Minnesota Department of Health

Adopted as Rule: November 2015

Toxicological Summary for: Bentazon

CAS**: 25057-89-0**

Synonyms: Bentazone, Basagran, Herbatox, Leader, Laddock, 3-Isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one 2,2-dioxide

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = 400 µg/L

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

$$= \frac{\text{(0.22 mg/kg/d) x (0.5) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 381 rounded to **400 µg/L**

Reference Dose/Concentration:	0.22 mg/kg-d (Wistar/HAN rats)
Source of toxicity value:	MDH, 2014
Point of Departure (POD):	100 mg/kg-d (NOAEL, Becker et al., 1986a in U.S. Environmental Protection Agency, 1998)
Human Equivalent Dose (MDH, 2011)	100 mg/kg-d x 0.22 = 22 mg/kg-day
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty to address the need for additional studies regarding thyroid effects
Critical effect(s):	Increased post-implantation loss and fetal resorptions
Co-critical effect(s):	Increased embryonic and fetal resorptions
Additivity endpoint(s):	Developmental; Female Reproductive System

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 60 µg/L

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

$$= \frac{\text{(0.033 mg/kg/d) x (0.5) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 57 rounded to **60 µg/L**

Reference Dose/Concentration:	0.033 mg/kg-d (Wistar/HAN rats)
Source of toxicity value:	MDH 2014
Point of Departure (POD):	15 mg/kg-d (NOAEL, Suter et al., 1989 in U.S.

	Environmental Protection Agency, 1998).
Human Equivalent Dose (MDH, 2011):	15 mg/kg-d x 0.22 = 3.3 mg/kg-d
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty to address the need for additional studies regarding thyroid effects that have been observed at other durations.
Critical effect(s):	Reduced pup body weight gains
Co-critical effect(s):	N/A
Additivity endpoint(s):	Developmental

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = 50 µg/L

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

$$= \frac{\text{(0.02 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.077 L/kg-d)}}$$

= 52 rounded to **50 µg/L**

Reference Dose/Concentration:	0.02 mg/kg-d (Beagle dogs)
Source of toxicity value:	MDH 2014
Point of Departure (POD):	3.2 mg/kg-d (NOAEL, Allen et al., 1989 in U.S. Environmental Protection Agency, 1998)
Human Equivalent Dose (MDH, 2011):	3.2 mg/kg-d x 0.62 = 2 mg/kg-d
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty to address the need for additional studies regarding thyroid effects
Critical effect(s):	Bloody stools, anemia, and decreased body weight gain
Co-critical effect(s):	N/A
Additivity endpoint(s):	Hematological (blood) system

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = 30 µg/L

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

$$= \frac{\text{(0.006 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.043L/kg-d)}}$$

= 28 rounded to **30 µg/L**

Reference Dose/Concentration:	0.006 mg/kg-d (B6C3F1 mice)
Source of toxicity value:	MDH, 2014
Point of Departure (POD):	12 mg/kg-d (LOAEL,Tajima et al.,1984 in U.S. Environmental Protection Agency, 1998)
Human Equivalent Dose (MDH, 2011):	12 mg/kg-d x 0.15 = 1.8 mg/kg-d
Total uncertainty factor:	300
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for

	intraspecies variability, and 10 for extrapolation from a LOAEL to a NOAEL
Critical effect(s):	Increased thyroid weight
Co-critical effect(s):	N/A
Additivity endpoint(s):	Thyroid

Cancer Health Risk Limit (cHRL) = "Not Applicable"

Volatile: No

Summary of Guidance Value History:
A noncancer Chronic Health-Based Value (HBV) of 200 µg/L was derived in 1998. In 2014 Acute, Short-term, Subchronic, and Chronic HBVs of 400, 60, 50 and 30 µg/L were derived. The HBVs were adopted into rule as HRLs in November 2015. The 2015 Chronic HRL is approximately 7 times lower than the 1998 HBV as a result of incorporating: 1) HED adjustments, 2) more recent intake rate data that include higher intakes early in life, and 3) rounding to one significant digit.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No	Yes	Yes	No
Effects?	Yes[1]	No	Yes[2]	Yes[3]	Yes[4]

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:

[1] Endocrine activity of bentazon per se has not been evaluated. However, alterations in thyroid organ weights have been noted and serve as the basis for the chronic RfD. A database uncertainty factor was incorporated into the acute, short-term and subchronic RfDs to address the need for additional studies regarding thyroid function.

[2] The acute and short-term RfDs are based on developmental effects such as post-implantation losses, fetal resorptions, and decreased pup body weights. Delays in ossification of multiple areas of the skeleton have also been described. Decreased pup body weight and body weight gains were also reported in animals dosed with up to 1500 times the short term RfD. One study reported animals experiencing partial abortions, embryonic resorptions, and no living fetuses at doses more than 5000 times the short term RfD.

[3] One male reproductive study in mice found no effects on spermatogenesis. The short-term RfD is based on incidence of postimplantation loss and fetal resorptions in animals dosed with bentazon. At 400 times the short-term RfD, animals had 100% postimplantation loses. There was a higher incidence of embryonic and fetal resorptions in animals treated with 300 times the short-term RfD.

[4] Neurotoxicity has not directly been studied for bentazon. Secondary observations in an animal study included sedation, ataxia and tremors at a dose more than 1500 times the subchronic RfD.

References:

Australian Government - Department of Health and Ageing. (2005). "ADI List, Acceptable Daily Intakes for Agricultural and Veterinary Chemicals." from http://www.health.gov.au/internet/main/publishing.nsf/content/E8F4D2F95D616584CA2573D700770C2A/$File/ADI-Dec12.pdf.

California EPA (Office of Environmental Health Hazard Assessment). (1999). "Public Health Goal for Bentazon In Drinking Water." from http://oehha.ca.gov/water/phg/pdf/bentaz_f.pdf.

California EPA (Office of Environmental Health Hazard Assessment). (2009). "Update of PHG - Bentazon." from http://oehha.ca.gov/water/phg/pdf/bentazon092809.pdf.

California State Water Resources Control Board (2011). "Compilation of Water Quality Goals."

Garagna, S., C. Vasco, et al. (2005). "Effects of a low dose of bentazon on spermatogenesis of mice exposed during foetal, postnatal and adult life." Toxicology **212**(2-3): 165-174.

Minnesota Department of Health (MDH). (2011). "MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses." from http://www.health.state.mn.us/divs/eh/risk/guidance/hedrefguide.pdf.

U.S. Environmental Protection Agency - Office of Drinking Water. (2012). "2012 Edition of the Drinking Water Standards and Health Advisories." from http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf.

U.S. Environmental Protection Agency - Office of Research and Development. (1988). "Recommendations for and Documentation of Biological Values for Use in Risk Assessment." from http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855.

U.S. Environmental Protection Agency - Office of the Science Advisor. (2011). "Recommended Use of Body Weight¾ as the Default Method in Derivation of the Oral Reference Dose." from http://www.epa.gov/raf/publications/pdfs/recommended-use-of-bw34.pdf.

U.S. Environmental Protection Agency - Regional Screening Tables. "Mid-Atlantic Risk Assessment - Regional Screening Table." from http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/Generic_Tables/index.htm

U.S. Environmental Protection Agency (1992). First and Second Peer Review of Bentazon.

U.S. Environmental Protection Agency (1994). "Reregistration Eligibility Decision (RED) for Bentazon."

U.S. Environmental Protection Agency. (1998). "Integrated Risk Information System Quickview for Bentazon." from http://www.epa.gov/iris/subst/0134.htm.

U.S. Environmental Protection Agency. (1998). "Toxicological Review of Bentazon (CAS No. 25057-89-0)." from http://www.epa.gov/iris/toxreviews/0134tr.pdf.

U.S. Geological Survey - Health-Based Screening Levels. from http://infotrek.er.usgs.gov/apex/f?p=HBSL:HOME:0.