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

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Toxicological Summary for: Pyroxasulfone

CAS: 447399-55-5
Synonyms: 3-[[5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)pyrazol-4-yl]methylsulfonyl]-5,5 dimethyl-4H-1,2-oxazole; KIH-485

Acute Non-Cancer Health-Based Value ($nHBV_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health-Based Value ($nHBV_{Short\text{-}term}$) = 40 µg/L

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

$$= \frac{\text{(0.058 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.290 L/kg-d)}^{**}}$$

= 40 µg/L

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5.

Reference Dose/Concentration:	HED/Total UF = 1.75/30 = 0.058 mg/kg-d (male Wistar rat)
Source of toxicity value:	Determined by MDH in 2025
Point of Departure (POD):	7.3 mg/kg-d ($NOAEL_{ADM}$, Covance 2004 as cited in (aci) EPA 2025)
Dose Adjustment Factor (DAF):	0.24 subchronic Wistar male rat; body weight scaling, default (MDH 2017 and US EPA 2011)
Human Equivalent Dose (HED):	POD x DAF = 7.3 mg/kg-d x 0.24 = 1.75 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics); 10 for intraspecies variability; 1 for database uncertainty
Critical effect(s):	Myocardial degeneration/necrosis in male rats
Co-critical effect(s):	None
Additivity endpoint(s):	Cardiovascular system

Subchronic Non-Cancer Health-Based Value ($nHBV_{Subchronic}$) = 40 µg/L

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

$$= \frac{\text{(0.039 mg/kg-d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.074 L/kg-d)}^{**}}$$

= 105 rounded to 100 µg/L

*Relative Source Contribution: MDH 2008, Section IV.E.1.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5.

Reference Dose/Concentration:	HED/Total UF = 1.18/30 = 0.039 mg/kg-d (female beagle)
Source of toxicity value:	Determined by MDH in 2025
Point of Departure (POD):	2.0 mg/kg-d ($NOAEL_{ADM}$, MPI 2008 aci EPA 2025)
Dose Adjustment Factor (DAF):	0.59 subchronic female dog; body weight scaling, default (US EPA 2011 and MDH 2017)
Human Equivalent Dose (HED):	POD x DAF = 2.0 mg/kg-d x 0.59 = 1.18 mg/kg-d
Total uncertainty factor (UF):	30
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics); 10 for intraspecies variability; 1 for database uncertainty
Critical effect(s):	Axonal demyelination in sciatic nerve and spinal cord (and related effects on motor function) of female beagles
Co-critical effect(s):	Axonal demyelination in sciatic nerves, myofiber degeneration in female dogs
Additivity endpoint(s):	Nervous system; Skeletal system

The Subchronic nHBV must be protective of shorter duration exposures that occur within the subchronic duration and, therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 40 µg/L. Additivity endpoints: Cardiovascular system

Chronic Non-Cancer Health-Based Value ($nHBV_{Chronic}$) = 40 µg/L

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

$$= \frac{\text{(0.039 mg/kg-d)}^{\#} \text{ x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.045 L/kg-d)}^{**}}$$

= 173 rounded to 200 µg/L

#The calculated Chronic RfD (0.057 mg/kg-d) is higher than the Subchronic RfD (0.039 mg/kg-d), which is based on nervous system effects. The Chronic RfD must be protective of all types of adverse effects that could occur as a result of chronic exposure, including subchronic effects (MDH 2008, page 34). Therefore, the Subchronic RfD is used in place of the calculated Chronic RfD when deriving chronic water guidance.
*Relative Source Contribution: MDH 2008, Section IV.E.1. An RSC of 0.2 was used instead of the default short-term RSC of 0.5 due to concerns that dietary intake per unit body weight was higher for infants than older children or adults.
**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2019, Exposure Factors Handbook, Tables 3-1, 3-3 and 3-5.

The Chronic nHBV must be protective of shorter duration exposures that occur within the chronic duration and, therefore, the Chronic nHBV is set equal to the Short-term nHBV of 40 µg/L. Additivity endpoints: Cardiovascular system

Cancer Health-Based Value (cHBV) = Not Applicable

Cancer classification:	Not Likely to be Carcinogenic to Humans at doses that do not cause crystals with subsequent calculi formation resulting in cellular damage of the urinary tract (EPA, 2025)
Tumor site(s):	Bladder

Statement for non-linear carcinogens:
MDH has determined that pyroxasulfone is a nonlinear carcinogen. This is due to its lack of genotoxicity and because some of the pre-neoplastic bladder effects observed after shorter exposures can progress to malignancy after longer exposures. Noncancer HBVs are based on effects that occur at doses lower than those causing pre-neoplastic bladder effects and are considered to be protective against cancer.

Volatility: Yes (low)

Summary of Guidance Value History:

Pyroxasulfone was previously evaluated by MDH as part of a noncancer pesticide rapid assessment (PRA) in 2014, and cancer pesticide rapid assessment in 2025. A noncancer PRA value of 5 µg/L was derived in for pyroxasulfone, while no value based on cancer was derived. In 2025, Short-term, Subchronic, and Chronic nHBVs were derived. The Short-term, Subchronic, and Chronic nHBVs have changed from the 2014 PRA as a result of 1) using MDH's most recent risk assessment methodology (multiduration guidance), and 2) incorporation of more toxicity information.

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	No	Yes	Yes	Yes	Yes
Effects observed?	-[1]	No[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1]No relevant information is available.

[2]Two studies evaluated the immunotoxicity of pyroxasulfone (evaluating antibody response) in rodents. No immune effects were observed at doses over 2,000 times higher than the Subchronic reference dose (RfD) (the lowest value derived).

[3]Changes to the brain (organ weight, altered morphology) and reduced body weight were observed in rat pups whose mothers were orally exposed to pyroxasulfone at doses 600-1,100 times greater than the Short-term RfD.

[4]Indicators of reproductive toxicity (i.e., reduced implantation rate and subsequent litter size) were noted at doses 2,300 times higher than the Short-term RfD in rats. Increased fetal resorptions were also noted in a developmental study in rabbits after dosing with concentrations 7,500 times higher than the Short-term RfD.

[5]The Subchronic RfD and Chronic RfD are based on neurotoxic effects (nerve degeneration and associated decrements in motor function) in female dogs and male mice, respectively, following ingestion of pyroxasulfone. A similar pattern of toxicity was observed in both sexes across species (mice, rats, dogs), under multiple exposure durations, bolstering the case that these effects resulted from pyroxasulfone administration. In addition, morphological changes were observed in the brains of rat pups whose mothers were exposed during gestation, as previously noted.

Resources Consulted During Review:

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