Providing Risk Context for Water Contaminants with Limited or No Toxicity Data

Helen Goeden[1], Martin Phillips[1], Ashley Suchomel[1], Naida Gavrelis[2], and Liz Bertelsen[2]

[1]Minnesota Department of Health, Saint Paul, MN; [2]Eastern Research Group, Inc. – Lexington, MA

Abstract # 1923

Helen Goeden | helen.goeden@state.mn.us | 651-201-4904

www.health.state.mn.us

ABSTRACT

The Minnesota Department of Health (MDH) is tasked with estimating the risk to humans from exposure to contaminants in drinking water. MDH typically employs standard risk assessment methodologies to derive health-based water guidance. These methodologies require *in vivo* chemical-specific toxicity data in order to develop water guidance values. Novel challenges are posed by advances in analytical methods and the subsequent detection of an increasing number and variety of environmental contaminants. The types of toxicological studies used in standard risk assessment methodologies have often not been performed or published for these contaminants. The results of *in vitro*, acute, or non-mammalian studies are sometimes available but their utility in the standard risk assessment process is not yet established. MDH has identified methods that could be used to provide risk context for chemicals with minimal toxicity data, with funding from the MN Clean Water, Land, and Legacy Amendment's Clean Water Fund. MDH worked with partners to critically review and test a range of published "generic" screening methods, extrapolation methods and computational tools. Three toxicological endpoints of particular concern were identified where available methods and tools may not be sufficiently protective: carcinogenicity, cholinesterase inhibition, and endocrine disruption. This initial finding, along with method testing results, was used to develop a systematic decision framework for evaluating water contaminants. The framework provides a stepwise assessment process starting with conservative benchmark values, incorporating chemical structure alerts, and progressing to more in-depth assessment depending upon the availability of toxicity information and predictive models (e.g., QSAR, biological, and hybrid models). MDH envisions using this decision framework to prioritize research needs and provide risk context for contaminant occurrence data, including chemical-specific water screening values when possible.

INTRODUCTION

The Problem:

- There are many chemicals found in surface, groundwater, and drinking water
- When a chemical is detected in drinking water, it creates a public health need to determine whether the concentration found in the water poses a risk to human health
- Many of these chemicals have not undergone traditional risk assessments to calculate a water guidance value

The Solution:

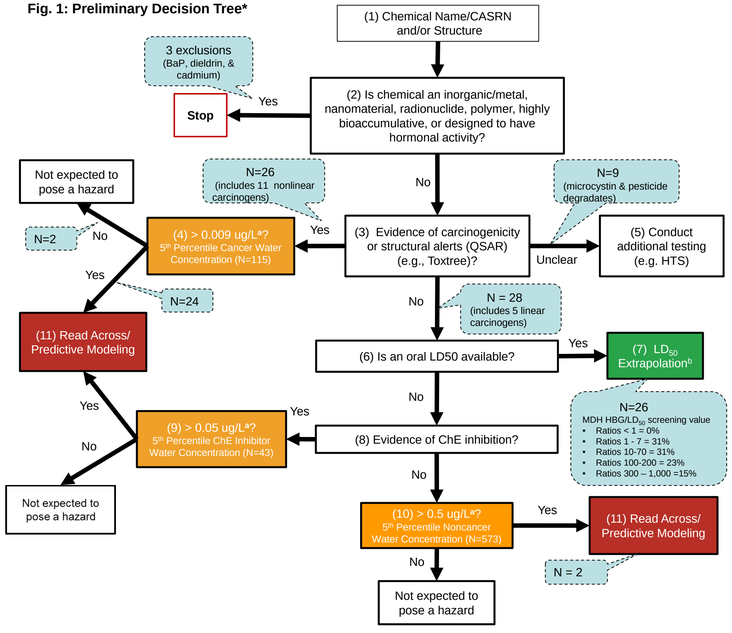
- Apply proven scientific methods to provide risk context until more robust guidance can be developed
- Explore the frontiers of risk assessment and toxicology testing in order to identify the most promising approaches that might be incorporated into a rapid water screening value
- Implement easy-to-use solutions that can be used by risk assessors without extensive additional training in computational or other non-traditional techniques

Minnesota Department of Health
Division of Environmental Health

PRELIMINARY DECISION TREE AND TEST RESULTS

A Preliminary Decision Tree (Fig. 1) was tested using a database of completed full toxicological reviews by MDH since 2008. This database consists of 66 chemicals/chemical groups, including: aromatic hydrocarbons, flame retardants, naturally occurring elements, pesticides, PFCs, plasticizers, solvents, pharmaceuticals, and personal care products. The results using MDH's 66 Health-based Guidance (HBGs) value are presented below.

Fig. 1: Preliminary Decision Tree*



[a] Benchmark based on 5th percentile value of non-excluded chemical water screening value derived from US EPA IRIS/HHBP toxicity values and MDH methodology (see equations below) or CalEPA Public Health Goals.
[b] LD_{50} extrapolation: oral LD_{50} / 17,000 Extrapolation Factor = LD_{50}-based chronic NOAEL. LD_{50}-NOAEL/100 UF = LD_{50}-based chronic RfD (Kramer et. al. 1996).

Screening water concentration for noncancer endpoints = (RfD * 0.5 RSC * 1000 µg/mg) /0.289 L/kg-d

$$\text{Screening water concentration for cancer endpoints} = \frac{(10^{-5}\text{ risk level} * 1000\ \mu g/mg)}{[(CSF^{*}10^{*}IR_{<2yr}{}^{*}2\ yr) + (CSF^{*}3^{*}IR_{2\text{-}16yr}{}^{*}14\ yr) + (CSF^{*}1^{*}IR_{16+yr}{}^{*}54\ yr)]/70\ yr}$$

** Benchmarks used for high level decision-making or initial screening, not intended to predict chemical-specific potency/toxicity. Framework can only provide risk context for detected chemicals whose detection limits are below the relevant screening values.*

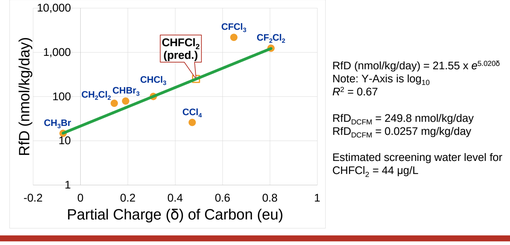
POTENTIAL APPLICATIONS

Scenario 1:
Monitoring of ambient groundwater and source water for community water systems resulted in the detection of 31 compounds. Health-based criteria are available for 19 (61%) and toxicity information is readily available for an additional 4 (13%). Questions from the public, legislature, and press regarding the level of concern for the remaining 8 (26%) detected chemicals need to be addressed.

Chemical	Level detected µg/L	Excluded?	Structural Alerts?	LD50-based Screening Level µg/L	Detected: Screening Level Ratio	Likely to pose a hazard?
3β-Coprostanol	0.248	Y	Considered highly bioaccumulative (log Kow =8.82) Cannot use Decision Tree			
Camphor	0.89	N	N	1.3	0.7	No
Cotinine	0.03	N	N	1.6	0.02	No
4-Cumylphenol	0.14	N	N	LD_{50} - not available Not ChE inhibitor	< 0.5 µg/L benchmark	No
Indole	0.24	N	N	1	0.24	No
5-Methyl-1*H*-benzotriazole	0.087	N	Unclear - Unable to run Toxtree Additional testing needed			
Triethyl citrate	0.01	N	N	6	0.002	No
Triphenyl phosphate	0.037	N	N	3.6	0.01	No

Scenario 2:
Residential drinking water well has been impacted by contaminants from a nearby closed landfill, including dichlorofluoromethane (DCFM) at 15 µg/L. No oral or inhalation toxicity values or data are available. Questions regarding potential health concerns and remediation need to be addressed. A simple read across can be conducted. Chronic oral RfD values were plotted against the partial charge of the central carbon atom (in electron units [eu]) calculated using the extended Hückel method implemented in ChemBio3D (Fig. 2). This led to a screening water value for $CHFCl_2$ of 44 µg/L. For comparison, chloroform ($CHCl_3$) has a guidance value of 30 µg/L.

Fig. 2: Reference Doses for Halomethanes vs. Central Carbon Partial Charge (δ)



RfD (nmol/kg/day) = 21.55 x $e^{5.0206}$
Note: Y-Axis is $\log_{10}$
R^2 = 0.67

RfD_{DCFM} = 249.8 nmol/kg/day
RfD_{DCFM} = 0.0257 mg/kg/day

Estimated screening water level for $CHFCl_2$ = 44 µg/L

GOAL

Develop a rapid, scientifically-sound, and risk-based methodology for estimating water screening values for chemicals with limited or no toxicity data

NEXT STEPS

The next steps of this project include:

- Refine decision tree criteria and methods used to determine exclusions (Box 2) and potential carcinogenic activity (Box 3).
- Confirm generic benchmark values (Boxes 4, 9 and 10).
- Explore the use of predictive modeling for estimating LD_{50} values and ChE inhibition (Boxes 6 and 8).
- Test the read across extrapolation method for additional chemical classes (Box 11).
- Determine how ongoing research in computational toxicology tools can be used to enhance and inform the framework.
- Perform additional testing and subject final decision tree to peer review.

• California Environmental Protection Agency (CalEPA). Office of Environmental Health Hazard Assessment. Public Health Goals. http://oehha.ca.gov/water/phg/
• Kramer et. al. 1996. Reg Tox Pharm 23:249-255
• Minnesota Department of Health (MDH) Human Health-based Water Guidance. http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html
• Stevens, J. Draft Report. 2012 Prepared for Minnesota Department of Health. http://www.health.state.mn.us/divs/eh/risk/guidance/dwec/execsumm.pdf.
• US Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS). http://www.epa.gov/iris/
• US EPA Office of Pesticide Programs. Human Health Benchmarks for Pesticides (HHBP). http://iaspub.epa.gov/apex/pesticides/f?p=HHBP:HOME

More information on MDH's Drinking Water Contaminants of Emerging Concern program can be found at: http://www.health.state.mn.us/cec

We would like to thank the rest of the Health Risk Assessment Unit for advice and assistance with this project.

This poster is available in alternative formats upon request.