CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

Acetone is a colorless volatile liquid at room temperature. It is water soluble and will volatize from soil and water. Acetone is used primarily as an intermediate in chemical production and as a solvent (ICIS 2017). It is used in many products, including paints and coatings, cleaning products, personal care products, and industrial products such as lubricants and plastics (CDR 2012, 2016).

In addition to its anthropogenic sources, acetone occurs naturally in the environment. Plants, trees, insects, and microbes emit acetone (Graedel et al. 1986; Isidorov et al. 1985; Khalil and Rasmussen 1992). Acetone is produced during human-made and natural combustion such as volcanic eruptions (Isidorov et al. 1990), forest fires (Graedel et al. 1986), vehicular exhaust (Graedel et al. 1986), trash incineration (Graedel et al. 1986), and smoking tobacco (Manning et al. 1983). Acetone is also formed endogenously in the human body as a byproduct of metabolism. Baseline levels of acetone vary from person to person. Children and adolescents tend to produce more endogenous acetone than adults due to their relatively high metabolic rates (Johanson 2012). People with diabetes may produce high levels of endogenous acetone in the process of metabolizing fatty acids in blood (Johanson 2012).

As a result of its emission during combustion, acetone is present in the air, leaving the general population susceptible to inhalation exposure. However, acetone levels in ambient air in the United States are low, ranging from less than 1 ppb (volume per volume) in remote areas (Cavanagh et al. 1969) to 6.9 ppb in urban air (Shah and Singh 1988). The low levels of acetone in ambient air reduce the concern for inhalation exposure in the general population. Individuals who smoke cigarettes, frequently use acetone-containing products in their home, or work in certain occupations may have higher risk of exposure.

Oral exposure to acetone may occur when people eat foods that contain acetone or drink water contaminated with acetone. Acetone has been detected in the volatile components of several fruits and vegetables (Bartley and Schwede 1989; Lovegren et al. 1979). No information on average dietary intake was found. Disulfiram, a medicine commonly used in alcohol aversion therapy, has been found to induce endogenous acetone production in humans and animals (DeMaster and Stevens 1988; Stowell et al. 1980). While acetone may already be present in water in low levels due to atmospheric deposition, landfill leaching and discharges from manufacturers can lead to increased levels of acetone in drinking water. Well water may be especially susceptible to acetone pollution due to acetone’s mobility in soil.

Dermal exposures may occur when individuals use products that contain acetone such as personal care (e.g., nail polish remover) or cleaning products or come into contact with water or soil containing acetone.

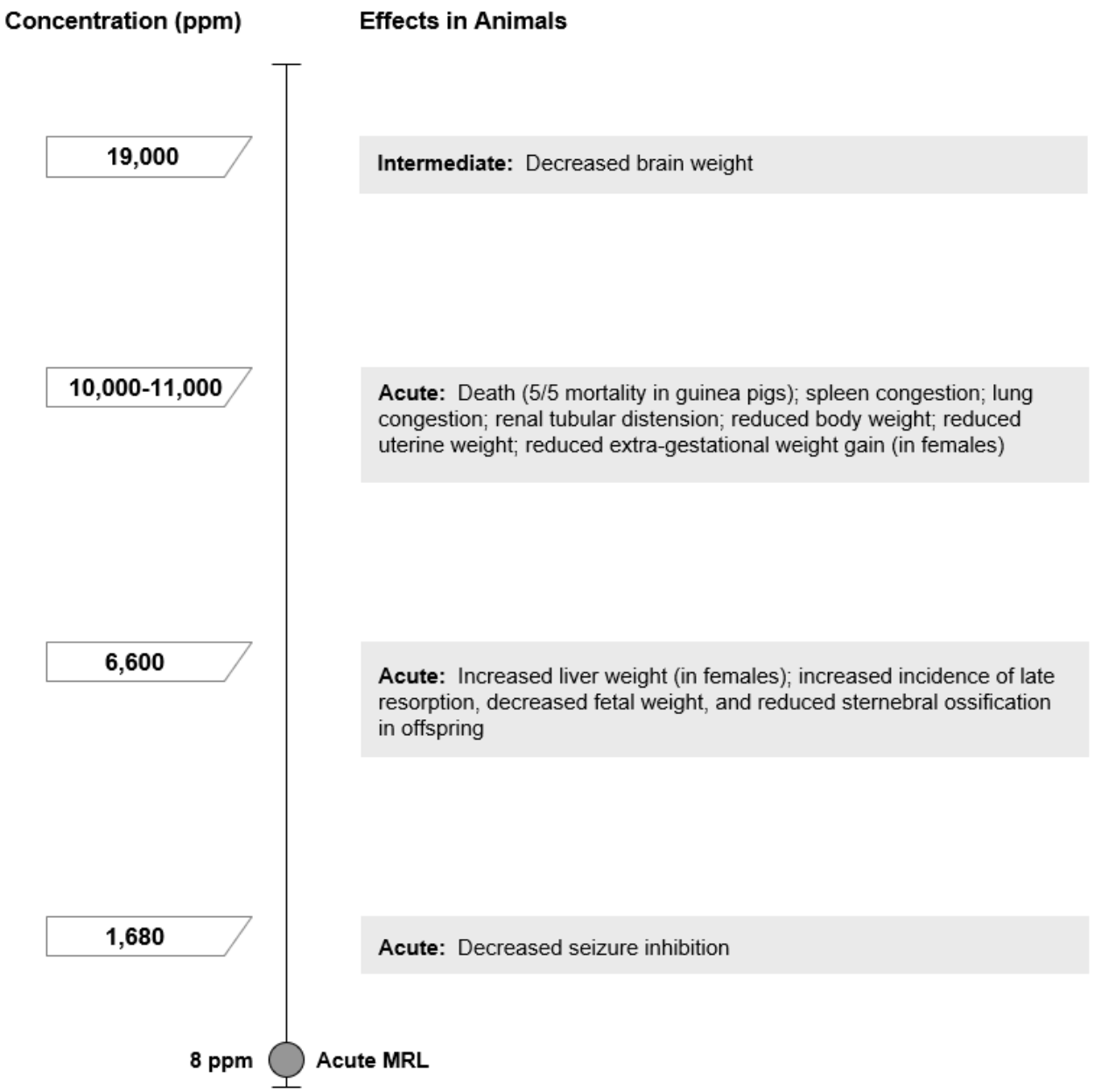
Acetone is produced endogenously by the human body, and this production varies from human to human. Therefore, baseline levels of acetone in the human body may also vary from person to person. Acetone in the body can be detected in exhaled breath, urine, blood, and breastmilk. However, because acetone is eliminated within 1–3 days, these biomarkers should only be used to monitor recent acetone exposure. While biomarkers are useful for assessing exposure to high levels of acetone found in, for example, occupational exposure studies, they are less accurate for the lower acetone levels found in the general population.

1.2 SUMMARY OF HEALTH EFFECTS

The health effects of acetone have been evaluated in epidemiology studies, controlled human trials, and experimental animal studies. Most studies examined acute inhalation or oral exposure to acetone. Both human and animal studies were located for the majority of the endpoints evaluated in this profile. However, body weight was only evaluated in animal studies, and no studies were located on the endocrine effects of acetone. Figures 1-1, 1-2, and 1-3 show the lowest-observed-adverse-effect levels (LOAELs) of acetone for various endpoints. The current body of literature suggests the following six main endpoints that are sensitive to acetone exposure:

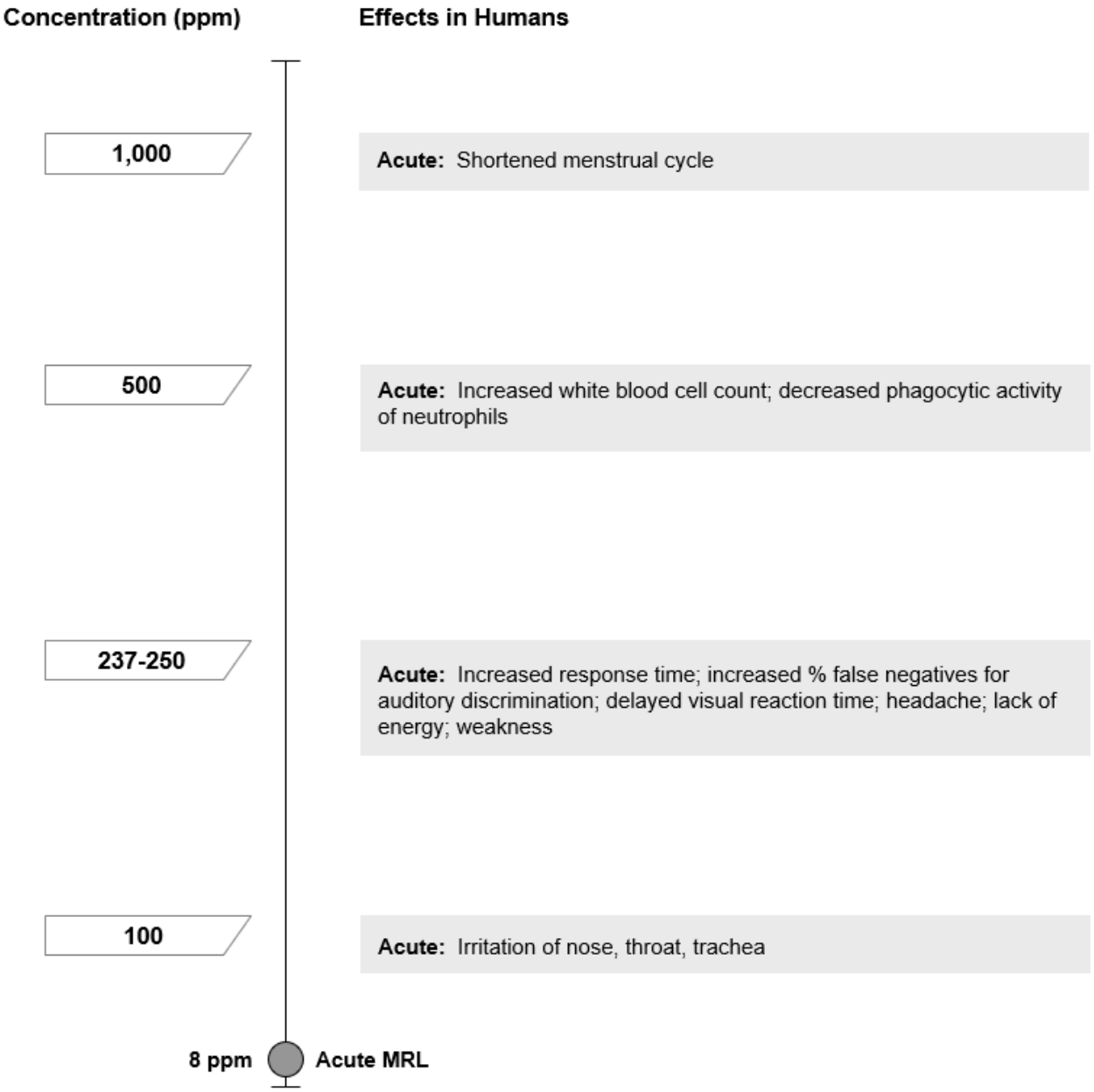
Neurological Effects. Neurological effects are the most common endpoint evaluated in the body of literature on acetone, occurring after oral or inhalation exposure. Neurological effects in humans exposed to acetone range from dizziness and headaches (Pomerantz 1950; Raleigh and McGee 1972) to dulling of reflexes (Chen et al. 2002; Haggard et al. 1944), unconsciousness (Ross 1973), and anger and hostility (Dick et al. 1989). Neurological effects, including narcosis, increases in anger and hostility, and loss of coordination have been observed in animals exposed to acetone (NTP 1988; Specht et al. 1939).

Figure 1-1. Health Effects Found in Animals Following Inhalation Exposure to Acetone*



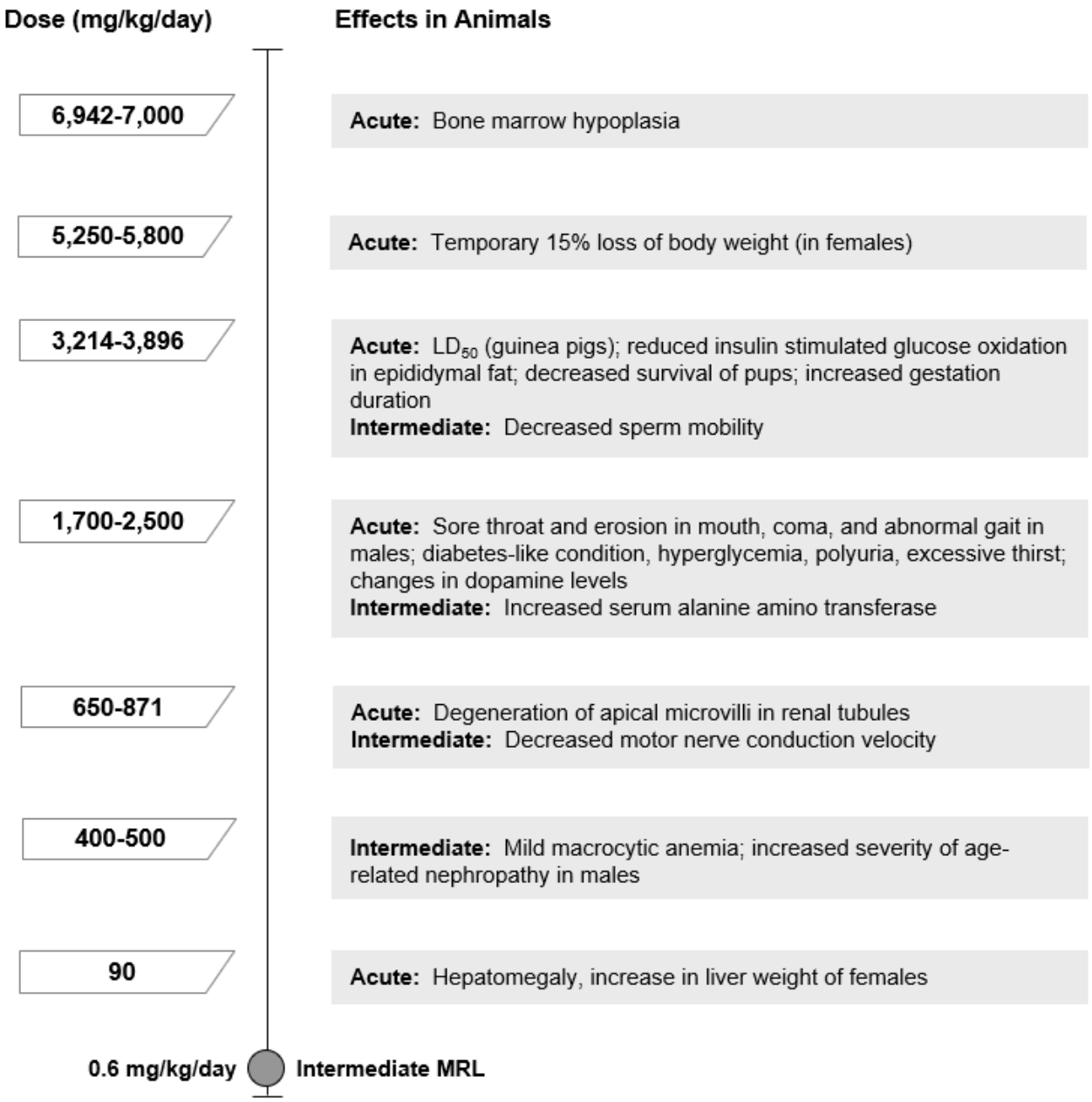
*Durations noted in Figure 1-1 refer to the duration of exposure that led to the specified health effect. See Chapter 2 for further discussion of the data presented in Figure 1-1.

Figure 1-2. Health Effects Found in Humans Following Inhalation Exposure to Acetone*



*Durations noted in Figure 1-2 refer to the duration of exposure that led to the specified health effect. See Chapter 2 for further discussion of the data presented in Figure 1-2.

Figure 1-3. Health Effects Found in Humans and Animals Following Oral Exposure to Acetone*



*Durations noted in Figure 1-3 refer to the duration of exposure that led to the specified health effect. See Chapter 2 for further discussion of the data presented in Figure 1-3.

Hematological Effects. Hematological effects due to acetone were found in human and animal studies following inhalation and oral exposure. Humans exposed to acetone showed increased white blood cell counts (Herman et al. 1997; Matsushita et al. 1969a, 1969b). Male rodents exposed to acetone in drinking water had bone marrow hypoplasia and signs of macrocytic anemia (Dietz et al. 1991; NTP 1991). Differences in hematological effects have been observed based on animal species and sex (American Biogenics Corp. 1986), which may signify males' higher susceptibility to acetone.

Renal Effects. Most renal effects associated with acetone exposure are based on oral exposure studies in animals. Increased kidney weight was found in rats and mice after oral acetone exposure (Dietz et al. 1991; NTP 1991), and male rats showed degeneration of the apical microvilli of renal tubules (Brown and Hewitt 1984). The renal lesions present in some studies were thought to be a sign of acetone-compounded nephropathy normally found in aging rodents (American Biogenics Corp. 1986; NTP 1991). Severe renal effects including moderate tubulointerstitial nephritis (Chen et al. 2002) and renal failure (Piatkowski et al. 2007) were reported in human case studies following inhalation exposure to acetone, but no epidemiologic studies verifying these effects were located.

Respiratory Effects. Human studies evaluating the respiratory effects of inhaled acetone exposure primarily found irritation of the nose, throat, trachea, and lungs. The irritating properties of acetone in humans have been noted both in workers who were exposed to acetone occupationally (Kiesswetter and Seeber 1995; Raleigh and McGee 1972; Ross 1973) and in volunteers under controlled laboratory conditions (Matsushita et al. 1969a, 1969b; Nelson et al. 1943). Animals exposed to higher concentrations of acetone had more severe respiratory effects including pulmonary congestion and hemorrhage (Specht et al. 1939). However, some animal studies did not observe respiratory effects on histopathological examination despite using high levels of acetone (Bruckner and Peterson 1981b; Schaper and Brost 1991).

Ocular Effects. Eye irritation has been associated with occupational (Mitran et al. 1997; Raleigh and McGee 1972) and voluntary (Matsushita et al. 1969a, 1969b; Nelson et al. 1943; Ross 1973) exposure to acetone. Unlike the other endpoints evaluated in this section, the ocular effects found in human and animal studies have primarily been observed following dermal exposure or direct eye-to-vapor contact.

Reproductive Effects. At high doses, acetone exposure has been associated with changes in testicular function such as decreases in sperm motility and increases in the numbers of abnormal sperm in rats but not mice (Dietz et al. 1991; NTP 1991). However, no changes in testicular morphology were observed,

and another study in rats by Larsen et al. (1991) found no significant decreases in male fertility. One study in male workers exposed to acetone and styrene found evidence of changes in sperm parameters (Jelnes et al. 1988).

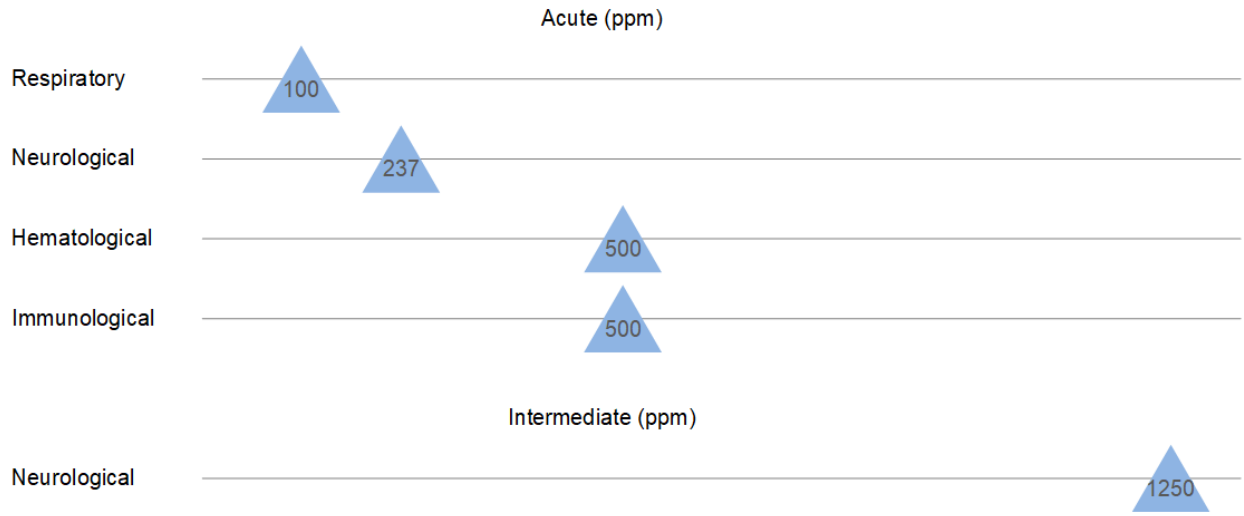
Acetone has not been evaluated by the Department of Health and Human Services or the International Agency for Research on Cancer (IARC) with regard to its carcinogenicity (IARC 2021; NTP 2021). The U.S. Environmental Protection Agency (EPA) determined that data are inadequate for an assessment of the human carcinogenic potential of acetone (EPA 2003).

1.3 MINIMAL RISK LEVELS (MRLs)

Minimal risk levels (MRLs) for inhalation and oral exposures to acetone were derived. Figures 1-4 and 1-5 summarize sensitive targets of acetone for inhalation and dermal exposures, respectively. As shown in Table 1-1 and discussed in greater detail in Appendix A, the inhalation database was only considered adequate for derivation of an acute-duration inhalation MRL for acetone. The oral database was only considered adequate for derivation of an intermediate-duration oral MRL.

Figure 1-4. Summary of Sensitive Targets of Acetone – Inhalation

The respiratory endpoint is the most sensitive target of acetone following inhalation exposure.
Numbers in triangles are the lowest LOAELs among health effects in humans.

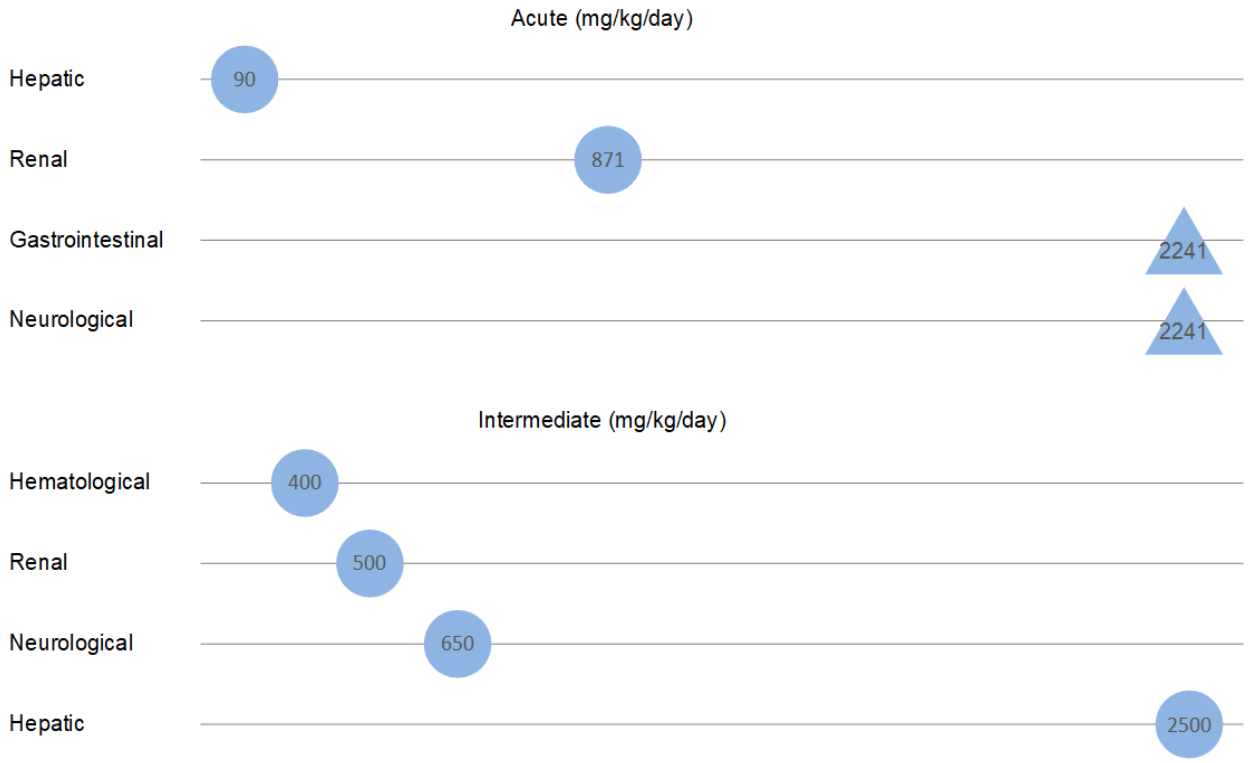


See Chapter 2 for further discussion of the data presented in Figure 1-4.

Figure 1-5. Summary of Sensitive Targets of Acetone – Oral

The hepatic and hematological endpoints are the most sensitive targets of acetone following oral exposure.

Numbers in triangles and circles are the lowest LOAELs among health effects in humans and animals, respectively.



See Chapter 2 for further discussion of the data presented in Figure 1-5.

Table 1-1. Minimal Risk Levels (MRLs) for Acetone[a]

Exposure duration	MRL	Critical effect	Point of departure/ human equivalent concentration	Uncertainty and modifying factor	Reference
Inhalation exposure (ppm)					
Acute	**8**	Neurobehavioral effects in humans	LOAEL: 237	UF: 30	Dick et al. 1989
Intermediate	Insufficient data for derivation of an MRL				
Chronic	Insufficient data for derivation of an MRL				
Oral exposure (mg acetone/kg/day)					
Acute	Insufficient data for derivation of an MRL				
Intermediate	**0.6**	Anemia with decreased reticulocyte count	$BMDL_{1SD}$: 57.0	UF: 100	Dietz et al. 1991; NTP 1991
Chronic	Insufficient data for derivation of an MRL				

[a]See Appendix A for additional information.

$BMDL_{1SD}$ = 95% lower confidence limit on the BMD (subscripts denote benchmark response: i.e., 1SD = dose associated with 1 standard deviation from the mean); LOAEL = lowest-observed-adverse-effect level; UF = uncertainty factor