated aquifer have also been shown to degrade aromatic JP-4 components under denitrifying (anaerobic) conditions, although at a very low rate (Hutchins et al. 1991).

5.3.2.3 Sediment and Soil

Considerable evidence exists to indicate that jet fuel is biodegraded in the soil. This is not unexpected since several components of jet fuel are known to be degraded by soil microorganisms. Application of shale-derived JP-4 to model soil core ecosystems resulted in increased production of carbon dioxide in

the system (Air Force 1981e, 1982c). Increased activity following addition of JP-4 to soil has been associated with increased microbial growth and decreased hydrocarbon residues (Song and Bartha 1990; Wang and Bartha 1990). The likely reason for this increase was increased activity of microorganisms that use the JP-4 component hydrocarbons. Laboratory comparisons of soil contaminated with JP-4 and uncontaminated soil showed that both degraded JP-4 hydrocarbons under aerobic conditions when nitrogen, phosphorus, and trace minerals were added (Yong and Mourato 1987). The uncontaminated soil had a lag time before biodegradation was initiated, whereas the contaminated soil showed immediate initiation of biodegradation. These data indicate the importance of microbial adaptation to biological breakdown of jet fuel in soil. Additional experiments in nonaerated soils showed that biodegradation of JP-4 hydrocarbons occurred under these conditions but was considerably reduced compared to degradation in aerated soils. Other studies have supported the evidence that most JP-4 degradation is aerobic (Song and Bartha 1990). In these experiments, decreased biodegradation in subsurface soils was associated with decreased oxygen. Model soil core ecosystems composed of contaminated soil taken from the site of a JP-4 spill were tested for biodegradation under a range of soil and water content conditions (Coho 1990). Two columns were vented with a mix of oxygen and nitrogen, and a control column was vented with nitrogen only. The venting rates were kept low to reduce losses through volatilization. An average of 44% of the original mass of JP-4 present in the soil (3,560 mg/kg moist soil; 4,590 mg/kg dry soil) was removed over the Sl-89-day experimental period. Biodegradation accounted for 93% of the total removed and volatilization accounted for 7%. The maximum rate of biodegradation, 14.3 mg/kg moist soil/day, occurred at a soil/water content of 72% saturation. The average rate of degradation due to microbial activity was about 10.6 mg/kg moist soil/day. Biodegradation of JP-4 has also been shown to be affected by soil type, temperature, and jet fuel concentration (Song et al. 1990). Biodegradation was greater in clay soil than sand or loam. The optimum temperature was 27 °C, with decreased degradation at higher and lower temperatures. The half-life of JP-4 in clay at 27 ºC was 3.5 weeks. Bioremediation treatment to increase the oxygen and mineral content of the soil decreased the half-life to 1.7 weeks. Some products of JP-4 metabolism appeared to be inhibitory to the microbiota, resulting in slightly decreased biodegradation rates at higher fuel concentrations (Song and Bartha 1990). At a concentration of 50 mg/g dry soil, 85% of the JP-4 had disappeared in 4 weeks, and with a concentration of 135 mg/g dry soil, 75% was degraded in 4 weeks. The components of JP-4 fuel found to be biodegradable in soil were tridecane, tetradecane and pentadecane, but undecane, dodecane and hexadecane were resistant to aerobic biodegradation (Dean-Ross 1993). Although anaerobic biodegradation of components in JP-4 fuel is slower than aerobic biodegradation, anaerobic

biodegradation of JP-4 fuel was observed in sediments. The carbon mineralization rate was most favorable at an added nitrate concentration of approximately 1 mmol and a pH of 6-7 (Bradley et al. 1992).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

JP-4 and JP-7 consist of various hydrocarbon components such as benzene, toluene, and xylene. These components can be measured in high concentrations in air, water, and soil.

5.4.1 Air

JP-4 and JP-7 enter the atmosphere through various mechanisms such as evaporation of spills, vaporization in loading and unloading operations, and burning in engines. JP-4 was detected in samples in a closed aircraft shelter that housed F-4 aircraft (Air Force 1981h). The JP-4 concentrations in the air ranged from 533 mg/m^3 (in the area of the shelter) to 1,160 mg/m^3 (in the vicinity of the refueler technician).

5.4.2 Water

Between 1986 and 1988, a hydrocarbon plume of JP-4 was discovered floating on the water table at the Federal Aviation Administration (FAA) Technical Center (Atlantic County, New Jersey) after JP-4 fuel contamination was discovered (EPA 1990b). The organic contaminants benzene, toluene, and naphthalene (identical to the components in jet fuel) were detected in groundwater samples at concentrations of 4,000, 3,100, and 1,000 ppb, respectively. The total volume of jet fuel-contaminated groundwater at the site was estimated to be 13.3 million gallons. In October of 1975, JP-4 was detected in water samples taken from the Defense Fuel Supply Center (Charleston, South Carolina) at a depth of 15 feet and at distances of 2.5 feet, 40 feet, and 50 feet from an 83,000-gallon fuel spill (Talts et al. 1977). From a distance of 25 feet, pure fuel was measured, while a concentration of 33 μg/mL was measured at 40 feet, and 22 μg/mL was measured at 50 feet.

Groundwater contamination was reported in East Bay Township, Michigan, in the vicinity of a U.S. Coast Guard Air Station (Twenter et al. 1985). The amount of toluene detected in groundwater samples was 74 μg/L. This concentration may possibly be attributed to JP-4 contamination, although

there were many other organics used on the base that could be sources of major groundwater contamination.

5.4.3 Soil

JP-4 as determined by total hydrocarbons in soil samples was detected at Robins Air Force Base (Georgia) at a depth of 1 meter in the soil around the site of a 20-year-old JP-4 spill; concentrations ranged from <0.1 µg/L at an approximate distance of 90 meters from the spill site to 180,000 µg/L within the vicinity of the fuel spill (EPA 1988a). Soil gas samples taken at 2 meters revealed a concentration ranging from <0.05 µg/L at an approximate distance of 50 meters from the fuel spill to a concentration of 310,000 µg/L in the vicinity of the fuel spill. Soil contamination of JP-4 hydrocarbons was also measured at the FAA Technical Center (Atlantic County, New Jersey); the maximum petroleum hydrocarbon concentration detected in surface soils was 284 ppm and the maximum concentration in subsurface soils was 18,500 ppm (EPA 1990b).

5.4.4 Other Environmental Media

No data were located that discussed concentrations of JP-4 or JP-7 in other environmental media such as food, fish and shellfish, or terrestrial plants and animals.

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

The National Occupational Exposure Survey, conducted by NIOSH between 1981 and 1983, estimated that 4,866 employees were exposed to JP-4 in the workplace (NOES 1990). No workplace exposure data were available for JP-7.

General population exposure to JP-4 and JP-7 is likely. However, exposure would be limited to populations living on or near Air Force bases where JP-4 and JP-7 are used in aircraft. These populations could be exposed to JP-4 and JP-7 from hydrocarbon release into air from aircraft or groundwater contaminated with spilled JP-4 or JP-7.

5. POTENTIAL FOR HUMAN EXPOSURE

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Air Force base workers engaged in fuel cell maintenance operations such as defueling and fueling aircraft and cleaning jet fuel spills are exposed to higher levels of JP-4 and JP-7 than those to which the general population is exposed (Bishop 1982). Other workers that are exposed to higher levels of JP-4 and JP-7 than the general population are component testers, engine testers, and mechanics (Knave et al. 1978). Maintenance workers who monitor fuel storage tanks may be exposed to jet fuels by inhalation or dermal exposure to draining water (due to condensation) from the fuel tanks (NIOSH 1989). Potentially high exposure through inhalation and dermal route may also occur for workers in petroleum plants that manufacture JP-4 and JP-7. Populations living on or very near Air Force bases, populations living near hazardous waste disposal sites for JP-4 and JP-7, and populations exposed as a result of spills and leaks that may occur during storage, transfer, and use of the these jet fuels are potentially exposed to higher levels of JP-4 and JP-7 than those to which the general population is exposed. However, data correlating the levels of these fuels or their biomarkers in body tissues and fluids (e.g., blood) with levels of exposure among these groups of population were not located.

Military pilots have a potentially higher risk of exposure to JP-4 and JP-7 than the general population. The concentration of JP-4 vapors sampled from the cockpit of an F-4 was 1,110 mg/m3 (Air Force 1981h).

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 JP-4 and JP-7 is available. Where adequate information is not available, ATSDR, in conjunction with 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 JP-4 and JP-7.

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. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the

identified data needs will be evaluated and prioritized, and a substance-specific research agenda may be proposed.

5.7.1 Identification of Data Needs

Physical and Chemical Properties. The values for many of the physicochemical parameters (e.g., K_{ow} K_{oc} and Henry's law constants) needed to model the fate and transport processes of JP-4 and JP-7 in the environment have not been determined. However, since these fuels are complex mixtures of hydrocarbons with small amounts of non-hydrocarbon additives, their behavior in the environment is determined by both the characteristics of the mixture and the characteristics of the individual components, making modeling based on physical and chemical properties difficult.

Production, Import/Export, Use, and Release and Disposal. Current production and import/export data are lacking and would aid in determining how pervasive the risk of exposure to JP-4 and JP-7 is to the general population. The uses of JP-4 and JP-7 are restricted to military aircraft (Air Force 1989b; IARC 1989). The primary releases to the environment come from in-flight jettisoning of fuel and from leaks and spills during storage, transfer, and use (IARC 1989; Talts et al. 1977; Twenter et al. 1985). Several disposal methods have been proposed, tested, and/or used (Elliot and DePaoli 1990; EPA 1990b; NIOSH 1989). However, data are needed on the risk posed by past disposal methods and improper disposal of the fuels.

According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit chemical release and off-site transfer information to the EPA. The Toxics Release Inventory (TRI), which contains this information for 1992, became available in May of 1994. This database will be updated yearly and should provide a list of industrial production facilities and emissions. However, since JP-4 and JP-7 are not reported under SARA Section 313, there are no data in the TRI.

Environmental Fate. The environmental fate of JP-4 has been studied extensively by the Air Force, EPA, and independent researchers. No data were located on the environmental fate of JP-7, although it can be assumed to behave in a manner similar to JP-4. Most JP-4 jettisoned in the atmosphere probably reacts photochemically to form ozone and particulates (Air Force 1981b, 1981e). Some of the fuel components or reactant products are probably transported by wind currents. The

primary fate process for JP-4 in water is volatilization, although some biodegradation and partitioning to sediment may occur (Air Force 1983f, 1988b; EPA 1985). The primary fate process for JP-4 spilled to soil is biodegradation (Air Force 1982c; Coho 1990; Song and Bartha 1990). A small fraction is likely to volatilize and some components may bind to soil particles. JP-4 that spills or leaks to soil migrates both horizontally and vertically, but that migration does not seem to be due primarily to leaching. Information on the degradation products of some of the components of JP-4 and JP-7 may be found in ATSDR profiles on benzene (ATSDR 1991a), toluene (ATSDR 1990), total xylenes (ATSDR 1991c), and polycyclic aromatic hydrocarbons (ATSDR 1991b). Components of jet fuel that migrate through the soil may contaminate groundwater (EPA 1990b; Talts et al. 1977). More information on chemical and light-mediated reactions of jet fuel components would help in assessing the persistence of jet fuel hydrocarbons in water and soil. In addition, more studies on the environmental fate of jet fuel under various water and soil conditions might provide insight into the variations in the fate of components that have been found under varying environmental conditions. Specifically, data pertaining to the interaction of JP-4 or JP-7 with various types of soils, including clays, sands, and mixtures would be useful, in order to determine horizontal and vertical migration patterns for assessing groundwater contamination in the vicinity of Air Force bases and hazardous waste sites. This information could also help in determining which jet fuel components persist in the environment and under what conditions.

Bioavailability from Environmental Media. There are no data on the absorption of JP-4 or JP-7 by the inhalation, oral, or dermal routes. However, several of the components of these fuels are known to be absorbed. For more information on absorption of individual components (e.g., benzene, xylene, toluene), see the ATSDR toxicological profiles on these compounds.

Food Chain Bioaccumulation. There are no data on the bioaccumulation or biomagnification of JP-4 or JP-7 in plants, aquatic organisms, or animals. Studies on the bioaccumulation of JP-4 and JP-7 are needed for plants, animals, and aquatic organisms, especially shellfish which, historically, have exhibited sensitivity to hydrocarbons. Data on a similar jet fuel, JP-8, suggest that bioaccumulation and biomagnification are low (Klein and Jenkins 1983). The mixtures are expected to separate into the individual components in the environment and these components are expected behave independently and differently in terms of their ability to accumulate in the food chain. For information on the bioaccumulation of the different components of JP-4 and JP-7 (e.g., benzene, xylene, toluene, ethylbenzene), see the ATSDR toxicological profiles for these compounds.

5. POTENTIAL FOR HUMAN EXPOSURE

Exposure Levels in Environmental Media. Some information exists on the levels of JP-4 and JP-7 in the air in closed buildings where the fuel is used (Air Force 1981h). Limited information was also located on levels in water and soil following spills or leaks (EPA 1988a, 1990b; Talts et al. 1977). No data were located on levels of jet fuels or component hydrocarbons in food, fish and shellfish, or terrestrial animals and plants. More data on levels in all environmental media are needed to fully assess the extent of exposure for populations with a high probability of exposure to jet fuels or their component hydrocarbons.

Exposure Levels in Humans. Certain populations are known to have a higher risk of exposure to JP-4, JP-7, and/or their component hydrocarbons. These are workers who manufacture or use the fuel; people living or working on Air Force bases where the fuel is stored and used; and populations living or working in the vicinity of a spill, leak, or dump site (Air Force 1981h; Bishop 1982; NIOSH 1989). More data are needed to assess the approximate levels of intermediate and chronic exposure for these populations.

Exposure Registries. No exposure registries for JP-4 and JP-7 were located. Components of JP-4 and JP-7 will be considered for inclusion in the National Exposure Registry in the future. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to exposure to these compounds.

5.7.2 Ongoing Studies

Investigations into the bioremediation of sites contaminated with jet fuels are providing information on the biodegradation of these compounds. Bioremediation studies are being conducted by the Department of the Interior, U.S. Geological Survey at a spill site in Charleston, South Carolina (FEDRIP 1994).

As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control and Prevention, will be analyzing human blood samples for certain components of JP-4 and JP-7 and other volatile organic compounds. These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population.

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring JP-4 and JP-7 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 JP-4 and JP-7. Rather, the intention is to identify well-established methods that are used as a the standard methods of analysis. Many of the analytical methods used to detect JP-4 and JP-7 in environmental samples are the methods approved by federal organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

6.1 BIOLOGICAL SAMPLES

No analytical methods were located for detecting either JP-4 or JP-7 in biological samples. For analytical methods information on some hydrocarbon components of jet fuels, see the ATSDR toxicological profiles for benzene (ATSDR 1991a), toluene (ATSDR 1990), xylenes (ATSDR 1991c), and polycyclic aromatic hydrocarbons (ATSDR 1991b).

6.2 ENVIRONMENTAL SAMPLES

Since JP-4 and JP-7 are composed of a complex mixture of hydrocarbons, there are few methods for the analysis of all of these components in environmental samples, but methods are reported for the analysis of some of the individual components or the amount of total hydrocarbon in the mixture (IARC 1989). The analysis of individual components usually involves separation of the components by column chromatography (i.e., packed or capillary column) followed by a suitable quantification method. These methods included gas chromatography (GC) and high-resolution gas chromatography (HRGC) combined with flame ionization detector (FID), or infrared (IR) spectroscopy. GC combined with mass spectrometry (MS) has been used to identify the principal hydrocarbon components present in jet fuels. Nuclear magnetic resonance (NMR), supercritical fluid chromatography (SFC)/FID, and laser raman spectroscopy can be used specifically to characterize the aromatic hydrocarbon makeup for

6. ANALYTICAL METHODS

JP-4 and JP-7 (Clarke et al. 1991; Di Sanzo and Yoder 1991; DOE 1981). Although no methods were located specifically for analyzing JP-7 in environmental samples, the methods used to measure the hydrocarbon components of JP-4 can be used for measuring the hydrocarbon components of JP-7. The few analytical methods that have been used are summarized in Table 6-l. Several of the jet fuel components have been discussed in detail in their individual ATSDR toxicological profiles (e.g., benzene and polycyclic aromatic hydrocarbons), which should be consulted for more information on analytical methods (ATSDR 1991a, 1991b).

Analytical methods for detecting JP-4 and jet fuel (petroleum naphtha and kerosene vapors) in air include IR spectroscopy and GC/FID (IARC 1989; NIOSH 1984; Thomas and Richardson 1981). The total hydrocarbon content of JP-4 in air can be determined by IR spectroscopy. The IR technique is best adapted to pure hydrocarbon exposures, such as exposure to JP-4. For both methods, samples are collected with either charcoal tubes or vapor monitor badges. Poor recovery (<75%) was obtained with the IR method using only Freon®113 as a desorbent. Recovery was improved (86-88%) using a mixture of Freon®1 13 and perchloroethylene. For the IR method, precision was excellent, ranging from 0.006% to 0.020% coefficient of variation (CV). Recoveries with the GCLFID method were excellent (97-101%) (NIOSH 1984; Thomas and Richardson 1981). For the GC/FID method, precision was also excellent (0.052% relative standard deviation [RSD]) (NIOSH 1984). Sensitivity for both methods is in the ppm range (IARC 1989; NIOSH 1984; Thomas and Richardson 1981).

GC/FID, HRGCLFID, and IR spectroscopy have been used to measure JP-4 in water (Puyear et al. 1981; Roberts and Thomas 1986). GCLFID was used to measure the major water-soluble hydrocarbons, the aliphatics and alkylbenzenes, of JP-4 (Puyear et al. 1981). The average recovery of all hydrocarbons tested (aliphatics and alkylbenzenes) was 43-72%; however, the recovery of the aliphatics only was 90-94% (Puyear et al. 1981). Overall recovery was improved from 43% to 72% with the use of ethyl acetate as an extraction solvent for JP-4. Under the chromatographic conditions used, the individual aliphatics were not well resolved. However, the alkylbenzenes were well separated and quantitation of each component was possible (Puyear et al. 1981). Sensitivity and precision were not reported (Puyear et al. 1981). The total hydrocarbon content of JP-4 in water can also be determined by IR spectroscopy (EPA 1978; Roberts and Thomas 1986) and fluorescence spectroscopy (ASTM 1982). Since JP-4 has a distinctive gas chromatographic profile, it is possible to distinguish JP-4 from other fuels present in environmental samples by examining selected peak areas or peak ratios for certain hydrocarbons (Roberts and Thomas 1986).

TABLE 6-1. Analytical Methods for Determining JP-4 and JP-7 in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (JP-4)	Collect air samples on charcoal tubes or vapor monitor badges; desorb hydrocarbons with Freon®113/ perchloroethylene (for IR method);	IR	0.4 mg/m^3	86-88	Thomas and Richardson 1981
	desorb with carbon disulfide (for GC/FID method)	GC/FID	NR	≥98	NIOSH 1984
Air (petroleum naptha and kerosene vapors)	Collect air sample on charcoal tube; desorb with carbon disulfide; inject aliquot	GC/FID	5 mg/m^3	97	IARC 1989; NIOSH 1984
Water (JP-4)	Concentrate water-soluble hydrocarbon components of JP-4 on Sep-Pak®; elute with ethyl acetate	GC/FID	NR	72	Puyear et al. 1981
Water (Total petroleum hydrocarbon)	Sample acidified to pH <2 extracted with Freon®113, extract passed through silica gel absorbent (EPA Method 418.1)	IR	<1 mg/L	NR	EPA 1978
Water (total petroleum hydrocarbon)	Extract with cyclohexane (ASTM D3650)	Fluorescence spectroscopy	NR	NR	ASTM 1982
Groundwater (JP-4)	Extract water sample with Freon®113; analyze by IR	IR	NR	NR	Roberts and Thomas 1986
	Extract water sample with isooctane three times; dry with anhydrous sodium sulfate; analyze by GC/FID	HRGC/FID	NR	NR	Roberts and Thomas 1986
Soil (JP-4)	Extract sample with methylene chloride in ultrasonic bath; clean up on microcolumn	GC/FID; GC/MS	NR	83.9	Vandegrift and Kampbell 1988

FID = flame ionization detector; GC = gas chromatography; HRGC = high-resolution gas chromatography; IR = infrared spectroscopy; JP-4 = jet propellant-4; JP-7 = jet propellant-7; MS = mass spectrometry; NR = not reported.

GC/FID has been used to quantify JP-4 in soil samples, while GC/MS has been used to identify the principal components in JP-4 (Vandegrift and Kampbell 1988). Sample preparation for GC/FID included extracting the fuel from soil with methylene chloride in an ultrasonic bath. Recovery was good (83.9%). Precision was adequate (12.6% CV). Sensitivity was in the low-ppm range (Vandegrift and Kampbell 1988).

Other methods reported for the analysis of the aromatic components in aircraft fuels, including JP-4, include HRGC combined with an ultraviolet detector (UVD), photoionization detector (PID), and GC combined with a nitrogen specific alkali-flame detector (AFD) (Air Force 1982a). Sample preparation includes fractionation of the fuel into an aromatic fraction and a nonaromatic fraction. The fractionation is accomplished by using adsorption column chromatography with silica gel, alumina, or Florisil. The aromatic fraction is then eluted using moderately polar solvents such as methylene chloride, benzene, or ethyl ether. The UV detector is specific for aromatic compounds. The estimated detection limits for benzenes and naphthalenes were 10 µg/mL and 2 µg rnL, respectively. Precision ranged from 5% to 10%. The photoionization detector is about 10 times as sensitive as a UVD or FID for the detection of aromatic hydrocarbons, although it does not provide the selectivity obtainable with the UVD. Nitrogen-containing compounds in fuels are detected using a nitrogen-specific AFD. A gas chromatographic method involving the simultaneous use of a UVD, FID, and AFD was recommended as a rapid, inexpensive, and selective method for the analysis of aircraft fuels (Air Force 1982a).

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 JP-4 and JP-7 is available. Where adequate information is not available, ATSDR, in conjunction with 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 JP-4 and JP-7.

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. This definition should not be

interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda may be proposed.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. No biomarkers of exposure were identified for JP-4 or JP-7. No standard procedures exist for identifying or quantifying exposure to JP-4 or JP-7 in biological media. Therefore, it is not possible to state whether existing methods are sensitive to measure background levels in the population or levels at which health effects occur. Biomonitoring studies are needed to adequately assess exposure to JP-4 and JP-7.

No biomarkers of effect were found for JP-7. Potential biomarkers for neurological effects of JP-4 are mild muscular weakness, staggering gait, and decreased sensitivity to painful stimuli (Davies 1964). No standard procedures exist for identifying and quantifying these biomarkers of effect for JP-4.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Methods exist for measuring the hydrocarbon components of jet fuels, specifically JP-4, in air, water, and soil (IARC 1989; NIOSH 1984; Puyear et al. 1981; Roberts and Thomas 1986; Thomas and Richardson 1981; Vandegrift and Kampbell 1988). Although no methods were located specifically for analyzing JP-7 in environmental samples, the methods used to measure the hydrocarbon components of JP-4 can be used for measuring the hydrocarbon components of JP-7. These methods are relatively sensitive, selective, and reliable and can be used to detect the levels of jet fuel components found in the environment and levels at which health effects occur. Sensitivity and precision data are needed for measuring the components in water. These data will aid in comparison of sensitivity and precision between methods and indicate where improvements in sensitivity are needed. This information will be useful in monitoring contamination in the environment,

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control and Prevention, is developing methods for the analysis of certain components of JP-4 and JP-7 and other volatile organic compounds in blood. These methods

use purge and trap methodology and magnetic sector mass spectrometry which gives detection limits in the low parts per trillion range.

No other ongoing studies were located for JP-4 or JP-7.

7. REGULATIONS AND ADVISORIES

The international, national, and state regulations and guidelines regarding JP-4 and JP-7 in air, water, and other media are summarized in Table 7- 1. There are only a few regulations that are specific to JP-4 and JP-7, but there are more regulations on the major components of JP-4 and JP-7.

ATSDR has derived an intermediate-duration inhalation MRL of 9 mg/m^3 for JP-4, based on an increase in hepatic toxicity observed in mice at 500 mg/m^3 (Air Force 1984b).

ATSDR has derived a chronic-duration inhalation MRL of 0.3 mg/m^3 for JP-7, based on an increase in hepatic toxicity observed in rats at 150 mg/m^3 (Air Force 1991).

Under the Hazardous Materials Transportation Act, aviation fuel is designated as a hazardous substance subject to special requirements for packaging, labeling, and transportation (DOT 1989). EPA has established guidelines to control air pollution from aircraft and aircraft engines (EPA 1982e, 1982f) and underground storage tank regulations for petroleum products (EPA 1988e).

7-1. Regulations and Guidelines Applicable to Jet Fuels[a]

Agency	Description	Information	Reference
INTERNATIONAL			
IARC	Carcinogenic classification of jet fuel	Group 3[b]	IARC 1989
NATIONAL			
Regulations:			
a. Air:			
AFOSH	PEL TWA (petroleum distillates [naphtha])	400 ppm	Air Force 1989b
	STEL (15 minutes) (petroleum distillates [naphtha])	500 ppm	Air Force 1989b
OSHA	PEL TWA (petroleum distillates [naphtha])	500 ppm	OSHA 1989 (29 CFR 1910.1000)
b. Other			
DOT	Hazardous Material Transportation Act: Aviation fuel is designated as a hazardous material subject to requirements for packaging, shipping, and transporting. (See fuel, aviation)	Yes	DOT 1989 (49 CFR 172.101 Appendix A)
EPA	Technical Standards and Corrective Action Requirements for Owners and Operators of Underground Storage Tanks (UST)	Yes	40 CFR 280 EPA 1988e
Guidelines:			
a. Air			
ACGIH	TLV TWA (gasoline) STEL (15 minutes) (gasoline)	300 ppm 500 ppm	ACGIH 1994 ACGIH 1994
EPA	Control of air pollution from aircraft and aircraft engines	Yes	EPA 1982e (40 CFR 87), 1982f
USAF OEHL	TLV TWA (informal guideline) -JP-4 STEL (informal guideline)-JP4	200 ppm 300 ppm	Air Force 1983d Air Force 1983d
c. Other			
EPA	Domestic water supply must be virtually free from oil and grease, particularly from the tastes and odors that emanate from petroleum products.	Yes	EPA 1986a
	Clean Water Act: Oil and grease are designated as conventional pollutants. Effluent limitations for oil and grease (polynuclear aromatic hydrocarbons) exist for almost all point sources under the general pretreatment standards for new and existing sources.	Yes	EPA 1988b (40 CFR 403.2), 1988c (40 CFR 401.16)

[a]International, national, and state regulations and guidelines regarding JP-4 and JP-7 in air, water and other media.

[b]Group 3 = Not classifiable as to human carcinogenicity.

ACGIH = American Conference of Governmental Industrial Hygienists; AFOSH = Air Force Office of Safety and Health; CFR = Code of Federal Regulations; DOT = Department of Transportation; EPA = Environmental Protection Agency; IARC = International Agency for Research on Cancer; JP-4 = jet propellant-4; JP-7 = jet propellant-7; OEHL = Occupational and Environmental Health Laboratory; OSHA = Occupational Safety and Health Administration; PEL = Permissible Exposure Limit; STEL = Short-Term Exposure Limit; TLV = Threshold Limit Value; TWA = Time-Weighted Average; USAF = United States Air Force

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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 chemi”Ea1 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, bnt serves as technical guidance to assist federal, state, and local officials.

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 Concentratiorq$_{(LO)}$ (LC_{50}) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

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

Lethal Time$_{(LO)}$ (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 dose of a chemical that is likely to be without an appreciable risk of adverse noncancerous effects 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.

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 µg/L for water, mg/kg/day for food, and µg/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 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 3 11 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.

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 Shour
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 non-technical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or chemical 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 chemical.

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.

The descriptive sentences (bullets) at the end of section 1.4 can be used to link significant health effects seen in humans and animals to chemical concentration and duration of exposure. These bullets give the reader a capsule understanding of the essential exposure-duration-effect relationships that have been developed in greater details throughout the rest of the profile. Significant effects at low and high doses are presented wherever the data permit.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1, 2-2, and 2-3) and figures (2-l and 2-2) are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, minimal risk levels (MRLs) to humans for noncancer endpoints, 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. Use the LSE tables and figures 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. 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), or Cancer Effect Levels (CELs). The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 2-l and Figure 2-l 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-l

(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 exists, 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

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Figure 2-l) and oral (LSE Figure 2-2) routes. Not all substances will have data on each route of exposure and will not therefore have all five of the tables and figures.

(2) Exposure Period Three exposure periods - acute (less than 15 days), intermediate (15 to 364 days), and chronic (365 days or more) are presented within each relevant route of exposure. In
this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect the major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(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 derive a NOAEL and a Less Serious LOAEL (also see the 2 " 18r" data points in Figure 2-l).

(5) Species The test species, whether animal or human, are identified in this column. Section 2.4, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 2.3, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(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 JP-4 and JP-7 via inhalation for 6 hours per day, 5 days per week, for 3 weeks. For a more complete review of the dosing regimen refer to the appropriate sections of the text or the original reference paper, i.e., Nitschke et al. 1981.

(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, 1 systemic effect (respiratory) was investigated.

(8) NOAEL A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest dose 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 endpoint used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(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 epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

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

LEGEND

See 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 concentrations for particular exposure periods.

(13) Exposure Period 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 exists. The same health effects appear in the LSE table.

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

(16) NOAEL In this example, 18r NOAEL is the critical endpoint for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates to 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 1 of 3 studies for which Cancer Effect Levels were derived. The diamond symbol refers to a Cancer Effect Level for the test species-mouse. 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 the 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

1 →

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

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect)		Reference
					Less serious (ppm)	Serious (ppm)	
2 → INTERMEDIATE EXPOSURE							
	5	6	7	8	9		10
3 → Systemic	↓	↓	↓	↓	↓		↓
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE							
					11		
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

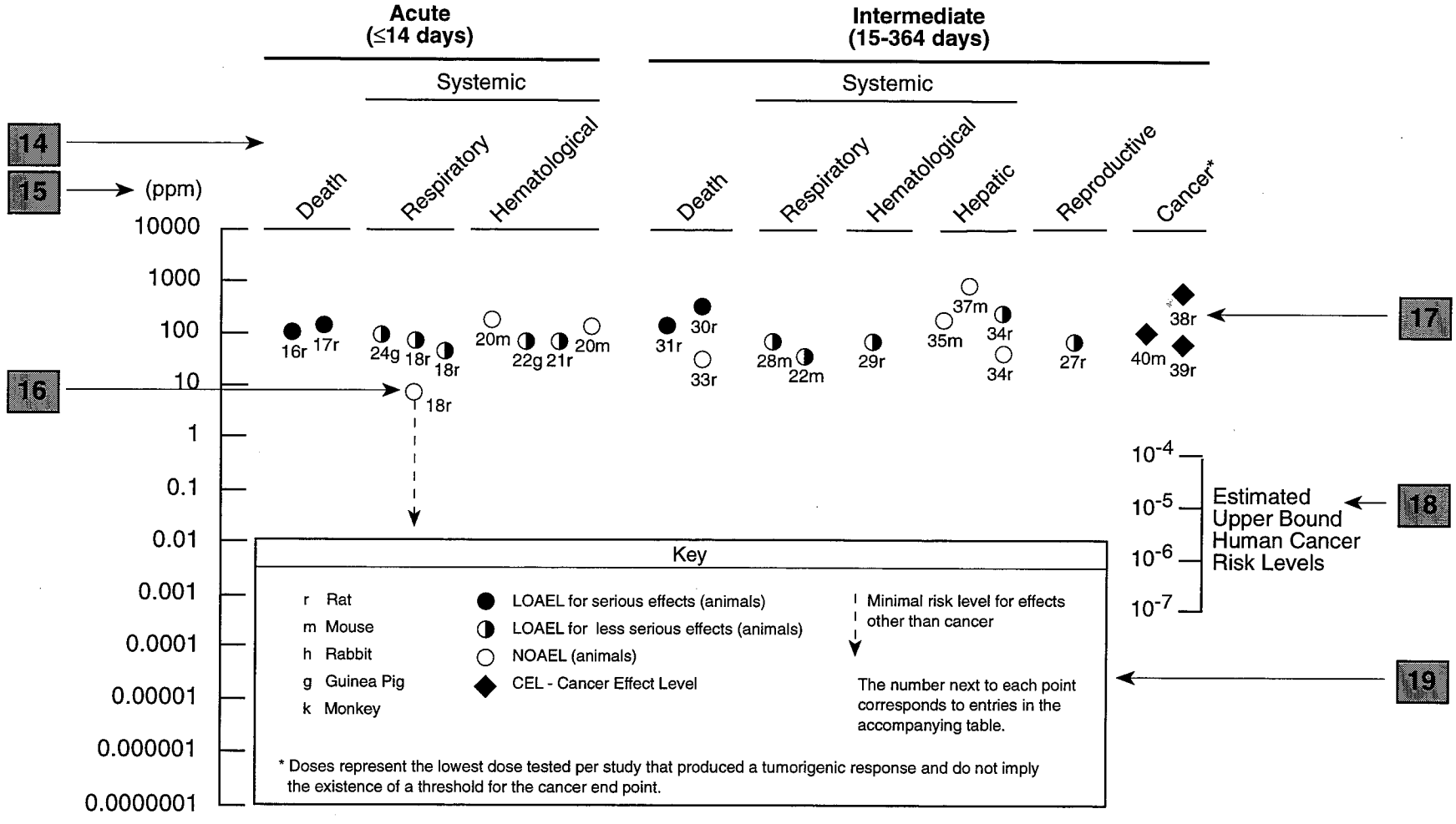
[a] The number corresponds to entries in Figure 2-1.

12 → [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 = days(s); hr = hour(s); LOAEL = lowest-observed-adverse-effect level; mo = month(s); NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s)

SAMPLE

13 → **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 toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health endpoints 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 covers endpoints in the same order they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, 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. Minimal risk levels (MRLs) for noncancer endpoints (if derived) and the endpoints from which they were derived are indicated and discussed.
Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, we have derived minimal risk levels (MRLs) for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action; but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2.4, “Relevance to Public Health,” contains basic information known about the substance. Other sections such as 2.7, “Interactions with Other Chemicals”, and 2.8, “Populations that are Unusually Susceptible” provide important supplemental information.

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To derive an MRL, ATSDR generally selects the most sensitive endpoint which, in its best judgement, represents the most sensitive human health 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 systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen endpoint 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. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both 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 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
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BSC	Board of Scientific Counselors
C	Centigrade
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
d	day
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
F	Fahrenheit
F_1	first filial generation
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
fpm	feet per minute
ft	foot
FR	Federal Register
g	gram
GC	gas chromatography
gen	generation
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
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient

L	liter
LC	liquid chromatography
LC_{Lo}	lethal concentration, low
LC_{50}	lethal concentration, 50% kill
LD_{Lo}	lethal dose, low
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
m	meter
mg	milligram
min	minute
mL	milliliter
mm	millimeter
mm Hg	millimeters of mercury
mmol	millimole
mo	month
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
ng	nanogram
nm	nanometer
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	proportionate 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

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STEL	short term exposure limit
STORET	STORAGE and RETRIEVAL
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TRI	Toxics Release Inventory
TWA	time-weighted average
U.S.	United States
UF	uncertainty factor
yr	year
WHO	World Health Organization
wk	week

>	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

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