Health Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: August 2018

Toxicological Summary for: Dieldrin

CAS: **60-57-1**

Synonyms: 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo-1,4-exo-5,8-dimethanonaphthalene

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 0.2 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.00011 mg/kg-d) x (0.5)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.285 L/kg-d)}^{**}}$$

= 0.19 rounded to **0.2 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration:	HED/Total UF = 0.00011 mg/kg-d (Squirrel Monkey)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	0.01 mg/kg-d (NOAEL, Smith et al. 1976)
Dose Adjustment Factor (DAF):	0.32 (Body weight scaling, subchronic Squirrel Monkey (USEPA, 2011) (Wisconsin, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 0.01 mg/kg-d x 0.32 = 0.0032 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Impaired learning
Co-critical effect(s):	Decrease in pup viability, increased preweaning pup mortality decreased antigen processing by alveolar macrophages, decreased tumor cell killing ability

Additivity endpoint(s):	Developmental, Immune system, Nervous system

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = $nHRL_{Short\text{-}term}$ = 0.2 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.00009 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.070 L/kg-d)}^{**}}$$

= 0.26 rounded to 0.3 µg/L

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration:	HED/Total UF = 0.00009 mg/kg-d (Beagle Dog)
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	0.005 mg/kg-d (NOAEL, Walker et al. 1969 aci USEPA, 2003)
Dose Adjustment Factor (DAF):	0.53 (Body weight scaling, 3 month female dog DAF) (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 0.005 mg/kg-d x 0.53 = 0.0027 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Increased plasma alkaline phosphatase (AP) activity,
Co-critical effect(s):	Decrease in pup viability, decreased litter size, decreased survival as a result of hyperesthetia in both dams and pups, decreased antigen processing by alveolar macrophages, decreased tumor cell killing ability, impaired learning
Additivity endpoint(s):	Developmental, Hepatic (liver) system, Immune system, Nervous system

The Subchronic nHRL must be protective of the short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 0.2 µg/L. Additivity endpoints: Developmental, Immune system, Nervous system.

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 0.2 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{}$$

(Chronic Intake Rate, L/kg-d)

$$= \frac{(0.000043 \text{ mg/kg-d}) \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.044\text{L/kg-d})^{**}}$$

= 0.19 rounded to **0.2 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration:	HED/Total UF = 0.000043 mg/kg-d (Carworth Farm E Rats))
Source of toxicity value:	Determined by MDH in 2016
Point of Departure (POD):	0.005 mg/kg-d (NOAEL, Walker et al. 1969 aci USEPA, 2003)
Dose Adjustment Factor (DAF):	0.26 (Body weight scaling, average chronic female rat (USEPA, 2011) (MDH, 2017)
Human Equivalent Dose (HED):	POD x DAF = 0.005 mg/kg-d x 0.26 = 0.0013 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability
Critical effect(s):	Increased relative liver weight
Co-critical effect(s):	Cerebral edema and small foci degeneration, decreased litter size, increased relative liver weight, decreased antigen processing by alveolar macrophages, decreased tumor cell killing ability
Additivity endpoint(s):	Developmental, Hepatic (liver) system, Immune system, Nervous system

Cancer Health Risk Limit (cHRL) = 0.006 µg/L

$$\frac{(\text{Additional Lifetime Cancer Risk, } 1 \times 10^{-5}) \times (\text{Conversion Factor, } 1000 \text{ µg/mg})}{(\text{Slope Factor, per mg/kg-d}) \times (\text{Lifetime Adjustment Factor}) \times (\text{Lifetime Intake Rate, L/kg-d})}$$

$$= \frac{(1 \times 10^{-5}) \times 1{,}000}{[(16 \times 2.5) \times 0.044 \text{ L/kg-day}]^{*}}$$

= 0.0057 rounded to **0.006 µg/L**

*Lifetime Adjustment Factor: MDH 2008, Section IV.E.2.
**Intake Rate: MDH 2008, Section IV.E.2. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Cancer classification:	B2, probable human carcinogen (USEPA, 1993) 2A probably carcinogenic to humans (IARC, 2016)
Slope factor (SF):	16 $(mg/kg\text{-}d)^{-1}$ (geometric mean of 13 slope factors from several mouse strains) (USEPA, 1993)
Source of cancer slope factor (SF):	USEPA, 1993
Tumor site(s):	Liver

Volatile: No

Summary of Guidance Value History:

A cancer health based value (HBV) of 0.02 µg/L was first derived in 1997. In 2009, acute, short-term, subchronic, chronic health risk limits (HRL) of 0.2 µg/L and a cancer HRL of 0.006 µg/L were derived. In 2016, MDH re-evaluated the HRLs. The 2016 values are the same as the 2009 values with the exception of the acute guidance being removed. However, the basis of the values has changed as the result of: 1) use of MDH's most recent risk assessment methodology, and 2) rounding to one significant digit. The 2016 guidance was adopted into rule as updated HRLs in 2018.

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	Yes	Yes	Yes	Yes	Yes
Effects observed?	No[1]	Yes[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1] No effect was found on levels of a limited number of circulating hormones (thyroxin, FSH, LH, TSH, prolactin, or growth hormone). There are some *in vivo* and *in vitro* data to suggest that dieldrin has weak estrogenic properties.

[2] Several studies in mice suggest that exposure may induce immunosuppression at dose levels similar to the short-term, subchronic, and chronic critical study HED LOAELs. Immune system has been listed as a short-term, subchronic, and chronic health endpoint.

[3] Several studies have demonstrated that dose levels similar to the short-term and subchronic critical study HED LOAELs can result in reduced pup survival, increase dopamine transporter levels and increase the incidence of hepatic lesions. Developmental effects has been listed as a short-term, subchronic, and chronic health endpoint.

[4] Several reproductive and multigenerational studies have been conducted. At levels within 3-6 fold slightly of the short-term and subchronic critical study HED LOAELs mothers were not able to adequately nurse their young because both the mother and offspring were too

hyperesthetic. Rats appear to be more sensitive than mice. Nervous system is listed as a short-term, subchronic and chronic health endpoint.

[5] Impaired learning, increases in dopamine transporters, and hyperesthetia were observed at the short-term, subchronic and chronic critical study HED LOAELs. Nervous system is listed as a short-term, subchronic and chronic critical health endpoint. As dose levels increase irritability, salivation, hyperexcitability, tremors followed by convulsions, loss of body weight, depression, prostrations, and death are observed.

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