Canadian Tissue Residue Guidelines for the Protection of Wildlife Consumers of Aquatic Biota

POLYCHLORINATED DIBENZO-*P*-DIOXINS AND POLYCHLORINATED DIBENZOFURANS (PCDD/Fs)

Polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), commonly known as dioxins and furans, respectively, are planar tricyclic aromatic compounds (WHO 1989). Combined, there are 210 possible congeners, but the 17 congeners that have chlorine atoms substituted in at least the 2,3,7, and 8 lateral positions are believed to be the most toxic. PCDD/Fs are omnipresent in the air, soil, sediments, and biota even though they have never been intentionally produced and have no known use (WHO 1989; Fiedler et al. 1990). They are by-products formed as a result of anthropogenic activities, including waste incineration, chemical manufacturing, petroleum refining, wood burning, metallurgical processes, fuel combustion (automobiles), residential oil combustion, and electric power generation, among others. Today, municipal waste incineration is one of the most significant sources of PCDD/Fs to the Canadian environment (Environment Canada 1999). Historically, pulp and paper mill effluent released significant amounts of PCDD/Fs, but major reductions have occurred since the Pulp and Paper Regulations of 1992 (Halliburton and Simpson 1999). Natural sources include forest fires and volcanic activity (Hicks and McColl 1995).

Because of their hydrophobic nature, the majority of PCDD/Fs released into aquatic systems ultimately become associated with the organic fraction of suspended and/or bed sediments and the lipid-rich tissues of aquatic organisms. Aquatic organisms may take up PCDD/Fs from water or sediment, or through the consumption of contaminated prey items. All 2,3,7,8-substituted PCDD/Fs readily accumulate in the tissues of aquatic organisms, though higher chlorinated PCDD/Fs generally accumulate to a lesser degree than lower chlorinated congeners. Bioconcentration factors (BCFs) and biota–sediment accumulation factors (BSAFs) are used to estimate the degree to which chemicals accumulate in biota relative to water and sediment, respectively (Oliver and Niimi 1985). Lipid-normalized bioconcentration factors ($BCFs_{lipid}$) recorded for 2,3,7,8-tetrachloro-*p*-dibenzo-dioxin (2,3,7,8-TCDD) are the highest of all congeners, ranging from 50 900 to 1 700 000 for resident freshwater species (Mehrle et al. 1988; Servos et al. 1989). BSAFs for 2,3,7,8-TCDD range from 0.03 to 0.85 and from 0.03 to 0.93 for freshwater and marine/estuarine systems, respectively (Batterman et al. 1989; van der Weiden et al. 1989a; Harding and Pomeroy 1990; Rubinstein et al. 1990). Accumulation from food may be the primary source of PCDD/Fs for some species (e.g., lake trout *[Salvelinus namaycush]*), but not for others (e.g., carp and guppies *[Poecilia reticulata]*) (Batterman et al. 1989; Loonen et al. 1993). Moreover, PCDD/Fs seem unusual in that they do not appear to biomagnify like other halogenated aromatics with comparable hydrophobicities (e.g., PCBs). The greatest biomagnification factors (BMFs) reported for PCDD/Fs are 32 and 76 for herring gulls *(Larus argentatus)* and mink *(Mustela vison)*, respectively (Braune and Norstrom 1989; Tillitt et al. 1996).

Toxicity

Mode of Action

The 2,3,7,8-substituted PCDD/Fs are thought to elicit most, if not all, of their toxicity via the aryl hydrocarbon *(Ah)* receptor, a protein present in mammals, birds, and fish (Clark et al. 1992; van den Heuvel and Lucier 1993). These congeners, as well as some polychlorinated biphenyls (PCBs), are potent ligands and activators of the *Ah* receptor. Binding of dioxin-like compounds to the *Ah* receptor correlates well to the induction of mixed-function oxidase (MFO) enzyme systems; however, linkages between enzyme induction and specific organ toxicity are unclear (Safe 1990; Brouwer 1991; De Vito et al. 1993). The toxic mode of action for non-2,3,7,8-substituted PCDD/Fs is not well understood.

Table 1. Canadian tissue residue guidelines for PCDD/Fs for the protection of wildlife consumers of aquatic biota (Environment Canada 2000).

Compound	Guideline value (ng TEQ·kg^{-1} diet ww)
PCDD/Fs	
Mammals	0.71*
Birds	4.75†

*Based on TEF values for mammals (van den Berg et al. 1998).
† Interim guideline, based on TEF values for birds (van den Berg et al. 1998); see text for details.

Toxic Equivalency Factors

Although 2,3,7,8-substituted PCDD/Fs act similarly on the *Ah* receptor, the degree of response incurred as a result of receptor binding varies by four orders of magnitude among individual congeners. Thus, environmental samples containing comparable concentrations of one or more congeners may differ drastically in toxic potency. Toxic equivalency factors (TEFs) have been developed to compare toxicities of environmental samples with different congener profiles (Table 2) (van den Berg et al. 1998). A number of sets of TEFs exist for mammalian and avian receptors. The most recent values were developed by the World Health Organization (WHO) (van den Berg et al. 1998). These TEFs were derived only for those congeners with *Ah* receptor-mediated responses and are based on all available scientific data, including in vitro, in ovo, and in vivo studies that examine a variety of endpoints. To apply TEFs, individual chemical concentrations within a sample are multiplied by their respective TEFs, and all products are summed to give a value expressed in toxic equivalency units (TEQs). The TEF/TEQ method takes into consideration the unique concentrations and toxicities of the individual congeners within a chemical mixture. This method, however, is unable to account for non-additive interactions that are known to occur among different chemicals. It may be difficult to extrapolate TEFs between species due to differences in toxicokinetics. Furthermore, TEFs are currently available for only a few select PCDD/F and PCB congeners. Thus, the influence of non-*Ah*-active congeners may go ignored. Despite these limitations, the dominant view in the scientific community is that the advantages of using the TEF/TEQ approach are far greater than the hazards associated with not using it.

Table 2. Chlorine substitution and toxic equivalency factors (TEFs) for selected PCDD and PCDF congeners (Environment Canada 2000).

	TEF*	
Structure	**Mammals**	**Birds**
PCDDs		
2,3,7,8-TCDD	1	1
1,2,3,7,8-PCDD	1	1
1,2,3,4,7,8-HCDD	0.1	0.05
1,2,3,6,7,8-HCDD	0.1	0.01
1,2,3,7,8,9-HCDD	0.1	0.1
1,2,3,4,6,7,8-HCDD	0.01	<0.001
OCDD	0.0001	0.0001
PCDFs		
2,3,7,8-TCDF	0.1	1
1,2,3,7,8-PCDF	0.05	0.1
2,3,4,7,8-PCDF	0.5	1
1,2,3,4,7,8-HCDF	0.1	0.1
1,2,3,6,7,8-HCDF	0.1	0.1
1,2,3,7,8,9-HCDF	0.1	0.1
2,3,4,6,7,8-HCDF	0.1	0.1
1,2,3,4,6,7,8-HCDF	0.01	0.01
1,2,3,4,7,8,9-HCDF	0.01	0.01
OCDF	0.0001	0.0001

*1998 WHO TEF values (van den Berg et al. 1998); see text for details.

The 1998 WHO TEFs for mammals and birds (Table 2) (van den Berg et al. 1998) were used in the derivation of the PCDD/F tissue residue guidelines (TRGs). TEQs calculated using the mammalian TEFs are abbreviated as TEQ_{mam}, and TEQs calculated using the avian TEFs are abbreviated as TEQ_{bird}. TEQ levels include 2,3,7,8-substituted PCDD/Fs only; "total TEQ" includes PCDD/Fs and PCBs. (See "Canadian tissue residue guidelines for the protection of wildlife consumers of aquatic biota: Polychlorinated biphenyls (PCBs)".)

Mammalian Toxicity

Most of the available toxicity information applies to 2,3,7,8-TCDD. Acute lethal doses of 2,3,7,8-TCDD span four orders of magnitude in mammalian receptors. Guinea pigs are most sensitive, with an LD_{50} of 0.6 $\mu g \cdot kg^{-1}$ bw (Schwetz et al. 1973). In contrast, single-dose oral LD_{50}s for male and female golden Syrian hamsters vary from 1157 to 5051 $\mu g \cdot kg^{-1}$ bw (Olson et al. 1980; Henck et al. 1981). Few data exist on the acute toxicity of 2,3,7,8-TCDD to wildlife species that consume aquatic biota; however, mink may be among the most sensitive species (LD_{50} = 4.2 $\mu g \cdot kg^{-1}$ bw) (Hochstein et al. 1988). For many species, mortality due to single doses of 2,3,7,8-TCDD is delayed (i.e., 5–45 d) (U.S. EPA 1987).

In addition to mortality, a number of sublethal effects may occur following acute exposure to 2,3,7,8-TCDD. For example, decreased body weight gain and/or food consumption are observed in guinea pigs, rats, and mink, but not in mice and hamsters (Greig et al. 1973; Hochstein et al. 1988; Nagao et al. 1993). Alterations to physiology (e.g., liver size and morphology) and physiological functions (e.g., heart rate and blood pressure) in mammalian receptors are associated also with acute

exposures to 2,3,7,8-TCDD (U.S. EPA 1987; Hermansky et al. 1988; Birnbaum et al. 1989a, 1989b; Hanberg et al. 1990; Lans et al. 1990).

Chronic oral exposure to relatively low levels of 2,3,7,8-TCDD may result in weight loss, hair loss, chloracne, and edema (Mukerjee et al. 1986). Common biochemical effects include induction of specific enzyme systems (e.g., MFO) and suppression of the immunological system (Vos et al. 1997/1998). Observed physiological effects include loss of fat; shrinkage of the thymus, spleen, and other lymphatic tissues; and alterations in the number of blood cells (WHO 1989; Lakshman et al. 1991).

Reduced growth and liver toxicity appear to be sensitive responses in mammals exposed to 2,3,7,8-TCDD. Rats fed 0.01 and 0.1 $\mu g \cdot kg^{-1} \cdot d^{-1}$ for 2 years experience increased mortality, decreased weight gain, and increased relative liver weight (Kociba et al. 1978). Those fed 0.01 $\mu g \cdot kg^{-1} \cdot d^{-1}$ have increased liver weights, but no changes in mortality or growth; there are no observable effects at the 0.001 $\mu g \cdot kg^{-1} \cdot d^{-1}$ dose. De Caprio et al. (1986) found that weanling guinea pigs of both sexes experience significant reductions in growth (22–39%) and increased liver weights (relative to body weights) when fed 0.0049 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ of 2,3,7,8-TCDD for 90 d. Also at this dose, males experience reduced relative thymus weights and elevated serum triglycerides, while females exhibit hepatocellular cytoplasmic inclusion bodies and lower serum alanine aminotransferase activities.

Numerous studies demonstrate that 2,3,7,8-TCDD is fetotoxic and teratogenic in rodents, with effects commonly observed at doses that are not overtly toxic to the mother. In rats, symptoms of fetotoxicity (decreased growth, hemorrhage, edema, and death of the fetus) are more sensitive indicators of toxicity than those of teratogenicity (cleft palate). For example, administration of a single oral dose of 2,3,7,8-TCDD (1.5 $\mu g \cdot kg^{-1}$ bw) to pregnant rats on gestation day 10 results in significant gastrointestinal hemorrhaging in the fetuses within 10 d (Olson et al. 1990). Increases in the incidence of cleft palate (38% incidence) in fetal rats does not occur until dams are dosed 18 $\mu g \cdot kg^{-1}$ bw and is accompanied by high fetal mortality (72%) and significant decrease in maternal body weight. In contrast to rats, teratogenic endpoints are more sensitive in mice, resulting in the induction of cleft palate (ED_{50} of 15.6 $\mu g \cdot kg^{-1}$ bw) and hydronephrosis (ED_{50} of 3.9 $\mu g \cdot kg^{-1}$ bw) at doses below those causing overt maternal or fetal toxicity (no effects at 18 $\mu g \cdot kg^{-1}$ bw) (Birnbaum et al. 1987; 1989a). Nursing may pose greater risk of 2,3,7,8-TCDD toxicity to young rodents than perinatal exposure as high levels of non-metabolized 2,3,7,8-TCDD are excreted in milk (Lucier et al. 1975). Research on nursing is limited, but neonate rats weigh significantly less when their mothers are exposed to 5.0 $\mu g \cdot kg^{-1}$ bw (or 0.5 $mg \cdot kg^{-1}$ $bw \cdot d^{-1}$) over the first 10 d of lactation (Lans et al. 1990).

Two studies assessing the cumulative effects of dioxin-like compounds (PCDD/Fs and PCBs) on reproduction and development in mammals are available. In one study, mink were fed diets containing 0, 10, 20, or 40% contaminated carp from Lake Michigan prior to and throughout the reproductive period (26 weeks total). Mink consumed an average of 0.011, 0.013, 0.012, and 0.015 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ of PCDD/Fs, or 0.23, 3.89, 7.34, and 10.2 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$ of TEQ_{mam}, respectively (Heaton et al. 1995). Females fed the 40% carp diet whelped significantly fewer kits, and all kits were either stillborn or dead within 1 d. There was a significant inverse dose-dependent response between weights of kits and proportion of carp in the maternal diet. Percent survival to 6 weeks of age (weaning) were 85, 28, 11.5, and 0% for the 0, 10, 20, and 40% carp diets, respectively. Relative organ weights of kits whelped and nursed by treated females were generally less than those of the control group (Tillitt et al. 1996).

In the second study, Sprague-Dawley rats fed 0, 2, or 20% chinook salmon from Lakes Huron and Ontario experienced no significant correlations through three generations among TEQ dietary intakes (up to 2.84 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$; based on I-TEFs[1]) and mating, fertility, viability, or lactating indices, save larger litters that occur among rats fed 20% fish diets (Feeley and Jordon 1998; Arnold et al. 1998; Feeley et al. 1998). The only statistically significant effect was that female offspring of the first and second generations had larger relative liver weights compared to controls.

Several studies indicate that chronic dietary exposure to low levels of 2,3,7,8-TCDD may result in an increased incidence of tumors in mammals (Kociba et al. 1978; U.S. Department of Health and Human Services 1980, 1982). Rats appear more sensitive than mice, and males more sensitive than females, for both species. A working group of the WHO convened to establish a tolerable daily intake (TDI) for humans concluded that 2,3,7,8-TCDD is carcinogenic in animals (but that results are inconclusive for humans) (cited in Schlatter 1994). It is also argued that

[1] International TEFs (NATO/CCMS 1988).

2,3,7,8-TCDD is both a promoter blocker and a promoter, with a net effect of an anticarcinogen (Kayajanian 1997).

Avian Toxicity

The majority of toxicity studies conducted on birds employed 2,3,7,8-TCDD. Single LD_{50}s of 2,3,7,8-TCDD range from 15 to >810 $\mu g \cdot kg^{-1}$ bw for bobwhite quail *(Colinus virginianus)* and the ringed turtle dove *(Streptopelia risoria)*, respectively (Hudson et al. 1984). Mallard ducks *(Anas platyrhynchos)* are also relatively resistant to this substance, with an LD_{50} of >108 $\mu g \cdot kg^{-1}$ bw (Hudson et al. 1984). Leghorn chickens *(Gallus domesticus)* exposed to a single 2,3,7,8-TCDD dose of 25–50 $\mu g \cdot kg^{-1}$ bw died 12–21 d later, with some birds experiencing weight loss and pericardial edema (Greig et al. 1973).

Few data were available to assess the effects of chronic exposures to 2,3,7,8-TCDD in birds, although data suggest that effects are similar to those observed in mammals. Significant mortality (80%) and edema occur in juvenile leghorn chickens administered 1 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$ of 2,3,7,8-TCDD for a period of 21 d; at daily doses of 10 $\mu g \cdot kg^{-1}$ bw, 100% mortality occurred within 15 d. The NOAEL for survival or edema in this study is 0.1 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$ (Schwetz et al. 1973). In a similar study, McKinney et al. (1976) reported significant declines in food consumption and body weight (i.e., reduced growth rate) of leghorn chicks exposed to 1.0 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$ of 2,3,7,8-TCDF via gastric intubation for 21 d. One of the six treated birds died at day 19, whereas none of three control birds died. At a dose of 5.0 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$ of 2,3,7,8-TCDF, chicks consumed less food than controls and died after an average of 11.5 d. Marked subcutaneous edema, ascites, and hydropericardium occurred more severely at the higher dose than at the lower dose (McKinney et al. 1976). Reduced food consumption and increased mortality occur also in ring-necked pheasants administered 2,3,7,8-TCDD as weekly doses of 1 $\mu g \cdot kg^{-1}$ bw (~0.14 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$) for 7 weeks by intraperitoneal injection (Nosek et al. 1992).

Only one study examining the effects of maternally administered dioxin on reproduction in birds is available. Female ring-necked pheasants treated with weekly 2,3,7,8-TCDD doses of 1 $\mu g \cdot kg^{-1}$ bw for 7 weeks (~0.14 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$) experience delayed onset of mortality in 57% of birds and significant reduction in egg production; embryos from those eggs have a significantly higher cumulative percent mortality. Effects on fertility or eggshell thickness index are not significant (Nosek et al. 1992). Birds treated similarly with 0–0.1 $\mu g \cdot kg^{-1}$ bw of 2,3,7,8-TCDD (~0.014 $\mu g \cdot kg^{-1}$ bw$\cdot d^{-1}$) experience no significant adverse effects.

In great blue herons *(Ardea herodias)*, brain asymmetry is commonly associated with 2,3,7,8-TCDD levels in eggs above 0.06 $\mu g \cdot kg^{-1}$ ww, though effects occur as low as 0.013 $\mu g \cdot kg^{-1}$ ww (Henshel 1998). EC_{50}s for asymmetry in brain angle, depth, height, and width are 0.053, 0.044, 0.040, and 0.032 $\mu g \cdot kg^{-1}$ ww of 2,3,7,8-TCDD and 0.099, 0.079, 0.083, and 0.065 $\mu g \cdot kg^{-1}$ ww of TEQs (based on Safe 1990 TEFs), respectively (Henshel 1998). Chick edema disease, characterized by jelly-like subcutaneous edema on the breast, occurs in 33.3 and 15% of great blue heron chicks hatched from eggs collected from Crofton and Vancouver, British Columbia, respectively; no edema occurs in chicks from Nicomekl, British Columbia (reference site) (Hart et al. 1991). Mean 2,3,7,8-TCDD levels in eggs are 0.211, 0.135, and 0.010 $\mu g \cdot kg^{-1}$ ww from the Crofton, Vancouver, and Nicomekl colonies, respectively (Hart et al. 1991). Bald eagles *(Haliaeetus leucocephalus)* appear to be relatively tolerant of dioxin toxicity. No significant concentration-related morphological, physiological, or histological effects were found in bald eagle chicks collected as eggs from pulp mill and references sites along the southern coast of British Columbia (Elliott et al. 1996). Total TEQ_{bird} concentrations range from 7.596 $\mu g \cdot kg^{-1}$ lipid in egg yolks from West Vancouver Island to 25.627 $\mu g \cdot kg^{-1}$ lipid in those from the Powell River (percentage of lipid ~8.8–23%); PCDD/Fs account for 22-60% of the total TEQ_{bird}.

Reduced nesting success, hatching success, survival, and weight and increased relative liver weight and incubation period were reported for Forster's terns *(Sterna forsteri)* from Lake Michigan (Green Bay, Wisconsin) for 1983 (Kubiak et al. 1989). 2,3,7,8-TCDD, H_6CDD, total PCDD, and total PCDF concentrations at Green Bay are 0.037, 0.037, 0.102, and 0.019 $\mu g \cdot kg^{-1}$egg, ww, respectively, whereas those of the reference site, Lake Pygan, are 0.008, 0.030., 0.025, and 0.009 $\mu g \cdot kg^{-1}$egg, ww, respectively. Reproductive impairment occurs in wood ducks *(Aix sponsa)* collected downstream from a point source in Arkansas. Researchers estimated a threshold TEQ level of 0.02–0.05 $\mu g \cdot kg^{-1}$ ww in eggs (based on I-TEFs) for nest success, hatching success, and duckling production (White and Seginak 1994; White and Hoffman 1995).

In the Netherlands, residue levels of PCDD/F TEQs (based on I-TEFs) in the yolk sac of cormorants

(Phalacrocorax carbo) correlate with head size, relative liver weight, shell weight, and yolk sac weight (van den Berg et al. 1994). Levels of individual congeners range from approximately 0.050 to 2.4 $\mu g \cdot kg^{-1}$ lipid. Common terns *(Sterna hirundo)* appear to be less sensitive as neither egg, hatchling, nor organ weights of those from the Netherlands are related to concentrations of dioxin-like compounds. The TEQ-based NOAEL for embryonic development in the common tern is below 4 $\mu g \cdot kg^{-1}$ lipid (based on TEFs from Bosveld et al. 1993) (Bosveld and van den Berg 1994).

Tissue Residue Guideline Derivation

The PCDD/F TRG for the protection of wildlife that consume aquatic biota was developed according to the CCME protocol (CCME 1998).

Guideline Derivation for PCDD/Fs

To develop the PCDD/F TRG, concentrations of individual or mixtures of congeners in food were first converted to TEQs for acceptable toxicity studies. This conversion was done using 1998 WHO TEFs (van den Berg et al. 1998). These latest TEFs differentiate between mammalian and avian receptors (Table 2). PCDD/F congeners incorporated into the TEQ include the 17 congeners substituted with chlorine atoms in at least the 2,3,7, and 8 lateral positions.

From daily diet doses of PCDD/F-based TEQs, a TDI was calculated for each study as the geometric mean of the LOAEL and NOAEL. According to the protocol (CCME 1998), when the NOAEL is not determined, it may be estimated by dividing the LOAEL by 5.6. It appears that this relationship holds for PCDD/F data (Environment Canada 2000). For the purposes of deriving a national value, the mammalian and avian RCs must be as inclusive as possible to accommodate all species and regions in Canada. Therefore, they are based on the highest mammalian and avian ratios of food intake to body weight (FI:bw) known for Canadian wildlife, namely 0.24 for female mink and 0.94 for Wilson's storm petrel (CCME 1998). These RC values apply to freshwater, marine, and estuarine systems. It is recognized that use of the highest FI:bw ratio may not always be appropriate (e.g., in areas where Wilson's storm petrel is not found). For this reason, RCs for a suite of mammalian and avian receptors have been calculated (Environment Canada 2000).

Mammalian Reference Concentration

A TDI based on the TEQ_{mam} of 0.17 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$ for significantly reduced growth rates in male and female weanling guinea pigs (De Caprio et al. 1986) was selected as the starting point for deriving mammalian RCs. In this study, weanling guinea pigs were fed diets containing 0–26 $ng \cdot kg^{-1}$ of 2,3,7,8-TCDD for 90 d. There are no observable effects at 0.1 or 0.6 $ng \cdot kg^{-1}$ diet. At 4.9 $ng \cdot kg^{-1}$ diet, male and female guinea pigs experience a 39 and 22% reduction in growth rates, respectively, relative to controls. At 26 $ng \cdot kg^{-1}$ diet, guinea pigs lose weight and 60% die (De Caprio et al. 1986). On a TEQ_{mam} basis, the NOAEL and LOAEL are 0.6 and 4.9 $ng \cdot kg^{-1}$ diet, respectively, as the TEF value for 2,3,7,8-TCDD is 1 (van den Berg et al. 1998). The geometric mean of the LOAEL and the NOAEL divided by a safety factor of 10 gives a TDI-based TEQ_{mam} of 0.17 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$. A safety factor of 10 was chosen to adjust from a subchronic to a chronic study and to accommodate differences in interspecies sensitivities to PCDD/Fs. An RC of 0.71 ng TEQ·kg^{-1} diet ww was obtained by dividing the TDI for guinea pigs by the highest FI:bw ratio for wild mammals (0.24) (CCME 1998).

Avian Reference Concentration

Avian data are sufficient to meet the minimum data requirements for an interim guideline (CCME 1998). In a 21-d test, 1-d-old white leghorn chicks exposed to 2,3,7,8-TCDF by oral intubation at a TEQ_{bird} dose of 1 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ experience reduced survival, food consumption, and body weights (McKinney et al. 1976). Similar, but more pronounced effects, including 100% mortality, occur in those dosed 5.0 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ of TEQ_{bird} (McKinney et al. 1976). A NOAEL based on a TEQ_{bird} of 0.18 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ was calculated by dividing the LOAEL of 1 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$ by 5.6 because this LOAEL was also the lowest dose tested (CCME 1998). A TDI based on a TEQ_{bird} of 42.4 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$ for white leghorn chickens was derived by dividing the geometric mean of the LOAEL and NOAEL by a safety factor of 10. For ring-necked pheasants, a TEQ_{bird}-based NOAEL and LOAEL of 0.014 and 0.14 $\mu g \cdot kg^{-1}$ $bw \cdot d^{-1}$, respectively, were calculated for significantly reduced egg production and increased mortality of embryos (Nosek et al. 1992). In this study, ring-necked pheasants were dosed via intraperitoneal injection once a week with 0, 0.01, 0.1, or 1.0 $\mu g \cdot kg^{-1}$ of 2,3,7,8-TCDD for 7 weeks (Nosek et al. 1992). A TDI based on a TEQ_{bird} of 4.47 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$ for ring-necked pheasants was derived by dividing the

geometric mean of the LOAEL and NOAEL by a safety factor of 10.

For both the chicken and ring-necked pheasant studies, a safety factor of 10 was chosen to adjust from a subchronic to a chronic study and to accommodate differences in interspecies sensitivities to PCDD/Fs and exposure routes.

That the TDI based on the TEQ_{bird} (42.4 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$) for white leghorn chickens is higher than that for ring-necked pheasants (4.47 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$) is inconsistent with reports indicating that white leghorn chickens may be inherently 10 times more sensitive to 2,3,7,8-TCDD and 2,3,7,8-TCDF exposure than ring-necked pheasants based on ethoxyresorufin-*O*-deethylase–inducing potency (Kennedy et al. 1996). A probable explanation for this discrepancy is the use of different exposure routes (intubation vs. injection) and different sensitivities among measured endpoints (growth vs. egg production and embryo mortality).

Dividing the lowest TDI based on the TEQ_{bird} (4.47 $ng \cdot kg^{-1}$ $bw \cdot d^{-1}$) by the highest FI:bw for wild birds (0.94 for Wilson's storm petrel) resulted in an avian RC based on a TEQ_{bird} of 4.75 $ng \cdot kg^{-1}$ diet.

PCDD/F Tissue Residue Guideline

According to protocol, the lowest RC among mammalian and avian species is adopted as the TRG. In the case PCDD/Fs, however, the TEQ-based mammalian and avian RCs are calculated using different sets of TEFs: those for mammals and birds, respectively. Thus, a single TEQ-based TRG cannot be recommended. Therefore, the lowest RC among available mammalian species is that for female mink *(Mustela vison)*, 0.71 $ng \cdot kg^{-1}$ diet ww; this value is adopted as the mammalian TRG for PCDD/Fs. The lowest RC among avian species is that for Wilson's storm petrel *(Oceanites oceanicus)*, 4.75 $ng \cdot kg^{-1}$ diet ww; this value is adopted as the avian TRG for PCDD/Fs. Each guideline refers to the TEQ concentration due to PCDD/Fs measured in an aquatic organism on a wet weight basis that is not expected to result in adverse effects on wildlife. The TRGs apply to freshwater, marine, and estuarine environments. The mammalian guideline is full, whereas the avian guideline is interim as avian toxicity data are only sufficient to satisfy minimum requirements for an interim guideline (Environment Canada 2000). The assumption is that by capturing the toxicity of the 2,3,7,8-substituted congeners, the TRG will also be protective of the non-2,3,7,8-substituted congeners.

In environments where both PCBs and PCDDs and PCDFs contribute significantly to the TEQ concentration in aquatic prey items, the Canadian TRG for PCBs should also be considered. As TRGs for both PCDD/Fs and PCBs are TEQ-based, the lower PCDD/F mammalian TRG should take precedence as the total TEQ_{mam} concentration (i.e., PCDD/F and PCB TEQs combined) in aquatic biota to protect mammalian consumers, while the lower PCB avian TRG should take precedence as the total TEQ_{bird} concentration in aquatic biota to protect avian consumers (Environment Canada 1998, 2000).

TEQ Levels in the Canadian Environment

Levels of TEQ_{mam} for several Canadian species of freshwater fish and invertebrates range from less than detection to 112 $ng \cdot kg^{-1}$ ww, with 34% of values below the mammalian TRG expressed as the TEQ_{mam} of 0.71 $ng \cdot kg^{-1}$ diet ww. TEQ_{bird} levels range from less than detection to 657 $ng \cdot kg^{-1}$ diet ww, with 36% of values below the avian TRG expressed as the TEQ_{bird} of 4.75 $ng \cdot kg^{-1}$ ww. Similar results apply to marine organisms. Total TEQ levels incorporating PCDD/F and PCB concentrations were all above the mammalian and avian TRGs, with the exception of zooplankton from Lake Ontario and a few white suckers *(Catostomus commersoni)* from Lake Superior (Environment Canada 2000). All of these percentages are biased insofar as sampling efforts have focused on sites with a history of contamination or a known source of PCDD/Fs, and thus are expected to contain elevated levels of TEQs. Where background or control sites are measured, 2,3,7,8-subsitituted PCDD/Fs are not usually detected, or if so, in such small amounts that the TEQ levels are below the guidelines.

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