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SECONDARY VALUES FOR METRIBUZIN (CAS No. 21087-64-9)

A search was conducted for information on the chemical properties and toxicity of metribuzin to human health and to fish and aquatic life using the following databases and search engines: ECOTOX (toxicity to fish and aquatic life), IRIS (Integrated Risk Information System; toxicity to human health), CHEMFATE (environmental fate), BIODEG (degradation), HSDB (Hazardous Substances Data Bank), CCRIS (Chemical Carcinogenesis Research Info System), ATSDR ToxFAQs (Agency for Toxic Substances and Disease Registry chemical fact sheets), and EXTOXNET (Extension Toxicology Network's pesticide information project). This search yielded some useful information on metribuzin's properties and toxicity.

Fish and Aquatic Life Secondary Values

To derive an acute toxicity criterion for fish and aquatic life, acute toxicity test results are required for at least one species in each of eight different families. Specific requirements and the data available to meet these requirements are found in Table 1. Following a search for information on the toxicity of metribuzin to fish and other aquatic life, it was determined that data are available to meet five out of the eight requirements. Because data are available for a Daphnid species, it was possible to calculate a secondary acute value for metribuzin.

Cold Water

To calculate a secondary acute value (SAV), the lowest genus mean acute value (GMAV) in the database is divided by the secondary acute factor (SAF; an adjustment factor corresponding to the number of satisfied requirements).

SAF for five out of eight requirements met = 6.1
Lowest GMAV = 20,392.26 µg/L (*Daphnia magna*)

SAV = GMAV/SAF
= 20,392.26 µg/L / 6.1
= 3,342.99 µg/L

Chronic data are currently available for *C. dubia* (Table 2) which meet acceptability requirements and which were collected by the same authors as the corresponding acute data for that species. Therefore, a secondary chronic value (SCV) may be calculated using this data plus default acute-chronic ratios.

SACR (secondary acute-chronic ratio) = Geometric mean of three species mean acute-chronic ratios (SMACRs).

SMACR 1 = 35,360 µg/L / 8,840 µg/L = 4.00

SMACR 2 = 18 (default)
SMACR 3 = 18 (default)

SACR = geometric mean of 4, 18, and 18 = 10.90

SCV = SAV/SACR
= 3,342.99 µg/L / 10.90
= 306.70 µg/L

So for cold water-designated waters, the secondary acute value is 3,343 µg/L and the secondary chronic value is 307 µg/L for metribuzin.

Warm Water Sportfish, Warm Water Forage Fish, Limited Forage Fish and Limited Aquatic Life

Because the lowest GMAV in the cold water database is for *Daphnia magna*, and because *Daphnia magna* will not drop out of the database for any of the remaining water body use classifications, secondary values calculated for cold water-designated waters will also apply for warm water sportfish, warm water forage fish, limited forage fish, and limited aquatic life designated waters.

Table 1. Requirements for calculation of an acute toxicity criterion for protection of aquatic life for metribuzin, and corresponding acute toxicity data.

Species Name	Common Name	Duration/ Endpoint	Value µg/L	Reference #[a]	Source
1. At least one salmonid fish in the family Salmonidae, in the class Osteichthyes.					
Oncorhynchus mykiss	**rainbow trout**	**96-h/LC50**	**99,000**	**1**	**AQUIRE**
Oncorhynchus mykiss	**rainbow trout**	**96-h/LC50**	**76,770**	**1**	**AQUIRE**
Oncorhynchus mykiss	**rainbow trout**	**96-h/LC50**	**147,000**	**1**	**AQUIRE**
Oncorhynchus mykiss	**rainbow trout**	**96-h/LC50**	**42,000**	**2**	**AQUIRE**
Species Mean Acute Value (SMAV) = 82,746.44					
2. At least one non-salmonid fish from another family in the class Osteichthyes, preferably a commercially or recreationally important warmwater species.					
Lepomis macrochirus	**bluegill**	**96-h/LC50**	**75,960**	**1**	**AQUIRE**
Lepomis macrochirus	**bluegill**	**96-h/LC50**	**131,300**	**1**	**AQUIRE**
Lepomis macrochirus	**bluegill**	**96-h/LC50**	**92,000**	**2**	**AQUIRE**
SMAV = 97,173.05					
3. At least one planktonic crustacean (e.g., cladoceran, copepod).					
Ceriodaphnia dubia	**water flea**	**48-h/LC50**	**35,360**	**3**	**AQUIRE**
SMAV = 35,360					
Daphnia magna	**water flea**	**48-h/EC50**	**4,200**	**1**	**AQUIRE**
Daphnia magna	**water flea**	**48-h/EC50**	**98,500**	**1**	**AQUIRE**
Daphnia magna	**water flea**	**48-h/EC50**	**4,180**	**1**	**AQUIRE**
Daphnia magna	**water flea**	**48-h/EC50**	**>100,000**	**2**	**AQUIRE**
SMAV = 20,392.26					
4. At least one benthic crustacean (e.g., ostracod, isopod, amphipod, crayfish).					

5. At least one insect (e.g., mayfly, dragonfly, damselfly, stonefly, caddisfly, mosquito, midge).

Chironomus thummi	**midge**	**48-h/EC50**	**43,500**	**4**	**AQUIRE**
Chironomus thummi	**midge**	**48-h/EC50**	**130,000**	**4**	**AQUIRE**

SMAV = 75,199.73

6. At least one fish or amphibian from a family in the phylum Chordata not already represented in one of the other subdivisions.

Ictalurus punctatus	**channel catfish**	**96-h/LC50**	**3,400**	**5**	**AQUIRE**
Ictalurus punctatus	**channel catfish**	**96-h/LC50**	**>100,000**	**2**	**AQUIRE**
Ictalurus punctatus	**channel catfish**	**96-h/LC50**	**>100,000**	**2**	**AQUIRE**

SMAV = 32,396.12

NOTE: For channel catfish and the water flea, the acute values varied by more than a factor of 10, but were equally split among low and high values. Since the values for the other species tended towards the high end of the range, all the values were used to calculate SMAVs.

7. At least one organism from a family in a phylum other than Arthropoda or Chordata (e.g., Rotifera, Annelida, Mollusca).

8. At least one organism from a family in any order of insect or any other phylum not already represented in subdivisions 1 through 7.

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[1]Office of Pesticide Programs. 2000. Environmental Effects Database (EEDB). Environmental Fate and Effects Division, U.S. EPA, Washington, D.C.

[2]Mayer, F.L.J. and M.R. Ellersieck. 1986. Manual of acute toxicity: Interpretation and data base for 410 chemicals and 66 species of freshwater animals. Resource Publication No. 160, U.S. Department of Interior, U.S. Fish and Wildlife Service, Washington, DC. 505 pp.

[3]Ort, M.P., J.F. Fairchild, and S.E. Finger. 1994. Acute and chronic effects of four commercial herbicide formulations on *Ceriodaphnia dubia*. Archives of Environmental Contamination and Toxicology 27(1):103-106.

[4]Buhl, K.J. and N.L. Faerber. 1989. Acute toxicity of selected herbicides and surfactants to larvae of the midge *Chironomus riparius*. Archives of Environmental Contamination and Toxicology 18(4):530-536.

[5]Clemens, H.P. and K.E. Sneed. 1959. Lethal doses of several commercial chemicals for fingerling channel catfish. Scientific Report on Fisheries No. 316, U.S. Department of Interior, U.S. Fish and Wildlife Service, Washington, DC. 10 pp.

Table 2. Requirements for calculation of a chronic toxicity criterion for the protection of aquatic life for metribuzin, and corresponding chronic toxicity data.

Species Name	Common Name	Duration/ Endpoint	Value µg/L	Reference #[a]	Source
1. At least one salmonid fish in the family Salmonidae, in the class Osteichthyes.					
2. At least one non-salmonid fish from another family in the class Osteichthyes, preferably a commercially or recreationally important warmwater species.					
3. At least one planktonic crustacean (e.g., cladoceran, copepod).					
Ceriodaphnia dubia	**water flea**	**7-d/MATC**	**8,840**	**1**	**AQUIRE**
4. At least one benthic crustacean (e.g., ostracod, isopod, amphipod, crayfish).					
5. At least one insect (e.g., mayfly, dragonfly, damselfly, stonefly, caddisfly, mosquito, midge).					
6. At least one fish or amphibian from a family in the phylum Chordata not already represented in one of the other subdivisions.					
7. At least one organism from a family in a phylum other than Arthropoda or Chordata (e.g., Rotifera, Annelida, Mollusca).					
8. At least one organism from a family in any order of insect or any other phylum not already represented in subdivisions 1 through 7.					

[1]Ort, M.P., J.F. Fairchild, and S.E. Finger. 1994. Acute and chronic effects of four commercial herbicide formulations on *Ceriodaphnia dubia*. Archives of Environmental Contamination and Toxicology 27(1):103-106.

HUMAN HEALTH

To calculate a criteria or secondary value for the protection of human health, it is first necessary to determine if the substance has been shown to be carcinogenic (which will result in the calculation of a human cancer criteria or secondary value) or not (which will result in the calculation of a human threshold criteria or secondary value). Metribuzin has been classified as Group D-- not classifiable as to human carcinogenicity, because of inadequate data (U.S. EPA's IRIS database). Because an oral reference dose and a log octanol water partition coefficient are available, a human threshold secondary value can be calculated for metribuzin.

There are several steps to calculating a human threshold secondary value: 1) calculation of the fraction of freely dissolved chemical; 2) calculation of the "baseline BAF"; 3) calculation of the "human health BAF"; and 4) calculation of the human threshold secondary value.

1) Calculation of the freely-dissolved fraction = f_{fd}

Given a standard dissolved organic carbon (DOC) concentration of 0.000002 Kg/L and a particulate organic carbon (POC) concentration of 0.00000004 Kg/L in water, the equation

$$f_{fd} = 1/\{1 + [(DOC)(K_{ow})/10] + [(POC)(K_{ow})]\}$$

can be reduced to:

$$= 1/\{1 + [(0.00000024\ Kg/L)(K_{ow})]\}$$

A log K_{ow} of 1.70 (K_{ow} of 50.1187) has been published for metribuzin (National Institutes of Health, Hazardous Substance Database).

$$f_{fd} = 1/\{1 + [(0.00000024\ Kg/L)(50.1187)]\}$$

$$= 1/1.000012$$

$$= \mathbf{1.0000}$$

2) Calculation of the baseline BAF

The baseline BAF is calculated according to the equations contained in 40 CFR part 132 (Final Water Quality Guidance for the Great Lakes System), Appendix B, using BAF data that was collected in one of four ways (listed in order of most preferred to least preferred):

a) a measured BAF from a field study
b) a predicted BAF based on field-measured BSAFs
c) a predicted BAF using a laboratory-measured bioconcentration factor (BCF) and a food chain multiplier (FCM)
d) a predicted BAF using a K_{ow} and a FCM

Currently, there are no BAFs, BSAFs, or BCFs available for metribuzin; therefore, the baseline BAF was calculated using the K_{ow} and a food chain multiplier (method d above).

Given metribuzin's log K_{ow} of 1.70 (K_{ow} of 50.1187), the FCMs (taken from table B-1 in GLI) are 1.005 for trophic level 3 (warm waters) and 1.000 for trophic level 4 (cold waters).

a) Cold Water

Baseline BAF = (FCM)(Kow)

= (1.000)(50.1187)

= 50.1187

b) Warm Waters

Baseline BAF = (FCM)(Kow)

= (1.005)(50.1187)

= 50.3693

3) Calculation of the human health BAF

a) Cold Water

BAF^{HH}_{TL4} = {[(baseline BAF)(0.044)] + 1} (f_{fd})

where

BAF^{HH}_{TL4} = Human health BAF for trophic level 4 (cold water)

baseline BAF = the baseline BAF (for cold waters) calculated in 2)

0.044 = fraction lipid value for cold water fish and aquatic life communities

f_{fd} = fraction freely dissolved

BAF^{HH}_{TL4} = {[(50.1187)(0.044)] + 1} (1.0000)

= **3.2052**

b) Warm Waters

BAF^{HH}_{TL3} = {[(baseline BAF)(0.013)] + 1} (f_{fd})

where

BAF^{HH}_{TL3} = Human health BAF for trophic level 3 (warm waters)

baseline BAF = the baseline BAF (for warm waters) calculated in 2)

0.013 = fraction lipid value for warm water fish and aquatic life communities

f_{fd} = fraction freely dissolved

BAF^{HH}_{TL3} = {[(50.3693)(0.013)] + 1} (1.0000)

= **1.6548**

4) Calculation of the human threshold secondary value

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

where

ADE = acceptable daily exposure (= oral reference dose, or RfD; = 0.025 mg/Kg/day for metribuzin (IRIS 2003))

70 Kg = average weight of an adult

RSC = relative source contribution to account for other routes of exposure (= 0.8 in the absence of other data)

W_H = average per capita daily water consumption (= 2 L/d for public water supplies, and 0.01 L/d for non-public water supplies)

F_H = average consumption of sport-caught fish in Wisconsin (= 0.02 Kg/d)

BAF = appropriate (cold or warm) human health BAF calculated in 3).

a) Public Water Supply/Cold Water

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

= [(0.025 mg/Kg/d)(70 Kg)(0.8)]/[**2** L/d + (0.02 Kg/d)(3.2052 L/Kg)]

= 0.6783 mg/L

= 678.3 µg/L

b) Public Water Supply/Warm Water Sportfish

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

= [(0.025 mg/Kg/d)(70 Kg)(0.8)]/[**2** L/d + (0.02 Kg/d)(1.6548 L/Kg)]

= 0.6886 mg/L

= 688.6 µg/L

c) Non-Public Water Supply/Cold Water

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

= [(0.025 mg/Kg/d)(70 Kg)(0.8)]/[**0.01** L/d + (0.02 Kg/d)(3.2052 L/Kg)]

= 18.8934 mg/L

= 18,893.4 µg/L

d) Non-Public Water Supply/Warm Waters (Warm Water Sportfish, Warm Water Forage Fish, and Limited Forage Fish designated waters)

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

= [(0.025 mg/Kg/d)(70 Kg)(0.8)]/[**0.01** L/d + (0.02 Kg/d)(1.6548 L/Kg)]

= 32.4826 mg/L

= 32,482.6 µg/L

e) Non-Public Water Supply/Limited Aquatic Life

Note: The Limited Aquatic Life classification applies to water bodies with no (or very few) fish present. Therefore, calculation of a human health threshold value for water bodies with this classification does not include a human health BAF since it is assumed that humans will not be exposed to metribuzin through consumption of fish in these areas.

Human Threshold Secondary Value = $[(ADE)(70\ Kg)(RSC)]/[W_H + (F_H)(BAF)]$

= [(0.025 mg/Kg/d)(70 Kg)(0.8)]/[**0.01** L/d + (0)]

= **140** mg/L

= **140,000 µg/L**

Chemical	CAS #	Category	Type of Secondary Value	Water Body Classification	Value (µg/L)
Metribuzin	21087-64-9	Fish and Aquatic	Acute	Cold, WWSF, WWFF, LFF, LAL	3,343
Metribuzin	21087-64-9	Fish and Aquatic	Chronic	Cold, WWSF, WWFF, LFF, LAL	307
Metribuzin	21087-64-9	Human Health	Human Threshold	Public Water Supply/Cold	678
Metribuzin	21087-64-9	Human Health	Human Threshold	Public Water Supply/WWSF	688
Metribuzin	21087-64-9	Human Health	Human Threshold	Non-Public Water Supply/Cold	18,893
Metribuzin	21087-64-9	Human Health	Human Threshold	Non-Public Water Supply/WWSF, WWFF, LFF	32,483
Metribuzin	21087-64-9	Human Health	Human Threshold	Non-Public Water Supply/LAL	140,000

Cold = cold water designated water bodies
WWSF = warm water sportfish designated water bodies
WWFF = warm water forage fish designated water bodies
LFF = limited forage fish designated water bodies
LAL = limited aquatic life designated water bodies (includes wetlands)