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The Canadian Ecological Screening Assessment for the Challenge on Bisphenol A

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Outline

1. The Ministerial Challenge

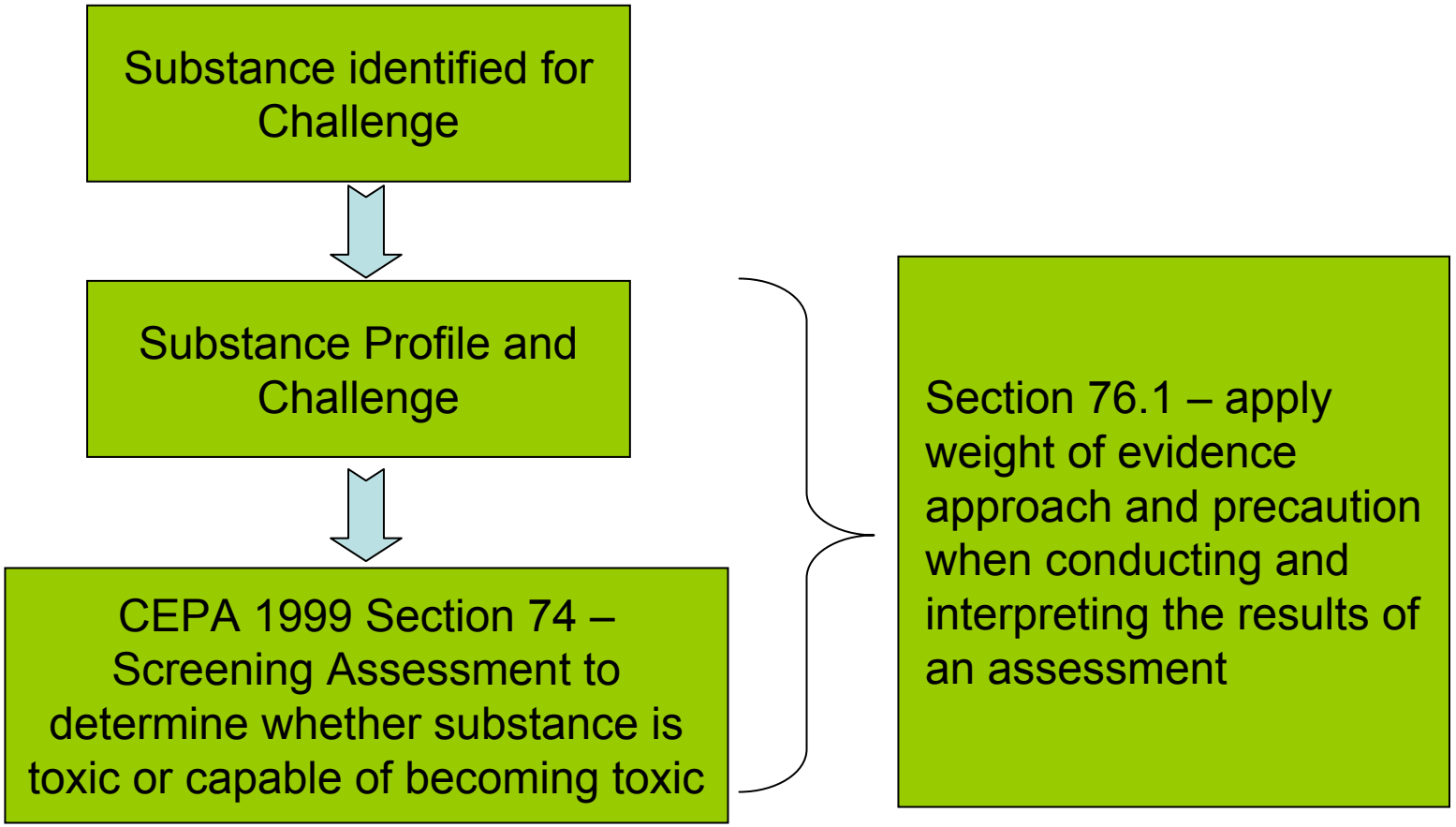
2. Highlights of the Bisphenol A Ecological Screening Assessment

3. Conclusions

The Ministerial Challenge

- A Notice was published in the *Canada Gazette,* Part I December 2006 outlining the Government of Canada's intended action for the Challenge.
- A plan for the assessment and management of substances believed to be in-commerce and identified as high priorities for action as a result of Categorization of the Canadian Domestic Substances List.
- The mandate provided under the Canadian Environmental Protection Act (CEPA 1999).
- High priority substances included those that met:
  - each of the ecological categorization criteria (persistence (P), bioaccumulation (B) and inherent toxicity to aquatic organisms (iT) and believed to be in commerce in Canada; and/or
  - the criteria for greatest or intermediate potential for exposure (GPE or IPE) and were identified as posing a high hazard to human health (evidence of carcinogenicity, mutagenicity, developmental toxicity or reproductive toxicity).
- Complemented with industry survey data to indicate that these substances were still in commerce today.

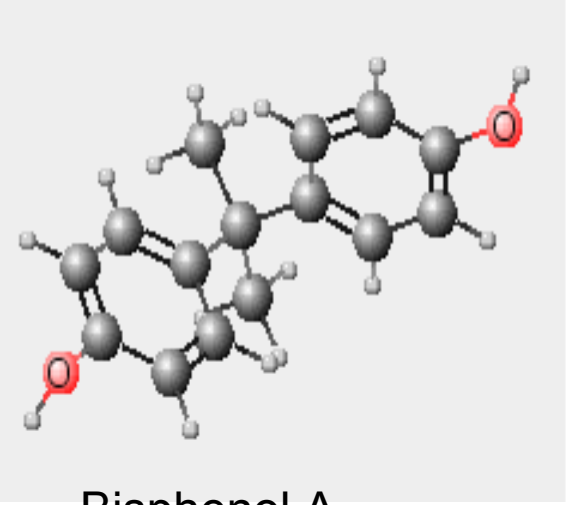
Moving to Screening Assessments for Substances under the Challenge



Assessment Approach

- Ecological assessment:
  - Evaluates entry, exposure and effects to determine risk to the environment.
  - Considers full range of the substance's properties observed in the environment or expected based on laboratory information and modeled data for these and related chemicals.
  - Develops conclusions based on broad range of considerations relevant to the ultimate risks that a substance may pose, such as persistence, bioaccumulation, risk quotients for different media, long-range transport, temporal trends, geographical distribution, sensitive habitats and species at risk.
- Assessments are subjected to Peer Reviews, and Public Consultation prior to finalization.

Highlights of the Bisphenol A Ecological Screening Assessment



Bisphenol A

CAS No. 80-05-7

$C_{15}H_{16}O_2$

Structure generated by Molecular Networks
http://www.molecular-networks.com/

Why was Bisphenol A Assessed?

- High priority for action under Ministerial Challenge.
- Met human health categorization criteria:
  - Greatest potential for human exposure; and
  - Classified on the basis of reproductive toxicity by the European Commission.
- Met ecological categorization criteria for inherent toxicity to aquatic organisms

Uses of Bisphenol A

- ~72% used in manufacture of polycarbonates, ~21% was used in epoxy resins, ~6% other applications (NTP 2007).
- Polycarbonates used for compact discs, food and beverage containers, water pipes, glazing applications, films, electronic equipment and automotive parts.
- Epoxy resins used for protective coatings (e.g., inside cans, lids, storage tanks), electrical laminates and adhesives.
- Main Canadian uses: plastic resin formulations, paperboard packaging, metal cans, industrial coatings, plasticizers, adhesives, chain oil, brake fluid, heat transfer fluid and lubricant formulations.

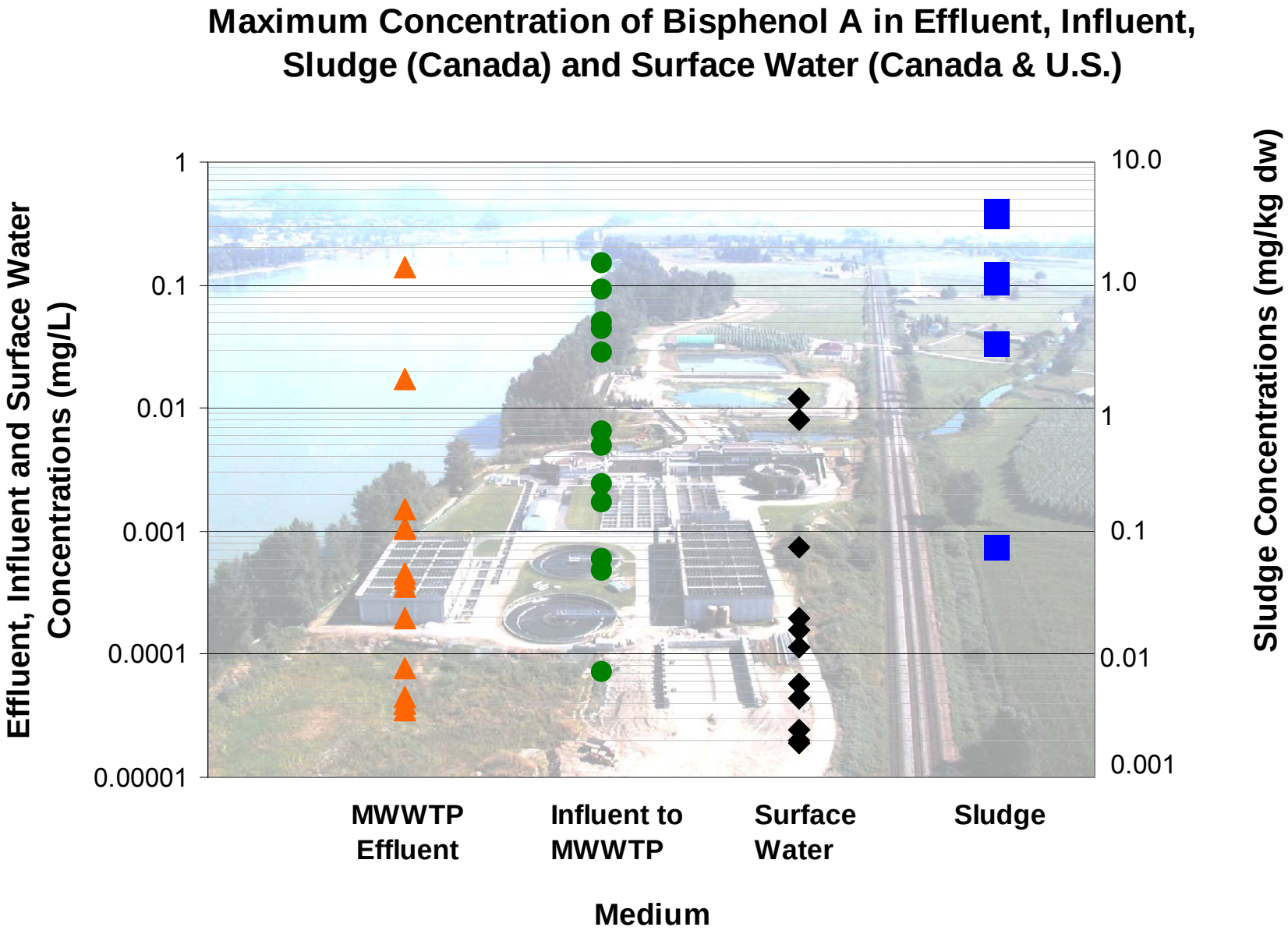
Considerations for Ecological Assessment: High and Increasing Production

- Global production 4 billion kg in 2006.
- 521 million kg (1990) to 736 million kg (1995) to ~1 billion kg (2000) in US (SRI Consulting 2007).
- CEPA 1999 Section 71 survey:
  - Not manufactured in Canada in 2006 at quantities greater than 100 kg.
  - In 2006, 26 Canadian companies reported use in the range of 100 000 to 1 000 000 kg, and approximately half a million kg was imported into Canada either alone, in a product, in a mixture or in a manufactured item.
  - Extent to which the reported values represent quantities of bisphenol A present in finished and semi-finished goods entering Canada from other parts of the world is unknown.

Environmental Releases

- Predominantly to surface water and land.
- Due to processing and product manufacturing, use of products and disposal.
  - E.g., washing residues during production and use, processing of materials, fugitive dust.
  - Identified in Canadian industrial discharges (Lee et al. 2002):
    - Paper and allied products ($<1.0 \times 10^{-5}$ to 0.149 mg/L);
    - Chemicals and chemical products (8.0×10^{-5} to 0.091 mg/L);
    - Textile industries (1.0×10^{-4} to 0.0005 mg/L);
    - Commercial laundries (7.5×10^{-4} to 0.044 mg/L); and
    - Plastic product manufacturing (5.0×10^{-5} – 0.002 mg/L).
- Effluent and sludge from municipal wastewater treatment facilities (MWWTPs).
- Median reduction of 68% (range 1 – 99%) in bisphenol A concentration at Canadian MWWTPs based on 36 influent/effluent pairs (Lee and Peart 2000).

Environmental Releases and Levels



Persistence and Bioaccumulation

- Rapid biodegradation under aerobic conditions.
  - Half-life = 1.2 days in water, 3 – 7 days in soil (Sarmah and Northcott 2008, Fent et al. 2003)
- Widespread detection in surface waters, MWWTP effluents.
- Measurement in media without direct input (e.g., groundwater) indicating that substance remains sufficiently long in the environment to move from its point of release into other environmental media.
- Based on observed stability with no degradation under anoxic conditions, bisphenol A is **considered to meet the Persistence criteria in sediments under CEPA 1999.**
  - No degradation in anaerobic river bed sediment slurry after 3 months of incubation (Roen and Abelovich 2000); stable in anoxic estuarine sediments after 120 days (Voordeckers et al. 2002).

- **Does not meet Bioaccumulation criteria under CEPA 1999**, but is bioavailable and can accumulate to some degree in organisms.
- Metabolism identified in fish, mammals, birds and plants.
  - In fish transformation to glucuronides

Pelagic and Terrestrial Effects

- Hazard to aquatic environment with L(E)C_{50} values at or approaching 1 mg/L and chronic NOEC equal or less than 0.1 mg/L. For example:
  - 96-hour EC_{50} = 1.0 – 3.1 mg/L (algae) (Alexander et al. 2008);
  - 96-hour LC_{50} = 1.0 mg/L (mysid shrimp, *Mysidopsis bahia)(*Hirano et al. 2004);
  - 7-day Lowest Observed Effect Concentration (LOEC) = 1.88 mg/L (*Ceriodaphnia dubia)(*Tatarazako et al. 2002);
  - 14-day LOEC = 1.0 mg/L (amphipod, *Gammarus pulex)(*Johnson et al. 2005);
  - 103-day LOEC = 0.00175 mg/L (brown trout, *Salmo trutta f. fario,* reduced semen quality)(Lahnsteiner et al. 2005).
- Adverse reproductive and developmental effects identified in terrestrial organisms. For example,
  - 14-day LOEC = 100 mg/kg dw (earthworm, *Eisenia sp.;* reproduction) (Johnson et al. 2005)
  - 23-week Lowest Observed Adverse Effect Level (LOAEL) = 100 mg/kg-bw per day (White Leghorn, *Gallus domesticus;* altered development of male phenotypes) (Furuya et al. 2006)

Endocrine Disruption

- Evidence of disruption to hormonal, reproductive and developmental processes for fish, aquatic invertebrates, amphibians and reptiles.
- Great variation in reported levels, but generally in the range 0.001 to 1 mg/L. Aquatic invertebrates generally show effects at lower concentrations than fish.
- Strong evidence of adverse effects, for instance:
  (1) following prolonged exposure at levels below those usually seen to elicit effects in standard toxicity tests (i.e., tests based on recognized methods which evaluate endpoints such as survival, reproduction and growth);
  (2) following brief low-dose exposure, particularly at sensitive developmental stages, with effects apparent later in the life cycle; and
  (3) on filial generations following parental exposure.

Risk Quotients: Background

- Risk quotient analysis is conservative and precautionary.
- Risk Quotient = Predicted Exposure Concentration (PEC) ÷ Predicted No Effect Concentration (PNEC).
- PEC = Measured or predicted environmental exposure level.
- PNEC = Critical Toxicity Value (CTV; usually an estimate of low toxic effect) ÷ Application Factor (AF, e.g., 10, 100, etc.).
- Quotients ≥ 1 indicate potential harmful risk.

- Risk quotient analysis conducted for pelagic, benthic, soil organisms and wildlife. Quotients below 1 for benthic and soil organisms and predatory wild birds.

Risk Quotient: Pelagic Organisms

- PEC = 0.00173 mg/L for surface water.
  - Based on effluent concentration of 0.0173 mg/L reported for Toronto area MWWTP effluent (Lee et al. 2004).
    - Highest reliable Canadian effluent concentration from a MWWTP providing secondary treatment.
  - Dilution factor of 10 to account for exposures in the immediate mixing zone.
- PNEC = 0.000175 mg/L.
  - Based on CTV of 0.00175 mg/L (103 day LOEC, reduced semen quality and delayed ovulation in brown trout).
  - Application factor = 10 (to account for variability in interspecies and intraspecies sensitivity and extrapolation from laboratory to field conditions).
- Q = 9.9; Potential identified for adverse risk to pelagic organisms.

Risk Quotients: Mammalian Wildlife

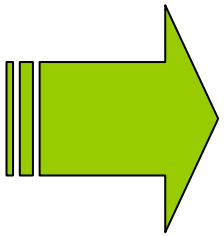
- Used an energetics model based on the general exposure approach for wildlife from the U.S. Environmental Protection Agency's (EPA) Exposure Factors Handbook (USEPA 1993).
- PEC estimated based on a calculation of the total daily intake (TDI, mg/kg-bw per day) of bisphenol A by sentinel species.

- TDI = $PEC_{wildlife}$
  - Calculation considers, concentration of bisphenol A in prey species (estimated for fish) and proportion which this species composes diet, metabolic rate of sentinel species, and gross energy of prey species.
- PEC_{mink} = 0.009 mg/kg-bw per day
- PEC_{otter} = 0.021 mg/kg-bw per day

Risk Quotients: Mammalian Wildlife (2)

- PNEC (mg/kg-bw per day) from repeated oral dose toxicity data normalized based on body weight to wildlife receptor.
- Based on the analysis of rodent studies by Health Canada, the dataset of neurodevelopmental and behavioural studies suggests potential effects in the range of 0.01 to 0.1 mg/kg-bw per day and higher.
- CTV = 0.01 – 0.1 mg/kg-bw per day
- $PNEC_{mink}$ = 0.0008 to 0.008 mg/kg-bw per day
- $PNEC_{otter}$ = 0.0005 to 0.005 mg/kg-bw per day

- Q_{mink} = 1.25 to 12.50
- Q_{otter} = 4.2 to 42.0



Potential for risk identified.

Bisphenol A Ecological Screening Assessment: Conclusions

- Based on lines of evidence relating to:
  - High and increasing production, environmental presence and stability, potential uptake and accumulation in biota, and environmental effects
- Bisphenol A found to meet criteria of subsection 64 (a) set out under the CEPA 1999.
  - Entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity.
  - Proposed addition to Schedule 1 under CEPA 1999.
- Final Assessment was published in *Canada Gazette* Part 1 on 18 October 2008.

Contact Information

- **Chemical Substances Web Site:**
  - www.chemicalsubstanceschimiques.gc.ca

- More information on the Challenge Program:

  Ecological Assessment Program
  Fontaine Building, 8th Floor
  200, Sacré-Coeur Boulevard
  Gatineau QC K1A 0H3
  T: 1-888-228-0530/819-956-9313
  F: 1-800-410-4314/819-953-4936
  Email: DSL.surveyco@ec.gc.ca (surveys and questionnaires)
  Existing.Substances.Existantes@ec.gc.ca (public comments)

Thank you for listening!

Addendum Slides

Ecological Criteria used in the Categorization of the Domestic Substances List

- Categorization criteria for Persistence and Bioaccumulation are identified in the Persistence and Bioaccumulation Regulations under CEPA 1999.

Persistence A substance is considered persistent if its transformation half-life satisfies the criterion in any one environmental medium or if it is subject to long-range transport		**Bioaccumulation**
Medium	**Half-life**	
Air Water Sediment Soil	≥2 days (or LRT) ≥6 months ≥1 year ≥6 months	BAF ≥ 5000 or BCF ≥ 5000 or log K_{ow} ≥ 5

- For a substance to be considered **Eco Inherently Toxic**, it must have an acute aquatic toxicity of < 1 mg/L, or a chronic aquatic toxicity of < 0.1 mg/L

Selected endpoint values relating to potential hormonal effects in fish

Test organism	Duration of test (days)	Endpoint observed	Lowest effect value (mg/L)	Reference
Fish:				
Carp	4	Vitellogenin induction	22.8	Letcher et al. 2005
Goldfish	8	Altered plasma calcium homeostasis	0.228	Suzuki et al. 2003
Rainbow trout	12	Vitellogenin induction	0.070	Lindholst et al. 2000
Carp	14	Altered sex steroid levels	0.001[1]	Mandich et al. 2007
Turbot	21	Altered steroid hormone balance	0.059[2]	Labadie and Budzinski 2006
Guppy	21	Reduced total sperm count	0.274[1]	Haubruge et al. 2000
Fathead minnow	21	Reduced egg number at spawning	0.500	Brian et al. 2007
Medaka	21	Vitellogenin induction	0.500	Tabata et al. 2004
Medaka	21	Altered gonad development	1.720	Kang et al. 2002
Medaka	60	Altered growth, sex ratio	1.820	Yokota et al. 2000
Zebrafish	Fertilization to adult (65-75 days)	Vitellogenin induction, altered gonad histology	0.375	Segner et al. 2003
Brown trout	103	Reduced sperm quality and motility; delayed ovulation, reduced percent ovulation	0.00175[1]	Lahnsteiner et al. 2005
Medaka	110	Altered gonad development	0.006[1]	Metcalfe et al. 2001

[1] Significant effects occurred at the lowest test concentration

[2] One test concentration

Selected endpoint values relating to potential hormonal effects in aquatic invertebrates

Test organism	Duration of test (days)	Endpoint observed	Lowest effect value (mg/L)	Reference
Copepod	21	Delayed development	0.00001[1]	Marcial et al. 2003
Mussel	21	Induction of vitellogenin-like proteins and spawning in both sexes	0.050[2]	Aarab et al. 2006
Mussel	21	Resorption of male and female gonads	0.050[2]	Ortiz-Zarragoitia and Cajaraville 2006
Mudsnail	56	Increased embryo production	0.001 (mg/kg)	Duft et al. 2003
Mudsnail	63	Increased embryo production	0.005	Jobling et al. 2004
Ramshorn snail	180	Increased egg and clutch production	0.0000483	Oehlmann et al. 2006
Chironomid	2 life cycles	Delayed emergence (2nd generation) mouthpart deformities	0.078 0.010	Segner et al. 2003

[1] Significant effects occurred at the lowest test concentration
[2] One test concentration

Selected endpoint values relating to potential hormonal effects in amphibians and reptiles

Test organism	Duration of test (days)	Endpoint observed	Lowest effect value (mg/L)	Reference
Amphibians:				
Frog	< 1	Competitive binding to estrogen receptor	0.107[3]	Suzuki et al. 2004
Frog	9	Suppressed metamorphosis	0.228[1]	Goto et al. 2006
Frog	75	Altered gonad development	0.228	Jagnytsch et al. 2006
Frog	84	Feminized sex ratio	0.0228	Kloas et al. 1999
Frog	90	No observable effect on larval growth, development or sexual differentiation	Highest: 0.500	Pickford et al. 2003
Frog	120	Feminized sex ratio at 0.0228 mg/L, no observable effect at 0.00228 and 0.228	0.0228	Levy et al. 2004
Reptiles:				
Caiman	10	Reversed gonadal sex and altered gonad structure	1.400[1] (mg/kg egg)	Stoker et al. 2003

[1] Significant effects occurred at the lowest test concentration
[2] Test concentration was reported as 4.7×10^{-7} M

Calculation of PEC Based on USEPA (1993)

- PEC estimated based on total daily intake (TDI, mg/kg-bw per day) for mink and otter.

$$TDI = \left[FMR\left(\frac{C_i \cdot P_i}{GE_i \cdot AE_i} \right) \right] \cdot Pt$$

  - Where:
    - FMR = normalized free metabolic rate of wildlife receptor of interest (236 kcal/kg-bw per day for mink and 183 kcal/kg-bw per day for river otter)
    - Ci = concentration of contaminant in the ith prey species (mg/kg-bw) (see below)
    - Pi = proportion of the ith prey species in the diet (unitless) (default = 35% for mink; 100% for otter)
    - GEi = gross energy of the ith prey species (default = 1240 kcal/kg-bw prey)
    - AEi = assimilation efficiency of the ith prey species by the wildlife receptor (default = 0.91)
    - Pt = proportion of the time the receptor spends in the contaminated area (50% for mink and 50% for otter)

Why Use Mink and Otter as Sentinel Species?

- Consumers of aquatic life (30% to 100% fish in diet)
- Good life history data (diet, metabolism, range, etc.)
- Well distributed throughout Canada in both freshwater and marine/estuarine habitats
- Relatively high metabolic needs so good focal species
- Exposed to contaminants in food and drinking water