Determining the health protective capability of analytical detection methods for short duration exposures

J.C. Lipscomb[1], S. Willison[1], E. Parry[1], S. Chattopadhyay[1], E. Silvestri[1], E. Snyder[2]
U.S. Environmental Protection Agency, Office of Research and Development, National Homeland Security Research Center
Cincinnati, OH[1] and Research Triangle Park, NC[2]
lipscomb.john@epa.gov
www2.epa.gov/homeland-security-research

Introduction

Water contamination may occur from accidental or intentional contamination of source water or drinking water. Water contamination raises questions about the nature and extent of contamination and once this is understood, for what application the water can be used, if any. Risk or exposure guideline values as well as analytical detection (quantitation) methods are needed to answer these questions. Optimally, (1) risk values are available for the route, duration of exposure and severity level of concern and (2) analytical methods are available for the chemical in drinking water with sensitivity to detect harmful concentrations of the chemical. Emergency response decisions made in the absence of either of these components will be accompanied by a level of uncertainty, against possible decisions must be weighed.

Recent events have showcased the vulnerability of water sources and systems to contamination and the challenges that water utilities face responding to these incidents. The sheer number of facilities that house toxic chemicals upstream from drinking water intakes and the volumes of chemical transported through our source waters further demonstrate their vulnerability. As evidenced by the methylcyclohexane-methanol (MCHM) contamination of the Elk River, the water source for the Charleston, WV metropolitan area, rapid decisions for returning drinking water systems to service are difficult without both appropriate and readily available risk values and analytical methods. To increase confidence in available analytic systems and inform development of analytic systems and future risk values, we assessed the state of the science regarding risk values and analytical methods for high priority chemicals.

The goal of the project is to inform the development of two approaches (see Figure 1):

1. An approach to work "forward" from risk or exposure guideline values to recommend sufficient detection capabilities, and
2. An approach to work "backward" from detection capabilities to recommend doses for toxicity testing.

Risk or Exposure Guideline Values

Risk represents the chance of harmful effects, while exposure describes the amount of an agent available at the exchange boundaries of the organism. Choice of use of a risk or exposure value *for emergency response applications* might be dependent on values:

Fit For Purpose

- developed by peer reviewed methods
- based on results from reliable studies using incident-concordant exposure durations
- provided by reputable organizations
- embodying an appropriate level of health conservatism
- addressing biological effect relevant to the decision at hand
- addressing escalation of effects with increasing doses

"Back extrapolation" of risk values developed for longer periods of exposure assumes:

- The same spectrum of effects will be observed at shorter and longer durations,
- The same effect will be the most sensitive effect at shorter and longer durations, and
- Long term doses can be accurately "compressed" into shorter durations.

Response severity increases with duration of exposure, and with dose. Three tiers of severity are generally identified in guideline value systems:

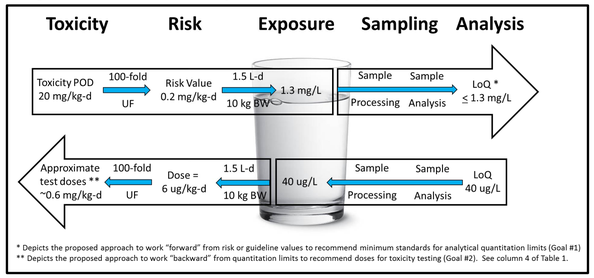
- Tier 1: normal compensatory changes or mild and reversible effects
- Tier 2: serious, irreversible or escape-impairing effects
- Tier 3: lethality

U.S. Environmental Protection Agency
Office of Research and Development

Chemical Selection & Results

- Chemical prioritization can be challenging due to thousands of potential candidates; however, factors can be applied to aid in chemical selection determination
- Federal Agencies (e.g., DHS, DoD, CDC, FDA, EPA) develop lists for chemicals of concern
- Available lists can be cross-referenced and chemical selection factors can be applied for chemical prioritization and determination
- The following factors were considered:
  - Commercial availability and/or synthetic feasibility
  - Federally recognized concern (Homeland Security Concern)
  - Inherent toxicity
  - Excluded metals

Figure 1. The relationship between risk, exposure and detection.

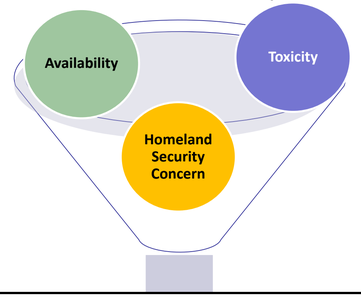


* Depicts the proposed approach to work "forward" from risk or guideline values to recommend minimum standards for analytical quantitation limits (Goal #1)
** Depicts the proposed approach to work "backward" from quantitation limits to recommend doses for toxicity testing (Goal #2). See column 4 of Table 1.

Table 1. Risk Values and Analytical Methods for priority chemicals.

Chemical	Risk Value (µg/L) [a]	Detection Method LOQ [d] (µg/L)	Approximate Doses for Toxicity Testing
Methamidophos	7	0.032	
Methyl parathion	13	10	
Phorate	1.3	10	
Aldicarb	6.7	0.2 [e]	
Cyanide, total	200	5 [e]	
Chlorpyrifos	20	0.05 [e]	
Diphacinone	10	0.125 [e, f]	
Acrylonitrile	67	1 [e, f]	
Disulfoton	0.27	0.05 [e, f]	
Acrylamide	6.7	10 [e, f]	
Parathion	20 [b]	10	
Acrolein	27 [b]	30 [f]	
Methylacrylonitrile	330 [c]	10 [e, f]	
Methyl hydrazine	6.7 [c]	- [g]	
Monocrotophos	-	40	600 µg/kg-d
Phosphamidon	-	0.11	3.45 µg/kg-d
Bromadiolone	-	0.125 [e, f]	1.9 µg/kg-d
Fluorosilicic acid	-	2000	30 mg/kg-d
Methyl fluoroacetate	-	50 [g]	750 µg/kg-d
Sodium fluoroacetate	-	50 [g]	750 µg/kg-d
BZ	-	- [g]	-

Figure 2. Chemical identification and prioritization.



Oral risk and exposure guideline values for durations of exposure less than "lifetime" or "chronic" for 21 priority chemicals were sought. *No values developed for emergency response were available for any chemical*. No other values were available for 8 priority chemicals; no other values for durations shorter than 15 days were available for 2 chemicals; no other values for durations shorter than subchronic were available for 2 chemicals.

Analytical method quantitation limit values were available for a majority of the chemicals of interest in drinking water. Some methods may not have all of the QA/QC criteria needed for drinking water standard methods; however, quantitation limits could still be obtained. Two chemicals did not have an appropriate analytical method to derive a quantitation limit value.

Table 2. Summary outcome.

OUTCOME
Risk values and detection limits available (13/21 chemicals)
Risk values not available, detection limits available (6/21 chemicals)
Risk values available, detection limits not available (1/21 chemicals)
Neither risk values nor detection limits available (1/21 chemicals)

[a] Only risk or exposure guideline values for durations of less than "chronic" or "lifetime" were considered for this analysis. When necessary, risk values were converted from value system-specific units to concentration in drinking water as shown on Figure 1. Values examined include EPA values for up to subchronic durations and ATSDR Acute and Intermediate values; the lowest value among those available is presented.
[b] No risk values available for durations shorter than 15 days.
[c] No risk values available for durations shorter than subchronic.
[d] Quantitation limit determined for the chemical in drinking water.
[e] Quantitation limit reported as lowest calibrated concentration.
[f] Quantitation limit derived from method that may not meet appropriate QA/QC criteria, data quality objectives, or is not available in desired environmental matrix.
[g] Environmental method not available.

Summary

Emergency response decisions are based on information and criteria that differ significantly from decisions made to protect general public health. These include the rare, if not once in a lifetime exposures presumed for emergency conditions; a smaller and sometimes well-characterized (even restricted) population exposed; and the likelihood of some adverse consequences accompanying some emergency response actions (e.g. evacuations). *Available information suggests that emergency response guideline values can be developed for many of these priority chemicals.* Emergency exposure guideline values should:

- include a lesser degree of health conservatism,
- identify the types of responses likely to occur with increasing exposure,
- quantify the exposures associated with responses of increasing severity, and
- reflect temporally-concordant toxicity data.

Many laboratory-based analytical detection systems are available and ensure the ability to recognize potentially harmful chemical exposures, enabling prompt emergency response decisions that embody an acceptable level of confidence. Key findings and some recommendations include:

- Risk or guideline exposure values enhance the value of information applicable when public health guideline values are exceeded.
- The ability to detect risk-associated concentrations is necessary to determine appropriate actions.
- Emergency Response guideline values *should* be developed for priority chemicals to better guide emergency management decisions.
- Available laboratory-based detection methods appear sufficient to detect concentrations associated with health-protective risk or guideline values for many priority chemicals.
- Analytical capability should be enhanced for several chemicals.
- Hand-held detection capabilities should be examined.

Selected References

NRC (National Research Council). 2001. Standing operating procedures for developing acute exposure guideline levels for hazardous chemicals. Washington, DC: National Academy Press.
U.S. EPA. 2011. Exposure factors handbook 2011 edition (final report). Washington, DC: U.S. Environmental Protection Agency. EPA/600/R-09/052F.
U.S. EPA. 2012. 2012 Edition of the Drinking Water Standards and Health Advisories. EPA 822-S-12-001. Office of Water, U.S. Environmental Protection Agency Washington, DC. https://nepis.epa.gov/Exe/ZyPDF.cgi/P100N01H.PDF?Dockey=P100N01H.PDF
U.S. EPA. 2017. Selected Analytical Methods for Environmental Remediation and Recovery (SAM) 2017. U.S. Environmental Protection Agency, Cincinnati, Ohio. https://www.epa.gov/homeland-security-research/sam.
U.S. EPA. 2017. Provisional Peer Reviewed Toxicity Values for Superfund (PPRTV). Office of Superfund Remediation and Technology Innovation, U.S. Environmental Protection Agency, Washington, DC 20460. https://hhpprtv.ornl.gov/pprtv_user.html
U.S. EPA. 2017. Human Health Benchmarks for Pesticides in Drinking Water. https://www.epa.gov/dwstandardsregulations/human-health-benchmarks-pesticides-drinking-water.
Young RA, Bast CB, Wood CS and Adeshina F. 2009. Overview of the Standing Operating Procedure (SOP) for the development of Provisional Advisory Levels (PALs). Inhalation Toxicol 21(S3):1-11.

This product (ORD-023690) was developed by National Homeland Security Research Center, a component of the U.S. Environmental Protection Agency's Office of Research and Development. This material has been reviewed and cleared for presentation in accord with established procedures, December, 2017. No official endorsements should be inferred; the content represents the views of the authors, and not necessarily those of the U.S. EPA.