



Web Publication Date: May 2024

Toxicological Summary for: Diketonitrile

CAS: 143701-75-1

Synonyms: DKN; 2-(cyclopropanecarbonyl)-3-[2-methylsulfonyl-4-(trifluoromethyl)phenyl]-3-

oxopropanenitrile; benzenepropanenitrile, alpha-(cyclopropylcarbonyl)-2-

(methylsulfonyl)-beta-oxo-4-(trifluoromethyl)-; RPA 202248

MDH finds there is insufficient toxicity information available for diketonitrile to develop chemicalspecific guidance for groundwater. The diketonitrile degradate guidance values will be issued as Risk Assessment Advice (RAA) and will be based on the Health-Based Values (HBVs) of the parent compound, isoxaflutole. This approach is consistent with the approach outlined in the Minnesota Statute 103H.201 Health Risk Limit Rules, Section 4717.7900 Chemical Breakdown Products.

Acute Non-Cancer Risk Assessment Advice (nRAA) = Not Derived (Insufficient Data)

Short-term Non-Cancer Risk Assessment Advice (nRAA) = $20 \mu g/L$

Subchronic Non-Cancer Risk Assessment Advice (nRAA) = 10 μg/L

Chronic Non-Cancer Risk Assessment Advice (nRAA) = $7 \mu g/L$

Cancer Risk Assessment Advice (cRAA) = Not Applicable

Statement for non-linear carcinogens:

MDH has determined that isoxaflutole is a nonlinear carcinogen given both its lack of genotoxicity and that the liver effects observed in shorter duration animal studies are known to progress to the types of liver tumors observed in longer duration studies. Accordingly, DKN is similarly considered a nonlinear carcinogen. The chronic RfD is considered protective against the key events observed in shorter duration studies and liver cancer.

Volatile: No

Summary of Guidance Value History:

In 2014, MDH developed a cancer pesticide rapid assessment of 9 µg/L and a noncancer rapid assessment of 7 µg/L for DKN based on the parent compound, isoxaflutole. Short-term, Subchronic, and Chronic Risk Assessment Advice (RAAs) of 20, 10, and 7 μg/L, respectively, were derived in 2024 also using isoxaflutole as a surrogate. The 2024 noncancer Chronic RAA of $7~\mu g/L$ is the same as the 2014 noncancer pesticide rapid assessment value despite using: 1) MDH's most recent risk assessment methodology; and 2) incorporation of more recent toxicological information. A cancer RAA was not derived in 2024 because MDH determined that isoxaflutole and DKN are nonlinear carcinogens and the noncancer Chronic RAA will be protective for cancer.

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	No	No	No
Effects observed?	_1	_1	_1	_1	_1

Comments on extent of testing or effects:

Resources Consulted During Review:

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- California EPA. Office of Environmental Health Hazard Assessment (OEHHA). https://oehha.ca.gov/chemicals/isoxaflutole

¹ Guidance values for diketonitrile are derived using data from the parent compound, isoxaflutole. DKN was not tested for endocrine, immunotoxicity, developmental, reproductive, or neurotoxicity related effects. For discussion of these effects following exposure to isoxaflutole, please see the <u>isoxaflutole summary sheet at</u> https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/isoxaflutole.pdf.

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- Mesnage, R., Biserni, M., Wozniak, E., Xenakis, T., Mein, C. A., & Antoniou, M. N. (2018). Comparison of transcriptome responses to glyphosate, isoxaflutole, quizalofop-p-ethyl and mesotrione in the HepaRG cell line. *Toxicol Rep*, *5*, 819-826. https://doi.org/10.1016/j.toxrep.2018.08.005
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