Use of margins of exposure and risk quotients in risk assessment

Fact sheet series: Topics in risk assessment of substances under the *Canadian Environmental Protection Act, 1999* (CEPA)

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Introduction

Margins of exposure (MOEs) and risk quotients (RQs) are measurements of potential risk used in the risk assessment of substances. Both MOEs and RQs are ratios of a substance's toxicity relative to its exposure to humans or other organisms. These ratios suggest whether adverse effects may happen in humans or in the environment at current or predicted exposure levels in Canada. Decision-making for ecological and human health assessments under CEPA is based on a weight of evidence approach that considers various lines of evidence to characterize health and ecological risks caused by substances (see the factsheet on Application of weight of evidence and precaution in risk assessment).

Margins of exposure

The MOE is the ratio usually calculated by determining a level of exposure in which harm to human heath is not expected to occur, and then dividing that by an estimated level of human exposure. A higher MOE denotes a larger buffer between a potential human health effect and exposure to a substance.

Data pertaining to human health are often from laboratory studies but there may be other data sources such as epidemiological studies. The level of exposure in which there is not expected to be a harm to human health is called a no-observed-adverse-effect level or concentration (NOAEL or NOAEC). Often a NOAEL or NOAEC is selected based on health effects observed at higher levels or concentrations in a study. A lowest level or concentration of exposure at which there is an adverse effect (LOAEL or LOAEC) may be used if a NOAEL or NOAEC is not available. Alternatively, measured data may be modelled to predict a value at which an effect of concern is not

expected. For more information, refer to the World Health Organization's Principles for modelling dose-response for the risk assessment of chemicals.

The level of human exposure takes into consideration the exposure scenario route, frequency, and duration. Exposure data may be measured, but in the absence of measured data are usually estimated in consideration of a substance's physical chemical properties as well as the expected exposure scenarios.

A MOE can be derived by comparing the NOAEL or NOAEC to an exposure level:

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MOE = Level in which harm to human health is not expected / Level of human exposure
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A MOE is specific to a human health value and exposure scenario for a substance. Multiple MOEs are often determined for a substance, given that there may be exposures to substances in different environmental media, food and beverages, or in products available to Canadians. In addition, for a single source of exposure, there may be multiple MOEs to account for different routes (oral, dermal, and inhalation) and durations of exposure. An MOE is not meant to be compared between substances or scenarios. For instance, if there is a 1000-fold difference between 2 MOEs, there is not an exact 1000-fold difference in risk to human health.

When considering the adequacy of the MOE, a larger value is typically required when there is uncertainty due to the hazard data available, or when there is an elevated concern related to seriousness of effect or steepness of a dose response curve. For instance, when a LOAEL is used to estimate the MOE, an additional uncertainty factor is considered applicable. For more information, refer to Health Canada's Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides.

Risk quotients

In ecological screening assessments, one line of evidence in risk characterization is the RQ, a ratio of a predicted environmental concentration (PEC) to a predicted no-effect concentration (PNEC). Ecological assessments often have PECs for multiple exposure scenarios, in which case there would be multiple RQs. It is key to note that RQs are just one line of evidence in risk characterization. Other lines of evidence (such as persistence and bioaccumulation potential) may also contribute to the evaluation of environmental risk of substances.

A PEC estimates the exposure to a substance in a particular environmental medium (such as water, air, sediment, or soil). Environmental exposure scenarios for a substance are selected based on ways it is most likely to be released. PECs are then calculated based on estimated or measured levels of exposure using monitoring data, modelling, and other information available from various sources. It is not possible to identify and fully characterize environmental exposure by calculating PECs for each

location with potential releases. Therefore, the environmental exposure scenarios presented in assessments are generic, rather than site-specific, and are not intended to be exhaustive.

A PNEC represents the concentration of a substance in an environmental medium that is unlikely to cause adverse effects to the structure or function of an exposed ecosystem. To determine PNECs in each environmental compartment (water, soil, and sediment), toxicity data for the substance(s) are collected for aquatic, benthic, and terrestrial organisms if available. For data-rich substances, the species sensitivity distribution (SSD) method is used to derive PNECs. This method models the variation in species sensitivities to the substance. An SSD aims to determine the concentration of a substance that will protect a certain percentage (for example, 95%) of the species in an ecosystem.

For substances that do not have the data to support an SSD method, an assessment factor (AF) method is used. When direct high-quality empirical data for the substance are lacking, reliable read-across and modelled toxicity data can also be added to the substance's dataset to derive a more accurate PNEC (see the factsheet on Use of analogues and read-across in risk assessment). Once the dataset is complete, the next step in the PNEC calculation is to select a critical toxicity value (CTV) and apply an AF in order to account for three main uncertainties within the ecotoxicity dataset. These uncertainties include:

- a lack of long-term ecotoxicity data on effects other than mortality
- inadequate representation by test species of the species variability within an ecosystem
- for substances with a specific mode of toxic action, a lack of toxicity data reflecting that mode of action

Finally, for each environmental medium (if data are available), the PNEC is calculated by dividing the CTV by the AF.

Once there are PECs and PNECs for the substance(s) in a particular environmental medium, the values can be compared to derive the RQ:

$$RQ = PEC / PNEC$$

Typically, RQ values that are well below 1 indicate that the potential for harm is low, which suggests that no further action is needed for the assessed substances. RQ values that are close to or above 1 indicate that an adverse ecological response caused by the substance is possible. In these cases a more precise or accurate evaluation of risks may be warranted. Often, risk management actions may be considered when RQ values are close to or greater than 1. In some cases, there will still be uncertainties in the level of risk even after using refinement procedures. Higher uncertainty corresponds to a lower strength of the evidence and a greater need to consider precaution. In general, it is important that the assessment approach is precautionary in cases where there is uncertainty in the PEC, the PNEC, or in other lines of evidence.