CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

Aldrin and dieldrin are highly chlorinated substances that were designed to control a variety of insects that are pests, such as termites. Thus, they can and are called insecticides and pesticides. Aldrin is readily converted to dieldrin under most environmental conditions and in the body. Aldrin was first produced in 1948, and dieldrin was first used in 1950. In 1970, the U.S. Department of Agriculture (USDA) canceled all uses for both aldrin and dieldrin based on concern that these chemicals are serious environmental hazards and are potentially carcinogenic. However, uses of these pesticides were not canceled by EPA until 1989.

Both aldrin and dieldrin are semi-volatile and slow to biodegrade. Large soil adsorption coefficients suggest low mobility in soils and a tendency to partition to suspended solids and sediment in the water column. Low levels of aldrin and dieldrin have been detected in soil, sediment, surface water, groundwater, and public water supplies. Dieldrin has been detected in food, such as root crops, dairy products, and meat.

Ingestion of drinking water or food items containing aldrin and/or dieldrin is the most likely route of exposure by the general population. However, exposure to aldrin and dieldrin is expected to be low since the compounds are no longer manufactured or used in the United States. In the most recently available biomonitoring data (samples taken in 2003–2004), aldrin and dieldrin serum levels were undetectable or very low. People living in areas surrounding hazardous waste sites that contain aldrin and/or dieldrin may be exposed primarily via dermal contact with, or ingestion of, contaminated soil since these compounds bind to soil particles. Aldrin and dieldrin possess high potential for bioaccumulation (based on log K_{ow} values in the range of 4–6). Aldrin and dieldrin have been observed to bioconcentrate in aquatic and terrestrial ecological systems. Aldrin is readily converted to dieldrin by epoxidation in biological systems.

1.2 SUMMARY OF HEALTH EFFECTS

Human data regarding the health effects of aldrin and dieldrin come from reports of occupationally-exposed cohorts, studies that employed self-reported use of aldrin or dieldrin and possible associations with health outcomes, studies that evaluated possible associations between dieldrin blood levels and

health outcomes, and case reports of accidental or intentional poisonings. Acute high-level exposure to aldrin or dieldrin in humans has resulted in central nervous system excitation culminating in convulsions and ultimately death. Longer-term exposure of humans in occupational settings has also been associated with adverse effects on the central nervous system. A few case reports have attributed liver and kidney toxicity and hemolytic anemia to intentional or accidental oral exposure to aldrin or dieldrin, but these effects were not observed in larger occupational studies. In general, the epidemiological data are lacking dose-response information.

Available studies in animals employed oral exposure (via diet, gavage, or capsule). As illustrated in Figure 1-1 (aldrin) and Figure 1-2 (dieldrin), the most sensitive common targets of aldrin and dieldrin toxicity appear to be hepatic, neurological, and reproductive endpoints. Body weight and developmental endpoints appear to be sensitive targets of aldrin and/or dieldrin toxicity as well. A systematic review of noncancer endpoints resulted in the following hazard identification conclusions (see Appendix C for more information):

- Body weight effects represent a presumed health effect endpoint for humans (aldrin)
- Hepatic effects represent a presumed health effect endpoint for humans (aldrin, dieldrin)
- Neurological effects represent a presumed health effect endpoint for humans (aldrin, dieldrin)
- Reproductive effects represent a presumed health effect endpoint for humans (aldrin, dieldrin)
- Developmental effects represent a presumed health effect endpoint for humans (aldrin, dieldrin)

Body Weight Effects. Decreases in body weight gain have been observed in rats and dogs exposed to aldrin in the diet for intermediate or chronic durations (Deichmann et al. 1970; NCI 1978a; Treon et al. 1955); weight loss has also been observed in dogs chronically exposed to aldrin (Fitzhugh et al. 1964).

Hepatic Effects. Increased relative liver weight and histopathologic changes were observed among rats administered aldrin or dieldrin in the diet for up to 2 years (Fitzhugh et al. 1964; Treon et al. 1951a; Walker et al. 1969).

Neurological Effects. Single or repeated oral exposure of laboratory animals to aldrin or dieldrin resulted in clinical signs of neurological impairment such as convulsions, tremors, twitching, and hyper-excitability; disrupted operant behavior; impaired learning; and neuronal degeneration (Burt 1975; Kitselman 1953; NCI 1978a, 1978b; Treon et al. 1951b; Walker et al. 1969).

Figure 1-1. Health Effects Found in Animals Following Oral Exposure to Aldrin

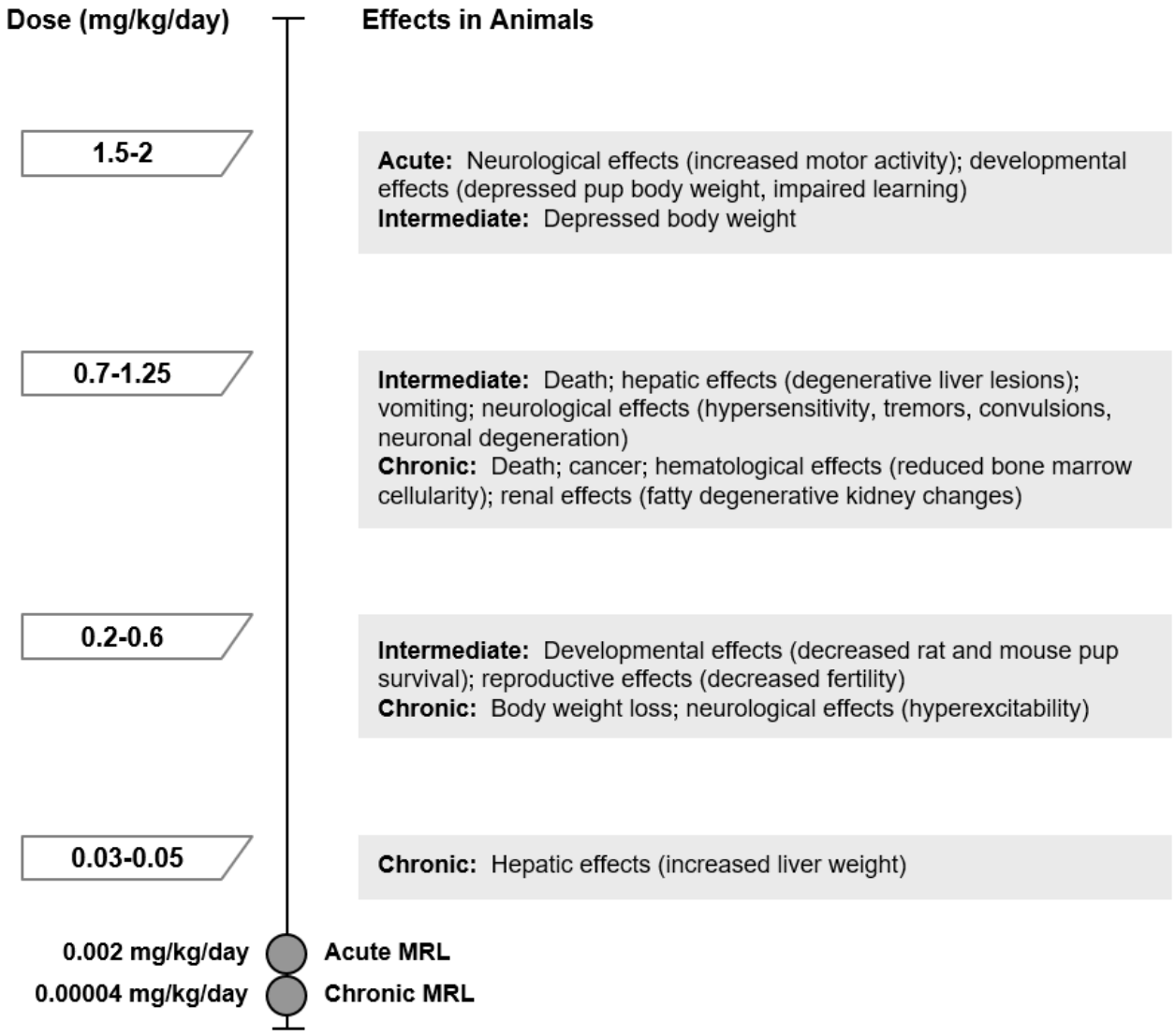
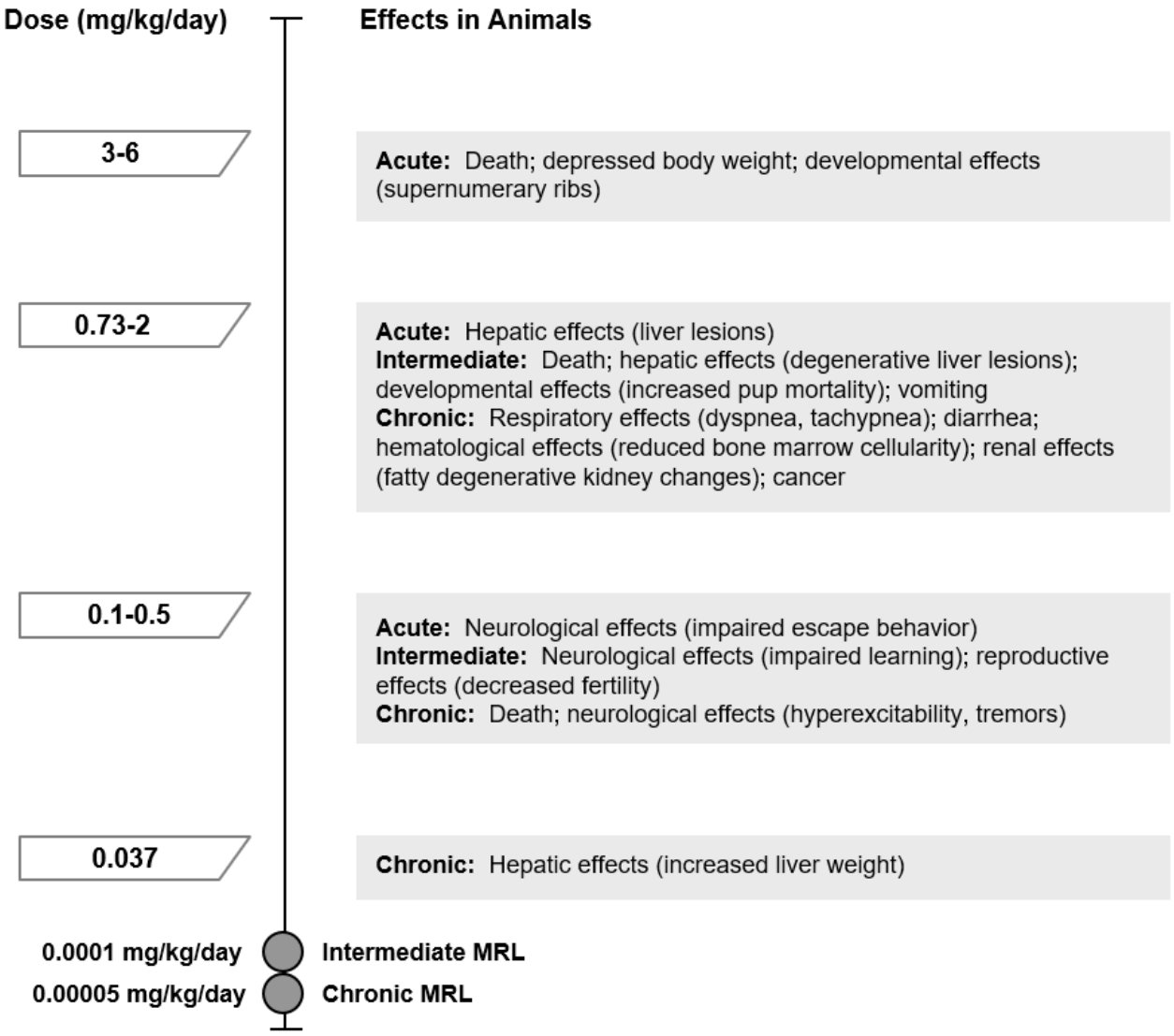


Figure 1-2. Health Effects Found in Animals Following Oral Exposure to Dieldrin



Reproductive Effects. In multi-generation reproduction studies in rodents, administration of aldrin or dieldrin in the diet resulted in decreased fertility (Keplinger et al. 1970; Treon et al. 1954a). Reproductive effects such as delayed estrus, reduced libido, lack of mammary function and development, and increased numbers of stillbirths were noted among dogs administered aldrin orally for 14 months prior to mating at doses as low as 0.15 mg/kg/day (Deichmann et al. 1971).

Developmental Effects. Increased postnatal mortality has been one of the most consistent developmental findings reported for aldrin and dieldrin in animals (Deichmann et al. 1971; Harr et al. 1970; Kitselman 1953; Treon et al. 1954a; Virgo and Bellward 1975). Aldrin or dieldrin exposure during gestation has resulted in some evidence of external malformations or skeletal anomalies in animals (Chernoff et al. 1975; Ottolenghi et al. 1974).

Cancer Effects. Increased incidences of liver tumors were reported in lifetime studies of multiple strains of mice administered aldrin or dieldrin in the diet (Davis and Fitzhugh 1962; Epstein 1975; Lipsky et al. 1989; Meierhenry et al. 1983; NCI 1978a; Reuber 1980; Tennekes et al. 1981; Thorpe and Walker 1973; Walker et al. 1973).

1.3 MINIMAL RISK LEVELS (MRLs)

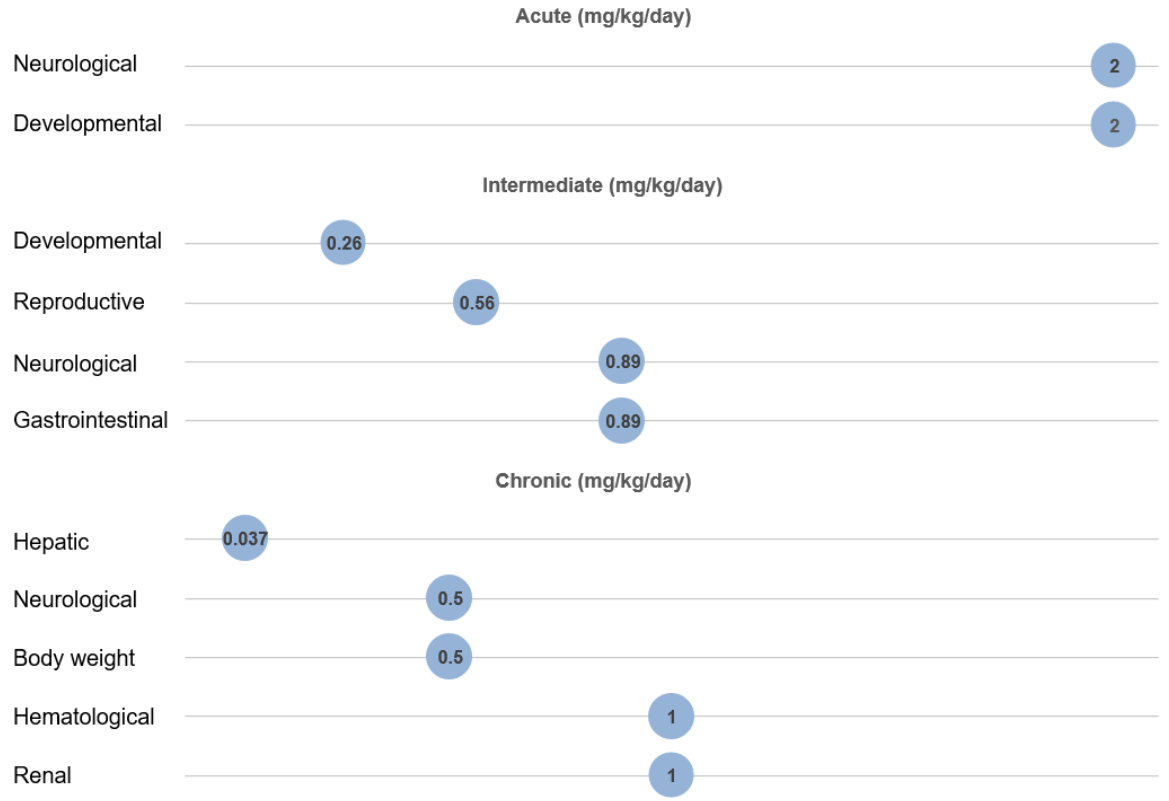
Aldrin. The inhalation database was considered inadequate for derivation of acute-, intermediate-, or chronic-duration inhalation MRLs for aldrin.

The oral database was considered inadequate for derivation of an intermediate-duration oral MRL for aldrin. The oral database was considered adequate for derivation of acute- and chronic-duration oral MRLs for aldrin. As presented in Figure 1-3, hepatic, developmental, and neurological endpoints are the most sensitive targets of aldrin toxicity following oral exposure.

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

The liver, developing organism, and nervous system are the most sensitive targets of aldrin oral exposure.

Numbers in circles are the lowest LOAELs for all health effects in animals; no reliable exposure-response human data were identified.



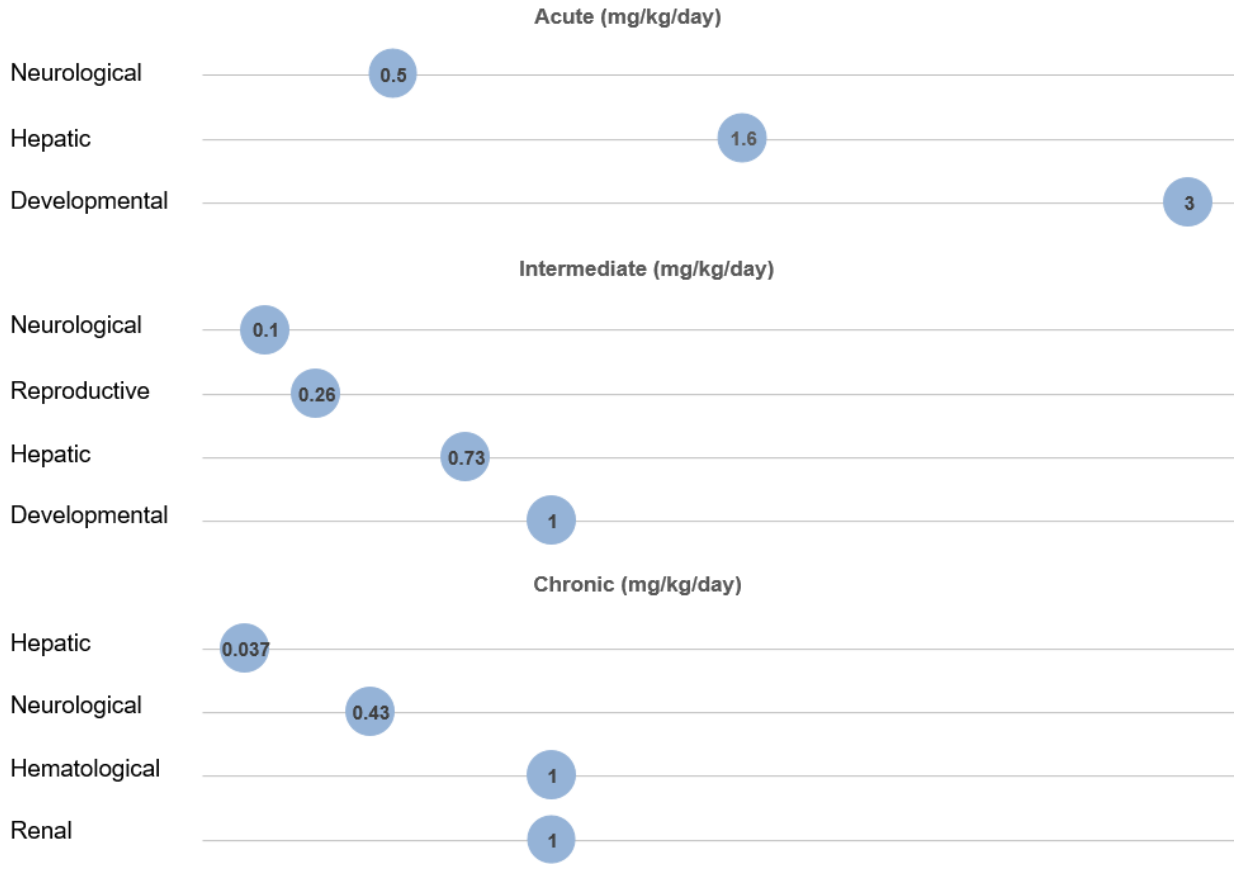
Dieldrin. The inhalation database was considered inadequate for derivation of acute-, intermediate-, or chronic-duration inhalation MRLs for dieldrin.

The oral database was considered inadequate for derivation of an acute-duration oral MRL for dieldrin. The oral database was considered adequate for derivation of intermediate- and chronic-duration oral MRLs for dieldrin. As presented in Figure 1-4, hepatic, neurological, and reproductive endpoints are the most sensitive targets of toxicity following oral exposure.

Figure 1-4. Summary of Sensitive Targets of Dieldrin – Oral

The nervous system, liver, and reproductive system are the most sensitive targets of dieldrin oral exposure.

Numbers in circles are the lowest LOAELs for all health effects in animals; no reliable exposure-response human data were identified.



The MRL values for aldrin are summarized in Table 1-1 and discussed in greater detail in Appendix A.

Table 1-1. Minimal Risk Levels (MRLs) for Aldrin[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	0.002 (2 µg/kg/day)	Neurotoxicity in offspring	2 (LOAEL)	1,000	Al-Hachim 1971
Intermediate	Insufficient data for MRL derivation				
Chronic	0.00004 (0.04 µg/kg/day)	Increased liver weight and histopathology	0.037 (LOAEL)	1,000	Fitzhugh et al. 1964

[a]See Appendix A for additional information.

LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level

The MRL values for dieldrin are summarized in Table 1-2 and discussed in greater detail in Appendix A.

Table 1-2. Minimal Risk Levels (MRLs) for Dieldrin[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	Insufficient data for MRL derivation				
Intermediate	0.0001 (0.1 µg/kg/day)	Neurotoxicity	0.01 (NOAEL)	100	Smith et al. 1976
Chronic	0.00005 (0.05 µg/kg/day)	Liver effects	0.005 (NOAEL)	100	Walker et al. 1969

[a]See Appendix A for additional information.

LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level