Health-Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
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Toxicological Summary for: Cyanazine and Atrazine Chlorinated Degradates

Cyanazine and atrazine are chlorotriazine herbicides. Cyanazine was used in Minnesota from the early 1970's through the 1990's, when its registration was cancelled (MDA 2020a). Atrazine is currently used in Minnesota and has been designated as a groundwater "common detection" chemical by the Minnesota Department of Agriculture (MDA 2020b). In the environment, atrazine and cyanazine break down into related chemicals called degradates. Cyanazine and atrazine form multiple environmental degradates (see Table 1 below).

Table 1. Cyanazine and Atrazine Degradates (EPA 2020, EPA 2018b, MDA 2020c, USGS 2005)

Cyanazine-specific Degradates [CASRN]	Atrazine-specific Degradates [CASRN]	Degradates Common to both Cyanazine and Atrazine [CASRN]
Cyanazine acid (CAC) [36576-43-9]	Ammeline* [645-92-1]	Deethyldeisopropylatrazine (DACT, DEDI, DDA) [3397-62-4]
Cyanazine amide (CAM) [36576-42-8]	Deethylatrazine (DEA) [6190-65-4]	
Deethylcyanazine (DEC) [21725-40-6]	Hydroxyatrazine (HA)* [2163-68-0]	Deisopropylatrazine (DIA) [1007-28-9]
Deethylcyanazine acid (DCAC) [36749-35-6]	Desethylhydroxyatrazine (HDEA)* [19988-24-0]	
Deethylcyanazine amide (DCAM) [36556-77-1]	Deisopropylhydroxyatrazine (HDIA)* [7313-54-4]	

* Hydroxy degradates are assessed using the rapid assessment value for hydroxyatrazine (20 µg/L) (MDH Updated 2020b).

Agencies in Minnesota are detecting various combinations of cyanazine, atrazine, and their degradates in Minnesota waters, including sources of drinking water.

Based on structural and toxicological similarities, the US Environmental Protection Agency (EPA) has divided chlorotriazine degradates (also referred to as metabolites by EPA) into two groups (US EPA 2018a, b):

1. chlorinated degradates that induce neuroendocrine effects, and
2. hydroxylated degradates that induce renal effects.

MDH, based on EPA's grouping, recommends use of hydroxyatrazine's Rapid Assessment value as a surrogate for other hydroxylated degradates (MDH, Updated 2020b). Health-based guidance values (HBGVs) are available for the parent chlorotriazine compounds cyanazine and atrazine (MDH, Updated 2020a). Chemical-specific guidance has not been developed for the remaining chlorinated degradates.

When no health risk limit or other health-based water value exists for a chemical breakdown product, due to minimal or absent toxicity information on the chemical breakdown product, it is MDH's practice to use the guidance value of the parent as the guidance value of the degradate. In cases where there are multiple degradates, the individual degradate water concentrations are added together and compared to the appropriate parent guidance value (Minnesota Rules, Part 4717.7900).

Cyanazine and atrazine have two chlorinated degradates in common (DACT and DIA). In order to assess potential health risks posed by these common chlorinated degradates, the risk assessor must determine which parent guidance value will be used for comparison to the sum of chlorinated degradate concentrations.

MDH is issuing the following Risk Assessment Advice for the chlorinated degradates of cyanazine and atrazine.

MDH recommends that if cyanazine or any of its specific degradates are present, water concentrations for the two common degradates should be summed with cyanazine and its specific degradates and the result compared to the cyanazine health risk limit (HRL) values.

Cyanazine (MDH 2018)

Acute nHRL = 3 µg/L	Additivity Endpoints – Developmental, Female reproductive system
Short-term nHRL = 3 µg/L	Additivity Endpoints – Developmental, Female reproductive system
Subchronic nHRL = 3 µg/L	Additivity Endpoints – Developmental, Female reproductive system, Hepatic (liver) system, Renal (kidney) system
Chronic nHRL = 1 µg/L	Additivity Endpoints – None

If cyanazine or its specific degradates are not present, it is appropriate to sum the water concentrations for the two common degradates with atrazine and its specific degradates and compare the resulting water concentration to the atrazine HRL. The rationale for this approach is that cyanazine has not been registered for nearly 20 years, while atrazine is still in use today.

Atrazine (MDH, updated 2020)

Chronic HRL_{MCL} – 3 µg/L*

*Note: since the atrazine HRL is based on the EPA maximum contaminant level (MCL) (U.S. EPA, 1995), MDH does not assign additivity endpoints to the atrazine HBGV.

Situations in which only one parent and its specific degradates have been sampled for, or only the common degradates are detected, require a site-specific review.

Volatile: No

Summary of Guidance Value History:

No previous MDH guidance exists for the chlorinated cyanazine and atrazine degradates in Table 1. The recommendation to use the cyanazine health-risk limit (HRL) values for cyanazine-specific degradates (i.e., CAC, CAM, DEC, DCAC and DCAM) as well as for the common degradates (i.e., DACT and DIA)

when cyanazine or its specific degradates are found represents new guidance. The recommendation to use the HRL value for atrazine, for the atrazine-specific degradate DEA, as well as for the common degradates (i.e., DACT and DIA) when cyanazine or its specific degradates are not found represents new guidance.

The hydroxyl degradates/metabolites are addressed through the use of hydroxyatrazine's 2014 pesticide rapid assessment value (20 µg/L). For more information on pesticide rapid assessment values, see: https://www.health.state.mn.us/communities/environment/risk/guidance/dwec/rapidpest.html .

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 effect?	No	No	Yes	Yes	No
Effects observed?	-	-	Yes[1]	Yes[1]	-

Comments on extent of testing or effects:

[1]There are limited studies on the developmental and reproductive effects of the cyanazine and atrazine degradates. Two studies reported various developmental and reproductive effects from exposure of rats to DEA, DIA, or DACT (Scialli, DeSesso, & Breckenridge, 2014; Stoker, Guidici, Laws, & Cooper, 2002). These effects included a delay in puberty and development of the reproductive tract in male rats, reduced fetal body weight, and post-implantation loss in pregnant female rats. EPA's grouping of DEA, DIA, and DACT with the parent compounds is, in part, based on similar toxicological effects.

Resources Consulted During Review:

European Chemicals Agency. REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) Registration Dossier - Cyanuric acid. Retrieved from https://echa.europa.eu/registration-dossier/-/registered-dossier/15028/7/9/1

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MDA. 2020c. Groundwater Cleanup Goals. Drinking Water Guidance Values Summary (June 2020). https://www.mda.state.mn.us/groundwater-cleanup-goals-guidance-document-28

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