



## Toxicological Summary for: S-Ethyl-N,N-dipropylthiocarbamate

CAS: 759-94-4

Synonyms: EPTC, Torbin, EPTAM, Eptam 6E, Eradicane, Stauffer R 1608, Alirox

**Acute Non-Cancer Health Based Value (nHBV<sub>acute</sub>) = 300 µg/L**

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Acute intake rate, L/kg-d})}$$

$$= \frac{(0.16 \text{ mg/kg-d}) \times (0.5^*) \times (1000 \text{ µg/mg})}{(0.285^{**} \text{ L/kg-d})}$$

$$= 281 \text{ rounded to } \mathbf{300 \text{ µg/L}}$$

\*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:	0.16 mg/kg-d (Ipk:APfSD rats)
Source of toxicity value:	MDH, 2015
Point of Departure (POD):	200 mg/kg-d (LOAEL, Brammer 1993 aci (U.S. Environmental Protection Agency 2011), MRIDs 43039701 and 43297401)
Human Equivalent Dose (MDH, 2011):	POD x DAF = 200 mg/kg-d x 0.24 = 48 mg/kg-day
Total uncertainty factor:	300
Uncertainty factor allocation:	3 for interspecies extrapolation (toxicodynamics); 10 for intraspecies variability; 10 for extrapolation from a LOAEL to a NOAEL due to the severity of the effect (brain necrosis).
Critical effect(s):	Necrosis of the pyriform/entorhinal cortex and/or dentate gyrus of the brain
Co-critical effect(s):	None
Additivity endpoint(s):	Nervous system

**Short-term Non-Cancer Health Based Value (nHBV<sub>Short-term</sub>) = 300 µg/L**

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

$$= \frac{(0.16 \text{ mg/kg-d}) \times (0.5^*) \times (1000 \text{ µg/mg})}{(0.285^{**} \text{ L/kg-d})}$$

$$= 281 \text{ rounded to } \mathbf{300 \text{ µg/L}}$$

\*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: 0.16 mg/kg-d (Wistar rats)  
Source of toxicity value: MDH, 2015  
Point of Departure (POD): 21.9 mg/kg-d (NOAEL, Lees 2004 aci (U.S. Environmental Protection Agency 2011), MRID 46319101)  
Human Equivalent Dose (MDH, 2011):  $POD \times DAF = 21.9 \text{ mg/kg-d} \times 0.22 = 4.8 \text{ mg/kg-day}$   
Total uncertainty factor: 30  
Uncertainty factor allocation: 3 for interspecies extrapolation (toxicodynamics); 10 for intraspecies variability  
Critical effect(s): Decreased pup weight at postnatal day 1, clinical signs of neurotoxicity in dams at parturition, increased whole litter losses  
Co-critical effect(s): Decreased pup body weight, decreased pup body weight gain  
Additivity endpoint(s): Developmental, Female Reproductive system, Nervous system

#### **Subchronic Non-Cancer Health Based Value (nHBV<sub>Subchronic</sub>) = 90 µg/L**

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic intake rate, L/kg-d})}$$
$$= \frac{(0.033 \text{ mg/kg-d}) \times (0.2^*) \times (1000 \text{ µg/mg})}{(0.070^{**} \text{ L/kg-d})}$$
$$= 94.3 \text{ rounded to } \mathbf{90 \text{ µg/L}}$$

\*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: 0.033 mg/kg-d (Sprague Dawley rats)  
Source of toxicity value: MDH, 2015  
Point of Departure (POD): 5 mg/kg-d in females, 4 mg/kg-d in males (NOAEL, Minor et al., 1982 aci (U.S. Environmental Protection Agency 2011), MRIDs 0012128 and 40420408, and Tisdell et al., 1986c aci (U.S. Environmental Protection Agency 2011), MRID 00161597)  
Human Equivalent Dose (MDH, 2011):  $\frac{[(POD \times DAF \text{ (females)}) + (POD \times DAF \text{ (males)})]/2}{1} = \frac{[(5 \text{ mg/kg-d} \times 0.22) + (4 \text{ mg/kg-day} \times 0.24)]/2}{1} = 1.0 \text{ mg/kg-day}$   
Total uncertainty factor: 30  
Uncertainty factor allocation: 3 for interspecies extrapolation (toxicodynamics); 10 for intraspecies variability  
Critical effect(s): Myocardial degeneration  
Co-critical effect(s): None  
Additivity endpoint(s): Cardiovascular system

**Chronic Non-Cancer Health Based Value (nHBV<sub>Chronic</sub>) = 40 µg/L**

$$\frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic intake rate, L/kg-d})}$$
$$= \frac{(0.0083 \text{ mg/kg-d}) \times (0.2^*) \times (1000 \text{ µg/mg})}{(0.044^{**} \text{ L/kg-d})}$$
$$= 37.7 \text{ rounded to } \mathbf{40 \text{ µg/L}}$$

\*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:	0.0083 mg/kg-d (Crl;CD(SD)BR rats)
Source of toxicity value:	MDH, 2015
Point of Departure (POD):	9 mg/kg-d (LOAEL, Dickie 1987 aci (U.S. Environmental Protection Agency 2011), MRID 40215001)
Human Equivalent Dose (MDH, 2011):	POD x DAF = 9 mg/kg-d x 0.28 = 2.5 mg/kg-day
Total uncertainty factor:	300
Uncertainty factor allocation:	3 for interspecies extrapolation (toxicodynamics); 10 for intraspecies variability; 10 for extrapolation from LOAEL to NOAEL because the effects were severe
Critical effect(s):	Cardiomyopathy
Co-critical effect(s):	Myocardial degeneration
Additivity endpoint(s):	Cardiovascular system

**Cancer Health Based Value (cHBV) = Not Applicable**

**Volatile: Yes (Moderate)**

**Summary of Guidance Value History:**

The previous 93/94 nHRL for EPTC is 200 µg/L. It represents the chronic duration and is derived from an EPA IRIS reference dose (RfD). There is also an MDH rapid assessment derived in 2014 of 80 µg/L. The current values for EPTC are 300 µg/L for the acute and short term duration, 90 µg/L for the subchronic duration and 40 µg/L for the chronic duration. There were no previous acute, short term or subchronic values. The reasons that the 2015 HBV for the chronic duration is 5x lower than the 1993 HRL are: 1) use of additional, more recent toxicity information; 2) use of enhanced duration-specific intake rates; and 3) rounding to one significant digit. In 2016 MDH updated the intake rate values used to derive guidance values. The updated intake rates did not result in any change to the nHBV values derived in 2015. MDH intends to re-evaluate guidance values on a five year cycle in order to keep guidance values current with scientific knowledge. Under this process EPTC would undergo re-evaluation in 2020.

**Summary of toxicity testing for health effects identified in the Health Standards Statute:**

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No	Yes	Yes	Yes
Effects?	No	No	Yes <sup>1</sup>	Yes <sup>2</sup>	Yes <sup>3</sup>

Note: 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. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

**Comments on extent of testing or effects:**

<sup>1</sup> Decreased pup body weight forms the basis for the short term RfD. Increased embryotoxicity was observed at 130-fold the acute RfD, along with fetal malformation at over 800-fold higher than the short term RfD.

<sup>2</sup> Total litter loss forms part of the basis of the short term RfD.

<sup>3</sup> Neurotoxicity forms the basis for the acute RfD. Effects seen included necrosis of the brain in adults exposed to EPTC, while neurobehavioral testing such as learning and memory tests did not show a difference in EPTC treated animals over control animals. Clinical signs such as hunched posture, pinched in sides, and hair standing on end in pregnant animals near the time of birth form the basis of the short term RfD. Several studies reported reduced brain weights in adult animals at doses more than 750-fold the subchronic RfD. Another study reported significant decreases in brain weights and neuronal necrosis at doses more than 250-fold the subchronic RfD.

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