Use of assessment factors in ecological risk assessment for deriving predicted no-effect concentrations

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

An ecological risk assessment determines the potential that a substance could adversely affect organisms, and includes the derivation of a predicted no-effect concentration (PNEC). A PNEC represents the concentration of a substance (in water, sediment, soil, or air) that is not expected to induce adverse effects in most organisms, in an ecosystem that is chronically exposed. For the majority of substances, ecotoxicity data are scarce and represent only a small number of species and effects. Therefore, risk assessors must apply certain assumptions to the available ecotoxicity data so that a derived PNEC is protective of as many species as possible. The general assumptions made when deriving a PNEC are:

1. Protecting the most sensitive species in an ecosystem will protect the ecosystem structure and function
2. Available ecotoxicity studies do not necessarily test the most sensitive species or the most sensitive endpoint
3. Using assessment factors (AFs) or species sensitivity distribution (SSD) approaches to derive a PNEC from ecotoxicity studies will protect the most sensitive species and, therefore, ecosystem function

SSD is the method recommended for deriving the PNEC of substances with larger datasets. Derivation of the SSD typically requires datasets that include chronic data for seven or more species representing primary producers (such as algae and plants), invertebrates (such as insects, clams and worms), and vertebrates (such as fish and frogs). An AF approach is recommended for assessing substances with datasets that are not suitable for constructing an SSD (for example, with too few species represented in the dataset). In the AF approach, a PNEC is calculated by dividing the selected critical toxicity value (CTV) by an AF. The CTV is an estimated or measured concentration of a substance that typically corresponds to an effect threshold, such as a low-observable (LOAEL), or no-observable adverse effect level

(NOAEL). When experimental data for a substance are limited, the AF approach may also consider data from close structural analogues and reliable modelled data in order to fill gaps within the dataset.

The AF approach used for decades by regulatory jurisdictions to derive PNECs for ecological risk assessment. Recent advances in our understanding of ecotoxicity, provide an opportunity to update the approach and improve transparency and consistency between assessors. A new AF approach developed by Environment and Climate Change Canada (Okonski *et al*., 2020 applies three main factors to the CTV to address uncertainties in the dataset:

1. The endpoint standardization factor (F_{ES}) to address differences in the study duration, severity and degree of effect between ecotoxicity endpoints
2. The species variation factor (F_{SV}) to address representation of ecosystem species
3. The mode of action factor (F_{MOA}) for substances with a specific mode of action that is not evidenced in the ecotoxicological dataset

F_{ES}

Toxicity tests used to derive a PNEC can vary in three important ways:

1. duration: the exposure period can range from a small fraction of the organism's lifespan to a larger fraction, or can include a sensitive life stage (such as reproduction)
2. severity of effect: the measured endpoint can range from mortality to non-lethal effects such as impaired growth
3. degree of effect: the measured endpoint can reflect an outcome that affects many organisms or a small percentage (for example, 50% mortality or 10% mortality), or the rate of effect to all organisms can be high or low (for example, 50% growth rate reduction or 10% reduction)

The F_{ES} represents extrapolations applied to the reported endpoint based on these three elements. The purpose of the F_{ES} is to standardize all endpoints, so that each may be considered to reflect a long-term, sub-lethal, no- or low-effect concentration.

If a study presents a long-term, sub-lethal, no- or low-effect level (chronic), no extrapolation is required (F_{ES} = 1). However, acute endpoints require extrapolation

for each of the above three elements in order to estimate long-term sub-lethal no-effect concentrations, and for acute studies, an F_{ES} of 10 is sufficient for most substances. For endpoints that require extrapolations based on one or two of the above elements, an F_{ES} of 5 is applied. For example, an F_{ES} of 5 would be applied to an endpoint that is long-term but lethal (for example, mortality reported in a 21-day daphnia reproduction study). All endpoints in the dataset are divided by an F_{ES} to standardize them to a long-term sub-lethal no- or low-effect level so that all of the data may be considered equally. The lowest standardized ecotoxicity value (SEV) is selected as the CTV, and this CTV will be used for PNEC calculation.

F_{ES} values

Is extrapolation needed for short-term to long-term exposure?	**Is extrapolation needed for lethal to sub-lethal effects?**	**Is extrapolation needed for median to no/low effect concentrations?**	**F_{ES}**
Yes	Yes	Yes	**10**
Yes/No	Yes/No	Yes/No	**5**
No	No	No	**1**

F_{SV}

In an SSD-based PNEC, the "hazardous concentration" at which 5% of species exhibit an effect from chronic exposure (HC_5) is often considered protective of sensitive species. When deriving an AF-based PNEC from a smaller dataset, the species variation factor (F_{SV}) is applied to estimate the HC_5. Statistical data analyses show that an AF-derived PNEC approaches the SSD-derived PNEC as the size and diversity of the dataset increases. Once a dataset includes testing on seven or more species across all three organism categories (primary producers, invertebrates, and vertebrates), AF- and SSD-derived PNECs become comparable. The F_{SV} therefore varies with the number of species and organism categories represented in the dataset. Larger F_{SV} values are used to reflect greater uncertainty when fewer species or categories of organisms are represented. A F_{SV} of 1 is employed for datasets comprising 7 or more species representing all three categories. F_{SV} values were selected based on the number of categories of organisms and number of species, such that each differs from its neighbor by a factor of approximately 2.

F_{SV} values

Number of categories*	1 species	2 to 3 species	4 to 6 species	7 or more species
1	50	20	10	5
2	x	10	5	2
3	x	5	2	1

* The 3 categories are: primary producers (such as algae and plants), invertebrates (such as insects, clams and worms), and vertebrates (such as fish, frogs, birds, mammals).

F_{MOA}

Another consideration for determining the AF is the mode of action (MoA) of the substance. The MoA describes how a substance causes an effect by initiating key events at the cellular level that lead to a functional or anatomical change, and contributes to an overall understanding of the substance's toxicity. When a substance has an MoA that involves interference with cell membranes, this is referred to as narcosis. A substance with a narcotic MoA is non-specific and elicits similar adverse effects in different organisms over a small range of concentrations. Substances with non-narcotic MoAs are reactive or specifically acting and may be more toxic to certain types of organisms than others. A F_{MOA} can be applied to address substances with a known or suspected non-narcotic mode of action.

- An F_{MOA} of 1 is applied to narcotic substances to acknowledge the small variation in effect levels across species from this MoA, when compared to non-narcotic substances
- An F_{MOA} of 2 is applied to non-narcotic substances whose MoA is expected to be applicable across species, and is expressed in the ecotoxicity data available for the substance
- An F_{MOA} of 5 is applied to substances that are non-narcotic in both short- and long-term exposures, where at least 1 of the expected MoA is not expressed in the available dataset
- An F_{MOA} of 10 is applied to substances that are narcotic in short-term exposures, and are expected to have 1 or more non-narcotic MoA in long-term exposures, where at least 1 of the expected MoA is not reflected in the available dataset
- The approach also allows for the use of custom factors, where warranted and well documented, derived from data for similar substances

Deriving a PNEC

After all three factors are determined, divide the ecotoxicity value by the F_{ES} to determine the SEV.

SEV = Ecotoxicity value ÷ F_{ES}

Select the CTV as the ecotoxicity value with the lowest SEV

Once the CTV has been selected, the PNEC can be calculated:

$PNEC = CTV \div AF = CTV \div (F_{ES} \times F_{SV} \times F_{MOA})$

Example of a PNEC calculation from a fictional dataset

Calculation of the SEV and selection of the CTV

Category	**Organism**	**Endpoint**	**Ecotoxicity value (mg/L)**	**F_{ES}**	**Standardized Ecotoxicity Value (SEV) (mg/L)**
Vertebrate	Carp	96-hour LC_{50}	34	10	3.4
Invertebrate	Water flea	48-hour EC_{50} (immobilization)	**15 (CTV)**	**10**	**1.5 (Lowest SEV)**
Invertebrate	Water flea	21-day EC_{10} (reproduction)	3	1	3
Primary Producer	Algae	72-hour EC_{50}	10	5	2

CTV = 15 mg/L because this was the ecotoxicity value that resulted in the lowest SEV

F_{ES} = 10 to extrapolate from acute severe-effect to chronic low- or no-effects value

F_{SV} = 5 because the dataset contains 3 different species covering 3 organism categories

F_{MOA} = 1 because the substance is thought to act through a narcotic mode of action

$PNEC = CTV \div (F_{ES} \times F_{SV} \times F_{MOA})$

$= 15 \text{ mg/L} \div (10 \times 5 \times 1)$

$= 0.3 \text{ mg/L}$

Consistency and transparency

The AF approach described here results in more consistent and predictable PNEC derivation. Additionally, the approach enables more transparency in communication of risk assessment outcomes as it describes how each toxicity data point contributes to the assessment factor. A more detailed account of the approach is available in Okonski *et al.* (2020).