Alternative approaches for evaluating and providing risk context for water contaminants with minimal toxicity data

Helen Goeden[1], Ashley Suchomel[1], Naida Gavrelis[2], Liz Bertelsen[2], Wendy Heiger-Bernays[3]

[1]Minnesota Department of Health – St. Paul, MN; [2]Eastern Research Group, Inc. – Lexington, MA; [3]Boston University School of Public Health – Boston, MA

Overview

The State of Minnesota monitors for contaminants of emerging concern (CECs) such as pharmaceuticals, personal care and household products, and unregulated industrial chemicals. The Minnesota Department of Health (MDH) is tasked with determining human health risks from exposure to contaminants in drinking water. Traditional risk assessment methods require chemical-specific toxicity data in order to develop numerical health-based guidance values for drinking water. However, many CECs have little to no available toxicity data, making it difficult to sufficiently evaluate the chemical.

With funding provided through the State of Minnesota Clean Water Fund of the Clean Water Land and Legacy Amendment MDH is exploring ways to integrate established, evolving and potentially novel approaches to assist in assessing potential human health risks associated with CECs detected in Minnesota waters for which little or no toxicity data exists.

MDH's goal is to develop a scientifically robust risk-based decision process to answer such questions as: Does the CEC pose a potential harm at detected concentrations? MDH worked with partners to identify, review and test a range of published "generic" screening methods, extrapolation methods and computational tools. The findings were used to develop a preliminary decision framework for evaluating chemicals detected in water. The overarching requirements considered in building the decision framework were:

- Scientifically defensible
- Health protective of susceptible populations (e.g., highly exposed or highly sensitive)
- Sufficiently robust to consider wide variety of chemicals and health effects.
- Supports rapid assessment (e.g., requires limited time, resources, data, and expertise)

Identified Methods

Generic

Percentile Approach

- Use of conservative statistic (e.g., 5th or 95th percentile) from a distribution of existing water guidance values.

Toxicological Threshold of Concern (TTC)

- Chronic acceptable daily intake values for different categories of chemicals (Munro et al 1996, Kroes et al 2004).
  - Carcinogen w/structural alert – 0.025 µg/kg-d (10^{-5} risk level)
  - Cholinesterase inhibitors – 0.3 µg/kg-d
  - Class III – 1.5 µg/kg-d

Chemical-Specific

LD50 Extrapolation

- Published LD50-to-chronic NOAEL extrapolation factor (17,000) recommended by Kramer et al (1996) combined with a UF of 100 to produce an LD50-based 'RfD'.

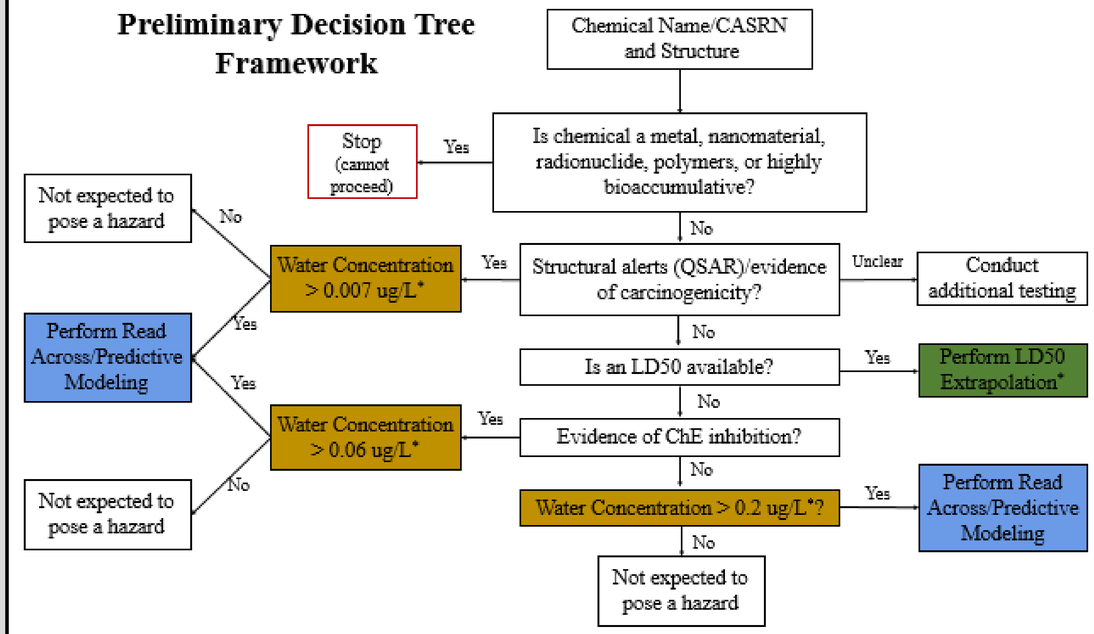
Virtually Safe Dose (VSD)

- 90-day study maximum tolerated dose/extrapolation factor (577,000) recommended by Gaylor and Gold (1995) equating to a 10^{-5} risk level.

Read Across/Predictive Modeling

- Infer toxicity from available toxicity information on similar chemicals.

Preliminary Decision Tree Framework



*Benchmark values used for high level decision-making or initial screening, not intended to predict chemical-specific potency/toxicity.

Results of Testing that Informed Preliminary Framework

Method	Chemical Class	Results of Testing Performed with MDH values	Results of Testing Performed with EPA IRIS/HHBP and CalEPA PHG Values	Used in Decision Tree Framework
Percentile Approach (5th Percentile)	Noncancer	0.3 µg/L (N=66)	EPA IRIS/HHBP[a] & CalEPA = 0.2 µg/L (N=666)	Yes
Percentile Approach (5th Percentile)	Cancer	0.005 µg/L (N=17)	EPA IRIS/HHBP[b] & CalEPA = 0.007 µg/L (N=133)	Yes
Percentile Approach (5th Percentile)	ChE Inhibitors	0.03 µg/L[a] (N=23)	EPA IRIS/HHBP[a] = 0.06 µg/L (N=46)	Yes
Percentile Approach (5th Percentile)	Endocrine Active	4.7 µg/L (N=14)	EPA IRIS/HHBP[a] & CalEPA = 0.3 µg/L (N=99)	Not necessary to differentiate
LD50	Noncancer	Protective[a] of 95% (N=57) (33% ≤ 10-fold of actual value)	EPA IRIS/HHBP[a] (N=46) Protective of ~93%	Yes
Read Across	All	Still Undergoing Testing	Still Undergoing Testing	Yes
VSD	Cancer	Protective of ~30%	--	No
TTC	Cancer with alert	10^{-5} risk value[b] ≈ 0.25 µg/L Protective of ~75%	--	No
TTC	ChE Inhibitors	Short-term[a] value ≈ 0.2 µg/L Protective of ~65%	--	No
TTC	Noncancer (Class III)	Short-term[c] value ≈ 1 µg/L Protective of ~90%	--	No

[a] Derived using MDH short-term algorithm: (RfD * 0.5 RSC * 1000 µg/mg) /0.289 L/kg-d

[b] Derived using MDH cancer algorithm which uses age dependent potency adjustment factors:

$$\frac{(10^{-5}\text{ risk level} * 1000\text{ ug/mg})}{[(CSF * 10 * IR_{<2yr} * 2yr) + (CSF * 3 * IR_{2-16yr} * 14yr) + (CSF * 1 * IR_{16+yr} * 54yr)]/70yr}$$

[c] Based on MDH screening algorithm: (ADI * 0.2 RSC * 1000 µg/mg) /0.289 L/kg-d

Next Steps

The next steps of this project are to:

- Complete testing of the suitability of read across extrapolation and the use of predictive modeling
- Determine whether ongoing research in computational toxicology tools can be utilized to enhance and inform the framework
- Refine framework decision criteria and additional testing of framework by taking a wide range of chemicals through the process.

Additional testing will help to validate the framework and reasoning. An independent peer review will provide confidence in the framework for use a screening tool for contaminants detected in Minnesota waters which have little or not available toxicity information.