

# **A Framework For The Derivation Of Environmental Quality Guidelines That Protect Apex Marine Mammals From Persistent Organic Pollutants (POPS)**

Kathleen McTavish, Juan José Alava, Tanya Brown, Magaidh Crossland, Neil Dangerfield, Brendan Hickie, Peter S. Ross, and Angeline Tillmanns

Fisheries and Oceans Canada  
Pacific Region  
Pacific Sciences Enterprise Centre  
4160 Marine Drive  
West Vancouver BC V7V 1H2

2024

**Canadian Technical Report of  
Fisheries and Aquatic Sciences 3582**



Fisheries and Oceans  
Canada

Pêches et Océans  
Canada

**Canada**

## **Canadian Technical Report of Fisheries and Aquatic Sciences**

Technical reports contain scientific and technical information that contributes to existing knowledge but which is not normally appropriate for primary literature. Technical reports are directed primarily toward a worldwide audience and have an international distribution. No restriction is placed on subject matter and the series reflects the broad interests and policies of Fisheries and Oceans Canada, namely, fisheries and aquatic sciences.

Technical reports may be cited as full publications. The correct citation appears above the abstract of each report. Each report is abstracted in the data base Aquatic Sciences and Fisheries Abstracts.

Technical reports are produced regionally but are numbered nationally. Requests for individual reports will be filled by the issuing establishment listed on the front cover and title page.

Numbers 1-456 in this series were issued as Technical Reports of the Fisheries Research Board of Canada. Numbers 457-714 were issued as Department of the Environment, Fisheries and Marine Service, Research and Development Directorate Technical Reports. Numbers 715-924 were issued as Department of Fisheries and Environment, Fisheries and Marine Service Technical Reports. The current series name was changed with report number 925.

## **Rapport technique canadien des sciences halieutiques et aquatiques**

Les rapports techniques contiennent des renseignements scientifiques et techniques qui constituent une contribution aux connaissances actuelles, mais qui ne sont pas normalement appropriés pour la publication dans un journal scientifique. Les rapports techniques sont destinés essentiellement à un public international et ils sont distribués à cet échelon. Il n'y a aucune restriction quant au sujet; de fait, la série reflète la vaste gamme des intérêts et des politiques de Pêches et Océans Canada, c'est-à-dire les sciences halieutiques et aquatiques.

Les rapports techniques peuvent être cités comme des publications à part entière. Le titre exact figure au-dessus du résumé de chaque rapport. Les rapports techniques sont résumés dans la base de données Résumés des sciences aquatiques et halieutiques.

Les rapports techniques sont produits à l'échelon régional, mais numérotés à l'échelon national. Les demandes de rapports seront satisfaites par l'établissement auteur dont le nom figure sur la couverture et la page du titre.

Les numéros 1 à 456 de cette série ont été publiés à titre de Rapports techniques de l'Office des recherches sur les pêcheries du Canada. Les numéros 457 à 714 sont parus à titre de Rapports techniques de la Direction générale de la recherche et du développement, Service des pêches et de la mer, ministère de l'Environnement. Les numéros 715 à 924 ont été publiés à titre de Rapports techniques du Service des pêches et de la mer, ministère des Pêches et de l'Environnement. Le nom actuel de la série a été établi lors de la parution du numéro 925.

Canadian Technical Report of  
Fisheries and Aquatic Sciences 3582

2024

A Framework For The Derivation Of Environmental Quality Guidelines That Protect Apex  
Marine Mammals From Persistent Organic Pollutants (POPs)

by

Kathleen McTavish<sup>1</sup>, Juan José Alava<sup>2, 5</sup>, Tanya Brown<sup>3,5</sup>, Magaidh Crossland<sup>1</sup>, Neil  
Dangerfield<sup>4</sup>, Brendan Hickie<sup>6</sup>, Peter S. Ross<sup>7</sup>, and Angeline Tillmanns<sup>8</sup>

Fisheries and Oceans Canada Pacific Science Enterprise Centre, Pacific Region 4160 Marine  
Drive West Vancouver, B.C., Canada V7V 1N6

<sup>1</sup> Environment and Climate Change Canada, 351 Boulevard Saint-Joseph, Gatineau, Quebec J8Y  
3Z5

<sup>2</sup> Ocean Pollution Research Unit, Institute for the Oceans and Fisheries, University of British  
Columbia, AERL 2202 Main Mall, Vancouver, BC V6T 1Z4 Canada

<sup>3</sup> Fisheries and Oceans Canada, 4160 Marine Drive, West Vancouver BC

<sup>4</sup> Fisheries and Oceans Canada, 9860 West Saanich Road, Sidney, BC V8L 4B2

<sup>5</sup> Simon Fraser University, 8888 University Drive, Burnaby BC V5A 1S6

<sup>6</sup> School of the Environment, Trent University, 1600 West Bank Drive, Peterborough ON K9L  
0G2

<sup>7</sup> Raincoast Conservation Foundation, PO Box 2429, Sidney BC V8L 3Y3

<sup>8</sup> British Columbia Ministry of Water, Land and Resource Stewardship, 525 Superior St.  
Victoria, B.C., V8V 3Y8

© His Majesty the King in Right of Canada, as represented by the Minister of the Department of Fisheries and Oceans, 2024

Cat. No. Fs97-6/3582E-PDF ISBN 978-0-660-69256-2 ISSN 1488-5379

Correct citation for this publication:

McTavish, K., Alava, J.J., Brown, T., Crossland, M., Dangerfield, N., Hickie, B., Ross, P.S., and Tillmanns, A. 2024. A Framework for the derivation of environmental quality guidelines that protect apex marine mammals from persistent organic pollutants (POPs). *Can. Tech. Rep. Fish. Aquat. Sci.* 3582: viii + 29p.

## Table Of Contents

1.	General Overview .....	1
1.1.	Introduction.....	1
1.2.	Selection of substances for guideline development .....	3
1.3.	Mixture considerations.....	4
2.	Derivation of a Toxicity Reference Value (TRV) for Marine Mammals .....	4
2.1.	What is a TRV and how is it derived? .....	4
2.2.	Selection of a point of departure (POD) .....	4
2.2.1.	Selection of an existing point of departure (POD).....	5
2.2.2.	Determination of a POD from laboratory dose-response data .....	5
2.2.3.	Marine mammal biomonitoring studies .....	5
2.3.	Selection of uncertainty factors.....	5
2.3.1.	Intraspecies variability .....	6
2.3.2.	Interspecies variability .....	6
2.3.3.	Data quality and quantity .....	6
2.4.	Calculation of the marine mammal TRV .....	6
2.5.	Consideration of carcinogenic effects.....	7
3.	Estimating concentrations in other environmental media .....	8
3.1.	Overview.....	8
3.2.	Biomagnification factor (Marine mammal:prey).....	8
3.3.	Bioaccumulation factor (prey:water) .....	11
3.4.	Estimating sediment concentrations.....	13
3.5.	Criteria for other models.....	14
4.	Calculation of the final environmental quality guidelines (EQG <sub>mm</sub> ) .....	14
4.1.	Diet guideline (DG <sub>mm</sub> ) .....	14
4.2.	Water quality guideline (WQG <sub>mm</sub> ).....	15
4.3.	Sediment quality guideline (SeQG <sub>mm</sub> ) .....	15
4.4.	Weight of evidence review .....	16
5.	Conclusion .....	16
6.	References.....	17
7.	Appendices.....	21
7.1.	Appendix A - Compilation and evaluation of toxicity data .....	21
7.2.	Appendix B – IB model input values and FI:BW estimates .....	24

## List Of Tables

Table 1. Mean calf BMFs for orca whales for a range of KOW values.	20
--	----

## List Of Figures

Figure 1. General steps for derivation of environmental quality guidelines for the protection of Canadian apex marine mammals from bioaccumulative substances..	8
Figure 2. Calculation pathways of EQGs for prey tissue, water, and sediment starting with a surrogate toxicity reference value (TRV).	18

## Acknowledgements

This draft was produced by the Marine Mammal Protocol Sub-Committee of the Southern Resident Killer Whale Contaminants Technical Working Group. Funding was provided by Environment Climate Change Canada (ECCC), Fisheries and Oceans Canada, and B.C. Ministry of Environment and Climate Change Strategy. Thank you to the various peer reviews for their valuable comments including Marie-Odile Fouchécourt for providing insight on human health risk assessment.

## Glossary

**Apex marine mammal** — a marine mammal species and species functional group at the top of the food chain/food web with no natural predators in their environment.

**Bioaccumulation** — general term describing a process by which chemical substances are accumulated by aquatic organisms from water directly or through consumption of food containing the chemicals (CCREM 1987).

**Bioconcentration** — A process by which there is a net accumulation of a chemical directly from water into aquatic organisms resulting from simultaneous uptake (e.g., by gill or epithelial tissue) and elimination (CCREM 1987).

**Biomagnification** — result of the processes of bioconcentration and bioaccumulation by which tissue concentrations of bioaccumulated chemicals increase as the chemical passes up through two or more trophic levels. The term implies an efficient transfer of chemicals from food to consumer so that residue concentrations increase systematically from one trophic level to the next (CCREM 1987).

**Biomarker** — a physiological, histological, or biochemical measurement that indicates an organism has experienced stress from contaminant exposure.

**Biomonitoring** — monitoring biological components of ecosystems (e.g., biomarkers, species presence/absence, diversity) to estimate organismic or ecosystem stress.

**Environmental Quality Guideline (EQG)** - scientifically derived numerical concentration or narrative statement considered to be protective of designated values in ambient conditions.

**K<sub>ow</sub>** — octanol/water partition coefficient. The ratio of a chemical's solubility in n-octanol and water at equilibrium. The logarithm of K<sub>ow</sub> is used as an indication of a chemical's propensity for bioconcentration by aquatic organisms (CCREM 1987).

**Mode of Action (MOA)** —the cellular or molecular mechanisms through which a toxic substance exerts its harmful effects on an organism.

**Point of Departure** — the point in a toxicological dose-response data set generally corresponding to an estimated low effect level or no effect level (e.g., BMDL, EC10, NOAEL, LOAEL).

**Tissue Residue** — chemical substance(s) in aquatic biota tissue, such as fish, shellfish, invertebrates, and aquatic plants on a whole body, wet weight basis.

**Trophic Magnification Factor** — represents the diet-weighted average biomagnification factor (BMF) of chemical residues across food webs.

**Toxicity Reference Value (TRV)** — TRVs for non-cancer effects are determined based on the threshold concentration or dose below which no adverse health effects are expected, usually determined from chronic toxicity data.

**Weight of Evidence** — a method for decision-making that involves consideration of multiple sources of information and lines of evidence.

## List of Acronyms

%OC	percent organic carbon
ADME	absorption, distribution, metabolism, and excretion
AOP	adverse outcome pathway
ATSDR	The Agency for Toxic Substances and Disease Registry
BAF	bioaccumulation factor
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
BMF	biomagnification factor
BSAF	biota-sediment accumulation factor
Bw	body weight
CCME	Canadian Council of Ministers of the Environment
CCREM	Canadian Council of Resource and Environment Ministers
DFO	Fisheries and Oceans Canada
DG <sub>mm</sub>	diet guideline for the protection of marine mammals
ECCC	Environment and Climate Change Canada
EC <sub>x</sub>	effect concentration causing response in x% of test organisms
ENV	British Columbia Ministry of Environment and Climate Change Strategy
EQG <sub>mm</sub>	environmental quality guideline for the protection of marine mammals
FI:BW	Food intake: body weight ratio IB model Individual-based model
KC	key characteristic
K <sub>oc</sub>	organic carbon-water partition coefficient
K <sub>ow</sub>	octanol-water partition coefficient
LOAEL	lowest observable adverse effect level
MATC	maximum acceptable toxicant concentration
MDL	method detection limit
MoA	mode of action
MoD	method of detection
NOAEL	no observable adverse effect level
PAH	polycyclic aromatic hydrocarbon
PBDE	polybrominated diphenyl ether
PCB	polychlorinated biphenyl
POD	point of departure
POP	persistent organic pollutant



QSAR	quantitative structure-activity relationship
SeQG <sub>mm</sub>	sediment quality guideline for the protection of marine mammals
SLEB	St. Lawrence Estuary Beluga
SRKW	Southern Resident Killer Whale
TMF	trophic magnification factor
TRV	toxicity reference value
UF	uncertainty factor
US EPA	United States Environmental Protection Agency
WoE	weight of evidence
WQG <sub>mm</sub>	water quality guideline for the protection of marine mammals
ww	wet weight

## Abstract

McTavish, K., Alava, J.J., Brown, T., Crossland, M., Dangerfield, N., Hickie, B., Ross, P.S., and Tillmanns, A. 2024. A Framework for the derivation of environmental quality guidelines that protect apex marine mammals from persistent organic pollutants (POPs). *Can. Tech. Rep. Fish. Aquat. Sci.* 3582: viii + 29p.

Marine mammals are generally long-lived, and often sit atop marine food webs, rendering them vulnerable to high levels of organic contaminants deemed to be persistent, bioaccumulative and toxic (PBT). In Canada, Southern Resident killer whales (*Orcinus orca*) and St Lawrence estuary beluga whales (*Delphinapterus leucas*) are among the world's most contaminated marine mammals. In both cases, high levels of PBT compounds have been cited as conservation threats, with populations listed as Endangered under the Species at Risk Act (COSEWIC 2018, DFO 2018). The lack of Environmental Quality Guidelines (EQGs) for the protection of long-lived, high trophic level species like these illustrates a significant gap in considering the important ecological process that leads to the heavy contamination of such species, namely biomagnification. Herein, we describe a framework to develop such guidelines for water, sediments, and marine mammal prey. In this framework, available marine mammal data are combined with rodent data generated for human health assessments to support a weight of evidence approach to guideline development. Ecological modelling is then used to calculate a cohesive set of EQGs for the protection of apex marine mammals from organic PBTs. We suggest that this draft framework serve as a basis for an operational protocol at the Canadian Council of Ministers of the Environment (CCME) and other agencies.

## Résumé

McTavish, K., Alava, J.J., Brown, T., Crossland, M., Dangerfield, N., Hickie, B., Ross, P.S., and Tillmanns, A. 2024. A Framework for the derivation of environmental quality guidelines that protect apex marine mammals from persistent organic pollutants (POPs). *Can. Tech. Rep. Fish. Aquat. Sci.* 3582: viii + 29p.

Les mammifères marins ont généralement une longue durée de vie et se retrouvent souvent au sommet des réseaux trophiques marins, ce qui les rend vulnérables à des niveaux élevés de contaminants organiques considérés comme étant persistants, bioaccumulables et toxiques (PBT). Au Canada, les orques résidentes du Sud (*Orcinus orca*) et les bélugas de l'estuaire du Saint-Laurent (*Delphinapterus leucas*) comptent parmi les mammifères marins les plus contaminés au monde. Dans les deux cas, les niveaux élevés de composés PBT ont été cités comme des menaces pour la conservation, avec des populations répertoriées comme étant en voie de disparition en vertu de la Loi sur les espèces en péril (COSEPAC 2018, MPO 2018). L'absence de Recommandations pour la qualité de l'environnement (RQE) pour la protection des espèces à longue durée de vie et à haut niveau trophique comme celles-ci illustre une lacune importante dans la prise en compte de l'importance du processus écologique qui mène à la forte contamination de ces espèces, à savoir la bioamplification. Ci-contre, nous décrivons un cadre permettant d'élaborer de telles recommandations pour l'eau, les sédiments et les proies des mammifères marins. Dans ce cadre, les données disponibles sur les mammifères marins sont combinées avec les données sur les rongeurs, générées pour les évaluations de la santé humaine afin de soutenir une approche fondée sur le poids de la preuve pour l'élaboration des recommandations. La modélisation écologique est ensuite utilisée pour calculer un ensemble cohérent de RQE pour la protection des mammifères marins apex contre les PBT organiques. Nous suggérons que ce projet de cadre sert comme base à un protocole opérationnel au Conseil canadien des ministres de l'environnement (CCME) et à d'autres agences.

# 1. General Overview

## 1.1. Introduction

This document describes a framework to inform the derivation of consistent and scientifically defensible environmental quality guidelines (EQGs) for the protection of apex marine mammals from organic contaminants deemed to be persistent, bioaccumulative and toxic (PBTs). An apex predator is a species at the top of the food chain or food web with no natural predators in their environment. Persistent, bioaccumulative and toxic contaminants bioaccumulate over time in biota, and increase with each trophic level in aquatic food webs. These contaminants biomagnify to levels in some marine mammals that can elicit harm through toxicity to endocrine, immune systems, and reproductive systems (Mos et al. 2010; Ross et al. 1996a; Brown et al. 2014; Desforges et al. 2016; Fair and Houde 2023). A weight of evidence has implicated PBTs, notably polychlorinated biphenyls (PCBs), in reduced reproductive output, increased susceptibility to disease and tumours, and developmental anomalies (De Guise et al. 1995; Fair and Houde 2023; Helle et al. 1976; Ross et al. 1996).

The persistence of many PBTs has led to very slow body burden responses and very slow declines in tissue burdens in marine mammals following government regulations or source controls (Ross et al. 2013). In the case of killer whales in the Northeastern Pacific, levels of PCBs are not yet declining, but still at steady state and expected to linger above effects thresholds for much of the 21st Century (Hickie et al. 2007; Alava et al. 2018). Such findings highlight the vulnerability of long-lived predators, but also the need for a new approach that would inform regulatory controls for certain chemicals and/or natural resource tools that protect such species from harm.

Environmental quality guidelines are scientifically-derived numerical concentrations or narrative statements considered to be protective of designated valued ecosystem components in ambient conditions. Guidelines developed following this framework are intended to serve as predicted no effect concentrations for apex marine mammals. EQGs are based solely on the toxicological health effects or hazards of specific substances or groups of substances and may serve several functions including: helping prevent pollution by providing targets for acceptable environmental quality; assisting in the evaluation of the concentrations of chemicals currently found in the environment (i.e., monitoring); serving as input and reference data for pollutant-food web bioaccumulation modelling, and informing risk management decisions. EQGs do not have any direct legal standing unless prescribed by regulation or binding agreements. An exceedance of an EQG does not necessarily imply that unacceptable risks are present, but that the potential for adverse effects may be increased and additional investigation and monitoring may be warranted.

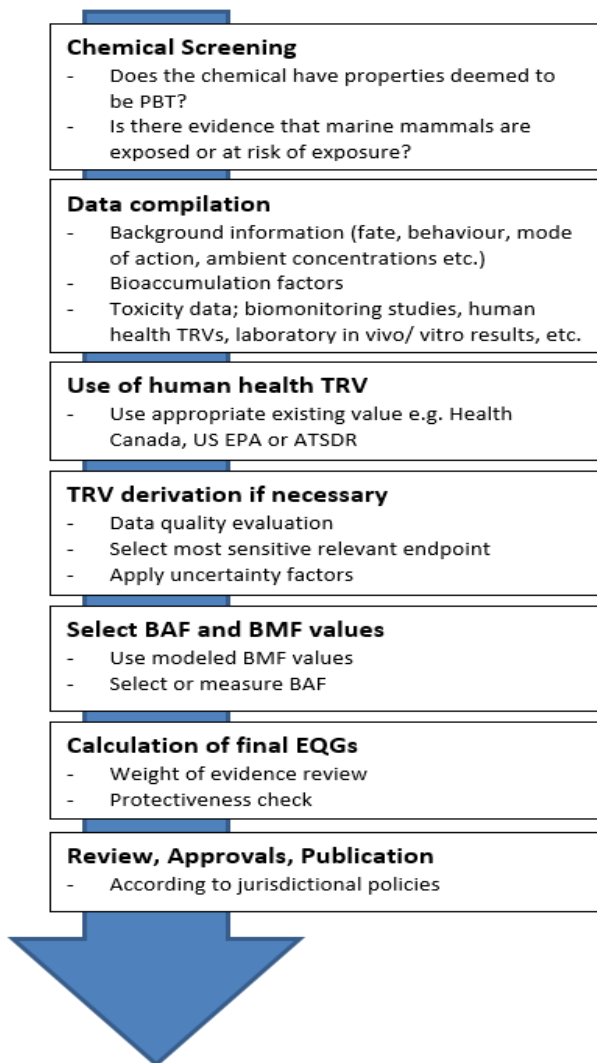
Guidelines are derived by multiple jurisdictions in Canada: nationally through CCME; federally through ECCC; and provincially through individual provincial or territorial environmental ministries. However, none of these jurisdictions have a protocol for deriving EQGs specifically for the protection of marine mammals. To our knowledge, no such EQGs exist in any jurisdiction around the world. The CCME *Protocol for the Derivation of Canadian Sediment Quality Guidelines for the Protection of Aquatic Life* (CCME 1995) was designed to protect benthic invertebrates living in the sediment rather than upper trophic level species and the CCME *Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life* (CCME 2007) does not consider mammals or bioaccumulation in their derivation. Although higher trophic levels are considered in the CCME *Protocol for the Derivation of Canadian Tissue Residue*

*Guidelines for the Protection of Wildlife that Consume Aquatic Biota* (CCME 1998), research over the past decades has demonstrated that the tissue residue guidelines for polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) (CCME 2001) are not protective of apex marine mammals (Hickie et al. 2007; Alava et al. 2012; Alava et al. 2016).

In this document, we describe a framework for the derivation of EQGs for the protection of apex marine mammals from organic PBTs, referred to as “this framework”. The approach outlined in this framework document is based on methodologies used for the CCME (1998) wildlife tissue residue guidelines as well as human health risk assessment methodologies. Available marine mammal data are combined with rodent data generated for human health assessments to support a weight of evidence (WoE) approach to guideline development (Ross 2000). Ecological modelling is then used to calculate EQGs for the protection of apex marine mammals from organic PBTs for three environmental compartments: marine mammal prey tissue, sediment, and water. The general steps of guideline derivation are summarized in Figure 1.

This document provides additional tools to consider when deriving or modifying protocols and EQGs to protect marine mammals by including: 1) more sensitive endpoints applicable to the protection of vulnerable individuals; 2) instructions for use of toxicity reference values (TRVs) derived for humans; 3) biomagnification factors (BMFs) to account for contaminant accumulation in apex marine mammals; and 4) a modelling approach to calculate guideline values in sediment and water as well as prey tissue.

Given the complexity associated with developing EQGs for marine mammals, including those associated with ecological modelling, this framework is offered as a framework for guideline derivation. Elements of this framework may not provide the best methodology for some substances. In these cases, it is suggested to include as many of the framework’s elements as possible in guideline derivation and document these in a clear and transparent manner.



**Figure 1.** General steps for the derivation of environmental quality guidelines for the protection of apex marine mammals from organic contaminants that are persistent, bioaccumulative and toxic.

Notes: TRV = Toxicity Reference Value; US EPA = United States Environmental Protection Agency; ATSDR = Agency for Toxic Substances and Disease Registry; BAF= Bioaccumulation Factor; BMF = Biomagnification Factor; EQGs = Environmental Quality Guidelines.

## 1.2. Selection of substances for guideline development

This framework is specifically intended for organic substances that are persistent, bioaccumulative and toxic. Bioaccumulative chemicals typically have a bioconcentration factor (BCF) or bioaccumulation factor (BAF)  $\geq 5,000$  and/or a  $\log K_{ow} \geq 5$ ; and are persistent in the environment (e.g., half-lives in water and sediment of  $\geq 182$  days and  $\geq 365$  days, respectively; Canada 2000; Gobas et al. 2009). The definition of ‘persistent’ and bioaccumulative’ adopted here aligns with those of the Canadian Environmental Protection Act (Canada 2000).

### **1.3. Mixture considerations**

Marine mammals and other aquatic biota are exposed to complex mixtures of contaminants, including many organic PBT compounds. Many organic PBTs co-occur in environmental media and may be found at high levels in apex marine mammals, including anthropogenically manufactured PCBs and PBDEs. Others may originate from natural sources or be altered through processes such as combustion, e.g. PAHs. Individual or population-level harm may occur as a result of a single contaminant class, or from a complex mixture of contaminants found in their tissues or prey. Guideline derivation should provide options to consider the use of Toxic Equivalency units or total concentrations for PBT classes (e.g. sum of 209 PCBs), as opposed to individual chemical constituents within a class (e.g. PCB-153).

## **2. Derivation of a Toxicity Reference Value (TRV) for Marine Mammals**

### **2.1. What is a TRV and how is it derived?**

A TRV is a parameter used to quantitatively assess potential risks to human health that are associated with exposure to a chemical or contaminant of concern (Health Canada, 2021). TRVs are published by various national and international agencies to characterize substance toxicity. They can be derived by dividing the point of departure (POD), which is the point in a toxicological dose-response data set that generally corresponds to an estimated low or no effect level, by an uncertainty factor (UF). Uncertainty factors, also known as safety factors or assessment factors, are numerical factors applied to the lowest value from an empirical toxicological dataset for a given substance to account for various uncertainties (Okonski et al. 2021).

Dose response data for marine mammals are rarely available given the ethical, legal, and logistical constraints required to obtain them. Therefore, human health TRVs, which are extrapolated from laboratory animal datasets (e.g., rats, mice, mink) (CCME 1998; US EPA 2014), should be used as a starting point for selecting a POD. Interspecies extrapolation is a process frequently used in human health risk assessment. Ross (2000) and Ross and Birnbaum (2003) highlighted the need for a weight of evidence approach in marine mammals, whereby, extrapolation of data from non-marine mammalian species to marine mammals is appropriate owing to: 1) the similarities in physiological systems and mechanisms of toxicity among mammals; 2) the lack of controlled studies to determine effects thresholds for marine mammals; and 3) similar protection goals (protection of the individual) for humans and marine mammals. Thus, like human risk assessment, it is reasonable to use the most conservative toxicity thresholds among available mammalian studies when deriving TRVs for apex marine mammals.

If there is, however, evidence to suggest that an alternate endpoint is preferred given the physiological, behavioural, ecological, and genetic or interspecies differences between marine mammals and humans, then an alternate POD may be selected from the prepared database.

### **2.2. Selection of a point of departure (POD)**

Two approaches are available for selecting a POD. The first, and most preferred approach, is to use an existing POD from a human health TRV. If a human health TRV and corresponding POD are not available or deemed inappropriate, a POD can be determined from a literature review.

### **2.2.1. Selection of an existing point of departure (POD)**

If available, human health TRVs can be used as a starting point for selecting a POD and associated uncertainty factors for calculating a TRV for marine mammals (Figure 1). Based on a toxicological dose-response data set, a POD is identified as either a no- or low-effect level. Multiple endpoints may be present in a toxicological dataset (e.g., a benchmark dose lower confidence limit (BMDL)<sup>1</sup>, a no observed adverse effect level (NOAEL), a lowest observed adverse effect level (LOAEL), or a maximum acceptable toxicant concentration (MATC)) and the selected POD is generally the lowest value among these four endpoints. Human health TRVs<sup>2</sup> should be compiled from various health agencies, including, but not limited to, Health Canada, the US EPA, California EPA, the World Health Organization, the Agency for Toxic Substances and Disease Registry (ATSDR), the European Food Safety Authority (EFSA), and the International Programme on Chemical Safety (IPCS). If multiple human health TRVs are available, then scientific judgement should be used to select the most appropriate one.

### **2.2.2. Determination of a POD from laboratory dose-response data**

If a human health TRV and its corresponding POD is unavailable or deemed inappropriate, a POD may be derived from the literature (Figure 1). This will involve collating and reviewing dose-response toxicity data on surrogate mammals using the criteria for data quality described in Appendix A. Once a toxicity database has been compiled, a POD is selected which is generally the most sensitive endpoint. Effects not previously noted in marine mammal studies may be available in laboratory studies, however given the similarities in mechanisms of toxicity across mammals, these endpoints should not be discounted without justification. The selection of the final POD should be done with the protection goal in mind, i.e., to be protective of individual marine mammals.

### **2.2.3. Marine mammal biomonitoring studies**

Marine mammal contaminant data, biomarker studies and meta-analyses that identify tissue residue concentrations and the related physiological endpoints should be summarized. Although the correlation in biomarker studies cannot be used to infer causality given the potential effects of other factors, including exposure to other chemicals (chemical mixtures), several studies systematically collated together can be used in a WoE approach to support the calculated EQGs.

## **2.3. Selection of uncertainty factors**

The UF is used to account for sources of uncertainty that cannot be estimated from the data set such as intraspecies variability including sensitive sub-populations, interspecies variability including differences in toxicodynamics and toxicokinetics, and data quality and quantity. Maximum uncertainty factors for each category are typically set at 10 though lower numbers are commonly used and applied in a multiplicative manner (Stedeford et al. 2007). Toxicology datasets involving well studied chemicals, marine mammals, and sensitive endpoints may rely on fewer or no UFs. Scientific judgement should be used to select an appropriate uncertainty factor and the rationale must be documented. If more than one UF is needed, selection of their values should be assessed collectively rather than in isolation from the other(s).

---

<sup>1</sup> The benchmark dose (BMD, or its lower confidence limit, BMDL) is a dose that produces a predetermined change in the response rate of an adverse effect (e.g., 1%, 5% or 10% of response compared to control, depending on the severity of the endpoint) and is obtained by fitting dose-response data with mathematical models.

<sup>2</sup> Terminology may vary depending on the agency (e.g., tolerable daily intake (TDI), reference dose (RfD), minimal risk level (MRL)).

### 2.3.1. Intraspecies variability

To some degree the biomagnification factor (BMF) will account for the intra-species uncertainty due to different life stages as all life stages are considered in the Individual Based (IB) model and the most sensitive life stage is selected for the BMF (see Section 3.2). However, if evidence suggests an additional UF is warranted the value should not exceed 10.

### 2.3.2. Interspecies variability

While allometric scaling of acute toxicity data may be warranted to account for interspecific differences, there is no evidence to support it for extrapolation of chronic toxicity data (Sample & Arenal 1999). Its use has therefore been discouraged for extrapolating chronic endpoints across species (Allard et al. 2010; Canada 2013). Interspecies scaling is done by using the food intake to body weight ratio. If adequate scientific rationale exists to include a further UF for inter-species extrapolation then it should not exceed 10.

### 2.3.3. Data quality and quantity

Most agencies recommend the use of an UF to account for deficiencies in the toxicological data set. Given that the original assessor will have the best understanding of the data set, the original UF for data deficiency should be retained if a POD from a human health TRV is used. If a new database is collated, the criteria in Appendix A should be used to assess the UF selection for toxicity database deficiencies.

## 2.4. Calculation of the marine mammal TRV

The selected POD, which is commonly reported as an oral dosage in food, must be adjusted to a daily intake rate by including the body weight (bw in kg) and daily food ingestion (g per day) of the test animal (Equation 1).

$$\text{Equation 1. } POD_{di} = \frac{\left[ \left( \frac{\text{mg chemical}}{\text{kg food}} \right) \times \left( \frac{\text{g food}}{\text{d}} \right) \times \frac{1\text{kg}}{1000\text{g}} \right]}{\text{kg bw}}$$

where:

$POD_{di}$  = POD converted to daily intake in  $\text{mg} \cdot \text{kg}^{-1}$  bw per day

POD = selected NOEL/BMDL/other endpoint reported as  $\text{mg chemical} \cdot \text{kg food}^{-1}$

bw = body weight in kg

d = day

Body weights and daily food ingestion, on a wet weight basis, should be used from the toxicity study from which the daily oral dose is reported. If these values are not available from the study, they may be obtained from the literature (e.g., Banfield 1974; Dunning 1993; NIOSH 1993). [1]

The final TRV is then calculated as:

$$\text{Equation 2. } TRV = \frac{POD}{UF_1 \times UF_2 \times \dots \times UF_X}$$

where:



TRV = tolerable daily intake ( $\text{mg}\cdot\text{kg}^{-1}$  bw per day)

POD = selected NOEL/BMDL/other endpoint adjusted to a daily intake rate in Eq 1 and reported in  $\text{mg}\cdot\text{kg}^{-1}$  bw per day

UF = product of the uncertainty factors

## 2.5. Consideration of carcinogenic effects

Marine mammals exposed to carcinogenic pollutants are at risk of developing cancer over their lifetime (Newman and Smith 2006; Gulland et al. 2020; Randhawa et al. 2015). The prevalence of cancer in marine mammals chronically exposed to POPs has been reported for free-ranging populations (e.g., SRKW and SLE beluga) inhabiting highly contaminated marine regions in the Northeastern Pacific Ocean and St. Lawrence Estuary (Gulland et al. 2020; Randhawa et al. 2015; Raverty et al. 2020). As this framework is concerned with protecting individual marine mammals rather than populations, it is important to consider the carcinogenic effects of the substance. As mentioned previously (Section 2.1), TRVs for non-cancer effects are determined based on the threshold below which no adverse effects are expected. In cases where sufficient data are available to demonstrate the occurrence of a threshold for cancer, the same procedure (POD divided by a global UF) can be used to derive a TRV for cancer. Otherwise (by default), it is assumed that any level of exposure to a carcinogenic substance is associated with a risk (probability) of developing cancer. The corresponding TRV refers to a cancer slope factor ( $\text{CSF}^3$ , expressed in  $(\text{mg}\cdot\text{kg}^{-1}$  bw per day) $^{-1}$ ), which can be converted<sup>4</sup> into a risk specific dose ( $\text{RSD}^5$ , expressed in  $\text{mg}\cdot\text{kg}^{-1}$  bw per day), as a dose corresponding to a given incremental risk. In the context of guidelines derivation, the incremental risk is directly related to the protection objective (i.e., the incremental risk associated with the guideline shall be deemed negligible or acceptable). For instance, in its guidance for federal contaminated sites, Health Canada (2021) considers that an incremental risk of  $10^{-5}$  (one in 100,000) is essentially negligible for humans and in the United States, an incremental risk of  $10^{-6}$  (one in 1,000,000) is retained as a Regional Screening Value for potentially carcinogenic chemicals (USEPA)<sup>6</sup>. To put these incremental risk values in perspective, the Canadian Cancer Society estimates that 4 in 10 (risk of 0.4) Canadians are expected to develop cancer during their lifetime<sup>7</sup>.

---

<sup>3</sup> The CSF is a measurement of risk. It corresponds to the risk of developing cancer associated to a lifetime average exposure dose of  $1 \text{ mg}\cdot\text{kg}^{-1}$  bw per day (e.g., a CSF of  $0.2 \text{ (mg}\cdot\text{kg}^{-1} \text{ bw per day)}^{-1}$ ) means that lifetime average exposure to  $1 \text{ mg}\cdot\text{kg}^{-1}$  bw per day may result in the development of cancer in 1 out of 5 individuals (probability of 0.2, or 20%) exposed under these conditions.

<sup>4</sup>  $\text{RSD} = \text{CSF} \cdot \text{Risk}$

<sup>5</sup> The RSD is the dose associated with a given risk (probability) to develop cancer. For instance, a dose associated to a risk of  $10^{-5}$  (i.e., a  $10^{-5}$  RSD) of  $0.00005 \text{ mg}\cdot\text{kg}^{-1}$  bw per day means that 1 out of 100,000 individuals (risk/probability of  $10^{-5}$ , i.e., 0.00001 or 0.001%) exposed over their lifetime to this average dose may develop cancer due to this substance.

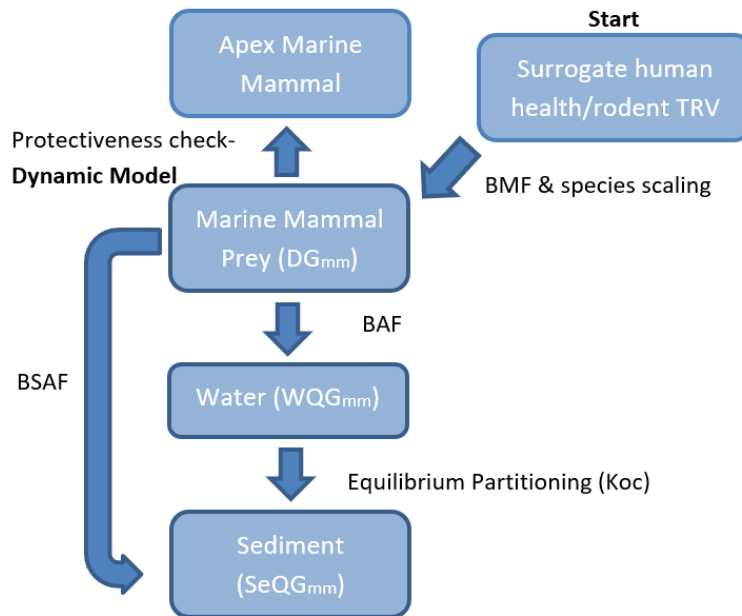
<sup>6</sup> Regional Screening Levels (RSLs) for Chemical Contaminants  
<https://www.epa.gov/risk/regional-screening-levels-rsls>

<sup>7</sup> <https://cancer.ca/en/research/cancer-statistics/cancer-statistics-at-a-glance> (site accessed March 2023)

### 3. Estimating concentrations in other environmental media

#### 3.1. Overview

Having established the TRV, empirical data and/or toxicokinetics/food web bioaccumulation models can be used to relate the TRV to the associated concentrations in prey tissue, water, and sediment. Protective prey tissue concentrations are derived by dividing the TRV by a biomagnification factor (BMF) which accounts for the biomagnification of the chemical in the marine mammal. Water concentrations are calculated by dividing the concentration in the biota or prey tissue by a bioaccumulation factor (BAF) and sediment guidelines are derived by dividing the concentration in biota or the prey tissue by a biota-sediment accumulation factor (BSAF) or by modelling the concentration in water and sediment using the chemical properties of the substance (e.g., the fugacity ratio or equilibrium partitioning method). This suite of bioaccumulation metric factors (i.e., BMF, BAF, BSAF) can be derived using field-based and/or food web modelling approaches, however, the uncertainty associated with calculating the guidelines increases when moving away from the TRV. Thus, the uncertainty associated with the sediment and water guidelines will be greater than the tissue diet guideline (see Figure 2).



**Figure 2. Pathways for the derivation of environmental quality guidelines (EQGs) for prey tissue, water, and sediment starting with a surrogate toxicity reference value (TRV).** BMF = biomagnification factor, BAF = bioaccumulation factor, K<sub>oc</sub> = organic carbon-water partition coefficient, BSAF = biota-sediment accumulation factor.

#### 3.2. Biomagnification factor (Marine mammal:prey)

A biomagnification factor (BMF) is the ratio of the chemical concentration in the tissue of a predator to the chemical concentration in the tissue of the prey at the next lowest trophic level (US EPA 2000; Gobas et

al. 2009). The ratio is unitless. For non-ionic chemicals and specific ionic chemicals with high  $K_{ow}$  values, the concentrations should be lipid-normalized.<sup>8</sup>

BMFs are used to estimate the prey tissue concentration that will be protective of marine mammals. The BMF estimates the concentration in marine mammal tissue that will occur after generations of exposure to the contaminant. In marine mammals the body burden of contaminants accumulates over a lifetime of exposure and calves are exposed to contaminants by way of placental and lactational transfer (Barrett et al. 2021; Desforges et al. 2012; Brown et al. 2016; Lee et al. 2023). Although laboratory feeding studies selected as the POD are typically chronic exposures, these are often less than one year and do not account for the long lifespans of marine mammals nor maternal transfer exposures.

BMFs can be estimated from ecological models or field data and these can be used together as modelled BMFs are often compared to field data for validation. If field-derived BMFs are available, they can be considered in a WoE approach. Field-derived BMFs, based on empirical tissue samples collected from predator and prey, can provide valuable estimates for guideline derivation. However, calculating field-derived BMFs have several uncertainties and limitations, including high cost, time, legal restrictions, and ethical implications when working with threatened and endangered species. Due to sampling restrictions, available data are limited to dart-biopsy (blubber tissue) sampling from free-ranging (wild) marine mammals, if official authorized licence allows, or/and tissue samples opportunistically collected from stranded animals or from subsistence harvests by indigenous communities, and may not necessarily represent all life stages or health conditions present in the population.

For this framework, it is recommended to use BMFs calculated using the individual-based (IB) model developed by Hickie and others (Hickie et al. 2000; 2005; 2007; 2013). A major advantage of this model is that it does not rely on ecosystem-specific input values, such as the contaminant concentration in fish, to calculate a BMF for a specific species and substance. This allows the output of the models to be applied to a wide range of contaminants without prior knowledge of concentrations in ecosystem compartments. The IB model has been parameterized for three apex marine mammal species in Canada: beluga whale (Hickie et al. 2000), killer whale (Hickie et al. 2007), and ringed seal (Hickie et al. 2005) which represent, respectively, the Atlantic, Pacific, and Arctic oceans in Canada.

The IB model reconstructs temporal trends in marine mammals by considering the toxicokinetics of the marine mammal (e.g., uptake, distribution, elimination) and life history characteristics and calculates the tissue concentration in the marine mammal at specific time intervals over its lifespan including the contaminant burden of offspring due to placenta transfer and nursing. The model loops upon itself until the contaminant concentrations reach steady state. In this way the model presents a multi-generation scenario (Hickie et al. 2007). The model produces multiple predicted BMFs for each sub-population (i.e., time-dependent for calves or pups, juveniles, adult females, and adult males), for the three species. The mean calf/pup value was selected to be protective of each respective species.

For this framework the overall mean calf/pup BMF for killer whales, belugas whales and Arctic ringed seals was chosen as a surrogate for marine mammal BMF (Table 1). These marine species were chosen as a surrogate for the other species of apex marine mammals representative of the three oceans bordering Canada applying the most recent IB model bioaccumulation model that includes  $K_{ow}$ -dependent terms. When considering life history traits, the selection of the killer whale is a suitable surrogate given that orca whales have the longest birth intervals (five years for killer whales vs three years for beluga whales and

---

<sup>8</sup> Note that at the time of publication, lipid-normalized BMFs cannot be applied to per- and polyfluoroalkyl substances (PFAS) as these ionic substances mainly bond to the protein content or fraction of animal tissues.

one year for ringed seals) which means orca females have the longest period to accumulate a contaminant burden between births which is then transferred to the orca calf via maternal transfer. Further, seals are known to have a greater capacity to biotransform organic chemicals such as PCBs which leads them to having lower BMFs.

$K_{ow}$ -specific equations were estimated from field data for PCBs for uptake efficiency from prey (McLachlan 1994) and partitioning to the milk (Cadieux et al. 2016) and field data for PCBs and PBDEs were used to estimate  $K_{ow}$  - specific equations for partitioning to the fetus (Desforges et al. 2012). These biological processes (i.e., digestion, gestation, and lactation) are not the result of simple equilibrium partitioning and require multiple steps which occur in both aqueous and lipid states and therefore, contrary to the positive relationship between  $K_{ow}$  and concentration in lipids, there is an inverse relationship between  $K_{ow}$  and uptake efficiency, partitioning to fetus, and partitioning to the milk (McLachlan 1994; Desforges et al. 2012; Cadieux et al. 2016). These relationships have not been tested for other POPs but, aside from PFAS that accumulates in proteins, it is anticipated that they will be similar across other lipophilic contaminants (Hickie pers. com. 2023).

**Table 1. Mean calf/pups BMFs (wet weight- based) for a range of KOW values.**

<b>Log K<sub>OW</sub></b>	<b>Arctic Ringed Seals (<i>Pusa hispida</i>)</b>	<b>Beluga Whales (<i>Delphinapterus leucas</i>)</b>	<b>Killer Whales (<i>Orcinus orca</i>)</b>
5	271	719	909
5.2	271	722	910
5.4	271	722	910
5.6	275	718	903
5.8	272	711	894
6	265	699	879
6.2	255	680	857
6.4	241	654	825
6.6	224	617	779
6.8	201	569	714
7	179	504	630
7.2	149	425	524
7.4	117	334	404
7.6	85	242	285
7.8	55	159	181
8.0	33	95	104
8.2	17	52	55
8.4	8.5	27	28

Notes: BMFs were estimated using the IB model (Hickie et al., 2000; 2005; 2007; 2013) that was updated to include K<sub>OW</sub> - specific equations for contaminant assimilation from prey and contaminant partitioning to milk and fetus. Input values for the IB model are given in Appendix B. Note that the input values include the assumption of negligible rates of biotransformation.

### **3.3. Bioaccumulation factor (prey:water)**

The bioaccumulation factor (BAF) is the ratio of contaminant concentration in the tissue of an organism (e.g., aquatic biota or the prey of marine mammal) to the contaminant concentration in water and/or aquatic

environment (Gobas et al. 2009) expressed in units of L·kg tissue on a wet, dry or lipid weight basis. The BAF approach is predicated on the following assumptions: both the organism and its food are exposed to the same concentration of contaminant in the water and the exposure concentration does not change substantially over time (i.e. steady state). Depending on the type of chemical and its properties, BAFs can be measured or predicted using one or more of the following methods:

- Measured BAFs derived from data obtained from a field study (i.e., field-measured BAFs, or Trophic Magnification Factors (TMFs))
- BAFs derived from laboratory measurements
- Predicted BAFs from models (e.g., AQUAWEB)

Field studies should be reviewed to ensure that the substance under investigation has reached steady state in the aquatic ecosystem or that water concentrations were averaged over a duration that is comparable to the time required for the substance to reach steady state (US EPA, 2000). Further, the study should be examined to ensure the aqueous concentrations were measured accurately, especially in older studies where cross contamination may have artificially increased BAF values (Borga et al. 2005).

The selection of a BAF involves collating literature values and selecting a value that is representative of each of the ocean regions where differences are noted. The final value selected will be the most conservative of the values to ensure the final EQGs are protective for all apex marine mammal predators.

Trophic magnification factors (TMFs) represent the “diet-weighted average BMF of chemical residues across food webs” (Burkhard et al. 2013). They are typically derived from the anti-log of the regression slope of the log of lipid-normalized chemical concentrations in organisms versus a spanning range of species trophic levels, which are determined from stable isotope ( $\delta^{15}\text{N}$ ) data (Borga et al. 2012). A recent review by Kidd et al. (2019) provides practical guidance on TMF use and selection for EQG derivation, including considering the following criteria when determining the reliability of TMF estimates:

- A minimum of two or three trophic levels.
- Measured contaminant concentrations in whole organisms.
- Lipid-normalizing concentrations of organic contaminants.
- Inclusion of several lower trophic level invertebrate taxa (e.g., zooplankton, benthic invertebrates).
- Balanced number of samples across trophic levels.
- Adequate and balanced samples for each trophic level.
- Inclusion of organisms known to be linked by diet through the food web.
- Measured contaminant concentrations are above detection limits in all samples.
- All organisms sampled are collected within a similar time frame (e.g., one season).
- Caution for potential upward bias of TMF estimates if homeotherms and air-breathing organisms (i.e., birds and mammals) are included in the data set.

If using TMFs, the final step is to estimate the BAF of the contaminant from water to plankton. Chemical-specific information for the BAF (either laboratory or field measurements) is preferable to assuming equilibrium but if no chemical-specific information is available then the equilibrium approach is acceptable. The final BAF for prey:water will then be the product of the  $\text{TMF}_{\text{prey:plankton}}$  and the  $\text{BAF}_{\text{plankton:water}}$ :

$$\text{Equation 3: } \text{BAF}_{\text{prey:water}} = [\text{TMF}_{\text{prey:plankton}}] \times [\text{BAF}_{\text{plankton:water}}]$$

### 3.4. Estimating sediment concentrations

Sediment concentrations can be estimated in two ways: either using the equilibrium partitioning approach, which estimates the bulk sediment concentration from the water concentration based on the organic carbon-normalized soil adsorption coefficient ( $K_{OC}$ ) (DiToro et al. 1991), or by using biota-sediment accumulation factor (BSAF) which is the ratio of the contaminant concentration in the tissue (in a wet weight basis or lipid normalized) of an organism to the contaminant concentration in the sediment (in a dry weight basis or total organic carbon (TOC) content-normalized) (Alava et al. 2012; Arblaster et al. 2015). Each of these methods are described below.

The equilibrium partitioning approach is applicable to non-ionic organic chemicals and assumes that the concentration between the organic carbon content of the sediment and the sediment pore water are in equilibrium (Di Toro et al. 1991). If the concentration in the water is known, an estimate of the concentration in sediment organic carbon can be calculated using the organic carbon-water partitioning coefficient and the percent organic carbon in the sediment.

Alternatively, a BSAF can be used to back calculate the concentration in the sediment given a known concentration in a biota. A BSAF can be measured either in the laboratory or in the field. Field measurements done on migratory or wide-ranging species can add challenges as contaminants can be accumulated from other locations. BSAFs are most applicable to site-specific assessments using sessile organisms. However, this bioaccumulation metric has been applied to marine mammals (e.g., southern resident killer whales) and their Critical Habitat (e.g., Alava et al. 2012; Arblaster et al. 2015; Lachmuth et al. 2010), and has the advantage of integrating biological processes not considered in the equilibrium approach. Like BAFs, a review is necessary to ensure the aquatic ecosystem is at equilibrium and that the appropriate analytical methods were used to prevent cross-contamination.

The BSAF is calculated as:

Equation 4. 
$$BSAF = \frac{C_t}{C_s}$$

Where:

BSAF = the biota-sediment accumulation factor

$C_t$  = concentration of chemical in the biota species ( $\text{g}\cdot\text{kg}^{-1}$  wet weight)

$C_s$  = concentration of contaminant in the sediment ( $\text{g}\cdot\text{kg}^{-1}$  dry weight) (Alava et al. 2012; Arblaster et al. 2015).

The BSAF can also be normalized in terms of lipid content and TOC fraction in the sediment, and the resulting units for  $C_t$  and  $C_s$  become  $\text{g}\cdot\text{kg}^{-1}$  lipid in biota and  $\text{g}\cdot\text{kg}^{-1}$  organic carbon in sediment, respectively (Alava et al. 2012; Arblaster et al. 2015).

Whenever possible, BSAFs should be used over the equilibrium approach. If using the BSAF approach, values should be collated for the three oceans bordering Canada. If BSAFs are not available for all three oceans and uncertainty exists as to its application to the remaining ocean(s) then the lower value of the two approaches (equilibrium partitioning vs BSAF) should be chosen.

### 3.5. Criteria for other models

It is possible that a model other than the IB model or AQUAWEB applied, respectively, for BMF and BAF predictions may be required due to properties of the contaminant. In these situations, the model selected must meet the following criteria:

- The model is well established and cited in the peer-reviewed literature.
- Code and equations are transparent and publicly available.
- Chemical/physical properties of the chemical are explicitly included in the model or available from a reputable source including (without being limited to):
  - $K_{ow}$ ;
  - Octanol-air partition coefficient ( $K_{OA}$ ); and
  - Sediment:water concentration ratio ( $C_s:C_w$ ).
- Site-specific environmental parameters of the ecosystem are assessed including:
  - mean water temperature;
  - concentration of particulate organic carbon in the water;
  - concentration of dissolved organic carbon in the water;
  - concentration of suspended solids in the water;
  - organic carbon content of the sediment (total organic carbon [TOC] content);
  - chemical concentration in the water; and
  - chemical concentration in the sediment (water temperature, salinity, pH).
- Sufficient quantity and quality of contaminant data for abiotic compartments (sediment and water).
- Reliable understanding of the composition and structure of the food web and dietary preferences of organisms.
- Site-specific biological properties and life history characteristics of biota are included (organism lipid content, dietary uptake rate, growth rate, organism wet weight or volume, diet % or organism feeding preferences).
- Available empirical data for biota (upper trophic level or/and apex predators) to test the performance of the model (model bias).

Food web bioaccumulation models meeting these modelling criteria are available and have been developed and applied for marine regions and ecosystems of the Northeastern Pacific, including British Columbia (Canada) and San Francisco Bay, California, US (see Supporting or Supplementary Information datasets published in Alava et al. 2012; Alava et al. 2016; Gobas and Arnot 2010).

## 4. Calculation of the final environmental quality guidelines ( $EQG_{mm}$ )

### 4.1. Diet guideline ( $DG_{mm}$ )

The dietary guideline for the tissue of marine mammal prey is an expected tissue residue concentration to be protective of apex marine mammals. When using field data or species specific models for the species deemed to be most sensitive, resulting BMFs may be used directly to determine the dietary guideline. The FI:BW ratio for the species specific BMF is used to convert the daily dietary dose to a diet tissue concentration CCME (1998) (Equation 5). Appendix B, Table 3 provides a list of food intake to body weight ratios (FI:BW) for the mammalian species from Table 1.



The  $DG_{mm}$  is calculated using the following equation:

$$\text{Equation 5. } DG_{mm} = \left( \frac{TRV}{(FI:BW) \times BMF} \right)$$

where:

$DG_{mm}$  = the diet guideline protective of marine mammals ( $\text{mg} \cdot \text{kg}^{-1}$  wet weight diet)

TRV = toxicity reference value established in section 2 ( $\text{mg} \cdot \text{kg}^{-1}$  bw per day)

FI:BW = food intake (kg wet weight diet per day) to body weight (kg bw) for the same species as the selected BMF.

BMF = biomagnification factor established in section 3.2 (unitless)

## 4.2. Water quality guideline ( $WQG_{mm}$ )

The water quality guideline is calculated using the following equation:

$$\text{Equation 6. } WQG_{mm} = \frac{DG_{mm}}{BAF_{\text{prey:water}}}$$

where:

$WQG_{mm}$  = water quality guideline protective of marine mammals ( $\text{mg} \cdot \text{L}^{-1}$ )

$DG_{mm}$  = diet guideline established in section 4.1. ( $\text{mg} \cdot \text{kg}^{-1}$  wet weight)

$BAF_{\text{prey:water}}$  = bioaccumulation factor established in section 3.3 ( $\text{L} \cdot \text{kg}^{-1}$  ww)

## 4.3. Sediment quality guideline ( $SeQG_{mm}$ )

The sediment quality guideline can be calculated using the equilibrium partitioning approach (DiToro et al. 1991) or using the BSAF (Alava et al. 2012; Arblaster et al. 2015). See section 3.4 for a discussion of these approaches.

Sediment concentrations can be calculated using the equilibrium partitioning approach using the following equation:

$$\text{Equation 7. } SeQG_{mm} = WQG_{mm} \times K_{oc} \times \%OC$$

where:

$SeQG_{mm}$  = sediment quality guideline protective of marine mammals ( $\text{mg} \cdot \text{kg}^{-1}$  dry weight sediment)

$WQG_{mm}$  = water quality guideline protective of marine mammals ( $\text{mg} \cdot \text{L}^{-1}$ )

$K_{oc}$  = organic carbon-water partition coefficient for the substance ( $\text{L} \cdot \text{kg}^{-1}$ )

% OC = percent organic carbon adjustment (typically to 1% to provide a conservative benchmark for which to compare monitoring data)

Before making comparisons to the  $SeQG_{mm}$ , monitoring data must be normalized to 1% OC to assess whether the guideline value is exceeded.

The following equation can be used to calculate the  $SeQG_{mm}$  using the BSAF (adapted from Alava et al. 2012; Arblaster et al. 2015):

$$\text{Equation 8. } SeQG_{mm} = \frac{DG_{mm}}{BSAF}$$

where:

SeQG<sub>mm</sub> = Sediment quality guideline protective of marine mammals (mg·kg<sup>-1</sup> sediment)

DG<sub>mm</sub> = diet guideline established in section 4.1. (mg·kg<sup>-1</sup> wet weight diet)

BSAF = biota-sediment accumulation factor (kg OC sediment/kg lipid biota or kg dw sediment/ kg ww biota)

#### 4.4. Weight of evidence review

A WoE approach is generally understood as a method for decision-making that involves consideration of multiple sources of information and lines of evidence. A WoE framework has been espoused for marine mammals, where cause-and-effect studies are lacking and extrapolation from other mammals (e.g. lab rodents) offers a resolution to such information gaps (Ross 2000). A WoE approach avoids relying solely on any one piece of information or line of evidence. A WoE approach may be applied at various stages of guideline development. It can be used to evaluate the quality of a single study, to assess similar studies for a particular parameter or endpoint, or to integrate information across multiple lines of evidence to support the choice of the final EQG. If it is not possible to follow the steps outlined in this framework, a WoE review should be completed that outlines all the lines of evidence compiled and considered that lead to the final recommended guideline.

Contaminant data from marine mammals is one line of evidence that can be used to assess the calculated guidelines. Although field studies cannot establish a clear causal effect given the presence of other contaminants and stressors, correlations between marine mammal tissue concentrations and a variety of effects (hormone levels, immunological endpoints and blood chemistry, genetic markers, or population level data such as pregnancy failure, lower birth rate, decreased survivability, and population decrease) together with observations from captive feeding studies do strongly suggest a relationship (e.g., Mos et al. 2010). The BMF values can be used to predict the concentration in blubber if marine mammals are exposed to the chemical concentration equal to the DG<sub>mm</sub>. Ideally, the DG<sub>mm</sub> would predict a biomonitored concentration lower than that found in the marine mammals in which an effect has occurred.

## 5. Conclusion

In conclusion, this document presents a comprehensive framework for the derivation of environmental quality guidelines aimed at protecting apex marine mammals from the harmful effects of persistent, bioaccumulative, and toxic contaminants. The vulnerabilities of these species to PBT contaminants underscores the need for specialized guidelines tailored to protect them. The recommended framework, building upon existing protocols, integrates marine mammal and lab rodent data through a weight of evidence approach, allowing for the calculation of EQGs in marine mammal prey tissue, sediment, and water. This framework provides a novel methodology to jurisdictions in Canada and beyond, where currently no EQG protocol specifically designed for the protection of marine mammals exists. By addressing the existing gap in EQGs for marine mammals, this framework provides a valuable and practical tool for regulators, researchers, and policymakers striving to mitigate the impact of PBTs on apex marine mammals. It is recommended that this framework be incorporated into guideline derivation processes in Canada, such as by the Canadian Council of Ministers of the Environment (CCME) and other agencies, to contribute to more effective protection of apex marine mammals and their ecosystems.

## 6. References

- Alava, J.J., Cisneros-Montemayor, A.M., Sumaila, R., Cheung, W.W.L. 2018. Projected amplification of food web bioaccumulation of MeHg and PCBs under climate change in the Northeastern Pacific. *Scientific Reports* 8:13460. doi:10.1038/s41598-018-31824-5
- Alava, J.J., Ross, P.S., Gobas, F.A.P.C. 2016. Food web bioaccumulation model for resident killer whales from the Northeastern Pacific Ocean as a tool for the derivation of PBDE-Sediment Quality Guidelines. *Arch. Environ. Contam. Toxicol.* 70(1): 155-168. doi: 10.1007/s00244-015-0215-y
- Alava, J. J., Ross, P. S., Lachmuth, C. L., Ford, J. K. B., Hickie, B., Gobas, F. A. P. C. (2012). Habitat-based PCB Environmental Quality Criteria for the Protection of Endangered Killer Whales (*Orcinus orca*). *Environ. Sci. Technol.* 46: 12655–12663.
- Allard, P., Fairbrother, A., Hope, B.K., Hull, R.N., Johnson, M.S., Kapustka, L., Mann, G., McDonald, B., Sample, B.E., 2010. Recommendations for the development and application of wildlife toxicity reference values. *Integr. Environ. Assess. Manag.* 6(1), pp.28-37. doi: 10.1897/IEAM\_2009-010.1
- Arblaster, J., Ikononou, M.G., Gobas, F.A., 2015. Toward ecosystem-based sediment quality guidelines for polychlorinated biphenyls (PCBs). *Integr. Environ. Assess. Manag.* 11(4), pp.689-700.
- Banfield, A.W.F. 1974. *The mammals of Canada*. National Museums of Canada. University of Toronto Press, Toronto.
- Barrett, H., Du, X., Houde, M., Lair, S., Verreault, J., Peng, H. 2021. Suspect and Nontarget Screening Revealed Class-Specific Temporal Trends (2000-2017) of Poly- and Perfluoroalkyl Substances in St. Lawrence Beluga Whales. *Environ. Sci. Technol.* 55: 1659-1671.
- Borgå, K., Fisk, A.T., Hargrave, B., Hoekstra, P.F., Swackhamer, D., Muir, D.C., 2005. Bioaccumulation factors for PCBs revisited. *Environ. Sci. Technol.* 39(12), pp.4523-4532.
- Borgå K, Kidd, K.A., Muir, D.C.G., Berglund, O., Conder, J.M., Gobas, F.A.P.C., Kucklick, J., Malm, O., Powell, D.E. 2012. Trophic magnification factors: Considerations of ecology, ecosystems and study design. *Integr. Environ. Assess. Manag.* 8:64–84.
- Brown, T.M., Ross, P.S., Reimer, K.J., Veldhoen, N., Dangerfield, N.J., Fisk, A.T., Helbing, C.C. 2014. PCB related effects thresholds as derived through gene transcript profiles in locally contaminated ringed seals (*Pusa hispida*) from Labrador, Canada. *Environmental Science and Technology*, 48(21): 12952-61.
- Brown, T.M., Ross, P.S., Reimer, K.J. 2016 Transplacental Transfer of Polychlorinated Biphenyls, Polybrominated Diphenylethers, and Organochlorine Pesticides in Ringed seals (*Pusa hispida*). *Archives of Environmental Contamination and Toxicology* 70: 20-27 DOI 10.1007/s00244-015-0191-2.
- Burkhard LP, Borga° K, Powell DE, Leonards P, Muir DCG, Parkerton TF, Woodburn KB. 2013. Improving the quality and scientific understanding of trophic magnification factors (TMFs). *Environ. Sci. Technol.* 47:1186–1187.
- Cadieux, M.A., Muir, D.C.G., Beland, P., Hickie, B.E. 2016. Lactational Transfer of Polychlorinated-Biphenyls (PCBs) and Other Organochlorines in St. Lawrence Beluga Whales (*Delphinapterus leucas*). *Arch. Environ. Contam. Toxicol.* 70:169-179.
- Canada. 2000. Canadian Environmental Protection Act: Persistence and Bioaccumulation Regulations, P.C. 2000-348, 23 March, 2000, SOR/2000-107, [Canada Gazette, Part II, vol. 134, no. 7, p. 607-612](#). PDF (1975 KB).
- Canada. 2013. Federal Contaminated Sites Action Plan (FCSAP) – ecological risk assessment guidance, module 2 : Selection or development of site-specific toxicity reference values .

CCME (Canadian Council of Ministers of the Environment). 1995. Protocol for the derivation of Canadian sediment quality guidelines for the protection of aquatic life. Available online <http://ceqg-rcqe.ccme.ca/download/en/226/>

CCME (Canadian Council of Ministers of the Environment). 1998. Protocol for the derivation of Canadian tissue residue guidelines for the protection of wildlife that consume aquatic biota. Available online at: <http://ceqg-rcqe.ccme.ca/download/en/290>

CCME (Canadian Council of Ministers of the Environment). 2001. Canadian tissue residue guidelines for the protection of wildlife consumers of aquatic biota: Polychlorinated biphenyls (PCBs). Updated. In: Canadian environmental quality guidelines, 1999, Canadian Council of Ministers of the Environment, Winnipeg. Available online at: <https://ccme.ca/en/res/polychlorinated-biphenyls-pcbs-canadian-tissue-residue-guidelines-for-the-protection-of-wildlife-consumers-of-aquatic-biota-en.pdf>

CCME (Canadian Council of Ministers of the Environment). 2007. A protocol for the derivation of water quality guidelines for the protection of aquatic life 2007. In: Canadian environmental quality guidelines, 1999, Canadian Council of Ministers of the Environment, 1999, Winnipeg.

CCREM (Canadian Council of Resource and Environment Ministers). 1987. Canadian Water Quality Guidelines. Prepared by the Task Force on Water Quality Guidelines. 1484 pp.

COSEWIC. 2018. COSEWIC assessment and status report on the Polar Bear *Ursus maritimus* in Canada. Committee on the Status of Endangered Wildlife in Canada. Ottawa. Xv + 113 pp. (<http://www.registrelep-sararegistry.gc.ca/default.asp?lang=en&n=24F7211B-1> ).

De Guise, S., D Martineau, P Béland, and M Fournier. Possible mechanisms of action of environmental contaminants on St. Lawrence beluga whales (*Delphinapterus leucas*). *Environ. Health. Perspect.* 103,: pp 73 - 77. doi: 10.1289/ehp.95103s473

Desforges, J-P.W., Ross, P.S., Loseto, L.L. 2012. Transplacental transfer of Polychlorinated Biphenyls and Polybrominated Diphenyl Ethers in Arctic Beluga Whales (*Delphinapterus Leucas*). *Environ. Toxicol. Chem.* 31:296-300.

Desforges, J.-P. W., Sonne, C., Levin, M., Siebert, U., De Guise, S., Dietz, R. 2016. Immunotoxic effects of environmental pollutants in marine mammals. *Environ. Int.* 86: 126–139. doi: 10.1016/j.envint.2015.10.007

DFO (Fisheries and Oceans Canada). 2018. Recovery Strategy for the Northern and Southern Resident Killer Whales (*Orcinus orca*) in Canada [Proposed]. Species at Risk Act Recovery Strategy Series, Fisheries & Oceans Canada, Ottawa, x + 84 pp.

Di Toro, D.M., Zarba, C.S., Hansen, D.J., Berry, W.J., Swartz, R.C., Cowan, C.E., Pavlou, S.P., Allen, H.E., Thomas, N.A., Paquin, P.R. 1991. Technical basis for establishing sediment quality criteria for nonionic organic chemicals using equilibrium partitioning. *Environ. Toxicol. Chem.* 10(12): 1541-1583.

Dunning, J.B. 1993. CRC handbook of avian masses. CRC Press, Boca Raton, FL.

Emmerich, C.H. and Harris, C.M., 2019. Minimum information and quality standards for conducting, reporting, and organizing in vitro research. Beshpalov A., Michel M., and Steckler T. Cham: Springer, 257, pp.177-96.

Fair, P.A., and Houde, M. 2023. Chapter 3.2.5 - Environmental endocrine-disrupting chemicals and their effects in marine mammals. In *Environmental Contaminants and Endocrine Health*. Edited by O. Carnevali and G. Hardiman. Elsevier Inc., Academic Press. pp. 283-306. doi: 10.1016/B978-0-12-824464-7.00017-9 .

Gobas, F. A. P. C., Arnot, J. 2010. Food web bioaccumulation model for polychlorinated biphenyls in San Francisco Bay, California, USA . *Environ. Toxicol. Chem.* 29: 1385–1395.

Gobas, F.A.P.C., de Wolf, W., Verbruggen, E., Plotzke, K., Burkhard, L., 2009. Revisiting bioaccumulation criteria for POPs and PBT assessments. *Integr. Environ. Assess. Manag.* 5: 624–637. [https://setac.onlinelibrary.wiley.com/doi/abs/10.1897/IEAM\\_2008-089.1](https://setac.onlinelibrary.wiley.com/doi/abs/10.1897/IEAM_2008-089.1)

Gulland, F., Hall, A.J., Ylitalo, G.M., Colegrove, K.M., Norris, T., Duignan, P.J., Halaska, B., Acevedo Whitehouse, K., Lowenstine, L.J., Deming, A.C., Rowles, T.K., 2020. Persistent contaminants and herpesvirus OthV1 are positively associated with cancer in wild California sea lions (*Zalophus californianus*). *Front. Mar. Sci.* 7:602565. doi :/10.3389/fmars.2020.602565

Health Canada (2021). Federal Contaminated Site Risk Assessment in Canada: Toxicological Reference Values (TRVs), Version 3.0.

Health Canada. 2021. Federal Contaminated Site Risk Assessment in Canada: Guidance on human health preliminary quantitative risk assessment (PQRA), version 3.0.

Helle, E., Olsson, M. and Jensen, S. 1976. DDT and PCB levels and reproduction in ringed seal from the Bothnian Bay. *Ambio* 5: 188–189.

Hickie, B.E., Cadieux, M.A., Riehl, K.N., Gregory, D.B., Alava, J.J., Fair, P.A. 2013. Modeling PCB Bioaccumulation in the Bottlenose Dolphin (*Tursiops truncatus*): Estimating a Dietary Threshold Concentration. *Environ. Sci. Technol.* 2103(47): 12314-12324.

Hickie, B.E., Kingsley, M.C.S., Hodson, P.V., Muir, D.C.G., Béland, P., Mackay, D. 2000. A modelling-based perspective on the past, present, and future polychlorinated biphenyl contamination of the St. Lawrence beluga whale (*Delphinapterus leucas*) population. *Fish. Aquat. Sci.* 57: 101-112.

Hickie, B.E., Muir, D.C.G., Addison, R.F., Hoekstra, P.F. 2005. Development and application of bioaccumulation models to assess persistent organic pollutant temporal trends in Arctic ringed seal (*Phoca hispida*) populations. *Sci. Total. Environ.* 351-352: 413-426.

Hickie, B.E., Ross, P.S., Macdonald, R.W., Ford, J.K.B. 2007. Killer whales (*Orcinus orca*) face protracted health risks associated with lifetime exposure to PCBs. *Environ.Sci.Technol.* 41: 6613-6619.

Kidd, K.A., Burkhard, L.P., Babut, M., Borgå, K., Muir, D.C., Perceval, O., Ruedel, H., Woodburn, K. and Embry, M.R., 2019. Practical advice for selecting or determining trophic magnification factors for application under the European Union Water Framework Directive. *Integr. Environ. Assess. Manag.* 15(2), pp.266-277. Lachmuth, C.L., Alava, J.J., Hickie, B.E., Johannessen, S.C., Macdonald, R.W., Ford, J.K.B., Ellis, G.M., Gobas, F.A.P.C., Ross, P.S. 2010. Ocean Disposal in Resident Killer Whale (*Orcinus orca*) Critical Habitat: Science in Support of Risk Management. DFO Can. Sci. Advis. Sec. Res. Doc. 2010/116. x + 172 p.

Lee, K., Alava, J.J., Cottrell, P., Cottrell, L., Grace, R., Zysk, I., Raverty, S. 2023. Emerging Contaminants and New POPs (PFAS and HBCDD) in Endangered Southern Resident and Bigg's (Transient) Killer Whales (*Orcinus orca*): In Utero Maternal Transfer and Pollution Management Implications. *Environmental Science & Technology*. doi: 10.1021/acs.est.2c04126

McLachlan, M.S. 1994. Model of the fate of hydrophobic contaminants in cows. *Environ Sci Technol.* 28:2407-2414.

Mos, L., Cameron, M., Jeffries, S. J., Koop; B.F., Ross, P.S. 2010. Risk-based analysis of PCB toxicity in harbour seals. *Integr. Environ. Assess. Manag.* 6:631–640.

Myatt, G.J., Ahlberg, E., Akahori, Y., Allen, D., Amberg, A., Anger, L.T., Aptula, A., Auerbach, S., Beilke, L., Bellion, P. Benigni, R., 2018. In silico toxicology protocols. *Regul. Toxicol. Pharmacol.* 96, pp.1-17.

Newman, S.J., Smith, S.A. 2006. Marine Mammal Neoplasia: A Review. *Vet. Pathol.* 43(6):863-880.

NIOSH (National Institute for Occupational Safety and Health). 1993. Registry of toxic effects of chemical substances. 6th ed. Rockville, MD.

Okonski, A.I., MacDonald, D.B., Potter, K. Bonnell, M., 2021. Deriving predicted no-effect concentrations (PNECs) using a novel assessment factor method. *Hum. ecol. risk assess.* 27(6), pp.1613-1635.

- Randhawa, N., Gulland, F., Ylitalo, G.M., DeLong, R., Mazet, J.A., 2015. Sentinel California sea lions provide insight into legacy organochlorine exposure trends and their association with cancer and infectious disease. *One Health* 1: 37-43.
- Raverty, S., St. Leger, J. S., Noren, D. P., Burek Huntington, K. B., Rotstein, D. S., Gulland, F. M. D., Ford, J. K. B., Hanson, M., Lambourn, D. M., Huggins, J., Delaney, M. A., Spaven, L., Rowles, T., Barre, L., Cottrell, P., Ellis, G., Goldstein, T., Terio, K., Duffield, D., Rice, J., Gaydos, J. K. 2020. Pathology Findings and Correlation with Body Condition Index in Stranded Killer Whales (*Orcinus orca*) in the Northeastern Pacific and Hawaii from 2004 to 2013. *PLoS One* 15: e0242505.
- Ross, P.S. 2000. Marine mammals as sentinels in ecological risk assessment. *Hum. ecol. risk assess.* 6: 29-46.
- Ross, P.S. Birnbaum, L.S. 2003. Integrated human and ecological risk assessment: A case study of persistent organic pollutants (POPs) in humans and wildlife. *Hum. ecol. risk assess.* 9(1): 303-324.
- Ross, P., De Swart, R., Addison, R., Van Loveren, H., Vos, J., Osterhaus, A. 1996a. Contaminant-induced immunotoxicity in harbour seals: wildlife at risk? *Toxicology* 112: 157–169. doi: 10.1016/0300-483x(96)03396-3
- Ross, P.S., De Swart, R.L., Addison, R.F., Van Loveren, H., Vos, J.G., and Osterhaus, A.D.M.E. 1996. Contaminant-induced immunotoxicity in harbour seals: wildlife at risk? *Toxicology* 112: 157-169.
- Ross, P.S., Noël, M., Lambourn, D., Dangerfield, N., Calambokidis, J., Jeffries, S. 2013. Declining concentrations of persistent PCBs, PBDEs, PCDFs, and PCNs in harbor seals (*Phoca vitulina*) from the Salish Sea. *Progress in Oceanography* 115: 160-170
- Sample, B., Arenal, C. 1999. Allometric Models for Interspecies Extrapolation of Wildlife Toxicity Data. *Bull. Environ. Contam. Toxicol.* 62, 653–663. doi: 10.1007/s001289900924
- Stedeford, T., Hsu, C. H., Zhao, Q. J., Dourson, M. L., Banasik, M. 2007. The application of non-default uncertainty factors in the US EPA’s Integrated Risk Information System (IRIS). Part I: UF (L), UF (S), and “other uncertainty factors”. *J. Environ. Sci. Health. Part C, Environmental Carcinogenesis & Ecotoxicology Reviews*, 25(3): 245-279. doi: 10.1080/10590500701569430
- US EPA (Environmental Protection Agency) 2000. Methodology for deriving ambient water quality criteria for the protection of human health (2000). U.S. Environmental Protection Agency. Washington, D.C. Final Report October 2000. EPA-822-B-00-004
- US EPA (Environmental Protection Agency) 2002. A Review of the Reference Dose and Reference Concentration Processes. Prepared for the Risk Assessment Forum. U.S. Environmental Protection Agency. Washington, D.C. Final Report December 2002. EPA/630/P-02/002F
- US EPA (Environmental Protection Agency). 2014 Guidance for applying quantitative data to develop data-derived extrapolation factors for interspecies and intraspecies extrapolation. Risk Assessment Forum, Office of the Science Advisor, Washington, DC; EPA/100/R-14/002.

## 7. Appendices

### 7.1. Appendix A - Compilation and evaluation of toxicity data

Given the sparsity of data for marine mammals and the desire to protect highly vulnerable individuals, endpoints are not restricted to the survival, reproduction, and growth endpoints traditionally used to develop guidelines. All endpoints are accepted if there is scientific evidence available that links the endpoint to an adverse outcome in a mammalian species. Adverse effects could include:

- Systemic toxicity such as to the liver, kidney, or general system.
- Neurotoxicity evidenced by behavioural differences or brain pathology.
- Reproductive toxicity that results in effects on fertility or the ability to reproduce.
- Endocrine toxicity that affects organs like the thyroid gland or circulating concentrations of hormones like estrogen, testosterone, or thyroid hormones.
- Developmental toxicity including effects on the developing fetus or maternal systemic effects that interfere with development.
- Immunotoxicity that affects immune system organs like the spleen and thymus, or general immune function disorders.

Acceptable endpoints include omics endpoints if they are anchored through a plausible adverse outcome pathway (AOP). An AOP consists of three main components: a molecular initiating event where the substance interacts with the biochemistry of the organism; key event(s) where the alteration in the biochemistry leads to an alteration in cell, tissue, or organ functioning; and an identified adverse outcome that has the potential to impair the growth, reproduction, and survival of an organism. Using AOPs is an emerging approach and most AOPs are still under development. It is not necessary to firmly establish each of the key events in the AOP but rather that the scientific literature has established a high likelihood that the pathway occurs.

All studies used in the development of a guideline must be evaluated to ensure acceptable laboratory, field, and/or computational practices were used in the design and execution of the study. The exception is studies previously screened and included in the ATSDR database or evaluated by Health Canada or the US EPA which can automatically be included with no additional screening.

Contamination, sampling procedure, sample preservation, storage, pre-concentration, and filtration may all be sources of errors rendering the task of achieving precision and accuracy complex. A thorough investigation of the data (technique and reliability) must be performed before considering the measured concentrations as acceptable values for a guideline derivation (CCME 2007).

While the evaluation of toxicological data should follow a basic format with certain requirements, scientific judgement is often required for the classification of studies. It is not mandatory for toxicity studies to follow standard design protocols; however, the data must be appropriate with respect to the substance in question. Nonstandard testing procedures can yield usable results and should be evaluated on a case-by-case basis for inclusion in the data set. Since standard protocols for toxicity testing may become outdated or are not always available or followed, a great deal of variability exists in the quality of published data.

To ensure a consistent scientific evaluation for each substance, the following questions should be used to evaluate the quality of each study for the following experimental approaches:

All Studies (criteria taken directly from US EPA 2002):

- What was the purpose of the study and is there a clearly delineated hypothesis?

- Is there sufficient description of the protocol, statistical analysis, and results to make an evaluation?
- Were the appropriate endpoints assessed in the study? Were the techniques used for the assessment scientifically sound?
- Were appropriate statistical techniques applied for each endpoint? Was the power of the study adequate to detect effects?
- Did the study establish dose-response relationships (e.g., LOAEL, EC10)?
- Is the shape of the dose-response curve consistent with the known toxicokinetics of the test compound?

In vivo laboratory dose-response studies from any mammal (criteria taken directly from US EPA 2002):

- Was the study sufficiently documented (e.g., conducted in accordance with good laboratory practices)?
- Were appropriate analytical techniques used to measure the stability, homogeneity, and actual level of the test substance in the study (in the water, feed, air, etc.)?
- Were the dose levels appropriate? What was the basis for choosing the dose levels?
- Was an appropriate method used to assign the animals to the dose groups?
- Was an appropriate route and matrix of exposure employed?
- Was the duration of exposure adequate for the study design?
- Were possible alterations in metabolism considered at the higher exposure levels?
- A clear dose-response relationship should be demonstrated in the study. Studies with limited treatment levels may be considered if other toxicological studies support the effect level.
- Dosage rates (in  $\text{mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ ), exposure duration, formulation, and administration method used in the study should be reported. Dosage rates that have been estimated are acceptable, but measured dosage rates are preferred.
- The substance should be administered in the test via the oral route (i.e., in food, in water, or by gavage). Dietary exposure studies are preferred. Tests using other administration methods (i.e., dermal, respiratory, intravenous, intramuscular, subcutaneous, or intra-peritoneal) should not be used unless sufficient supportive information on the pharmacokinetics (absorption, distribution, metabolism, and excretion) of the substance was available and the dosage was measured. [1]

In-vitro studies (criteria from Emmerich and Harris 2019)

- Does the methodology include all minimum information requirements of the experiment type? If none exist, is information given on buffer (e.g., cell culture medium), lysis conditions, sample preparation and handling and incubation times?
- Are the sources of all materials (e.g., cells, antibodies, enzymes, proteins, nucleic acids, chemicals) clearly listed, including vendor, catalogue number, and lot number?
- For non-commercially sourced materials, were the necessary quality control analysis conducted to validate their identity, purity, and biological activity.
- Was the source of recombinant proteins reported? This includes the sequence, expression system, purification, and analysis for purity and bioactivity.
- Were inhibitors and compounds specifically screened to identify off-target effects?
- Were the methods for purifying and preparing cell lines described?
- Were antibodies screened for specificity and cross-reactivity?
- Did the study design include adequate replication and randomization?
- Was the statistical analysis clearly described and the corresponding sample size and error bars reported?



In silico studies (criteria from Myatt et al. 2018)

- Were all steps and methodologies transparently documented, including the exact software used? (Though not essential, it is best practice for researchers to supply the data and code so the experiment can be replicated.)
- Was the training data set of high quality?
- Did the model have a high prediction reliability?
- Was the selection of structural descriptors biologically meaningful?
- Support in the literature for the relationships between structural descriptors and toxicological effect?
- Were the results explained in relation to current toxicological knowledge?
- Were weaknesses in the approach and necessary steps for further validation clearly described?

## 7.2. Appendix B – IB model input values and FI:BW estimates

Table B1. The parameters and input values for orca and beluga below are taken from Hickie et al. 2007.

Time parameters	Orca	Beluga
Years model runs after weaning (68)	68	68
First possible year of pregnancy (15)	15	9
Julian day of copulation	35	35
Julian day of birth	545	455
Julian day of weaning	1278	1278
Number of days between standard output reports	60	120
Percentage of weaning time calf is in food transition	20	20
n/a	n/a	n/a
Stage specific food intake multipliers	n/a	n/a
Food multiplier for juvenile (eg 1.3)	1.3	1.3
Food multiplier for adult (eg 1.3)	1.3	1.3
Food multiplier during pregnancy (eg 1.3)	1.3	1.3
Food multiplier during lactating (eg 1.3)	1.3	1.3
n/a	n/a	n/a
Body compartment parameters	n/a	n/a
Maximum blubber proportion of body wt	0.29	0.4
Minimum blubber proportion of body wt	0.28	0.4
Fetal blubber proportion of body wt	0.17	0.17
Lipid proportion of blubber female	0.4	0.8
Lipid proportion of core	0.05	0.05
Ratio of support:fetal mass at term	1	1.0
Nonpregnant base uterus weight	0.05	0.05
Ratio of placental:support mass	0.25	0.25
n/a	n/a	n/a
Female Orca growth parameters	n/a	n/a
Max length parameter	564	365
Gompertz B value length	0.885	0.8805

Table B1 continued. The parameters and input values for orca and beluga below are taken from Hickie et al. 2007.

Time parameters	Orca	Beluga
Gompertz K value length	0.27000	0.00044
Max weight parameter	2703	680
Gompertz b value weight	2.7	2.572
Gompertz k value weight	0.00046	0.00044
n/a	n/a	n/a
Male Orca growth parameters	n/a	n/a
Max length parameter	683	416
Gompertz B value length	1.08	0.987
Gompertz K value length	0.1752	0.000375
Max weight parameter	5015	995
Gompertz B value weight	3.3	2.895
Gompertz K value weight	0.00046	0.000375
Lipid proportion of blubber male (0.4)	0.4	0.8
n/a	n/a	n/a
Stage specific metabolic rate multipliers	n/a	n/a
1.5-3.0 x BMR for neonate (lact)	4	4
1.5-3.0 x BMR for first year	4	4
1.5-3.0 x BMR for juvenile	4	4
1.5-3.0 x BMR for adult (non-reprod/male)	4	4
1.5-3.0 x BMR for adult (pregnant)	4	4
1.5-3.0 x BMR for adult (lactating)	4	4
n/a	n/a	n/a
Energetics parameters	n/a	n/a
kcal·kg <sup>-1</sup> food (1800)	1800	1778
Digestibility of food (~0.6-0.9)	0.82	0.82
kcal reqd to add 1kg core mass (~9100)	9100	9100
kcal reqd to add 1kg blubber mass (~9100)	9100	9100
kcal reqd to add 1kg fetus/uterus mass (~9100)	9100	9100

Table B1 continued. The parameters and input values for orca and beluga below are taken from Hickie et al. 2007.

Time parameters	Orca	Beluga
Energetics parameters	n/a	n/a
kcal·kg <sup>-1</sup> blubber energy density (~8500)	8500	8500
Energy efficiency of blubber mobilization (~0.9)	0.9	0.9
kcal·kg <sup>-1</sup> milk energy density (~3325)	3325	3000
Lipid proportion in milk (~0.26)	0.3	0.27
Digestibility of milk (~0.9)	0.9	0.9
Energy efficiency in milk production (~0.9)	0.9	0.9
n/a	n/a	n/a
Contaminant kinetics terms	n/a	n/a
log K <sub>OW</sub> for chemical	6.8	6.8
TOX assimilation from food (~0.8)	0.724	0.724
TOX assimilation from milk (~0.8)	0.9	0.9
Blubber-milk TOX partition coefficient (0.6-1.0)	0.490	0.490
Adult TOX whole-body clearance rate (per day)	0.00009	0.000055
Neonate TOX whole-body clearance rate (per day)	0.00009	0.000055
Placenta effect on mother-fetus partition (0.6-1.0)	0.556	0.556
n/a	n/a	n/a
Diet Energy Content Calculation kcal·kg <sup>-1</sup> wet wt	n/a	n/a
Protein % of wet wt (5600 kcal·kg <sup>-1</sup> )	20	20
Lipid % of wet wt (9400 kcal·kg <sup>-1</sup> )	8.0	7.0
n/a	n/a	n/a
Pregnant in Years	15,20,25, 30,35,40	10,13,16, 19,22,25, 28,31,34

\* K<sub>OW</sub> dependent parameter. Tox assimilation from food equation is given in McLachlan 1994; blubber-milk tox partition coefficient equation is given in Cadieux et al. 2016; and placenta effect on mother-fetus partition equation is given in Desforges et al. 2012.

Table B2. The parameters and input values for ringed seal below are taken from Hickie et al. 2007.

Time parameters	Ringed Seal
Years model runs after weaning (~20)	25
First possible year of pregnancy (7+)	7
Julian day of birth (April 1 = 90)	90
Julian day of weaning and copulation	130
Julian day of implantation (Aug 4 = 215)	215
Julian day of moult start	180
Julian day of moult END	210
Number of days between standard output reports	30
Stage specific food intake multipliers	n/a
Food multiplier for juvenile	1.3
Food multiplier for adult	1.3
Food multiplier during moult	0.7
Food multiplier during lactating	0.6
n/a	n/a
Body compartment parameters	n/a
Maximum blubber proportion of body wt	0.4
Minimum blubber proportion of body wt	0.25
Fetal blubber proportion of body wt	0.055
Lipid proportion of blubber	0.8
Lipid proportion of core	0.05
Ratio of support:fetal mass at term	1.0
Nonpregnant base uterus weight	0.05
Ratio of placental:support mass	0.25
n/a	n/a
Female growth parameters	n/a
Max Length Parameter (cm)	126.85
Gompertz B value	0.3377
Gompertz K value	0.00032
Length-wt slope (cm---kg)	3.2544
Length-wt constant	5.0596
n/a	n/a
Male growth parameters	n/a
Max Length Parameter (cm)	131.21
Gompertz B value	0.400
Gompertz K value	0.0005
Length-wt slope (cm---kg)	3.0685
Length-wt constant	4.693
n/a	n/a
Stage specific metabolic rate multipliers	n/a
1.5-4.0 x BMR for neonate (lact)	1.0
1.5-4.0 x BMR for first year	4.0

Table B2. Continued. The parameters and input values for ringed seal below are taken from Hickie et al. 2007.

Time parameters	Ringed Seal
Stage specific metabolic rate multipliers	n/a
1.5-4.0 x BMR for juvenile	4.0
1.5-4.0 x BMR for adult (non-reprod/male)	4.0
1.5-4.0 x BMR for adult (pregnant)	4.0
1.5-4.0 x BMR for adult (lactating)	4.0
Metabolic rate modifier for moulting	0.8
n/a	n/a
Energetics parameters	n/a
kcal·kg <sup>-1</sup> food	1684
Digestibility of food	0.82
kcal reqd to add 1kg core mass	9100
kcal reqd to add 1kg blubber mass	9100
kcal reqd to add 1kg fetus/uterus mass	9100
kcal·kg <sup>-1</sup> blubber energy density	8500
Energy efficiency of blubber mobilization	0.9
kcal·kg <sup>-1</sup> milk energy density	4000
Lipid proportion in milk	0.38
Digestibility of milk	0.9
Energy efficiency in milk production	0.9
n/a	n/a
Contaminant kinetics terms	n/a
Name of contaminant in this run	Kow Trial
log Kow for chemical	6.8
TOX assimilation from food	0.724
TOX assimilation from milk	0.9
Blubber-milk TOX partition coefficient (0.6-1.0)	0.490
Adult TOX whole-body clearance rate (per day)	0.000027
Neonate TOX whole-body clearance rate	0.000027
Placenta effect on mother-fetus partition (0.6-1.0)	0.556
n/a	n/a
Diet Energy Content Calculation kcal·kg <sup>-1</sup> wet wt	n/a
Protein % of wet wt (5600 kcal·kg <sup>-1</sup> )	20
Lipid % of wet wt (9400 kcal·kg <sup>-1</sup> )	6.0
n/a	n/a
Pregnant in Years	8,19,11,13,14,15,17,19,20,22,23

Table B3. FI:BW rates (percent of body weight per day) for five subgroups of Arctic ringed seals, beluga whales and killer whales estimated with the individual-based bioaccumulation models. Juvenile are considered to be from ages 1.2 to 10 years for beluga and 1.0 to 15 years for killer whales. Differences between the two species are primary due to differences in body mass.

n/a	Juveniles	Adult Males 10-60 years	Adult Females		
			Non-Pregnant	Pregnant	Nursing
Arctic Ringed Seals	$8.8 \pm 1.2$	$7.6 \pm 0.3$	$8.3 \pm 0.5$	$8.5 \pm 0.6$	$10.4 \pm 1.8$
Beluga Whales	$5.1 \pm 0.7$	$3.5 \pm 0.2$	$3.8 \pm 0.1$	$4.2 \pm 0.4$	$4.8 \pm 0.3$
Killer Whales	$3.5 \pm 0.8$	$2.3 \pm 0.1$	$2.7 \pm 0.1$	$2.8 \pm 0.1$	$3.3 \pm 0.3$