CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

ATSDR's *Toxicological Profile for Dinitrocresols* was released in 1995. In order to update the literature in this profile, ATSDR conducted a literature search focused on health effects information as described in Appendix B. Chapters 2 and 3 were revised to reflect the most current health effects data. In some cases, other sections of the profile were updated as needed or for consistency with the updated health effects data. However, the focus of the update to this profile is on health effects information.

Dinitrocresols are a group of organic chemicals that can contain up to 18 individual compounds. 4,6-Dinitro-*o*-cresol (DNOC) is the most commercially important dinitrocresol. DNOC is a yellow solid with no smell; it dissolves slightly in water. DNOC in water and soil does not easily evaporate to air. DNOC was primarily used to protect fruit trees and other food crops from insect damage. However, the U.S. Environmental Protection Agency (EPA) has cancelled its registration as a pesticide. In the 1930s, DNOC was used in pills for reducing weight. It is no longer used for this purpose because of bad effects on health. The most likely source of exposure for the general population is from contaminated drinking water. Populations living near sites containing DNOC wastes may be exposed by breathing contaminated air as well.

1.2 SUMMARY OF HEALTH EFFECTS

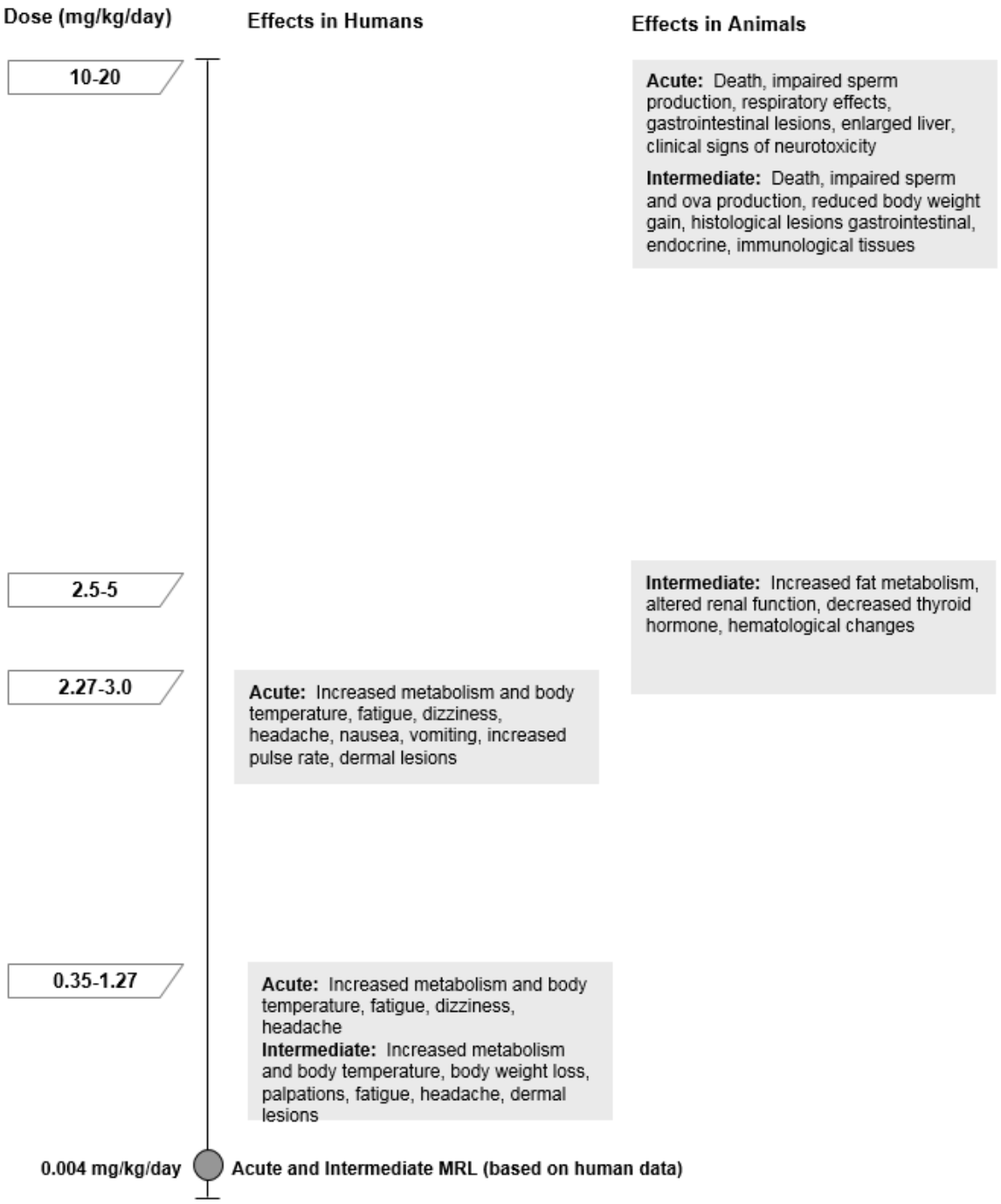
DNOC uncouples oxidative phosphorylation, resulting in energy being given off as heat and manifested as hyperthermia. In an attempt to reduce body temperature, the body increases respiratory rate and heart rate as part of a compensatory mechanism. The most significant and sensitive effects resulting from acute, intermediate, or chronic exposure are related to increased basal metabolic rates in humans. Overexposure to DNOC has resulted in death in humans and animals.

Increased pulse rate, respiratory rate, and profuse sweating were commonly seen in humans and animals exposed to DNOC. Neurological signs such as lethargy, depression, and peripheral neuritis have occurred in humans exposed to DNOC. Maculopapular urticarial eruptions were also observed in humans after oral exposure; this effect was not seen in animals. DNOC has been associated with cataract formation in humans. Cataract formation is an important reason why the government and the medical community stopped use of DNOC and dinitrophenol for weight loss in humans. A limited number of animal studies reported DNOC-induced effects on sperm and lack of corpora lutea production. There are no reliable

human data regarding DNOC-induced reproductive or developmental effects. No data were located regarding potential for DNOC to cause cancer in humans or animals. However, clastogenicity has been demonstrated in both *in vivo* and *in vitro* human and animal test systems.

As illustrated in Figure 1-1, the most sensitive effects following oral exposure are cardiovascular, metabolic, immunological (dermal allergic reactions), and neurological effects.

Figure 1-1. Health Effects Found in Animals and Humans Following Oral Exposure to Dinitrocresols



1.3 MINIMAL RISK LEVELS (MRLs)

As presented in Figure 1-2, limited inhalation data from animals indicate metabolic and hematological systems as particularly sensitive targets of DNOC toxicity. However, the available information is considered insufficient to derive inhalation MRLs for DNOC. As presented in Figure 1-3, available oral data from humans identify metabolism, neurological, cardiovascular, and immunological systems as the most sensitive targets of DNOC toxicity; laboratory animal data generally support the findings in humans. The MRL values for acute- and intermediate-duration oral exposure to DNOC are summarized in Table 1-1 and discussed in greater detail in Appendix A.

Figure 1-2. Summary of Sensitive Targets of Dinitrocresols – Inhalation

The hematological and metabolic systems are the most sensitive target of dinitrocresols.
Based on the lowest LOAELs (mg/m^3) among health effects in animals; no human data were identified.

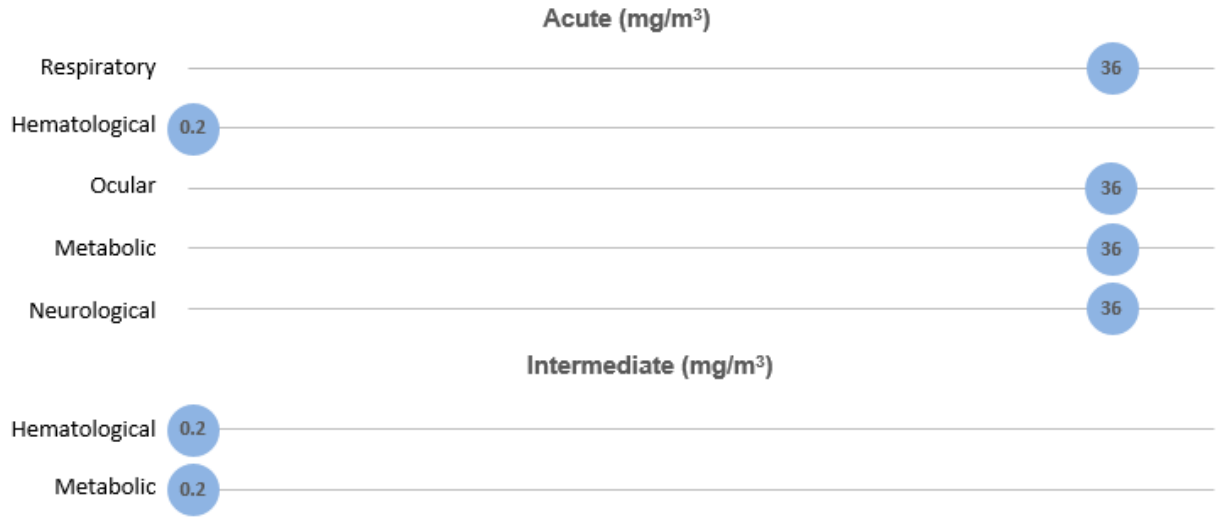


Figure 1-3. Summary of Sensitive Targets of Dinitrocresols – Oral

Metabolism, cardiovascular system, immunological system, and nervous system are the most sensitive targets of dinitrocresols

Numbers in triangles and circles are the lowest LOAELs (mg/kg/day) among health effects in humans and animals, respectively

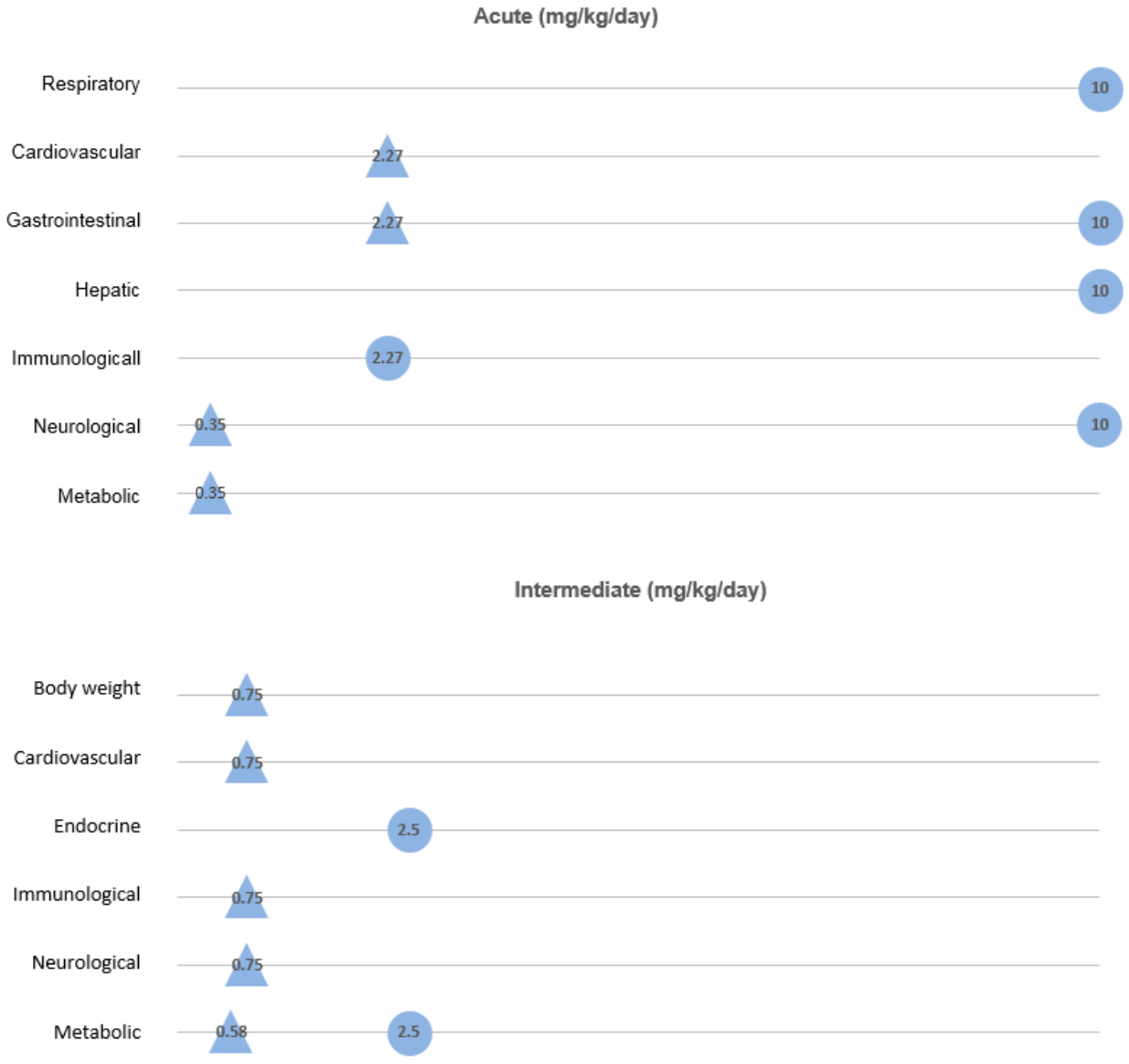


Table 1-1. Minimal Risk Levels (MRLs) for Dinitrocresols[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure (ppm)					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				
Oral exposure (mg/kg/day)					
Acute[b]	0.004	Neurological effects	0.35 (LOAEL)	100	Plotz 1936
Intermediate[b]	0.004	Neurological effects	0.35 (LOAEL)	100	Plotz 1936
Chronic	Insufficient data for MRL derivation				

[a]See Appendix A for additional information.
[b]MRL derived for 4,6-dinitro-*o*-cresol.

LOAEL = lowest-observed-adverse-effect level