ATTACHMENT A "Risk 101"

Risk Assessment Methodology for Health Risk Limits Derivation, Summarized from 2023 SONAR[1]

The Minnesota Department of Health (MDH) derives Health Risk Limits (HRLs) based on United States Environmental Protection Agency (EPA) risk assessment methods and guidelines. Risk assessment methods require that MDH determine: the health effects associated with a chemical and the lowest dose at which an adverse effect may arise; an evaluation of human exposure; and an integration of these and other considerations that may contribute to human health risk. The following is a brief step-wise description of the approach MDH's scientists use to calculate the HRLs.

An MDH-derived HRL is the concentration of a chemical in drinking water that is likely to pose little or no health risk to humans, including vulnerable subpopulations, based on current levels of scientific understanding. Vulnerable populations vary depending on the chemical of interest, but may include: fetuses, infants, pregnant women, prepubescent childrenn, and others. The HRL concentration is a function of how toxic a chemical is (that is, the minimum quantity that will cause health effects), the duration of exposure, and the amount of water individuals drink during the exposure period. In addition, a HRL value incorporates several adjustment factors to account for uncertainty in our understanding of a chemical's health risks.

1) Toxicity Evaluation – Noncancer Effects

Rather than wait until health effects are evident in humans, the accepted method for assessing potential toxicity to humans is through controlled laboratory studies using mammals (the term "animal" shall be used throughout to describe mammalian species). In toxicity testing, animals are divided into groups and each group is administered one of several doses of a chemical, usually daily, over a set period of time. Testing has two goals: (1.) to identify the hazard or toxic effects caused by the chemical, and; (2.) to evaluate the relationship between the dose and the animal's response. The dose-response relationship may vary depending on when (e.g., the life stage) during the life stage and for how long (duration) the exposure occurred.

In evaluating the dose and the response for noncancer health effects, researchers seek to determine the lowest dose where adverse effects related to dosing are observed (the "lowest observed adverse effect level," or LOAEL) and the highest dose where no adverse effects related to dosing are observed (the "no observed adverse effect level," or NOAEL). By definition, LOAELs and NOAELs can only be a dose used in the study of interest. A newer analysis method, benchmark dose (BMD) modeling, uses statistical modeling to evaluate a dose-response dataset using a pre-determined effect level. Modeling assesses the shape of the dose response relationship and allows scientists to calculate a dose where a given response level (e.g., 10% change in organ weight) is expected to be seen. While not all datasets are compatible with BMD modeling, when feasible, it is preferable to a NOAEL/LOAEL approach because it considers the entire dose-response curve rather than relying on discrete dose points. BMD modeling is now a standard risk assessment practice that is used by many state, federal, and international regulatory agencies; indeed, the US EPA developed and maintains a free-to-use BMD modeling software that is employed by MDH and other states to evaluate appropriate datasets.

The dose resulting from dose-response evaluation (also referred to as a point of departure (POD) dose) serves as the starting point for deriving health-protective concentrations for environmental media.

The dose level selected from the dose-response evaluation of the animal study(s) is identified as a point of departure dose (POD). The dose to the laboratory animal is converted to a human equivalent dose (HED) by adjusting for differences in how these species handle the chemical in the body. An HED represents the dose to humans that would result in the same internal dose as the dose administered to the laboratory animal species, assuming that the toxic response is similar in the two species.

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[1] MDH. 2023 Statement of Need and Reasonableness (SONAR), as cited in MDH 2023 SONAR. (https://www.health.state.mn.us/communities/environment/risk/docs/rules/hrlsonar23full.pdf).

The HED is then reduced by variability and uncertainty factors (UFs) to account for what is not known about a chemical's toxicity to a human population. The factors account for:

- UF_A - uncertainty in extrapolating from animal data to humans (e.g., it may not be known whether humans are more or less sensitive than the test animal);
- UF_H - variation in sensitivity among human individuals (e.g., variability in internal dose levels or sensitivity to the toxicological effects);
- UF_S - uncertainty in extrapolating from effects observed in a short-term study to potential effects from a longer exposure;
- UF_L - uncertainty associated with using a study in which health effects were found at all doses tested (lowest dose was a LOAEL and no NOAEL was identified); and
- UF_{DB} - deficiencies (data gaps) in available data.

In the absence of chemical-specific information, each of the five factors is typically assigned a value between 1 and 10. Values of 1, $10^{0.5}$ and 10 are most common. Values assigned to all factors are multiplied to determine the overall uncertainty factor. By convention, half-power values (e.g., $10^{0.5}$) are factored as whole numbers when they occur singly but as powers or logs when they occur in tandem. For example, individual UFs of 3 and 10 would be expressed as 30 (3×10^1), whereas individual UFs of 3 and 3 would be expressed as 10 ($10^{0.5} \times 10^{0.5} = 10^1$).

The HED is divided by the product of the uncertainty and variability factors to calculate a reference dose (RfD). An RfD is expressed in milligrams of chemical per kilogram of body weight per day (mg/kg-day) and is defined as an estimate of a dose level that is likely to be without an appreciable risk of adverse effects.

2) Exposure

HRLs must be protective against adverse health effects from short-term as well as long-term exposures to contaminants in drinking water. MDH considers sensitive life stages and subpopulations as well as the magnitude and duration of exposure necessary to elicit a toxic effect. Intake rate is expressed as the quantity of water consumed per kilogram of body weight per day (L/kg-day). Studies of water consumption indicate that infants and young children drink more water for their body weight than do adults. Newborns derive all, or nearly all, their nutrition from liquid. Intake rates fall rapidly with age; by age seven, intake rates are nearly the same as those of adults.

MDH uses water intake rates that are recommended by US EPA Exposures Factor Handbook (EPA 2019). These rates are based on data collected from individuals across the US as part of the US Department of Agriculture's Continuing Survey of Food Intake by Individuals (CSFII) survey.

3) Risk Characterization

An RfD incorporates information about the toxicity of a single chemical associated with a given dose. Exposure to a chemical may result from multiple sources. The Groundwater Protection Act requires that MDH use a "relative source contribution" (RSC) factor when deriving HRLs for noncancer effects. The RSC allocates only a portion of the RfD to exposure from ingestion of water, and reserves the remainder of the RfD for other water-related exposures (e.g., inhalation of volatilized chemicals, dermal absorption) as well as exposures via other contaminated media such as food, air, and soil. MDH has relied upon EPA's Exposure Decision Tree approach (EPA 2000) to facilitate determining appropriate default RSC values.

MDH combines the above information into an equation for noncancer health effects:

$$\text{Noncancer HRL } (\mu g/L) = \frac{\text{RfD (mg/kg-d) x RSC x 1,000 } \mu g/mg}{\text{Intake Rate (L/kg-d)}}$$

References:

Minnesota Department of Health 2023. Statement of Need and Reasonableness in the Matter of Proposed Rules Relating to Health Risk Limits for Groundwater. Available online: https://www.health.state.mn.us/communities/environment/risk/docs/rules/hrlsonar23full.pdf