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 on the toxicology of used mineral-based crankcase oil. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

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

This profile will focus on the properties of *used* mineral-based crankcase oil because most of the mineral-based crankcase oil at hazardous waste sites is expected to be previously used oil. It is important to make the distinction between new and used mineral-based crankcase oil because the characteristics of mineral-based crankcase oil change with use (Vazquez-Duhalt 1989). An important difference between new and used motor oil is the heavy metal content. This difference is extremely important because many of the metals are harmful to human health and living organisms. These metals originate from the fuel and from motor wear. Used oil contains high concentrations of lead, zinc, calcium, barium, and magnesium along with lower concentrations of iron, sodium, copper, aluminium, chromium, manganese, potassium, nickel, tin, silicon, boron, and molybdenum (Vasquez-Duhalt 1989). Concentrations of lead in used mineral-based crankcase oil were likely higher when leaded gasoline was used.

Mineral-based crankcase oils are manufactured using highly refined base oils and contain up to 20% of a variety of additives such as viscosity index improvers, detergents/dispersants, antiwear additives, pour-point depressants, and antioxidants (IARC 1984; Kirk-Othmer 1981). During use, the high temperatures and friction cause changes such as oxidation, nitration, and cracking of polymers in the component chemicals (Vazquez-Duhalt 1989). In addition, a variety of substances such as fuel, water, antifreeze, dust, and various combustion products such as polycyclic aromatic hydrocarbons (PAHs), metals, and metallic oxides accumulate in the oil. The degree of chemical change and accumulation of

contaminants in the oil increases with use and varies depending on the type of fuel used and the mechanical properties of the engine.

In an engine lubricating system, the required quantity of lubricant is transported where it is needed in the engine. The lubricant protects against wear, reduces friction, cleans the engine of dirt and residue (detergent), protects against corrosion, cools the engine, and seals the pistons (Van Donkelaar 1990). Additives are added to lubricating oils to improve its physical and chemical properties. Consequently, lubricating oils have high additive contents (up to 20%), especially detergents and dispersants which constitute 2-15% of oil weight (Vasquez-Duhalt 1989). However, several of the oil additives are toxic environmental contaminants, e.g., zinc dithiophosphate and zinc diary1 or dialkyl dithiophosphates (ZDTPs); calcium alkyl phenates; magnesium, sodium, and calcium sulphonates; tricresyl phosphates; molybdenum disulfide; heavy metal soaps; and other organometallic compounds that contain heavy metals. Hence, very high levels of zinc and cadmium are found in new motor oil-approximately 1,500 μg/g of zinc and 87 μg/kg of cadmium (Hewstone 1994a; Vasquez-Duhalt 1989). Although ZDTPs have a low acute systemic toxicity, they can cause eye damage and skin irritation (Hewstone 1994a). Prolonged exposure to high concentrations of ZDTPs, calcium alkyl phenates, and magnesium, sodium, and calcium sulphonates had significant effects on the reproductive organs of male rabbits (testicular atrophy and reduction or absence of spermatozoa) which appeared to be species specific. The absorption of tricresyl phosphates caused peripheral nervous system damage, leading to neuromuscular problems (Hewstone 1994a).

In a crankcase-lubricated engine, the oil compartment acts as a sink for heavy molecular incomplete combustion products such as PAHs and their analogs (Scheepers and Bos 1992). Thus, contaminants such as PAHs, which are formed via combustion, can accumulate in the oil by a factor of up to 1,000. PAHs are known to be highly toxic environmental contaminants with carcinogenic and mutagenic properties. They leave the engine in various ways, such as via particulates, oil leaks, and uncontrolled oil changes, which then accumulates in the environment. One hundred and forty different PAHs have been found in the used oil of crankcase-lubricated engines. These PAHs are also preseni'in much lower quantities in new or fresh oil (Van Donkelaar 1990).

Used mineral-based crankcase oil is a complex mixture of metals and PAHs. When motor oils undergo thermal decomposition, gasoline combustion products are formed, significantly increasing the levels of PAHs which contribute to the carcinogenic and mutagenic properties of the oils (Bingham

1988; Ingram et al. 1994). Hence, it is difficult to define the precise composition of used mineralbased crankcase oil because of the variety of chemical additives that may be present and the varying degrees of chemical decomposition and contaminant accumulation. Therefore, rather than describing toxicities associated with individual components, the following discussion focuses on information obtained in studies that have examined the effects of exposure to samples of used mineral-based crankcase oil. In several studies, composite samples of used mineral-based crankcase oil have been employed; these studies may therefore provide a more generalized picture of toxicities associated with exposure. However, it should be noted that the results of any one study may not be representative of effects occurring with similar exposures to other samples of used mineral-based crankcase oil.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others 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, reproductive, developmental, 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. “Serious” effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). “Less serious” effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, “less serious” LOAEL, or “serious” LOAEL, and’that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between “less serious” and “serious” effects. The distinction between “less serious” effects and “serious” effects is considered to be important because it helps the users of the profiles to

identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining 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 Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others 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 or exposure levels below which no adverse effects have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of used mineral-based crankcase oil are indicated in Table 2-3.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

2.2.1 Inhalation Exposure

2.2.1.1 Death

No studies were located regarding death in humans or animals after inhalation exposure to used mineral-based crankcase oil.

2.2.1.2 Systemic Effects

No studies were located regarding musculoskeletal or renal effects in humans or animals after inhalation exposure to used mineral-based crankcase oil.

The systemic effects observed after inhalation exposure are discussed below. Although some qualitative information was located for cardiovascular, gastrointestinal, hematological, hepatic, dermal and ocular effects, NOAELs and/or LOAELs for these effects were not identified. The highest

NOAEL value for respiratory effects in guinea pigs after an acute-duration inhalation exposure to used mineral-based crankcase oil is recorded in Table 2-1 and plotted in Figure 2-1.

Respiratory Effects. Ten-minute exposures of volunteers to aerosols of used mineral-based crankcase oils resulted in mild-to-moderate nose and throat irritation (Dautrebande and Capps 1950). If a respiratory filter mask was worn, the degree of irritation was decreased to none-to-mild even at twofold higher concentrations. Insufficient information was provided in the report to convert the exposure levels used in this study, expressed as ppm by weight, to mg/m^3. In another study in which inhalation exposures occurred as the result of leakage of the aerosol from inside goggles designed to assess ocular exposures, chest tightness (but no nose irritation) was reported (Dautrebande et al. 1951). Concentrations of the used mineral-based crankcase oil in ambient air were not measured in this study; however effects were observed in one of three volunteers exposed within the goggles to 42 mg/m^3 and in another to 84 mg/m^3. Both of these studies are limited in that they were conducted over 40 years ago and are of limited value in predicting effects of current formulations that have been used in present-day engines. No studies were located regarding the respiratory effects in humans after longer term exposure to aerosols of used mineral-based crankcase oil.

Guinea pigs exposed for 1 hour to an aerosol of used mineral-based crankcase oil at concentrations as high as 222 mg/m^3 showed no adverse effects on pulmonary function (Costa and Amdur 1979a). Studies in animals on the respiratory effects of longer-term exposures were not found.

Cardiovascular Effects. Blood pressure was elevated in 37% of the mechanics, 7% of the apprentice mechanics, and 18% of the miscellaneous workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). However, interpretation of these results is severely limited because of the absence of comparison with a control population, the likelihood of dermal as well as inhalation exposures, the high probability of exposure to other causative substances, and the failure to consider other confounding factors.

No studies were located regarding cardiovascular effects in animals after inhalation exposure to used mineral-based crankcase oil.

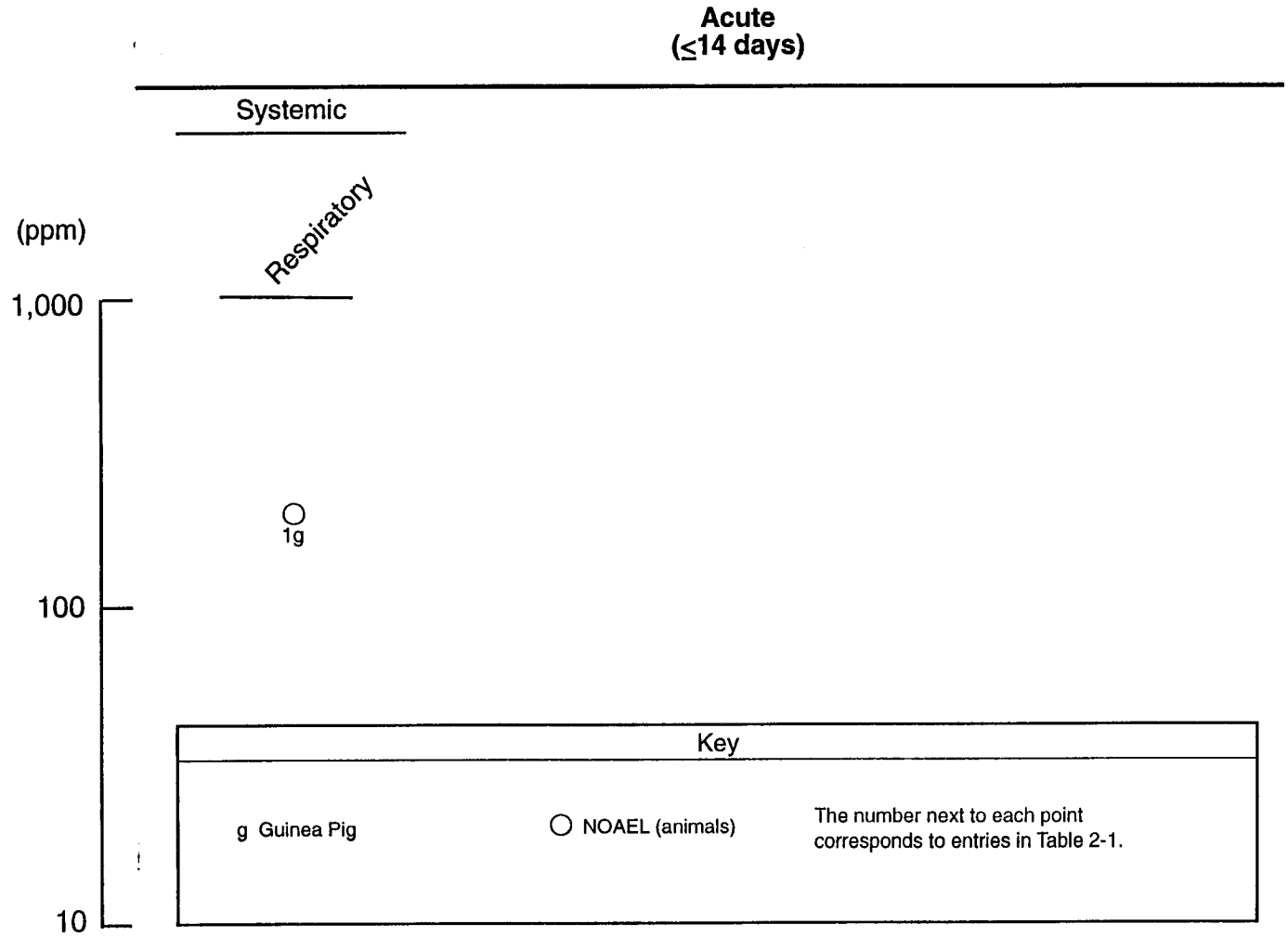
TABLE 2-1. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Inhalation

Key [a] to figure	Species (strain)	Exposure duration/ frequency	System	NOAEL (ppm)	LOAEL (effect)		Reference
					Less serious (ppm)	Serious (ppm)	
ACUTE EXPOSURE							
Systemic							
1	Gn pig (NS)	1 hr	Resp	222			Costa and Amdur 1979a

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

Gn pig = guinea pig; hr = hour; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; NS = not specified; Resp = respiratory

Figure 2-1. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Inhalation



Gastrointestinal Effects. The incidence of gastrointestinal effects (stomach pain, constipation, anorexia) did not appear to be increased in an epidemiologic study of mechanics and apprentice mechanics from auto shops in Denmark (Clausen and Rastogi 1977). As indicated above under Cardiovascular Effects, interpretation of these results is severely limited because of the absence of a comparison with a control population, the likelihood of dermal as well as inhalation exposures, the high probability of exposure to other causative substances, and the failure to consider other confounding factors.

No studies were located regarding gastrointestinal effects in animals after inhalation exposure to used mineral-based crankcase oil.

Hematological Effects. Lower than normal hematocrit and mean corpuscular hemoglobin were observed in several mechanics and apprentice mechanics in an epidemiologic study examining health effects among auto shop workers (Clausen and Rastogi 1977). A significant correlation was seen between the lead level and delta-aminolevulinic acid dehydratase (δ-ALAD) activity in the blood of both normal subjects and autoworkers (Spear-man's rank analysis, $p < 0.001$). In the blood of autoworkers, the δ-ALAD activity was depressed because of the higher blood lead levels. The lead levels in whole blood of all autoworkers was significantly higher than that of control subjects (Wilcoxon's test, $p < 0.002$) (Clausen and Rastogi 1977). Elevated blood lead levels were observed in 52% of the mechanics when compared to levels in controls not employed in the auto industry (Wilcoxon's test, $p < 0.002$). In several cases, the elevated lead levels correlated with decreases in hematocrit and mean corpuscular hemoglobin, suggesting that the effects may have been related to blood lead levels (Clausen and Rastogi 1977). Eastin et al. (1983) demonstrated that in ducks and pheasants fed diets containing up to 4.5% of used mineral-based crankcase oil, δ-ALAD was significantly decreased (ANOVA and Tukey's HSD test, $p <0.05$). No effects on hematocrit or hemoglobin concentration were seen. δ-ALAD is one of the most sensitive and one of the first enzymes in the pathway for heme synthesis which is inhibited by lead. In the absence of effects on hemoglobin and hematocrit, it is an early biological indicator of subclinical lead poisoning in humans and birds (Goyer 1996).

The study by Eastin et al. (1983) suggests that used oil is a source of lead exposure and hematoxicity in mechanics (Clausen and Rastogi 1977). Other studies by Blakley and Brockman (1976), Osweiler

et al. (1973), and Sas (1989) also support the conclusion that lead poisoning is a probable hazard from exposure to used crankcase oils. High blood lead levels have been associated with anemia (see the ATSDR profile on lead [ATSDR 1993b]). Although used mineral-based crankcase oil was determined to be one source of lead exposure, other sources of lead exposure (exhaust gas, gasoline, gear oil) may also have contributed to the effects observed.

No studies were located regarding the hematological effects of used mineral-based crankcase oil in animals after inhalation exposure.

Hepatic Effects. Increased serum bilirubin and thymol reaction (indicative of increased serum alkaline phosphatase) were observed in 14% of the mechanics examined in a study of auto shops in Denmark (Clausen and Rastogi 1977). In addition, 11% of the mechanics had elevated serum alanine and aspartate aminotransferase and lactate dehydrogenase activities, suggesting hepatic damage. However, it is unclear whether dermal exposures, substances other than used mineral-based crankcase oil, or diseases unrelated to employment may have contributed to the effects observed. Also, it is unknown whether these effects were significantly increased relative to a control population.

No studies were located regarding hepatic effects in animals after inhalation exposure to used mineral-based crankcase oil.

Dermal Effects. Skin irritation has been reported in epidemiological and experimental studies of humans after exposure to used mineral-based crankcase oil (Clausen and Rastogi 1977; Dautrebande and Capps 1950). However, these effects were probably due to direct contact of aerosols or volatile components with these tissues and will be discussed under the section dealing with effects of dermal exposures.

No studies were located regarding dermal effects in animals after inhalation exposure to used mineral-based crankcase oil.

Ocular Effects. Eye irritation has been reported in epidemiological and experimental studies of humans after exposure to used mineral-based crankcase oil (Clausen and Rastogi 1977; Dautrebande and Capps 1950). However, these effects were probably due to direct contact of aerosols or volatile

components with these tissues and will be discussed under the section dealing with effects of dermal exposures.

No studies were located regarding ocular effects in animals after inhalation exposure to used mineral-based crankcase oil.

2.2.1.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological and lymphoreticular effects in humans or animals after inhalation exposure to used mineral-based crankcase oil.

2.2.1.4 Neurological Effects

Examination of workers from 10 auto shops in Denmark revealed headaches in the morning among 14% and headaches in the evening among 20% of the mechanics (Clausen and Rastogi 1977). Tremors in the hands were reported by 11% of the mechanics. However, as indicated above under Cardiovascular Effects, interpretation of these results is severely limited because of the absence of a comparison with a control population, the likelihood of dermal as well as inhalation exposures, the high probability of exposure to other causative substances, and the failure to consider other confounding factors.

Exposure of rats (head-only) to an aerosol of filtered used mineral-based crankcase oil (concentration not specified) for 7 hours resulted in no adverse effects on behavior during a 40-day postexposure observation period (DOT 1983). Similarly, no adverse effects were observed in chickens during or following a 7-hour exposure to an aerosol of used mineral-based crankcase oil (concentration not specified). The chickens were placed in either head-only exposure chambers or given whole body exposures. The motor oil tested was obtained from a turboprop aircraft (used for 165 hours). The study was limited as the actual dose in the breathing space and particle size was not measured, and only a small number of animals were tested. No control group was used. (DOT 1983).

No studies were located regarding the following health effects in humans or animals after inhalation exposure to used mineral-based crankcase oil.

2.2.1.5 Reproductive Effects

2.2.1.6 Developmental Effects

2.2.1.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.5.

2.2.1.8 Cancer

An epidemiological study of the incidence of renal pelvic and bladder cancer among workers in Sweden between 1961 and 1979 showed no significant increases in relative risk among workers exposed to motor oil or oil mists (excluding mists from cutting oils or fluids) (Steineck et al. 1989). This study was limited as the time, dose, and route of exposure were not provided. Also confounding factors were not separated out, the substances that subjects were exposed to were not clearly defined, and the job descriptions of the workers may have been erroneous. No studies were located regarding the incidence of other cancer types among humans exposed by inhalation to used mineral-based crankcase oil.

No studies were located regarding cancer in animals after inhalation exposure to used mineral-based crankcase oil.

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding death in humans after oral exposure to used mineral-based crankcase oil.

No deaths were observed in rats for up to 14 days after ingestion of 22,500 mg/kg of used mineral-based crankcase oil (API 1980b; Beck et al. 1984; Vernot et al. 1990). However, increased mortality was observed among cattle believed to have ingested discarded used mineral-based crankcase oil (Osweiler et al. 1973). Tissue lead levels were elevated in the cattle, and toxic symptoms observed in the affected cattle were attributed to ingestion of lead contained in the used oil. Fatalities among

cattle ingesting used mineral-based crankcase oil have also been attributed to molybdenum contained in the used oil (Sas 1989). It was suggested that the ingested molybdenum caused death as a result of central nervous system hypoxia.

2.2.2.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, musculoskeletal, renal, or ocular effects in humans or animals after oral exposure to used mineral-based crankcase oil. The systemic effects observed after oral exposure are discussed below. The highest NOAEL and LOAEL values for systemic effects in rats after an acute-duration oral exposure to used mineral-based crankcase oil are recorded in Table 2-2 and plotted in Figure 2-2.

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans after oral exposure to used mineral-based crankcase oil.

No effects were observed in rats for up to 14 days after ingestion of 22,500 mg/kg of used mineral-based crankcase oil, while a single oral dose of 9,000 mg/kg of used mineral-based crankcase oil resulted in oily diarrhea in exposed rats (API 1980b; Beck et al. 1984; Vemot et al. 1990). Diarrhea was also observed in some cattle that grazed for at least 2 weeks in a pasture contaminated with used mineral-based crankcase oil (Sas 1989). This effect is not unexpected because medicinal-grade mineral oil is used as a cathartic (Fingl 1980); however, other chemicals present in used mineral-based crankcase oil may have contributed to the laxative effect.

Hematological Effects. No studies were located regarding hematological effects in humans after oral exposure to used mineral-based crankcase oil.

Anemia was observed in cattle that had ingested an unknown amount of used mineral-based crankcase oil while grazing in a pasture (Sas 1989). The used oil had molybdenum bisulfide present as an additive. The anemia was attributed to increased molybdenum intake and molybdenum-induced copper deficiency. No effects on hematocrit or hemoglobin concentration were observed in ducks and pheasants given diets containing up to 4.5% used mineral-based crankcase oil (Eastin et al. 1983). However, δ-ALAD activity was significantly decreased in the ducks and pheasants in a dose-related manner at all dietary concentrations (0.5%, 1.5%, and 4.5%) (ANOVA and Tukey's HSD test,

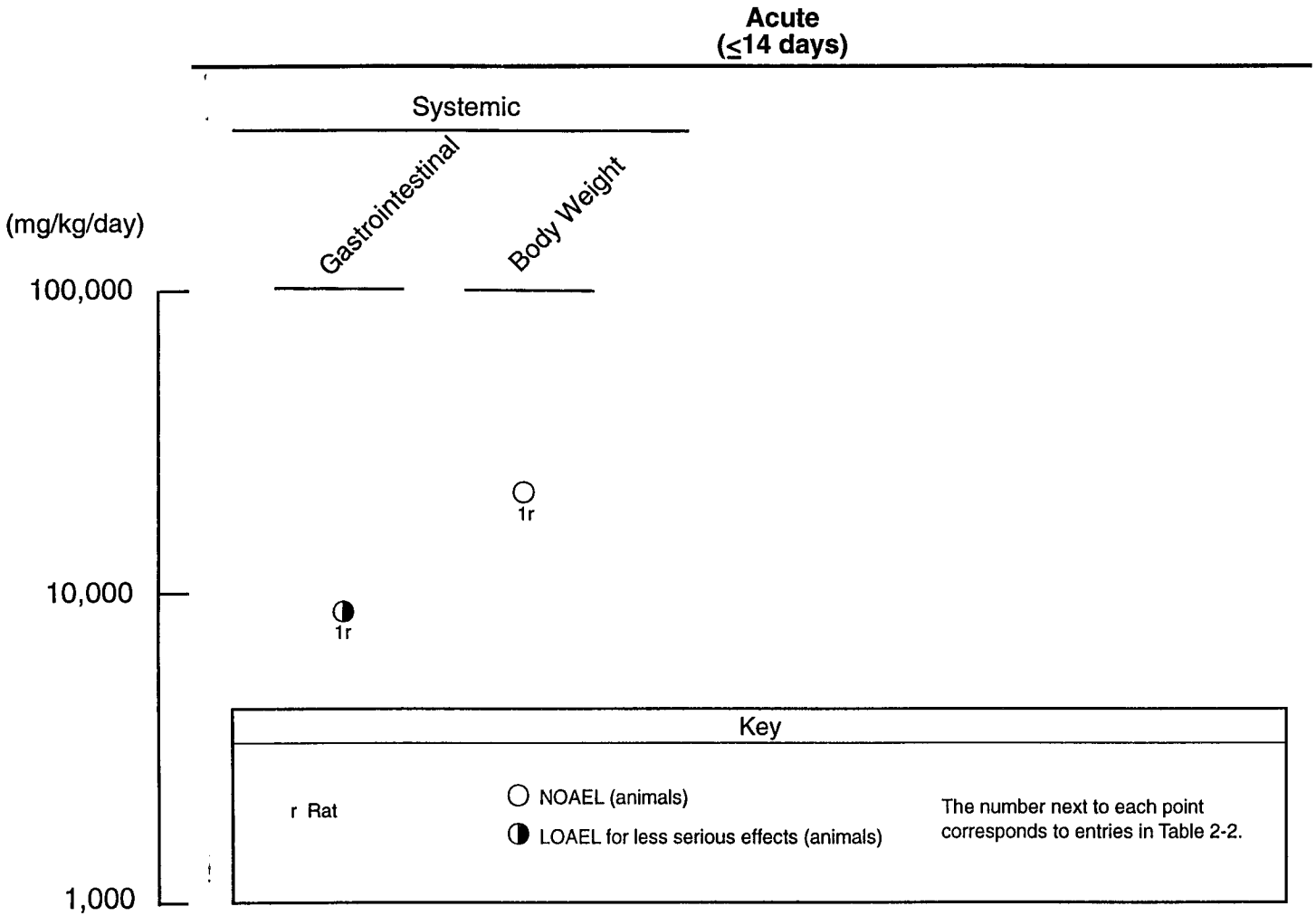
TABLE 2-2. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Oral

Key [a] to figure	Species (strain)	Exposure duration/ frequency (specific route)	System	NOAEL (mg/kg/day)	LOAEL (effect)			Reference
					Less serious (mg/kg/day)		Serious (mg/kg/day)	
ACUTE EXPOSURE								
Systemic								
1	Rat (Sprague Dawley)	once (G)	Gastro		9000	(oily diarrhea)		API 1980; Beck et al. 1984; Vernot et al. 1990
			Other	22500				

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

(G) = gavage; Gastro = gastrointestinal; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level

Figure 2-2. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Oral



p <0.05). The decrease in δ-ALAD activity suggests an effect on heme synthesis, but in the absence of effects on hemoglobin concentration or hematocrit, the toxicological significance of this change is unclear. δ-ALAD is one of the most sensitive and one of the first enzymes in the pathway for heme synthesis which is inhibited by lead. In the absence of effects on hemoglobin and hematocrit, it serves as an early biological indicator of subclinical lead poisoning in humans and birds (Goyer 1996).

Hepatic Effects. No studies were located regarding hepatic effects in humans after oral exposure to used mineral-based crankcase oil.

The only information located regarding hepatic effects after oral exposure to used mineral-based crankcase oil was a study that showed a significant increase in serum aspartate aminotransferase activity in ducks after 3 weeks of dietary exposure at a dietary concentration of 4.5% (Eastin et al. 1983) (ANOVA and Tukey's HSD test, p <0.05). No effects were observed on the serum levels of alanine aminotransferase, uric acid, glucose, triglycerides, total protein, and cholesterol after l-3 weeks of dietary exposure of ducks and pheasants to dietary concentrations of used mineral-based crankcase oil as high as 4.5%.

Dermal Effects. No studies were located regarding dermal effects in humans after oral exposure to used mineral-based crankcase oil.

Cattle that ingested used mineral-based crankcase oil in a pasture for at least 2 weeks had decreased pigmentation in the hair around the eyes (Sas 1989). This effect may have been the result of a molybdenum-induced copper deficiency. No other information was located regarding dermal effects in animals after oral exposure to used mineral-based crankcase oil.

Body Weight Effects. No studies were located regarding body weight effects in humans after oral exposure to used mineral-based crankcase oil.

No effects on body weight gain or growth were observed in rats that received single doses of used mineral-based crankcase oil as high as 22,500 mg/kg (API 1980b; Beck et al. 1984; Vernot et al. 1990) or in ducks or pheasants that ingested an unspecified amount of used mineral-based crankcase oil in their diets for up to 3 weeks (Eastin et al. 1983). The lack of effects on body weight gain or

growth probably indicates that higher doses of used crankcase oil in the diet would have been tolerated.

2.2.2.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological or lymphoreticular effects in humans or animals after oral exposure to used mineral-based crankcase oil.

2.2.2.4 Neurological Effects

No studies were located regarding neurological effects in humans after oral exposure to used mineral-based crankcase oil.

Cattle that ingested an unspecified amount of used mineral-based crankcase oil as a result of grazing in contaminated pastures for approximately one year have shown a number of neurological disorders (Osweiler et al. 1973; Sas 1989). Blindness, muscle twitching, hyperirritability, depression, and convulsions were observed and attributed to lead poisoning (Osweiler et al. 1973). Muscle tremors and weakness were observed in another study (Sas 1989). These effects may be associated with molybdenum-induced copper deficiency.

No studies were located regarding the following health effects in humans or animals after oral exposure to used mineral-based crankcase oil.

2.2.2.5 Reproductive Effects

2.2.2.6 Developmental Effects

2.2.2.7 Genotoxic Effects

Genotoxicity studies are discussed in Section 2.5.

2.2.2.8 Cancer

No studies were located regarding cancer in humans or animals after oral exposure to used mineral-based crankcase oil.

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding death in humans after dermal exposure to used mineral-based crankcase oil.

Contact of 5 mL/kg (4,500 mg/kg) of used mineral-based crankcase oil with either abraded or intact sites on the backs of rabbits (approximately 30% of the total surface area of the rabbits) for 24 hours resulted in no mortality (API 1980b; Beck et al. 1984; Vemot et al. 1990). No increase in death rate was reported in a skin-painting study in mice in which 1,667 mg/kg was applied to the backs of male C3WHeJ mice (precise area of application was not specified) twice per week for 2 years (API 1983). Negative controls included a group of mice that were untreated and one group that was treated with toluene. Positive controls included a group that was treated with 0.05% or 0.15% benzo(a)pyrene (a known carcinogen) in toluene. Survival was slightly decreased in mice treated with used motor oil at weeks 91 (22% survival versus 36% in controls) and 104 (10% versus 22% in controls). The study is limited as only one dose was studied and only males were used (API 1983).

2.2.3.2 Systemic Effects

No studies were located regarding musculoskeletal effects in humans or animals after dermal exposure to used mineral-based crankcase oil. The systemic effects observed after dermal exposure are discussed below: The highest NOAEL and LOAEL values for each end point in each species and duration category after dermal exposure to used mineral-based crankcase oil are recorded in Table 2-3.

TABLE 2-3. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Dermal

Species (strain)	Exposure duration/ frequency (specific route)	System	NOAEL	LOAEL (effect) Less serious		Serious		Reference
ACUTE EXPOSURE								
Systemic								
Rabbit (New Zealand White)	2 wks 5d/wk 24hr/d	Hepatic	8 mL/kg					API 1980; Beck et al. 1984
		Renal	8 mL/kg					
		Dermal				8 mL/kg	(acanthosis, chronic inflammation, dermal congestion, edema, hyperkeratosis, hair loss)	
		Other		8 mL/kg	(decreased food consumption, 18% weight loss)			
Rabbit (New Zealand White)	24 hr	Dermal		5 mL	(slight erythema)			API 1980; Beck et al. 1984; Vernot et al. 1990
Rabbit (New Zealand White)	24 hr	Dermal		0.5 mL	(very slight erythema)			API 1980; Beck et al. 1984; Vernot et al. 1990

TABLE 2-3. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Dermal (continued)

Species (strain)	Exposure duration/ frequency (specific route)	System	NOAEL (mg/kg/day)	LOAEL (effect) Less serious (mg/kg/day)		Serious (mg/kg/day)		Reference
Rabbit (New Zealand White)	once	Ocular		0.1 mL				API 1980; Beck et al. 1984; Vernot et al. 1990
INTERMEDIATE EXPOSURE								
Systemic								
Gn pig (albino)	3.5 wks 3x/wk 6hr/d	Dermal		0.5 mL	(none-to-slight erythema)			Vernot et al. 1990
Immuno/Lymphor								
Gn pig (albino)	3.5 wks 3x/wk 6hr/d		0.5 mL					API 1980; Beck et al. 1984
CHRONIC EXPOSURE								
Systemic								
Mouse (C3H/HeJ)	104 wks 2d/wk	Dermal				1667 mg/kg	(acanthosis, hyperkeratosis, and fibrosis of skin)	API 1983
		Body wt	1667 mg/kg					

TABLE 2-3. Levels of Significant Exposure to Used Mineral-based Crankcase Oil - Dermal (continued)

Species (strain)	Exposure duration/ frequency (specific route)	System	NOAEL (mg/kg/day)	LOAEL (effect)			Reference
				Less serious (mg/kg/day)	Serious (mg/kg/day)		
Cancer							
Mouse (C3H/HeJ)	104 wks 2d/wk				1667 mg/kg	(CEL - dermal papillomas, keratocanthomas, squamous cell carcinomas, and hemangiosarcomas)	API 1983
Mouse (CFLP)	104 wks 2x/wk				60 mg/kg	(CEL - dermal papillomas and carcinomas)	Grimmer et al. 1982a, 1982b, 1983
Mouse (C3H/HeJ)	approx 79 wks 3x/wk				900 mg/kg	(CEL - dermal papillomas and carcinomas)	McKee and Plutnick 1989
Mouse (C3H/HeJ)	104 wk 2x/wk				1667 mg/kg	(CEL - skin)	Schreiner and Mackerer 1982; University of Cincinnati 1980

approx = approximately; Body wt = body weight; CEL = cancer effect level; d = day(s); Gn pig = guinea pig; hr = hour(s); Immuno/Lymphor = Immunological and Lymphoreticular; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level; wk(s) = week(s); x = time(s)

Respiratory Effects. Volunteers, whose eyes were exposed to aerosols of used mineral-based crankcase oil at concentrations ranging from 42 to 84 mg/m^3 in specially designed goggles, reported chest tightness (Dautrebande et al. 1951). The method of exposure used in this study was designed to limit inhalation exposures, but it is unlikely that inhalation exposure was completely prevented. Thus, it is unclear whether the chest tightness represented an effect stemming directly from the ocular exposure or whether inhalation of the test material contributed to the feeling of chest tightness. Furthermore, the data were collected over 40 years ago, and formulations have changed considerably since that time.

No increase in the incidence of pneumonia was noted in mice that received dermal doses of 1,667 mg/kg/day, applied to their backs twice a week, for 2 years. However, this study is limited in that only half of the animals treated (n=50) were examined histologically (API 1983).

Cardiovascular Effects. High blood pressure was noted in 37% of the mechanics, 7% of the apprentice mechanics, and 18% of the miscellaneous workers examined in a study of workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). However, interpretation of these results is severely limited because of the absence of comparison with a control population, the likelihood of inhalation as well as dermal exposures, the high probability of exposure to other causative substances, and the failure to consider other confounding factors such as diseases unrelated to exposure.

No studies were located regarding cardiovascular effects in animals after derrnal exposure to used mineral-based crankcase oil.

Gastrointestinal Effects. The incidence of gastrointestinal effects such as stomach pain, constipation, or anorexia was not increased in a group of mechanics and apprentice mechanics from auto shops in Denmark (Clausen and Rastogi 1977). However, interpretation of these results is severely limited-because of the absence of comparison with a control population, the likelihood of inhalation as well as dermal exposures, the high probability of exposure to other causative substances, and the failure to consider confounding factors.

No studies were located regarding gastrointestinal effects in animals after dermal exposure to used mineral-based crankcase oil.

Hematological Effects. Lower than normal hematocrit and mean corpuscular hemoglobin were observed in a number of mechanics and apprentice mechanics in a study of workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). Elevated blood lead levels were observed in 52% of the mechanics when compared to controls. In several cases, the elevated lead levels were correlated with the decreases in hematocrit and mean corpuscular hemoglobin, suggesting that the effects may have been related to blood lead levels. High blood lead levels have been associated with anemia (see the ATSDR profile on lead [ATSDR 1993b]). Used mineral-based crankcase oil was determined to be one source of lead exposure, but other sources of lead exposure (exhaust gas, gasoline, gear oil) may have been contributors.

No studies were located regarding hematological effects in animals after dermal exposure to used mineral-based crankcase oil.

Hepatic Effects. Increased serum levels of bilirubin and thymol reaction (indicative of increased serum alkaline phosphatase) were observed in 14% of the mechanics examined in a study of workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). Elevated serum alanine and aspartate aminotransferase and lactate dehydrogenase were also found in 11% of the mechanics. However, interpretation of these results is limited because of the absence of comparison with a control population, the likelihood of inhalation as well as dermal exposures, the high probability of exposure to other causative substances, and the failure to consider other confounding factors (such as diseases unrelated to employment).

Histopathological analysis of livers of rabbits dermally exposed to 8 mL/kg of used mineral-based crankcase oil on a 4-inch-square area of their backs for 5 days/week for 2 weeks showed no marked increase in adverse effects on the liver (API 1980b; Beck et al. 1984; Vemot et al. 1990). No studies regarding the hepatic effects of longer-term dermal exposure of animals to used mineral-based crankcase oil were located.

Renal Effects. No studies were located regarding renal effects in humans after dermal exposure to used mineral-based crankcase oil.

Histopathological analyses of kidneys and urinary bladders from rabbits given dermal applications of 8 mL/kg of used mineral-based crankcase oil on a 4-inch-square area of their backs 5 days/week for 2 weeks showed no adverse effects (API 1980b; Beck et al. 1984; Vernot et al. 1990). No increase in the incidence of renal necrosis or chronic interstitial nephritis was observed in mice receiving dermal doses of 1,667 mg/kg/day on their backs, twice a week, for 2 years (API 1983). However, this study is limited in that only half of the animals treated were examined histologically.

Dermal Effects. Rashes on the hands or arms were reported by 29% of the mechanics in a study of workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). However, interpretation of this result is difficult because other chemical exposures may have contributed to the effects observed.

A single 5-mL dose of used mineral-based crankcase oil maintained in contact with abraded and intact skin on the backs of rabbits (approximately 30% of the total surface area) for 24 hours caused slight erythema (API 1980b; Beck et al. 1984; Vemot et al. 1990). At 0.5 mL, the amount of erythema noted in the l-inch-square area of application after a 24-hour exposure was very slight, and no redness was observed on either intact or abraded sites on rabbits by 72 hours postexposure. Daily application of 8 mL/kg of used mineral-based crankcase oil to a 4-inch-square area on the backs of rabbits for 24 hours/day, 5 days/week, for 2 weeks resulted in irritation at the application site and hair loss on adjacent tissues. Histopathological examination of the skin showed acanthosis, chronic inflammation, dermal congestion, edema, and hyperkeratosis (API 1980b; Beck et al. 1984). In contrast, daily application of 0.5 mL of used mineral-based crankcase oil to a l-inch-square area on the back of guinea pigs for 6 hours/day, 3 days/week, for 3.5 weeks resulted in only none-to-slight erythema (API 1980b; Beck et al. 1984; Vemot et al. 1990). Dermal application of 1,667 mg/kg (50 mg applied to an unspecified area on the backs of each animal) two times a week for 104 weeks resulted in a slightly increased incidence of acanthosis and hyperkeratosis and slightly increased severity of fibrosis in C3H/HeJ mice (API 1983).

Dermal exposure of rats to 125-167 mg/kg/day of used mineral-based crankcase oil for 3 days resulted in increased activity of microsomal enzyme activity of the skin (Rahimtula et al. 1982). Similar

effects were observed following a single dose of an unspecified amount of used mineral-based crankcase oil (Rahimtula et al. 1984). This is considered to be an adaptive effect.

Ocular Effects. Mild-to-moderate eye irritation was reported by volunteers exposed to aerosols of used mineral-based crankcase oil (Dautrebande and Capps 1950; Dautrebande et al. 1951). Although considerable variability in individual sensitivities was observed, mild eye irritation was observed in at least one of the subjects at exposure levels as low as 18.9 mg/m^3. It is likely that the eye irritation was due to direct contact of the aerosol with the eye.

Instillation of 0.1 mL of used mineral-based crankcase oil into the eyes of rabbits resulted in slight swelling and conjunctival redness in the eye of only one of the six rabbits tested (API 1980b; Beck et al. 1984; Vernot et al. 1990). Thus, the oil was classified as nonirritating.

Body Weight Effects. No studies were located regarding body weight effects in humans after dermal exposure to used mineral-based crankcase oil.

Exposure of a 4-inch-square area on the backs of rabbits to 8 mL/kg of used mineral-based crankcase oil for 24 hours/day, 5 days/week, for 2 weeks resulted in marked decrease in food consumption and weight loss (API 1980b; Beck et al. 1984; Vernot et al. 1990). The biological basis for the decreased food consumption was not identified. In contrast, application of a somewhat lower dose (1,667 mg/kg/day) to an unspecified area on the backs of mice 2 days/week for 2 years resulted in no effect on body weight gain (API 1983).

2.2.3.3 Immunological and Lymphoreticular Effects

No studies were located regarding immunological or lymphoreticular effects in humans after dermal exposure to used mineral-based crankcase oil.

No sensitization was observed in guinea pigs when challenged 2 weeks after a 3 day/week, 3.5-week exposure to 0.5 mL/day (API 1980b; Beck et al. 1984; Vernot et al. 1990). However, the positive control group also did not exhibit sensitization. Other studies examining the immunological effects of used mineral-based crankcase oil after dermal exposure were not located. The NOAEL for

sensitization after acute-duration dermal exposure to used mineral-based crankcase oil is recorded in Table 2-3.

2.2.3.4 Neurological Effects

Examination of workers from 10 auto shops in Denmark revealed headaches in the morning among 14% and headaches in the evening among 20% of the mechanics (Clausen and Rastogi 1977). Tremors of the hands were reported by 11% of the mechanics. It is unclear whether the incidence of these findings are elevated relative to those in a control population. Also, exposures to substances other than used mineral-based crankcase oil, as well as other confounding factors (such as lifestyle or preexisting diseases) may have contributed to the effects observed.

No studies were located regarding neurological effects in animals after dermal exposure to used mineral-based crankcase oil.

2.2.3.5 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals after dermal exposure to used mineral-based crankcase oil.

2.2.3.6 Developmental Effects

No studies were located regarding developmental effects in humans or animals after dermal exposure to used mineral-based crankcase oil.

2.2.3.7 Genotoxic Effects

Genotoxic carcinogens exert their carcinogenic effects by damaging DNA. There are two types of genotoxic carcinogens: (1) direct acting carcinogens (or ultimate carcinogens), which bind directly to DNA and other cellular macromolecules, and (2) precarcinogens (or procarcinogens), which have to be bioactivated either directly or indirectly to ultimate carcinogens. These ultimate carcinogens, which are electrophilic in nature, are highly reactive. They bind directly to DNA to form DNA adducts, producing tumors. Polycyclic aromatic compounds (PAHs), for example, benzo[a]pyrene, are among

the various chemical carcinogens found in this second category. Bioactivation occurs mainly in the liver but also in the lung and skin. Most of the reactions in this process, which converts certain chemically stable compounds to chemically reactive metabolites, are catalyzed by the cytochrome P450 (CYP450)-dependent monooxygenase systems. Most aromatic compounds like the PAHs are converted to epoxides, which are extremely reactive metabolites, by the CYP450 system. These epoxides bind to DNA to form DNA adducts, resulting in necrosis and/or cancer (Lu 1991).

In humans, absorption of PAHs after therapeutic or occupational exposure occurs mainly through the skin. Inhalation exposure is less likely. No studies were located regarding mutagenic or clastogenic effects in humans following dermal exposure to used mineral-based crankcase oil. However, dermal application of used mineral-based crankcase oil to the shaved backs of mice produced DNA adducts in the skin and the lungs, indicating that used mineral-based crankcase oil was genotoxic (Carmichael et al. 1990; Schoket et al. 1989). A single application of about 50 mg of used gasoline or diesel engine crankcase oil to the shaved backs of male Parkes mice produced adducts in DNA isolated from the skin 24 hours after treatment. Analysis of the adducts by thin-layer chromatography showed that the number and variety of adducts found in the skin with oil from gasoline-powered engines was greater than that observed with either unused oil or oil from diesel engines. No adducts were observed in the lung following a single application, but lung adducts were observed after treatment on 4 consecutive days (Schoket et al. 1989). Similar to the effects in the skin, oil from gasoline-powered engines produced a response in the lungs, but the number and variety of adducts found in the lung were less than in the skin. The levels of skin ($p < 0.05$) and lung DNA ($p < 0.01$) adducts produced by gasoline engine oil correlated with an index of oil use (calculated as the product of miles since the last oil change and total engine mileage). The total PAH concentration in gasoline engine oil proved to be a good predictor of adduct levels. When adduct levels were compared with the concentrations of individual PAHs in the oil, the best correlation was with benz(a)anthracene; skin DNA, $\delta = 0.91$ ($p < 0.0l$) and lung DNA, $\delta = 0.96$ ($p < 0.01$). The correlation with benzo(a)pyrene was poor, and was not statistically significant (Carmichael et al. 1990).

To identify further the PAHs responsible for the major adducts, Carmichael et al. (1992) fractionated one of the samples of used gasoline engine oil studied by Carmichael et al. (1990). They then painted the fractions on the shaved backs of male Parkes mice (four/group), and identified the adducts formed in skin DNA. In addition, individual PAHs dissolved in unused motor oil at concentrations similar to those detected in the unfractionated used oil were evaluated in this assay. Based on this analysis, the

major adducts produced in mouse skin by used gasoline engine oil were attributed to reactive metabolites of the PAHs benzo(*b*)naphtho(1,2-*d*)thiophene, benzo(*c*)phenanthrene, benzo(*g,h,i*)-fluoranthene, chrysene, benzo(*a*)pyrene, and benzo(*g,h,i*)perylene, several of which are known genotoxins and carcinogens (ATSDR 1990c). The study authors did not provide any explanation for the different PAHs implicated in the two studies. However, the concentrations of benzo(*c*)phenanthrene, benzo(*g,h,i*)fluoranthene and chrysene were significantly correlated with adduct levels in the study by Carmichael et al. (1990).

Other genotoxicity studies are discussed in Section 2.5.

2.2.3.8 Cancer

An epidemiological study of the incidence of renal pelvic and bladder cancer among workers in Sweden between 1961 and 1979 showed no significant increases in relative risk among workers exposed to motor oil or oil mists other than mists from cutting oils or fluids (Steineck et al. 1989). This study was limited as the time, dose, and route of exposure were not provided. Also, confounding factors were not separated out, the substances subjects were exposed to were not clearly defined, and the job descriptions of the workers may have been erroneous. No studies were located regarding the incidence of other types of cancer among humans dermally exposed to used mineral-based crankcase oil.

Several studies have examined the dermal carcinogenicity of used mineral-based crankcase oil in mice (API 1983; Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989). These studies have shown that the incidence of dermal papillomas and carcinomas among male C3H/HEJ mice (API 1983; McKee and Plutnick 1989) and female CFLP mice (Grimmer et al. 1982a, 1982b, 1983) are increased after chronic-duration dermal exposure to used mineral-based crankcase oil from gasoline-powered cars. The greatest tumor incidence was observed in mice exposed to oil from cars driven the longest distances prior to removing the oil (McKee and Plutnick 1989), and no tumors were observed in mice exposed to unused motor oil (API 1983; McKee and Plutnick 1989), indicating that carcinogens accumulated in the oil during its use. The increase in carcinogenicity was attributed to accumulation of PAHs in the oils because the tumor incidence correlated with PAH content of the oil (McKee and Plutnick 1989). Fractionation of the oil showed tumor induction only with the fraction containing PAHs with more than three rings (Grimmer et al. 1982a, 1982b, 1983). In contrast, a study by Ingram

et al. (1994) of the main mutagenic components of a carcinogenic oil by fractionation and testing in the modified Ames assay showed that the mutagenicity of PAHs with l-3 rings was greater than that of PAHs with 4-6 rings. The authors concluded that the 4-6 ring PAHs were not the main mutagenic components of the oil examined, and therefore the mutagenic components may be different from the carcinogenic components. In contrast to used mineral-based crankcase oil from gasoline-powered automobiles, used mineral-based crankcase oil from diesel-powered automobiles showed no increase in tumor incidence, even when the diesel-powered automobiles were driven extremely long distances prior to removal of the oil (McKee and Plutnick 1989). The CELs for dermal tumors observed in mice after chronic-duration exposure to used mineral-based crankcase oil are recorded in Table 2-3.

In the past, increased mutagenicity and cancer mortality have been associated with exposure to the PAHs present in complex mixtures such as skin oils of roofing workers (Wolff et al. 1982), used metalworking cutting oils or mineral oils (Apostoli et al. 1993; Bingham 1988; Cruickshank and Squire 1950; Eyres 1981; Roy et al. 1988), diesel soot particles (Vogl and Elstner 1989), coal tar (Clonfero et al. 1986; Jongeneelen et al. 1988c; Wheeler et al. 1981), petroleum products (Witschi et al. 1987), cigarette smoke, diesel exhausts, and air pollution (Bond et al. 1988; Gallagher et al 1990; Iyer et al. 1990; Schenker et al. 1984; Siemiatycki et al. 1988; Woskie et al. 1988). The carcinogenic potential of these complex mixtures is related to their PAH content. Benzo[a]pyrene (BaP), a PAH, is mainly associated with the carcinogenicity of complex mixtures. However, a study by Warshawsky et al. (1993) showed that BaP alone was not responsible for the observed potency of these mixtures. The presence of other low carcinogenic compounds, e.g., methylbenz[a]anthracenes and straight chain aliphatics, can also contribute to carcinogenicity. It is possible that these compounds may play a role in the formation of tumors following exposure to used mineral-based crankcase oils.

2.3 TOXICOKINETICS

Used mineral-based crankcase oil is a complex mixture of PAHs and metals. Consequently, it is difficult to determine its toxicokinetics because of the extensive variability in its composition and also because of a lack of definitive data for either humans or animals. However, a brief discussion of the toxicokinetics of the toxic components of used crankcase oil e.g., heavy metals such as lead, cadmium, chromium amongst others, and PAHs is provided. Additional information regarding the toxicokinetics of individual components of used mineral-based crankcase oil can be found in ATSDR profiles for the components.

No human studies were located regarding the toxicokinetics of used mineral-based crankcase oil. Only a very limited number of animal studies were located. Data based on studies of poisoning in cattle indicate that lead and other metals in used mineral-based crankcase oil may be absorbed and distributed to various tissues following oral exposure and that the feces is a significant path of excretion (Blakely and Brockman 1976; Osweiler et al. 1973). Limited rodent data indicate that, following oral exposure, used mineral-based crankcase oil is absorbed and excreted in the feces. PAHs found in used mineral-based crankcase oil are absorbed and distributed to various tissues as indicated by the presence of PAH-DNA adducts in the skin and lungs of male mice that were dermally exposed to used mineral-based crankcase oil. As PAHs are lipophilic compounds, they are mainly stored in adipose tissue and secreted in milk (Lu 1991). In both humans and animals, lead is stored in the skeletal and soft tissue pool, cadmium is accumulated in the kidneys, while molybdenum is stored somewhat in the liver and rapidly excreted in the urine and in the bile. The half-life of cadmium is 30 years, and hence, is excreted very slowly. The kidney is the primary target organ of cadmium. It damages the renal proximal tubules, forming lesions and causing urinary excretion of small-molecule proteins, amino acids and glucose. Chromium also damages the proximal tubules (Lu 1991). No other information regarding the toxicokinetics of used mineral-based crankcase oil was located.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

No studies were located regarding the absorption of used mineral-based crankcase oil in humans or animals after inhalation. Insufficient information was available from inhalation toxicity studies to determine whether absorption through the respiratory tract may have occurred.

2.3.1.2 Oral Exposure

No studies were located regarding the absorption of used mineral-based crankcase oil in-humans after oral exposure.

The few animal studies available indicate that lead and other metals in used mineral-based crankcase oil may be absorbed following ingestion (Blakley and Brockman 1976; Osweiler et al. 1973; Sas 1989). Ingestion of used mineral-based crankcase oil was determined to be the source of elevated

tissue lead levels in 22 cases of lead toxicosis in cattle (Blakley and Brockman 1976). Blood lead levels (0.98 ppm) from cattle with lead poisoning from all sources (oil, batteries, paint, chemical, and unknown) averaged 13-fold higher than in controls. A mean blood lead level of 0.78 ppm was measured in another study of cattle (80 cases) with lead poisoning (Osweiler et al. 1973). The source of the lead was determined to be ingestion of used mineral-based crankcase oil in 29% of the cases. In neither study was information provided on the dose, duration of exposure, or absorption rates. Molybdenum levels were elevated by two orders of magnitude in the livers and kidneys of cattle that ingested used mineral-based crankcase oil known to contain molybdenum bisulfide as an additive (Sas 1989).

2.3.1.3 Dermal Exposure

No studies were located regarding the absorption of used mineral-based crankcase oil in humans after dermal exposure.

The few studies available indicate that PAHs found in used mineral-based crankcase oil can penetrate the outer layer of skin as shown by the finding of PAH-DNA adducts in the skin of male mice receiving a single dermal application or four daily applications of used mineral-based crankcase oil (≈40-50 mg) (Carmichael et al. 1990; Schoket et al. 1989). PAH-DNA adducts were also found in the lungs, suggesting that PAHs found in used mineral-based crankcase oil or metabolites may be systemically available following dermal application (Carmichael et al. 1990; Schoket et al. 1989).

2.3.2 Distribution

Petroleum hydrocarbons are lipophilic. Therefore, they would tend to distribute in fatty tissue (Rozman and Klaassen 1996). Among the metals found in used mineral-based crankcase oil, lead is stored in skeletal tissue, cadmium accumulates in the kidneys, and molybdenum tends to accumulate in the liver (Goyer-1996). Specific data regarding the distribution of components of used mineral-based crankcase oil following different routes of exposure can be found in compound specific ATSDR Profiles.

2.3.2.1 Inhalation Exposure

No studies were located regarding the distribution of used mineral-based crankcase oil in humans or animals after inhalation exposure.

2.3.2.2 Oral Exposure

No studies were located regarding the distribution of used mineral-based crankcase oil in humans after oral exposure.

Studies of poisoning in cattle indicate that metals found in used mineral-based crankcase oil are distributed to various tissues (Blakley and Brockman 1976; Osweiler et al. 1973; Sas 1989). In studies examining the distribution of lead, the kidneys appear to be the major site of lead accumulation (Blakley and Brockman 1976; Osweiler et al. 1973). Lead levels were elevated ≈100-fold, 24-fold, 4-fold, and 460-fold in the kidney, liver, brain, and rumen contents, respectively. The respective values were statistically different ($p<0.05$) for all tissues except the brain. The rumen contents exhibited a high degree of variability. The source of the lead was determined to be ingestion of used mineral-based crankcase oil in 22 cases (Blakley and Brockman 1976). In another study of cattle (80 cases) with lead poisoning, mean tissue levels of lead were 29.7 and 57.7 ppm in the liver and kidney, respectively (Osweiler et al. 1973). The source of the lead was determined to be ingestion of used mineral-based crankcase oil in 29% of the cases. Molybdenum concentrations in the livers and kidneys of cows that ingested used mineral-based crankcase oil known to contain molybdenum bisulfide as an additive were found to exceed normal physiological concentrations by two orders of magnitude (Sas 1989). Very limited information on the dose and duration of exposure was provided in these studies.

2.3.2.3 Dermal Exposure

No data were located regarding the distribution of used mineral-based crankcase oil in humans after dermal exposure.

Animal data indicate that PAHs found in used mineral-based crankcase oil are found in tissues other than the skin of dermally exposed mice (Carmichael et al. 1990; Schoket et al. 1989). PAH-DNA

adducts were found in both the skin and lungs of male mice receiving either one or four daily applications of used mineral-based crankcase oil (≈1,333-1,780 mg/kg) (Carmichael et al. 1990; Schoket et al. 1989).

2.3.3 Metabolism

No studies were located regarding the metabolism of used mineral-based crankcase oil in humans or animals.

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

No studies were located regarding the excretion of used mineral-based crankcase oil in humans or animals after inhalation exposure.

2.3.4.2 Oral Exposure

No studies were located regarding the excretion of used mineral-based crankcase oil in humans after oral exposure.

Very limited animal data, based on a study of lead poisoning in cattle (90 cases), indicate that the feces is a significant path of excretion (Blakley and Brockman 1976). Lead levels in the feces were >160-fold the normal level. The source of the lead was determined to be ingestion of used mineral-based crankcase oil in 22 cases (Blakley and Brockman 1976). No data on dose, duration of exposure, or excretion rates were provided. Rats given a single oral dose (9,000 or 22,500 mg/kg) of used mineral-based crankcase oil excreted the oil in the feces as evidenced by dose-related increases in oily diarrhea (API 1980b; Beck et al. 1984; Vernot et al. 1990). However, it is unclear whether the oil excreted in the feces represented mainly unabsorbed oil.

2.3.4.3 Dermal Exposure

No studies were located regarding the excretion of used mineral-based crankcase oil in humans or animals after dermal exposure.

2.4 MECHANISMS OF ACTION

Although the toxicity of used mineral-based crankcase oil has not been fully investigated, the toxicity of used oil is attributed to additives and contaminants in the oil such as PAHs, lead, molybdenum, chromium, zinc, cadmium, copper, and silicon. New (unused) mineral-based crankcase oil and refinery streams are, by comparison, relatively nontoxic (API 1979, 1980a, 1983; Beck et al. 1984). In contrast, systemic toxicity and death in cattle that ingested used mineral-based crankcase oil had been attributed in one instance to lead accumulation in the oil (Osweiler et al. 1973), and in another to molybdenum present as an additive in the oil that was ingested (Sas 1989). The toxicity in the report by Sas (1989) was attributed to molybdenum present in the used oil. The molybdenum was suggested to cause hypochromic microcytic anemia and death as a result of molybdenum-induced copper deficiency. The molybdenum was suggested to have caused the formation of copper-thiomolybdate complexes in both the rumen and in the blood, thereby decreasing the copper available for absorption or for use by copper-requiring enzymes. The mechanism of the lead-induced toxicity was not specified in the report by Osweiler et al. (1973), but detailed information describing the fundamental mechanisms for lead-mediated effects may be found in the ATSDR profile on lead (ATSDR 1993b).

One of the target organs of lead is the hematopoietic system. It inhibits δ-ALAD, a zinc-dependent enzyme, by displacing zinc and hence, the synthesis of heme. Heme is the main component of hemoglobin (Lu 1991). The nervous system is also a target of lead. Young, developing children and unborn fetuses are extremely susceptible to lead toxicity. High blood levels of lead results in encephalopathy, ataxia, stupor, coma and convulsions, peripheral neuropathy, decreased attention span and mental retardation. Chronic lead exposure induces inclusion bodies in the nuclei ofrenal proximal tubular cells. Lead also results in renal adenocarcinoma in animals (Lu 1991). However, it should be noted that current lead levels in fuels, oils and additives are considerably lower due to stringent rules and regulations. Hence, the risk of toxic effects from lead exposure has been reduced.

Acute exposure to cadmium results in local irritation. Exposure via inhalation to cadmium results in pulmonary edema and chemical pneumonitis. Oral exposure results in nausea, vomiting and abdominal pain (Lu 1991). Cadmium is a probable human carcinogen. Like lead, cadmium also accumulates in the lysosomes of the renal proximal tubular cells as cadmium-metallothionein complex, where the cadmium complex degrades and releases Cd^{2+}. The cadmium ion (Cd^{2+}) inhibits the proteolytic enzymes in the lysosomes and damages the cell (Lu 1991). Chromium is a known human carcinogen. Occupational exposure to chromium induces lung cancer, which is thought to be caused by hexavalent chromium. Hexavalent chromium is rapidly taken up by cells and converted to trivalent chromium intracellularly. The trivalent chromium ion is extremely reactive and binds to nucleic acid, initiating the carcinogenic process. Hexavalent chromium is extremely corrosive and causes nasal and skin ulcers (Lu 1991).

PAHs are potent inducers of microsomal enzymes. Hence, they can enhance the metabolism of steroids such as estradiol and androsterone which affect the reproductive system (Lu 1991). Because of their effects on enzymes, PAHs can affect the toxicity of other chemicals and promote carcinogenesis in the liver, induce immunosuppression (depressed immune system) and adversely affect reproductive functions (Lu 1991).

The carcinogenicity of used mineral-based crankcase oil has been attributed to accumulations of PAHs, lead, molybdenum, chromium, zinc, cadmium, copper, and silicon in the oil (Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989) based on the correlation of tumor incidence with the PAH content of the oil and the isolation and testing of PAH-containing fractions of the oil for carcinogenicity. The concentration of PAHs was increased in used oil, and PAHs containing more than three rings contributed to 70% of the total carcinogenicity in used oil. In several studies, benzolalpyrene present in automobile exhaust condensate, crankcase oil (used oil), and smoke condensate contributed to 10, 18, and 5-8% respectively of the total carcinogenicity observed (Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989).

In contrast, a study by Ingram et al. (1994) of the main mutagenic components of a carcinogenic oil by fractionation and testing in the modified Ames assay showed that the mutagenicity of PAHs with l-3 rings was greater than that of PAHs with 4-6 rings. The authors concluded that the 4-6 ring PAHs were not the main mutagenic components of the oil examined, and therefore the mutagenic components may be different from the carcinogenic components. However, the information on the

carcinogenicity of used mineral-based crankcase oil in humans is very limited. Genotoxicity studies with used mineral-based crankcase oil support the conclusion that PAHs contained in the used oil may be responsible for the carcinogenicity that has been observed (Carmichael et al. 1990, 1991, 1992; Hermann et al. 1980b; Peake and Parker 1980; Schoket et al. 1989; Schreiner and Mackerer 1982). Further information on the mutagenicity and carcinogenicity of PAHs may be found in the ATSDR profile on PAHs (ATSDR 1990c).

2.5 RELEVANCE TO PUBLIC HEALTH

Persons in the vicinity of hazardous waste sites are likely to be exposed to used mineral-based crankcase oil primarily via skin contact or ingestion of contaminated soil. Used mineral-based crankcase oil may also be found in surface water as a result of runoff. Because of its poor volatility, inhalation exposure is unlikely unless the oil is aerosolized. Its poor solubility suggests that drinking water exposures are also unlikely. However, chemical constituents (especially metals) of used mineral-based crankcase oil may be released from the oil into the environment, and significant exposure to toxic constituents may occur in the drinking water or as the result of bioaccumulation in foods.

Relatively little is known about the toxicity of used mineral-based crankcase oil. Few studies have been reported which examined the toxicity of used mineral-based crankcase oil. Studies examining the toxicity of the naphthenic and paraffinic base stocks used to formulate mineral-based crankcase oil indicate that these base stocks are relatively nontoxic (API 1983; Beck et al. 1984). Thus, the toxicity associated with exposure to used mineral-based crankcase oil does not appear to be due to the oil present in used mineral-based crankcase oil. Rather, the toxicity that has been observed has been attributed to additives present in the oil (up to 25% of mineral-based crankcase oil formulations) or to decomposition products or contaminants that build up in the oil with use. Thus, results of studies are likely to be specific for the particular additive composition or use characteristics of oil that was used and may not be able to be generalized to all exposures to used mineral-based crankcase oil. For example, lead contamination of oil is expected to be substantially greater in oil from engines using leaded gasolines than from engines powered with unleaded gasolines.

Few well-conducted studies exist that have examined the toxicity of used mineral-based crankcase oil. Furthermore, correlations between exposure and effects in humans are extremely tenuous. For example, a study of mechanics and other auto workers occupationally exposed to used mineral-based

crankcase oil (as well as a variety of other potentially causative substances) suggests that the skin, blood, liver, nervous system, and cardiovascular system may be target organs. However, strong correlations between effects in these organs and exposure to used mineral-based crankcase oil were not established. Inhalation studies in humans suggest that used mineral-based crankcase oil is minimally irritating to the tissues of the respiratory tract, but exposure levels were not well described. Animal data are somewhat more reliable. However, some of the information comes from case reports in species, such as cattle, in which extrapolation to human effects is more difficult. Acute inhalation studies in guinea pigs support the human data indicating that used mineral-based crankcase oil is only minimally irritating to the tissues of the respiratory tract.

Reports of toxicity associated with ingestion of used mineral-based crankcase oil have shown that large oral doses with low levels of metal contamination are tolerated by rats without death or overt toxic signs other than diarrhea. However, cattle ingesting used oil in contaminated pastures have died and shown marked hematological toxicity and neurotoxicity. Cows that ingested used mineral-based crankcase oil during grazing developed clinical lead toxicosis from used crankcase oil or lead containing paint from paint buckets or from sides of buildings or fences with flaking or peeling paint (Osweiler et al. 1973). Oil, paint, grease, trash piles, and lead storage batteries were frequent sources of lead poisoning in 67% of the cases. Of the 67%, oil accounted for 29% of all bovine lead poisoning cases. The source of oil was primarily used crankcase oil (Osweiler et al. 1973). The death of cows in central Hungary was due to molybdenum-induced secondary copper deficiency. The origin of environmental molybdenum was used motor oil containing molybdenum bisulfide as an additive, which had polluted the cows' pasture. The animals had been grazing on the contaminated area for 2 weeks before their illnesses and deaths (Sas 1989). Acute-duration dermal and ocular exposures in rodents have generally resulted in negligible eye irritation and only low-grade dermal irritation. Repeated dermal applications in rabbits have resulted in weight loss of an unknown etiology, suggesting that toxicity may not be limited to the skin.

Carcinogenicity and genotoxicity studies have shown that used mineral-based crankcase oil is carcinogenic to the skin after long-term dermal exposures. The carcinogenicity is most likely due to PAHs found in the oil. Although neoplasia and skin cancer are a possible hazard from repeated dermal exposure to used crankcase oil, this has not been conclusively established, even though used motor oil is genotoxic using the Ames test. Respiratory and ocular discomfort and irritation are possible from short-term exposure to high concentrations of oil mist, aerosol, or exhaust from autos

with inadequate piston rings. At hazardous waste sites, respiratory, cardiovascular, or gastrointestinal effects are unlikely. Hematological effects appear possible with repeated inhalation or dermal contact with oil contaminated with lead, but would probably not occur at hazardous waste sites.

The potential toxicity of lead and other heavy metals in the oil, such as copper, molybdenum, and cadmium, etc. has been noted and would occur upon sufficient exposure to oil or by ingestion of contaminated groundwater. Hepatic, renal, immunological, or neurological effects on fetal development also appear likely. The dose, route, and frequency of exposure are very important in predicting systemic effects from used motor oil. The amount of potential exposure to used motor oil at hazardous waste sites appears to be minimal. The hazard associated with such exposures is anticipated to be low, but adequate data for a comprehensive risk assessment are not available.

Acute effects associated with ingestion of used motor oil are unlikely for humans, but not impossible. Children could accidentally ingest used motor oil. Used crankcase oil stored in homes of do-it-yourself mechanics would be the source of such oil.

Repeated dermal exposure by mechanics and others, respiratory and ocular exposure in closed spaces by mechanics working with motorized vehicles, and oral exposure of children is likely. Exposure to water soluble components, e.g., metals, in contaminated drinking water is also possible.

As noted above, most of the toxicity of used mineral-based crankcase oil has been attributed to additives present in the oil or contaminants that have accumulated in the oil with use. Elements commonly found as additives or contaminants in used mineral-based crankcase oil include lead, zinc, calcium, barium, magnesium, iron, sodium, cadmium, copper, aluminum, chromium, manganese, potassium, nickel, tin, silicon, boron, and molybdenum (Vazquez-Duhalt 1989). In addition, PAHs increase in oil with use (Vazquez-Duhalt 1989). In some cases, observed toxicity has been correlated with individual constituents of the used oil, but this aspect of toxicity with used mineral-based crankcase oil has not been extensively studied. For information on the toxicities associated with exposures to specific contaminants or additives in used mineral-based crankcase oil, see the ATSDR profiles on PAHs (ATSDR 1990c), lead (ATSDR 1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

Minimal Risk Levels for Used Mineral-based Crankcase Oil

As indicated in the introduction to Chapter 2, the composition of used mineral-based crankcase oil is expected to vary depending on the specific additives present in the oil, the type of fuel used, the mechanical condition of the engine, and how long the oil was used. Thus, the NOAEL and LOAEL values presented in Section 2.2 must be considered only as extremely rough estimates of exposure levels associated with the effects observed. Because of the substantial amount of uncertainty regarding these values, no meaningful MRL values could be derived.

Death. No studies were located that reported deaths in humans attributable to exposure to used mineral-based crankcase oil. Studies in rats have shown that ingestion of large doses of used mineral-based crankcase oil over a short period may be well tolerated (API 1980b; Beck et al. 1984; Vemot et al. 1990), but ingestion by cattle while grazing in contaminated pastures resulted in the deaths of several animals (Osweiler et al. 1973; Sas 1989). The deaths of the cattle were attributed to lead and molybdenum in the oil. It is unknown whether the rats and cattle ingested used mineral-based crankcase oils with similar metal contamination. Acute-duration dermal exposures of rabbits (API 1980b; Beck et al. 1984; Vernot et al. 1990) and chronic-duration dermal exposures of mice to used mineral-based crankcase oil (API 1983) did not result in increased mortality. Thus, it is unlikely that persons exposed through skin contact with used mineral-based crankcase oil are at risk of death. However, it is possible that ingestion of sufficient amounts of oil may result in death among susceptible groups in the population depending on the specific contaminant content of the oil. For additional information on death associated with known contaminants of used mineral-based crankcase oil, see the other ATSDR profiles noted above in the introduction to Section 2.5.

Systemic Effects

Respiratory Effects. Inhalation exposure of volunteers to aerosols of used mineral-based crankcase oil for a few minutes has resulted in nose and throat irritation (Dautrebande and Capps 1956) and a feeling of chest tightness (Dautrebande et al. 1951). Animal studies have not, however, shown effects of acute-duration exposure to used mineral-based crankcase oil on pulmonary function. Guinea pigs exposed for up to 1 hour at concentrations as high as 222 mg/m^3 showed no evidence of pulmonary irritation (Costa and Amdur 1979b). Animal studies examining the effects of *unused* mineral-based crankcase oil have shown infectious focal pneumonia and interstitial inflammation in monkeys after

chronic-duration inhalation exposure (Lushbaugh et al. 1950). Thus, the possibility exists that chronic-duration exposure to used mineral-based crankcase oil may also result in similar effects. In addition, exposure to minerals oils present in laxatives and various aerolized industrial materials by inhalation or aspiration causes exogenous lipoid or lipid pneumonia (oil droplets in the lungs) and proliferative fibrosis of the lung (Fan and Graham 1994; Spickard and Hirschmann 1994). However, lipid pneumonia has not been widely observed after inhalation of unused mineral-based crankcase oil (Lushbaugh et al. 1950; Shoshkes et al. 1950) except when aspiration of the material was induced (Gerarde 1963). Because it is unlikely that persons at hazardous waste sites would be exposed to aerosols of used mineral-based crankcase oil, and inhalation is an unlikely route of exposure, respiratory effects from exposures at hazardous waste sites are also highly unlikely to occur.

Cardiovascular Effects. Elevated blood pressure has been reported in a number of workers with occupational exposure to used mineral-based crankcase oil (Clausen and Rastogi 1977). However, it is unclear whether other environmental, genetic, pathophysiological, or behavioral factors may have caused the increase in blood pressure. Systematic studies of whether a significant correlation exists between elevated blood pressure and exposure to used mineral-based crankcase oil have not been performed. Thus, insufficient information exists to determine whether persons exposed to used mineral-based crankcase oil at hazardous waste sites may be at an increased risk of elevated blood pressure.

Gastrointestinal Effects. No increase in clinical signs of gastrointestinal toxicity (stomach pain, constipation, anorexia) was found in workers occupationally exposed to used mineral-based crankcase oil (Clausen and Rastogi 1977). However, diarrhea has been observed in rats (API 1980b; Beck et al. 1984; Vernot et al. 1990) and cattle (Osweiler et al. 1973) that ingested used mineral-based crankcase oil. Medicinal-grade mineral oil is used therapeutically as an emollient laxative acting to soften the stool by retarding reabsorption of water from the gastrointestinal tract (Fingl 1980). Thus, it is likely that used mineral-based crankcase oil is acting at least in part by the same mechanism. A slight irritant effect on-the-gastrointestinal tract by additives or contaminants cannot be eliminated based on the stomach irritation observed in monkeys. Hyperplastic gastritis has been observed in monkeys that were believed to have swallowed significant amounts of inhaled aerosols of *unused* mineral-based crankcase oil (Lushbaugh et al. 1950). While the component of *unused* oil responsible for the gastritis was not identified, it is possible that such a component is also present in used mineral-based crankcase

oil. Thus, the possibility exists that ingestion of large amounts of used mineral-based crankcase oil may result in diarrhea or stomach damage.

Hematological Effects. Lower than normal hematocrit and mean corpuscular hemoglobin have been observed in several workers with occupational exposure to used mineral-based crankcase oil (Clausen and Rastogi 1977). In several cases, the hematological effects correlated with elevated blood lead levels suggesting a role of lead in the effects observed. However, sources of lead exposure other than from used mineral-based crankcase oil and other causes for the blood effects were not eliminated. Ingestion of used mineral-based crankcase oil by ducks and pheasants resulted in dose-related decreases in δ-ALAD activity (Eastin et al. 1983). Since δ-ALAD is involved in heme synthesis and is sensitive to inhibition by lead, this study supports the possibility that lead in used mineral-based crankcase oil may have contributed to the anemia observed in the auto workers. Ingestion of used mineral-based crankcase oil containing high levels of molybdenum resulted in anemia in cattle (Sas 1989). Thus, the possibility exists that anemia may occur in persons exposed to lead or molybdenum in used mineral-based crankcase oil.

Hepatic Effects. Limited epidemiological data show that a small percentage of workers with occupational exposure to used mineral-based crankcase oil had elevated clinical chemistry values indicative of liver damage (increased serum bilirubin, alanine and aspartate aminotransferases, lactate dehydrogenase, and thymol reaction) (Clausen and Rastogi 1977). However, other environmental or behavioral factors were not eliminated as potential causes. Animal data have not shown biochemical evidence after intermediate-duration oral exposure (Eastin et al. 1983) or histopathological evidence of hepatic toxicity after acute-duration dermal exposure (API 1980b; Beck et al. 1984; Vemot et al. 1990). Insufficient information exists to predict whether persons exposed to used mineral-based crankcase oil at hazardous waste sites will exhibit hepatotoxicity.

Renal Effects. No studies were located that reported renal effects in humans attributable to exposure to used mineral-based crankcase oil. The only information regarding renal effects in animals after exposure to used mineral-based crankcase oil came from a 2-week dermal study in rabbits that indicated no histopathological evidence of toxicity of the kidneys and urinary bladder (API 1980b; Beck et al. 1984; Vemot et al. 1990). Insufficient information was located to determine whether renal toxicity may result from exposure to used mineral-based crankcase oil at hazardous waste sites.

Dermal Effects. Skin rashes on the hands and arms were reported by a number of workers exposed to used mineral-based crankcase oil (Clausen and Rastogi 1977). However, it was not established whether used mineral-based crankcase oil was the causative agent. Studies in rabbits (API 1980b; Beck et al. 1984; Vemot et al. 1990) and mice (API 1983) have shown that dermal exposure to used mineral-based crankcase oil results in mild-to-moderate skin irritation. In rabbits, multiple exposures also resulted in hair loss adjacent to the application site (API 1980b; Beck et al. 1984; Vemot et al. 1990). Monkeys chronically exposed (whole-body) to aerosols of *unused* mineral-based crankcase oil also experienced extensive hair loss (Lushbaugh et al. 1950). It is unknown whether the underlying cause for the hair loss is similar in these two studies, but the data suggest that components present in both unused and used mineral-based crankcase oil may result in some degree of hair loss.

Ocular Effects. Volunteers exposed to aerosols of used mineral-based crankcase oil have reported eye irritation (Dautrebande and Capps 1950; Dautrebande et al. 1951). In contrast, negligible irritation was noted in rabbits when 0.1 mL was directly instilled into the eye (API 1980b; Beck et al. 1984; Vernot et al. 1990). This apparent discrepancy may be due to the differing compositions of the samples of the used mineral-based crankcase oil that were tested. It is unlikely that persons at hazardous waste sites would be exposed to aerosols of used mineral-based crankcase oil. However, dermal exposure is possible and eye irritation from used mineral-based crankcase oils may occur.

Body Weight Effects. No studies were located regarding body weight effects in humans after exposure to used mineral-based crankcase oil. No effects on body weight gain or growth were observed in rats that received single doses or used mineral-based crankcase as high as 22,500 mg/kg (API 1980b; Beck et al. 1984; Vemot et al. 1990) nor in mice (API 1983).

In contrast, 8 mL/kg of used mineral-based crankcase applied on the backs of rabbits 24 hours/day, 5 days/week, for 2 weeks resulted in a marked decrease in food consumption and weight loss (API 1980a; Beck et al. 1984; Vemot et al. 1990). The biological basis for the decreased food consumption was not identified.

Immunological and Lymphoreticular Effects. Extremely little information was located regarding immunological effects of used mineral-based crankcase oil in humans or animals. A dermal sensitization study conducted with guinea pigs showed no sensitization potential (API 1980b; Beck et al. 1984; Vemot et al. 1990), but the positive control also failed to show sensitization. Other aspects

of immune function were not assessed. Thus, some uncertainty exists regarding the likelihood of contact dermatitis following exposure to used mineral-based crankcase oil near hazardous waste sites.

Neurological Effects. Limited information was located regarding neurological effects in humans or animals after exposure to used mineral-based crankcase oil. A study of a group of auto workers showed headaches and/or tremors of the hands in a small number of the exposed workers (Clausen and Rastogi 1977). However, it was not established whether the used mineral-based crankcase oil was the causative agent. Studies in rodents have not reported overt neurotoxicity following inhalation, oral, or dermal exposure to used mineral-based crankcase oil, but cattle that have ingested used mineral-based crankcase oil have shown muscle tremors, weakness, blindness, muscle twitching, hyperirritability, depression, and convulsions (Osweiler et al. 1973; Sas 1989). The neurological effects in the study by Osweiler et al. (1973) were attributed to lead poisoning, and those in the study by Sas (1989) were attributed to molybdenum poisoning. Insufficient information exists to determine whether persons exposed to used mineral-based crankcase oil at hazardous waste sites may experience adverse neurological effects.

Reproductive Effects. No information was located regarding reproductive effects in humans or animals after exposure to used mineral-based crankcase oil.

Developmental Effects. No information was located regarding developmental effects in humans or animals after inhalation, oral, or dermal exposure to used mineral-based crankcase oil. However, a study by Hoffmann and Albers (1984) investigated the potential embryotoxicity and teratogenicity of automotive virgin crankcase oil and waste crankcase oil in mallard *(Anus platyrhynchos)* eggs. The oil was applied to upright fertile eggs with a microliter pipet by streaking the surface just below the air space and allowing the oil to spread freely (Hoffmann and Albers 1984). Application of waste crankcase oil significantly affected embryonic survival. It had an LD_{50} of 5.3 µL/egg (=90 µg/g egg) compared to that of virgin crankcase oil, which was 23.5 µL/egg. At doses below the LD_{50}, waste crankcase oil also resulted in more survivors with severe abnormalities, including defects of the brain (anencephaly and exencephaly) and of the eye (microphthalmia), than with virgin crankcase oil (Hoffmann and Albers 1984).

An egg-painting study using quail and ducks showed decreased growth and survival in both quail and duck fetuses, edema, incomplete ossification, and exencephaly in quail; and hemorrhages, edema,

incomplete ossification, anencephaly, and microphthalmia in ducks (Hoffman et al. 1982a). In addition, quail and duck embryos and/or hatchlings showed low hemoglobin and decreased blood and liver δ-ALAD. The toxicity was attributed to the lead and aromatic hydrocarbon content of the used oil rather than to asphyxiation since higher volumes of other oils were not toxic. The presence of heavy metals in the oil may be a significant factor in its toxicity. Automotive waste oil contained 4,600 ppm lead, which caused a significant depression of red blood cell δ-ALAD activity and decreased hemoglobin concentration in mallard and bobwhite embryos (Hoffmann and Albers 1984; Hoffman et al. 1982a). It is unknown whether comparable developmental toxicity would be observed in persons exposed to used mineral-based crankcase oil. It should be noted here that painting or injecting bird eggs with used crankcase oil is very different from performing reproductive toxicity tests using mammalian species. In the mammalian situation, the pregnant animal is treated or administered the substance. In addition, there are fundamental maternal, circulatory, excretory, and metabolic influences which determine exposure to the fetus, qualitatively and quantitatively. Hence, the relevance to humans of bird egg toxicity after exposure to used mineral-based crankcase oil is remote.

Genotoxic Effects. No standard *in vivo* or *in vitro* genotoxicity studies of used crankcase oil in mammalian test systems were located, but several studies (Carmichael et al. 1990, 1991, 1992; Schoket et al. 1989) identified DNA adducts formed by acute-duration dermal application of used mineral-based crankcase oils and suggested that specific DNA adducts may be attributed to the reaction of specific PAHs with DNA. PAHs, like benzo[a]pyrene, induce certain drug-metabolizing enzymes, mainly the cytochrome P4501A subfamily (CYPIA), which is also known as CYP448 and aryl hydrocarbon hydroxylase (AHH). The CYPIA enzymes metabolize PAHs into epoxides, which are then hydroxylated to dihydrodiols and are noncarcinogenic. However, further epoxidation of the dihydrodiols by the CYPIA enzymes generates reactive “electrophilic” species which are capable of binding and damaging DNA by forming DNA adducts, resulting in necrosis and/or cancer. However, while these experiments clearly show that PAHs in used motor oil interacted with DNA, most adducts would be repaired, and few would result in genetic lesions. Thus, the rate of repair and the final outcome of the DNA damage is of considerable interest.

Similarly, DNA adducts were formed when human skin cultures were exposed to used oils (Carmichael et al. 1991). Application of diesel engine oil resulted in fewer adducts than did gasoline engine oil in both *in vivo* and *in vitro* test systems. Qualitative differences in the adducts formed in the human and mouse skin culture systems were consistent with the metabolism of certain PAHs by

species-specific pathways. Based on the comparison of DNA-adducts formed by fractionated oils with those formed by individual PAHs, Carmichael et al. (1992) attributed the major adducts produced in mouse skin by used gasoline engine oil to reactive metabolites of benzo(*b*)naphtho(l,2-*d*)thiophene, benzo(*c*)phenanthrene, benzo(*g,h,i*)fluoranthene, chrysene, benzo(*a*)pyrene, and benzo(*g,h,i*)perylene. Used mineral-based crankcase oil also contains compounds that induce aryl hydrocarbon hydroxylases (AHHs) (Rahimtula et al. 1982). As with the adducts observed in the dermal studies, only unrepaired adducts would result in genetic lesions. Furthermore, it is not known how well the skin cell culture system simulates dermal exposure *in vivo*.

Used mineral-based crankcase oil from gasoline-powered automobiles is consistently positive in *Salmonella typhimurium*/mammalian microsome mutagenicity assays in the presence or absence of S9 activation, but the revertant yield is higher with the S9-activated material (Blackbum et al. 1983; Granella and Clonfero 1991; Pasquini and Monarca 1983; Payne et al. 1978; Peake and Parker 1980; Rahimtula et al. 1984; Schreiner and Mackerer 1982). The strongest mutagenic responses are generally observed in strains TA98 and TA100. *Unused* mineral-based crankcase oil is generally negative in this assay in both the presence and absence of S9 activation (Granella and Clonfero 1991; Pasquini and Monarca 1983; Schreiner and Mackerer 1982). Key genotoxicity studies using *S. typhimurium* are presented in Table 2-4.

The mutagenicity of oil appears to increase as a function of the mileage since the last oil change. An increase in the number of revertants/mg oil, induced with or without S9, was observed in repeated sampling of the motor oil in one car (EPA 1980d). The level of skin and lung adducts produced by dermal application of used engine oil to male mice correlated with an index of oil use calculated as the product of the number of miles since the last oil change and the total engine mileage (Carmichael et al. 1990). Not all studies have shown similar results, but possible methodological differences may have accounted for the differing results. In a comparison of used oils from eight different cars, no correlation was observed between mutagenicity and engine age or miles since the last oil change (Dutcher et al. l-986), but no analysis was conducted to determine whether there was a correlation with engine age *and* miles since the last oil change. Such a correlation could have been missed because the newer cars tended to have higher mileage since the last oil change. The water-soluble fraction of used mineral-based crankcase oil was not mutagenic with or without S9 activation, but this fraction was obtained in a highly diluted form, and toxic levels were not tested (Vandermeulen et al. 1985).

TABLE 2-4. Genotoxicity of Used Mineral-based Crankcase Oil *In Vitro*

Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms:				
Gasoline engine oil				
Salmonella typhimurium	Gene mutation	+	+	Abdelnasser et al. 1986
S. typhimurium	Gene mutation	+	+	Blackburn et al. 1983
S. typhimurium	Gene mutation	+	+	Dutcher et al. 1986
S. typhimurium	Gene mutation	+	+	Granella and Clonfero 1991
S. typhimurium	Gene mutation	+	ND	Hermann et al. 1980a
S. typhimurium	Gene mutation	+	ND	Hermann et al. 1980b
S. typhimurium	Gene mutation	+	+	EPA 1980d
S. typhimurium	Gene mutation	+	+	Manabe et al. 1984
S. typhimurium	Gene mutation	+	+	Pasquini and Monarca 1983
S. typhimurium	Gene mutation	+	–	Payne et al. 1978
S. typhimurium	Gene mutation	+	+	Peake and Parker 1980
S. typhimurium	Gene mutation	+	+	Rahimtula et al. 1984
S. typhimurium	Gene mutation	+	+	Schreiner and Mackerer 1982
S. typhimurium	Gene mutation	+	+	Vandermeulen et al. 1985
Diesel engine oil				
S. typhimurium	Gene mutation	+	+	Dutcher and Clark 1981
S. typhimurium	Gene mutation	+	+	Dutcher et al. 1986
S. typhimurium	Gene mutation	ND	+	Manabe et al. 1984

+ = positive result; – = negative result; ND = not determined

Data regarding the mutagenicity of used oil from diesel engines are much more limited than those regarding used gasoline engine oil. However, there is evidence that nonactivated and S9-activated diesel engine oil is mutagenic in *S. typhimurium* strain TA98 (Dutcher and Clark 1981; Dutcher et al. 1986). In another study, extracts of diesel engine oils were reported to cause a small increase in TA98 mutants (EPA 1980d). Diesel engine oil was less potent than gasoline engine crankcase oil in the induction of DNA adducts following dermal application to mice *in vivo* (Carmichael et al. 1990, 1991; Schoket et al. 1989) and application to mouse or human skin cultures *in vitro* (Carmichael et al. 1991). The lower mutagenicity of diesel engine oils may be attributable to the lower mileage since the last oil change, compared to oil from gasoline-powered engines. However, this would not be expected to affect the human health risk since diesel engine oil is changed more frequently than oil in gasoline-powered engines.

The *Salmonella* assay has also been used by several investigators to compare the mutagenicity of different samples of used mineral-based crankcase oil and to identify the mutagenic components in the complex chemical mixture found in used mineral-based crankcase oil. The data regarding the specific PAHs that account for the mutagenicity of used crankcase oil are contradictory. As discussed above, some inconsistencies may arise from variations in the oil used. In an early experiment, the mutagenic activity of used oil largely did not migrate together with benzopyrene or benzanthracene (isomers not reported) on thin-layer chromatography plates (Payne et al. 1978). Most of the mutagenicity of another oil sample was attributed to PAHs containing four, five, or six fused aromatic rings (Hermann et al. 1980b). The PAH with the largest contribution to the mutagenicity was benzo(a)pyrene. Most of the adducts found following dermal treatment of mice with used mineral-based crankcase oil were attributed to metabolites of PAHs with four or fewer aromatic rings. These data are too limited and contradictory to determine which compounds are responsible for much of the mutagenic activity of used mineral-based crankcase oil.

Results from the controlled “aging” of new oil under defined conditions suggest that nitrated PAHs or other compounds generated by reaction of the oil with nitrogen dioxide account for much of the direct-acting mutagenic activity of used oil. Exposure to nitrogen dioxide markedly increased the yield of revertants induced by fresh crankcase oil in *S. typhimurium* strain TA98 with or without S9 activation. By contrast, heating the oil to 100°C for 100 hours, or exposing it to air, sulfur dioxide, or hydrogen sulfide did not result in the production of mutagenic material (Abdelnasser et al. 1986). Thin-layer chromatographic fractionation revealed that the composition of mutagenic compounds in used oil was

similar to that in fresh oil treated with heat and nitrogen dioxide. The study authors suggested that these mutagenic species are nitrated PAHs. Other authors have also implicated reaction with nitrogen dioxide in the production of mutagenic compounds (Naughton and Jespersen 1991).

Genetic analysis has also indicated that a major portion of the mutagenic activity of used mineralbased crankcase oil in the absence of S9 activation is due to nitroaromatic compounds (nitroPAHs). The yield of revertants induced in TA98 by a dimethyl sulfoxide extract of used mineral-based crankcase oil in the absence of S9 was reduced by about 65% in the nitroreductase-deficient strain TA98NR (Blackburn et al. 1983), a finding confirmed by Manabe et al. (1984). 1-Nitropyrene (1-NP) and 1,6-dinitropyrene (diNP) were tentatively identified as direct-acting mutagenic compounds in used mineral-based crankcase oil. Thus, the direct-acting mutagenic activity of used mineral-based crankcase oil is largely attributed to nitroaromatic compounds, while the mutagenic activity that requires S9 activation is attributed largely to PAH metabolites. Nitro-PAHs can be metabolized to aromatic amine derivatives, some of which are capable of inducing urinary bladder cancer in humans (Iyer et al. 1990). 1-NP is also capable of generating oxidants or reactive oxygen species such as the superoxide radical (Nachtman 1986), which can react with and damage cellular molecules (DNA, lipids, proteins) or activate genotoxic substances such as PAHs, which can eventually lead to cancer (Sun 1990). These oxidants are also generated in the body by white blood cells as a defense mechanism during inflammation (Sun 1990). Reactive oxygen species are thought to play a role in the toxicity and mutagenicity of diesel soot (Vogl and Elstner 1989) and in the metabolic activation of PAHs in mouse skin (Kensler et al. 1987). 1-NP, diNP, and trinitropyrene were shown to be potent lung DNA binding agents in the absence of the inducing agent, BaP, but were extremely potent after pretreatment with BaP (Howard et al 1986). Hence, it is possible that 1-NP and diNP may play a role in the toxicity of used mineral-based crankcase oil by generating superoxide radicals which can damage cells and lead to the development of cancer.

Although no genotoxicity data were located regarding used mineral-based crankcase oil in mammalian systems, the evidence suggests that it can be mutagenic to humans. Crankcase oil accumulates PAHs, many of which are known genotoxins and fractionate together with mutagenic activity in the oil. Oil from gasoline engines would presumably be more mutagenic than oil from diesel engines. No possible explanations were located for the higher mutagenic potency of oil from gasoline engines. Used oil is mutagenic in the *Salmonella* mutation assay, the mutagenic activity is stronger in the presence of S9 activation, and DNA adducts are found in cutaneous DNA following application of used oil to mice *in*

vivo or to samples of human or mouse skin *in vitro*. Thus, the genotoxicity data support the data from animal studies indicating that dermal exposure to used mineral-based crankcase oil can cause cancer. The genotoxicity data also suggest that used mineral-based crankcase oil may be a developmental toxicant. Therefore, dermal exposure to used mineral-based crankcase oil may pose a human health hazard.

Cancer. Limited information was located regarding the carcinogenicity of used mineral-based crankcase oil in humans. An epidemiological study of workers in Sweden indicated that the risk of developing renal pelvic and bladder cancer was not increased in workers exposed to motor oil (Steineck et al. 1989), but no information was located regarding the development of other types of cancer. Studies in mice demonstrate that chronic-duration dermal exposure to used mineral-based crankcase oil results in an increased incidence of dermal papillomas and carcinomas (API 1983; Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989). The tumor incidence correlated with the PAH content of the oil (Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989). DNA adducts were identified in both the skin and lungs of mice that had received dermal treatments for l-4 days (Carmichael et al. 1990; Schoket et al. 1989), suggesting that tumor development in organs other than the skin may be possible.

Based on the information from the mouse studies, IARC has determined that one sample of used mineral-based crankcase oil showed sufficient evidence for carcinogenicity in animals; however, data are inadequate to evaluate used mineral-based crankcase oil as a class “since the possible carcinogenic activity of individual products is dependent upon the quality of the base oils used, the nature and concentration of additives and contaminants, and the conditions of use” (IARC 1984). EPA and the Department of Health and Human Services have not classified used mineral-based crankcase oil as to its carcinogenicity. The IARC cancer classification reflects the uncertainty regarding the composition of different batches of used mineral-based crankcase oil.

2.6 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).

Due to a nascent understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. 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 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 used mineral-based crankcase oil are discussed in Section 2.6.1.

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 not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by used mineral-based crankcase oil are discussed in Section 2.6.2.

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 increasein absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.8, Populations That Are Unusually Susceptible.

2.6.1 Biomarkers Used to Identify or Quantify Exposure to Used Mineral-based Crankcase Oil

No information was located regarding biomarkers that could be used to identify exposure to used mineral-based crankcase oil. However, biomarkers for PAHs such as DNA adduct formation (Carmichael et al. 1990; Schoket et al. 1989) or biomarkers for metals such as metal content of the blood (Clausen and Rastogi 1977; Osweiler et al. 1973; Sas 1989) or decreased δ-aminolevulinic acid dehydratase in blood (Clausen and Rastogi 1977; Eastin et al. 1983; Hoffman et al. 1982a) have been identified as possible indicators of exposure to chemicals found in used mineral-based crankcase oil. It should be noted that these biomarkers are not specific for exposure to used mineral-based crankcase oil itself but may be specific for toxic chemicals found in the oil. Any substance containing PAHs and/or heavy metals could be the source of exposure. Although there are valid tests to measure biomarkers of exposure, high blood lead for instance, the presence of a biomarker does not necessarily imply exposure to used motor oil. Hence, evidence of exposure to used mineral-based crankcase oil must first be determined before biomarkers of exposure to metals or PAHs are used to help confirm exposure to used mineral-based crankcase oil. Biomarkers for exposure to metals and aromatic hydrocarbons are discussed in more detail in ATSDR profiles on the following substances: PAHs (ATSDR 1990c), lead (ATSDR 1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

2.6.2 Biomarkers Used to Characterize Effects Caused by Used Mineral-based Crankcase Oil

While the health effects of exposure to used mineral-based crankcase oil have not been fully described, some indicators of toxicity have been identified that may be useful in characterizing potential effects. Hematological analyses for hemoglobin or hematocrit could be useful for predicting anemia (Clausen and Rastogi 1977). Analyses for serum copper and ceruloplasmin levels may be useful in detecting copper deficiency (Sas 1989), and examination of skin for the formation of elevated levels of DNA adducts (Carmichael et al. 1990, 1991, 1992; Schoket et al. 1989) may be indicative of potentially genotoxic exposures. The biomarkers mentioned are specific for toxic materials which may be components of used motor oil, but are not specific for used motor oil itself. For further descriptions of the utility of these biomarkers in characterizing effects of individual chemicals potentially found in used mineral-based crankcase oil, see the ATSDR profiles on PAHs (ATSDR 1990c), lead (ATSDR

1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

2.7 INTERACTIONS WITH OTHER SUBSTANCES

Extremely limited and conflicting information was located regarding interactions of used mineral-based crankcase oil with other chemicals. As very little is known about this subject, the discussion is necessarily quite limited. While a decrease in the pulmonary irritancy of sulfur dioxide in guinea pigs was reported by Costa and Amdur (1979a) when aerosols of used mineral-based crankcase oil were administered simultaneously with sulfur dioxide, human subjects experienced an increase in eye, nose, and throat irritation when exposed to aerosols containing both used mineral-based crankcase oil and sulfur dioxide (Dautrebande and Capps 1950). The differences in the results may be due to differences in the end points examined or in the amount or composition of the samples of used mineral-based crankcase oil that were employed, but they do not appear to be attributable to differences in the concentration of sulfur dioxide. Other interactions reported included less-than-additive eye, nose, and throat irritation reported by human subjects exposed to aerosols of combinations of used mineral-based crankcase oil with either carbon black, a combination of sulfur dioxide and carbon black, or a combination of sulfur trioxide and carbon black (Dautrebande and Capps 1950).

2.8 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to used mineral-based crankcase oil than will most persons exposed to the same level of used mineral-based crankcase oil in the environment. Reasons include genetic make-up, developmental stage, age, health and nutritional status (including dietary habits that may increase susceptibility, such as inconsistent diets or nutritional deficiencies), and substance exposure history (including smoking). These parameters may result in decreased function of the detoxification and excretory processes (mainly hepatic, renal, and respiratory) or the pre-existing compromised function of target organs (including effects or clearance rates and any resulting end-product metabolites). 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 on toxic effects of used mineral-based crankcase oil did not identify specific populations that are known to be unusually susceptible to its effects. Depending on the additive and contaminant composition of individual oils, various populations may be expected to be particularly susceptible. The groups with high susceptibility would be expected to vary with the constituents of the oil. It is beyond the scope of this profile to detail all possible exposure scenarios and the respective sensitive groups. However, certain populations with high susceptibility to PAH or lead toxicity will be summarized below. For additional information on the populations that may be expected to be susceptible to the toxicities of PAHs, lead, and other potential constituents, see the ATSDR profiles on PAHs (ATSDR 1990c), lead (ATSDR 1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

Persons repeatedly exposed to used motor oil would potentially be a very susceptible group (see Section 5.6). Populations expected to show an increased susceptibility to toxic effects of PAHs include persons with induced aryl hydrocarbon hydroxylase activity (the enzyme responsible for transformation of PAHs to reactive intermediates), those with nutritional deficiencies in vitamins A, C, and D, iron, and riboflavin (an increased cancer incidence has been seen under these conditions), and persons with genetic diseases affecting DNA repair capabilities (ATSDR 1990c). Assuming used mineral-based crankcase oil has carcinogenic components, persons who smoke and those with excessive sun exposure may show increased carcinogenicity because particulates in cigarette smoke and ultraviolet radiation potentiate the carcinogenic response to PAH exposure. Also, the very young and persons without fully functional immune systems may be impaired in their ability to resist PAH-induced toxicity (ATSDR 1990c). The very young and the very old, for reasons of physiology and metabolism, would also be expected to be more susceptible than the “normal” adult population to any adverse effect of exposure to used motor oil, as would be persons with a Vitamin A, C, or D deficiency. Deficiencies in Vitamins C and D enhances lead and cadmium toxicity.

Populations that may be more susceptible to the toxic effects of lead exposure include young children (<5 years old), pregnant women, the elderly, smokers, alcoholics, and people with genetic diseases

affecting heme synthesis, and nutritional deficiencies (ATSDR 1993b). Children have a greater gastrointestinal absorption of lead and lower blood thresholds for hematological and neurological effects induced by lead exposure. Dietary deficiencies in calcium and iron potentiate the toxicity of lead. Pregnant women and the elderly may have increased blood lead levels because of greater mobilization from bone. Persons who consume large amounts of alcohol may be at increased risk of hematological, neurological, and hepatotoxic effects of lead because of alcohol's synergistic effects on these tissues (ATSDR 1993b).

2.9 METHODS FOR REDUCING TOXIC EFFECTS

This section describes clinical practice and research concerning methods for reducing toxic effects of exposure to used mineral-based crankcase oil. 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 used mineral-based crankcase oil. When specific exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice.

2.9.1 Reducing Peak Absorption Following Exposure

Treatment recommendations are sufficiently general for virtually any mineral oil exposure. There are no specific methods for used mineral-based crankcase oil. Because the volatility of used mineralbased crankcase oil is expected to be negligible and inhalation exposure is a concern only in situations where aerosols may be generated, exposure to used mineral-based crankcase oil is expected to occur mainly via the oral and dermal routes. Effects of dermal exposures may be limited by washing exposed skin with mild green (lipophilic) soap (Ellenhorn and Barceloux 1988). Care should be taken not to abrade the skin, since dermal abrasions may facilitate the absorption of toxic chemicals found in the oil. Virtually nothing is known about the absorption of used mineral-based crankcase oil from the gastrointestinal tract, but toxicity studies suggest that absorption of chemicals (contaminants or additives) found in the oil may be toxicologically significant (Osweiler et al. 1973; Sas 1989). Therefore, it may be desirable to take steps to reduce absorption of chemicals found in the oil. This is especially true for those chemicals whose absorption is augmented in the presence of oil. In general, steps taken to reduce the gastrointestinal absorption of chemicals found in the oil should be tailored to practices known to be effective for the constituents of concern (Ellenhorn and Barceloux 1988; Goldfrank et al. 1990; Haddad and Winchester 1990). Since the risk of aspiration of used mineral-

based crankcase oil is not as great as with many hydrocarbons (Gerarde 1963; Goldfrank et al. 1990), induction of emesis may be a viable means of removing the oil from the gastrointestinal tract. Gastric lavage has been recommended only in unconscious patients with the use of a cuffed endotracheal tube to limit aspiration that could result in induction of lipid pneumonia (Gerarde 1963; Goldfrank et al. 1990). Activated charcoal has not been shown to be effective in adsorbing petroleum distillates (Goldfrank et al. 1990) but may be effective in limiting the absorption of other chemicals found in the oil. Cathartics may help speed removal from the gastrointestinal tract; however, the used mineralbased crankcase oil may itself act as a cathartic if sufficiently large amounts are ingested. If additional cathartics are required, osmotic cathartics such as sorbitol are preferable to mineral oil cathartics because of the possibility of aspiration of the oil (Ellenhorn and Barceloux 1988; Haddad and Winchester 1990).

2.9.2 Reducing Body Burden

Available information indicates that the toxicity of used mineral-based crankcase oil is primarily a function of the toxicities of additives or contaminants found in the oil. Therefore, steps used to reduce the body burden should be tailored to the specific additives or contaminants of concern. It is beyond the scope of this profile to present the methods associated with decreasing body levels of all of the potential chemicals of concern. However, a brief discussion of lead and PAHs is provided as they are the primary hazardous constituents associated with used motor oil. In adults and children, approximately 94% and 73% of the total body burden of lead is found in bones, respectively (ATSDR 1993b). Currently, chelating agents are used to reduce the body burden of lead and hence, its toxicity. All of the chelating agents bind inorganic lead and facilitate the transfer of lead from soft tissues to the circulation where it can be excreted. Since excretion of chelated lead is via the kidney, caution should be used in patients with renal failure. The standard chelating agents currently used are dimercaprol (British Anti-Lewisite or BAL) and ethylenediaminetetraacetic acid (EDTA). Both these agents are administered parenterally (ATSDR 1993b).

Currently, there are no known methods available for reducing the body burden of PAHs. PAHs are rapidly metabolized and conjugated to form water-soluble metabolites that are completely eliminated in the urine and feces within a matter of days (ATSDR 1990c). No data are available on the kinetics of PAHs following chronic exposure, so it is not known if PAHs or their metabolites bioaccumulate in these exposure situations. Given the relatively rapid and complete excretion following short-term

exposures, it is unlikely that PAHs will bioaccumulate to a large extent. However, since PAHs are lipophilic, it is possible that the unmetabolized parent compound could accumulate in fat tissue (ATSDR 1990c). It is possible that high-fat diets may favor accumulation of parent PAHs in lipids so that they are not metabolized to reactive intermediates or water-soluble conjugates. Therefore, modulating body fat content may reduce the body burden of PAHs by hastening their metabolism to water-soluble conjugates. However, this may result in increased toxicity due to the increased metabolism to reactive metabolites (ATSDR 1990c).

For substance-specific information on methods that may be effective in reducing levels of other individual chemicals potentially found in used mineral-based crankcase oil, see the ATSDR profiles on PAHs (ATSDR 1990c), lead (ATSDR 1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

2.9.3 Interfering with the Mechanism of Action for Toxic Effects

As indicated above in the section on mechanisms of action, the toxicity of used mineral-based crankcase oil has been attributed primarily to additives or contaminants found in the oil. As both the additive composition and contaminants are likely to vary depending on the brand of oil used and its use characteristics, steps taken to interfere with mechanisms underlying toxic responses should be tailored to the individual chemicals of concern. It is beyond the scope of this profile to address actions that may be taken to interfere with the mechanisms of action of all potential toxic additives or contaminants. However, a brief discussion of lead and PAHs is provided as they are the primary hazardous constituents associated with used motor oil. Chelating agents are used to prevent the toxicity of lead by reducing the body burden. All of the chelating agents bind inorganic lead and facilitate the transfer of lead from soft tissues to the circulation where it can be excreted. BAL chelates both intracellular and extracellular stores of lead. BAL-lead chelates are excreted mainly in the bile and some in the urine. BAL is used in individuals with renal impairment (ATSDR 1993b). For adults that are symptomatic or have blood lead levels >70 μg/dL and for children (symptomatic or asymptomatic) with blood lead levels >70 μg/dL, therapy with BAL is followed by EDTA. For asymptomatic children with blood lead levels >45-69 μg/dL, EDTA chelation therapy is used. 2,3-Dimercaptoseccinia acid (DSMA) is an orally administered chelating agent approved by the FDA

for treating children with blood levels >45 μg/dL. DSMA is also being used to treat lead poisoning in adults (ATSDR 1993b).

The toxic and carcinogenic effects of PAHs are thought to be mediated by reactive diol-epoxide intermediates that interact directly with DNA and RNA, producing adducts. These adducts result in neoplastic transformation and interfere with the normal functioning of rapidly proliferating tissues. The reactive intermediates are formed when PAHs are biotransformed by the cytochrome P450 enzymes (ATSDR 1990c). Interference with these metabolic pathways, by inactivation of the activated diol epoxides, or a reduction in tissue levels of cytochrome P450 enzymes responsible for forming the reactive intermediates, could reduce the toxic and carcinogenic effects of PAHs. Various drugs, such as cobaltous chloride, SKF-535A and 6-nitro-1,2,3-benzothiadiazole can inhibit the cytochrome P450 enzymes. Because PAHs are detoxified by conjugation with substances such as glutathione, sufficient glutathione stores in the body may reduce the chances of toxic effects following acute exposure to PAHs.

For additional chemical-specific information see the ATSDR profiles on PAHs (ATSDR 1990c), lead (ATSDR 1993b), zinc (ATSDR 1989b), cadmium (ATSDR 1992d), copper (ATSDR 1990b), chromium (ATSDR 1993a), nickel (ATSDR 1992f), barium (ATSDR 1992b), boron (ATSDR 1992c), manganese (ATSDR 1992e), tin (ATSDR 1992g), and aluminum (ATSDR 1992a).

2.10 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 used mineral-based crankcase oil 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 usedmineral-based crankcase oil.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean

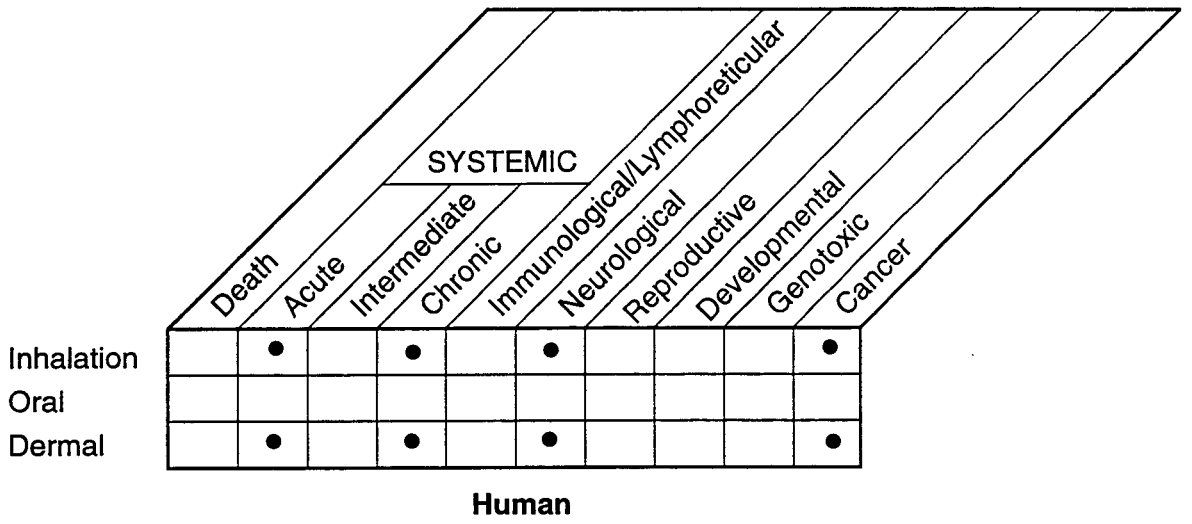
that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.10.1 Existing Information on Health Effects of Used Mineral-based Crankcase Oil

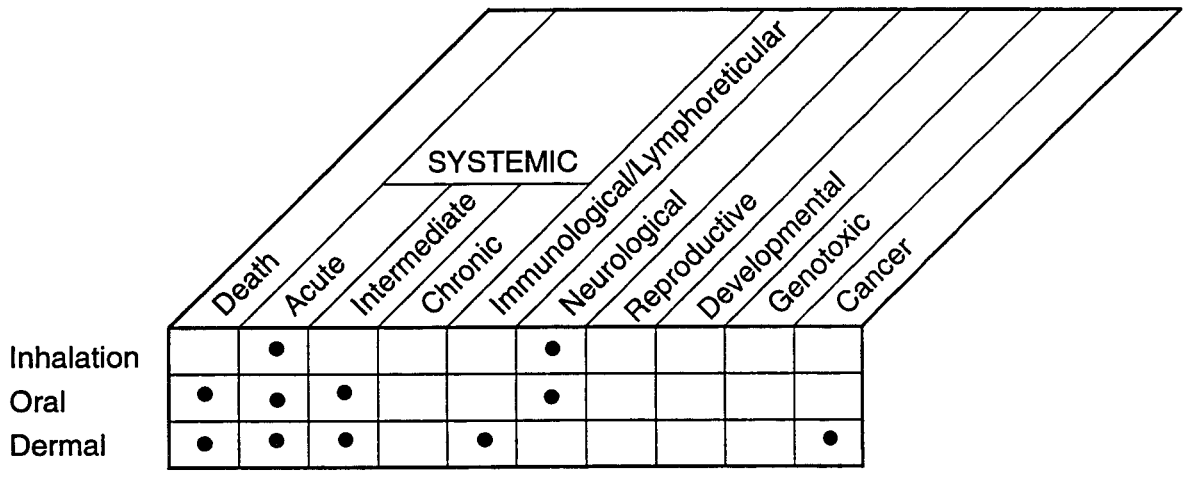
The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to used mineral-based crankcase oil are summarized in Figure 2-3. The purpose of this figure is to illustrate the existing information concerning the health effects of used mineral-based crankcase oil. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need." A data need, as defined in ATSDR's Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles (ATSDR 1989a), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

As seen in Figure 2-3, a large number of gaps exist in current knowledge of the health effects of used mineral-based crankcase oil in humans and animals. Data from humans are limited to two studies in which volunteers were exposed briefly to aerosols of used mineral-based crankcase oil (Dautrebande and Capps 1950; Dautrebande et al. 1951) and two epidemiology studies of persons exposed occupationally to used mineral-based crankcase oil (Clausen and Rastogi 1977; Steineck et al. 1989). Animal data are also limited, consisting of a series of acute oral and dermal toxicity and irritation tests in rodents (API 1980b; Beck et al. 1984; Vemot et al. 1990), two acute-duration inhalation toxicity studies in rodents (Costa and Amdur 1979b; DOT 1983), an acute-to-intermediate-duration dietary study in ducks and pheasants (Eastin et al. 1983), two case reports of poisonings in cattle that grazed in contaminated pastures (Osweiler et al. 1973; Sas 1989), and a number of skin-painting oncogenicity studies in mice (API 1983; Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989).

FIGURE 2-3. Existing Information on Health Effects of Used Mineral-based Crankcase Oil



Human



Animal

● Existing Studies

2.10.2 Identification of Data Needs

Acute-Duration Exposure. Studies exist that have examined the effects of acute-duration inhalation, oral, and dermal exposures to used mineral-based crankcase oil in humans and/or animals (API 1980b; Beck et al. 1984; Costa and Amdur 1979b; Dautrebande and Capps 1950; Dautrebande et al. 1951; DOT 1983; Eastin et al. 1983; Vemot et al. 1990). However, no MRLs were derived for acute-duration inhalation or oral exposure to used mineral-based crankcase oil. This was due in part to the lack of reliable dose-response data and in part to the variability in the composition of batches of used mineral-based crankcase oil. Inhalation studies in humans identified mild eye, nose, and throat irritation as toxic end points (Dautrebande and Capps 1950; Dautrebande et al. 1951), but a study with guinea pigs showed no effect on pulmonary function (Costa and Amdur 1979a). In addition, an acute-duration inhalation study in rats showed no overt effects on either behavior or on pathology at necropsy (DOT 1983). An acute oral LD_{50} study in rats showed no lethality, but oily diarrhea was observed following administration of large oral doses (API 1980b; Beck et al. 1984; Vemot et al. 1990). Acute-duration dermal studies in rabbits identified slight-to-moderate skin irritation, but only negligible eye irritation was reported (API 1980b; Beck et al. 1984; Vemot et al. 1990). Repeated dermal doses in rabbits resulted in emaciation, but no specific systemic cause for the weight loss was identified (API 1980b; Beck et al. 1984; Vemot et al. 1990). This suggests that toxicity other than mild eye and skin irritation is possible with acute-duration exposures. The emaciation is probably due to reduced food intake, effects on intestinal absorption, general systemic toxicity or stress which alters metabolism, or a combination of these factors. What is required is a study in which food intake is carefully measured, histopathology and clinical chemistry is performed, and metal content of major organs is determined. Additional acute-duration inhalation studies are not warranted at this time since inhalation exposure to used mineral-based crankcase oil is unlikely.

Intermediate-Duration Exposure. No intermediate-duration inhalation or oral MRLs were derived for used mineral-based crankcase oil because of the absence of reliable dose-response data and variability in the composition of different batches of used mineral-based crankcase oil. No intermediate-duration inhalation studies were located, but such studies do not appear necessary at this time since inhalation exposures are not expected to occur unless the oil becomes aerosolized. Case reports of intermediate-duration oral exposures in cattle suggest that effects associated with metal toxicity may occur (Osweiler et al. 1973; Sas 1989). In addition, a study examining the health effects

associated with intermediate-duration exposure of monkeys to *unused* mineral-based crankcase oil indicated that severe gastrointestinal damage may occur with ingestion (Lushbaugh et al. 1950). Since used mineral-based crankcase oil may contain the same chemical that was responsible for the effects of exposure to the unused oil, similar effects may occur with intermediate-duration ingestion of used oil. These effects have not been thoroughly studied, and a well-conducted 90-day oral study in animals could provide valuable information about target organs in humans and exposure levels associated with toxicity. The only intermediate-duration dermal study that was located was a dermal sensitization study in guinea pigs that reported only effects on the skin (API 1980b; Beck et al. 1984; Vemot et al. 1990). As indicated in the repeated-dose, acute-duration study described above, target organs other than the skin are possible. Therefore, a 21- or 90-day dermal toxicity study in animals could provide valuable information regarding effects likely to occur in persons with intermediate-duration dermal exposures. The variations in used oil composition must be adequately dealt with for such studies to be meaningful. Pooled composite samples or possibly several pooled samples from vehicles driven a range of mileages would be required. A dermal study could provide information on potential systemic effects of used oil applied to the skin. Four consecutive daily applications of used motor oil to the skin of mice produced adducts in the DNA of the lung (Schoket et al. 1989). Evaluation of DNA adducts in the major organs, assays for red blood cell δ-ALAD to detect lead poisoning, measurement of concentrations of specific metals in serum and selected organs, and histopathologic examination of major organs should be performed in such a study.

Chronic-Duration Exposure and Cancer. No chronic-duration inhalation or oral MRLs were derived for used mineral-based crankcase oil because of the absence of reliable dose-response data and variability in the composition of different batches of used mineral-based crankcase oil. The only information located regarding the effects of chronic-duration exposure to used mineral-based crankcase oil in humans was a report of health effects experienced by a number of mechanics and other auto workers from 10 auto shops in Denmark (Clausen and Rastogi 1977). Additional studies examining health effects of chronic oral and dermal exposures among exposed populations would provide valuable information regarding the potential for such effects in similarly exposed populations. Chronic-duration animal studies with used mineral-based crankcase oil are limited to studies whose intent was to identify dermal carcinogenicity, and therefore other types of toxicity were not examined (Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989) or were examined incompletely (API 1983). Additional animal studies examining the health effects of chronic-duration oral and dermal exposures to used mineral-based crankcase oil, as well as water-soluble constituents of the used oil are

necessary to identify health effects that may be associated with such exposures. For the chronic oral study, daily administration of the water soluble components of used motor oil may be most useful for assessing risk around hazardous waste sites, as these components may leach into drinking water.

The only information located regarding carcinogenicity in humans after exposure to used mineral-based crankcase oil was a study that showed that persons with occupational exposure are not at an increased risk of renal pelvic or bladder cancer (Steineck et al. 1989). No information was located regarding the occurrence of other types of cancer in humans exposed to used mineral-based crankcase oil. Studies in mice have demonstrated that chronic-duration cutaneous exposure to used mineralbased crankcase oil increases the incidence of skin tumors (API 1983; Grimmer et al. 1982a, 1982b, 1983; McKee and Plutnick 1989). Thus, similar tumors may occur in exposed human populations. Additional studies directed at determining the cancer incidence in persons with chronic-duration dermal exposure to used mineral-based crankcase oil (occupational studies) could provide information on whether similar effects may occur in chronically exposed populations. However, epidemiology studies in which the effects of chronic dermal exposure to used motor oil are evaluated are often not very practical. The individuals who have repeated contact with used oil in service stations and garages do not, as a group, remain on the job for extended periods of time; hence a suitable population is almost impossible to find. A study examining the carcinogenicity of chronic-duration oral exposures to used mineral-based crankcase oil in rodents may provide information on whether persons exposed similarly might expect an increased risk of cancer.

Genotoxicity. No genotoxicity data were located regarding used mineral-based crankcase oil in mammalian systems. However, results from Salmonella mutation assays (Dutcher et al. 1986; Granella and Clonfero 1991; EPA 1980d; Manabe et al. 1984; Pasquini and Monarca 1983; Payne et al. 1978; Peake and Parker 1980; Schreiner and Mackerer 1982) and the formation of DNA adducts in the skin following cutaneous application of used mineral-based crankcase oil (Carmichael et al. 1990, 1992; Schoket et al. 1989) suggest that this substance may be mutagenic in humans. Additional *in vitro* mutagenicity tests in mammalian cells and *in vivo* analyses such as tests for chromosomal aberrations or micronucleus tests could provide more conclusive evidence for the genotoxicity of used mineral-based crankcase oil in humans. In addition, tests assessing DNA adducts in tissues of animals exposed experimentally could provide useful information about the distribution of such changes in the body.

Reproductive Toxicity. No information was located regarding the reproductive toxicity of used mineral-based crankcase oil in humans or animals. As the oral and dermal routes are the most likely routes of exposure to used mineral-based crankcase oil, intermediate-duration studies in animals using these routes of exposure and examining the effects on reproductive organs would be a useful first step in assessing the reproductive toxicity of this substance.

Developmental Toxicity. The only information located regarding developmental toxicity came from an egg-painting study using ducks and quail (Hoffman et al. 1982a) and another study in which used and virgin crankcase oil was injected into mallard eggs (Hoffmann and Albers 1984). These studies suggest that the developing bird fetus may be at risk when exposed to chemicals found in used mineral-based crankcase oil. Studies in mammals designed to assess the toxicity of used mineralbased crankcase oil following oral or dermal exposure during gestation could provide valuable information regarding the likelihood of developmental toxicity with maternal exposure. Toxicokinetic studies of known contaminants such as lead or PAHs in pregnant animals when administered in a mineral oil carrier could also provide information on the likelihood of fetal exposure.

Immunotoxicity. The only information located regarding immunological effects of used mineralbased crankcase oil came from a dermal sensitization study using guinea pigs that showed no sensitization after intermediate-duration exposure (API 1980b; Beck et al. 1984; Vernot et al. 1990). However, the positive control group also failed to show a potentiation of the dermal response in this study. Thus, the results are inconclusive. Since workers with exposure to used mineral-based crankcase oil report a moderate incidence of skin rashes on the hands and arms (not specified whether the rashes were allergic in nature) (Clausen and Rastogi 1977), an additional skin sensitization study could provide valuable information. In addition, if a subchronic oral or dermal exposure study in animals were conducted, examination of effects on lymphoid tissue and leukocyte content could also provide information indicating whether the immune system may be adversely affected. A test of bacterial infectivity could also provide information regarding immune function. Also, measurement of blood levels of immunoglobulins may provide subtle, but useful, information.

Neurotoxicity. Information regarding the neurotoxic potential of used mineral-based crankcase oil is largely anecdotal in nature. Limited information from a report of health effects in mechanics and other auto workers suggests that neurotoxic effects may be associated with occupational exposure to used mineral-based crankcase oil (Clausen and Rastogi 1977). In addition, cattle that ingested used

mineral-based crankcase oil showed marked neurotoxicity (Osweiler et al. 1973; Sas 1989). Additional experimental studies in animals examining the potential for neurotoxicity after oral and dermal exposures under controlled conditions could provide valuable information as to whether persons exposed to used mineral-based crankcase oil under such conditions may be expected to experience adverse neurological effects. Neurotoxicity of crankcase oils can be evaluated as part of the subchronic oral or dermal studies.

Epidemiological and Human Dosimetry Studies. Limited information was located regarding epidemiological analyses of exposed populations. Renal, pelvic, and bladder cancers among workers exposed to motor oil was examined in a study assessing the incidence of these tumor types among different occupational groups (Steineck et al. 1989), and health effects and blood lead levels were examined among workers in a small number of auto shops in Denmark (Clausen and Rastogi 1977). Assessing the health effects among various groups of workers occupationally exposed to used mineral-based crankcase oil could be valuable in establishing cause/effect relationships that would be helpful in monitoring populations living near hazardous waste sites.

Biomarkers of Exposure and Effect

Exposure. No information was located regarding biomarkers that are specific for exposure to used mineral-based crankcase oil. The available literature on health effects of used mineral-based crankcase oil indicates a few biomarkers of exposure for specific chemicals found in used mineral-based crankcase oil such as metal content of the blood (Clausen and Rastogi 1977; Osweiler et al. 1973; Sas 1989) or DNA-adduct formation with PAHs (Carmichael et al. 1990; Schoket et al. 1989) . However, since the toxicity of used mineral-based crankcase oil is expected to vary with chemical content, effective biomarkers for exposure would also be expected to vary with chemical content of the oil. Thus, additional research regarding biomarkers of exposure should be addressed on a chemical-specific basis.

Effect. As discussed above for biomarkers of exposure, no information was located regarding biomarkers that were specific for effects of used mineral-based crankcase oil. Examination of the literature on health effects of used mineral-based crankcase oil indicated that DNA-adduct formation by PAHs may be an indicator of the genotoxic potential of used mineral-based crankcase oil. However, the chemical content of used mineral-based crankcase oil is expected to vary greatly, and

additional research regarding other biomarkers of effect should be addressed on a chemical-specific basis.

Absorption, Distribution, Metabolism, and Excretion. No information was located regarding the metabolism of used mineral-based crankcase oil, and only very limited animal data were located regarding absorption, distribution, and excretion following oral and dermal exposures to used mineral-based crankcase oil (API 1980b; Beck et al. 1984; Blakley and Brockman 1976; Carmichael et al. 1990; Osweiler et al. 1973; Sas 1989; Schoket et al. 1989; Vemot et al. 1990). No other quantitative data were located regarding the absorption, distribution, metabolism, and excretion of used mineral-based crankcase oil following inhalation, oral, or dermal exposure in humans or animals. Therefore, acute, intermediate, and chronic exposure 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 and dose for the primary chemical constituents of concern. A definitive pharmacokinetics study of absorption of PAHs, lead, and other potentially toxic materials administered in mineral oil through the intact skin of animals would be useful. Once that information is available, the actual hazard associated with dermal exposure can be estimated. In addition, animal and human data are needed to identify target organs among multiple species.

Comparative Toxicokinetics. No studies were located regarding comparative toxicokinetics of used mineral-based crankcase oil. Human and animal data are needed in order to examine toxicokinetics across species, i.e., in humans and animals of 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.

Methods for Reducing Toxic Effects. Although the mechanisms of absorption of used mineralbased crankcase oil from the gastrointestinal tract and skin have not been studied, methods have been identified that may be useful for reducing absorption of used mineral-based crankcase oil from these areas. For example, washing with mild lipophilic soap has been recommended for removal from exposed skin (Ellenhorn and Barceloux 1988), and induction of emesis, gastric lavage, and administration of activated charcoal and/or osmotic cathartics have been suggested for decreasing gastrointestinal absorption (Ellenhom and Barceloux 1988; Goldfrank et al. 1990; Haddad and Winchester 1990). Additional research into the mechanisms of absorption of used mineral-based crankcase oil and/or chemicals contained in the oil through the skin or the gastrointestinal tract could

provide a basis for developing more specific methods for reducing absorption. No specific methods were identified for reducing the body burden or for interfering with the mechanisms of action of used mineral-based crankcase oil. Such mitigation strategies would best be approached on a substance-specific basis depending on the additives or contaminants in the oil that are believed to be of toxicological significance. Until specific toxic effects are clearly defined, methods for reducing toxic effects must remain generalized.

2.10.3 On-going Studies

No information was located regarding on-going studies evaluating either the health effects or toxicokinetics of used mineral-based crankcase oil.