2012 Risk Assessment Advice for Groundwater
Health Risk Assessment Unit, Environmental Health Division
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Chemical Name: Metribuzin Degradates: DA, DK, and DADK
CAS: 35045-02-4 (DA); 56507-37-0 (DK); 52236-30-3 (DADK)

Metribuzin DA: Desaminometribuzin;
6-(1,1-dimethylethyl)-3-(methylthio)- 1,2,4-triazin-5-(4H)-one

Metribuzin DK: Diketometribuzin;
4-amino-6-(1,1-dimethylethyl)-3,5-(diketo)-1,2,4-triazin-5-(2H,4H)-dione

Metribuzin DADK: Desaminodiketometribuzin;
6-(1,1-dimethylethyl)-3,5-(diketo)- 1,2,4-triazin-5-(2H,4H)-dione

MDH finds the currently available toxicity data for metribuzin DA, DK, and DADK insufficient to develop chemical specific health-based guidance for groundwater. A repeat dose toxicity study is available only for metribuzin DADK. In the DADK 28-day study in rats (Krotlinger, 1996, as cited in the EU Draft Assessment Report (DAR), 2006), neurological effects similar to those observed in studies of metribuzin were reported at similar doses. In this same study thyroid effects were also reported for DADK although at higher doses than for the parent. In the 2006 EU DAR, the peer review concluded that relative to the parent compound metribuzin the metabolite metribuzin DADK exhibited comparable toxicity.

Metribuzin DA, DK, and DADK are the predominant metabolites following oral exposures to metribuzin and also have been found as environmental degradates. Health-Based Values (HBVs) are available for the parent compound, metribuzin. Based on the lack of sufficient information to derive chemical specific health-based guidance values for metribuzin DA, DK, and DADK, MDH recommends using the HBVs for the parent compound, metribuzin. This recommendation is consistent with the guidelines noted in Minnesota Administrative Rules Part 4717.7900 Chemical Breakdown Products.

The HBV values for metribuzin are: Acute – 30ug/L; Short-term, Subchronic and Chronic - 10 µg/L. For additional information on the derivation of HBV values for metribuzin see: https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/metribuzin.pdf.

Volatile: No (low volatility)

Summary of Guidance Value History:
In 2010, MDH applied the guidance values for the parent compound, metribuzin, to the metribuzin DA, DK, and DADK degradates due to a lack of chemical specific information for the degradates. The metribuzin HBVs were 40 ug/L for the Acute duration and 10 ug/L for the Short-term, Subchronic, and Chronic

durations. MDH reevaluated the parent metribuzin HBVs in 2012 to incorporate Human Equivalent Dose (HED) methodology. The resulting Acute HBV is 30 ug/L, which is1.5 fold lower than the 2010 value. The Short-term, Subchronic, and Chronic HBVs of 10 ug/L are unchanged.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observation	No	No	No	Secondary Observation
Effects?	Yes[1]	--	--	--	Yes[1]

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] Thyroid effects (e.g. alteration in thyroid hormone levels) and neurological effects (e.g. reduced motility, staggered gait, and narrowed and/or closed eyelids) were reported in a 28-day repeat dose toxicity study of metribuzin DADK in rats (Kotlinger, 1996). No comparable studies were available for metribuzin DA and DK. (Note: the unpublished study included here is cited in the EU Draft Assessment Report, 2006.)

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