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Toxicity reference values for mink exposed to 2,3,7,8-tetrachlodibenzo-*p*-dioxin (TCDD) equivalents (TEQs)

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Abstract

Dietary and tissue residue-based toxicity reference values (TRVs) were derived for mink from the published results of studies in which mink were exposed to polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), biphenyls (PCBs), or related compounds. Because the primary mechanism of toxic action at the least concentration for these compounds is related to activation of the aryl hydrocarbon receptor (AhR), TRVs were described on the basis of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) equivalents (TEQ). Each published study was critically reviewed for its usefulness in deriving a TRV based on the following criteria: (1) close relatedness of the test species to the wildlife receptor of concern (only mink studies were reviewed in this paper); (2) chronic duration of exposure which included sensitive life stages to evaluate potential developmental and reproductive effects; (3) measurement of ecologically relevant endpoints; (4) availability of congener-specific data to calculate TEQ concentrations; and (5) minimal impact of co-contaminants. Dietary TRVs for mink exposed to TEQ ranged from 12.1 to 56.6 ng TEQ/kg feed (wet weight) for the no observable adverse effect level (NOAEL) and from 50.4 to 242 ng TEQ/kg feed (wet weight) for the lowest observable adverse effect level (LOAEL). TRVs based on tissue residue concentrations ranged from 50.2 to 77.8 ng TEQ/kg liver (wet weight) for the no observable adverse effect concentration (NOAEC) and the value was 189 ng TEQ/kg liver (wet weight) for the lowest observable adverse effect concentration (LOAEC). Selection of a TRV should be based on studies of compounds that are most similar to those at a site of interest. In particular, it was determined that the effects of PCDFs could not be accurately predicted from the use of TEQ-based TRVs developed from studies of PCDDs or PCBs. Risk assessors should be aware that exceedance of these TRVs would not necessarily be expected to lead to ecologically relevant adverse effects because of the inherently conservative assumptions made in the TRV derivation process.

Keywords: Ecological risk assessment; Dioxin; PCDDs; PCDFs; PCBs; Furans

1. Introduction

Mink (*Mustela vison*) are an important, albeit seldom seen, species that can be at risk in aquatic ecosystems contaminated with persistent, bioaccumulative, and toxic (PBT) pollutants (Platonow and Karstad, 1973; Aulerich et al., 1974; Hornshaw et al., 1983; Kihlstrom et al., 1992; Hochstein et al., 1998; Brunstrom et al., 2001). Mink have been found to bioaccumulate specific congeners of PBT pollutants such as polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), biphenyls (PCBs), and related compounds based on field studies of wild mink (Haffner et al., 1998; Millsap et al., 2004; Martin et al., 2006a, b) and laboratory exposures of ranch mink (Ringer et al., 1972; Tillitt et al., 1996; Halbrook et al., 1999; Bursian et al., 2006a–c). In addition, mink have been found

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to be one of the most sensitive species to the toxic effects of these compounds (Heaton et al., 1995; Tillitt et al., 1996). It is for these reasons that mink are one of the most commonly selected receptors in ecological risk assessments (ERAs) for sites involving aquatic habitats with elevated concentrations of PCDDs, PCDFs, PCBs, and related compounds (USEPA, 1995, 2000, 2005a; Sample et al., 1996; GES/MDEQ, 2003). In order to effectively protect mink and have the best estimate of risk possible, it is important to reduce uncertainty regarding potential exposure by direct measurement of tissue residue concentrations in mink and their primary dietary items *and* to have a good understanding of toxicity thresholds.

From the early 1970s to the present, numerous toxicological studies have been conducted with mink (reviewed herein). However, many of these studies have been conducted with individual congeners, congener cocktails, various site-specific environmental mixtures (including some with potentially significant concentrations of co-contaminants), and conducted under different conditions, experimental designs, time periods, and with different endpoints. Because of these differences among studies, interpretation of individual studies and comparison among studies and derivation of appropriate toxicity reference values (TRVs) can be difficult. In addition, selection of the most appropriate study to form the basis of a TRV to assess risk at specific sites is not always straightforward. This is particularly true when using the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) equivalent (TEQ) approach to describe threshold concentrations for one class of compounds from another. Thus, the overall objective of this paper is to critically review and summarize available toxicological studies and provide guidance on the selection of the most appropriate and scientifically defensible TRVs for mink exposed to PCDDs, PCDFs, PCBs, and related compounds expressed as TEQ. While it is beyond the scope of this paper to provide a comprehensive review of all mink toxicity data for these compounds, the focus will be on those data that provide toxicological information for ecologically relevant endpoints in response to chronic, dietary exposures. The limitations of the various studies are also discussed. Finally, the predictive capacity of the calculated TRV values will be assessed by comparing them to those derived in other laboratory and field studies of mink exposed to aryl hydrocarbon receptor (AhR)-active compounds, either singly to the same compound or in mixtures.

1.1. PCDDS, PCDFs, PCBs, TEFs, TEQ, and relative potencies

Theoretically, there are 75, 135, and 209 possible congeners of PCDDs, PCDFs and PCBs, respectively (Erickson, 1997). These congeners vary in the number and position of chlorine substitutions. Despite their structural relatedness, each of these congeners has different physical–chemical properties that affect their fate, transport, and bioavailability in the environment (Erickson, 1997). In the environment, PCDD, PCDF, and PCB congeners are predominantly associated with particulate material, such as sediments, suspended material, and soils (Erickson, 1997). Of the PCDD, PCDF, and PCB congeners, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD), also referred to as TCDD, is considered to be the most potent and is the one most studied (Van den Berg et al., 1998, 2006). Observed effects of TCDD and related chemicals in wildlife and laboratory animals include biochemical adaptive changes such as enzyme induction, developmental deformities, reproductive failure, liver damage, wasting syndrome, and death (Giesy et al., 1994a; Blankenship and Giesy, 2002; Hilscherova et al., 2003). While there are a number of other structurally related polychlorinated, diaromatic compounds, in most situations the above-listed compounds account for most of the toxic potency of environmental mixtures (Giesy et al., 1994b; Blankenship et al., 2000).

Toxicity equivalency factors (TEFs) are used to allow assessment of the additive toxicity of PCDDs, PCDFs and similar compounds that act through a common mechanism of action when they occur in mixtures (Giesy et al., 1994b; Van den Berg et al., 1998, 2006; Blankenship et al., 2000). The critical mechanism of action which results in the least allowable exposure to a mixture of TCDD and related compounds at the cellular level is primarily mediated via the AhR (Giesy and Kannan, 1998; Kannan et al., 2000; Blankenship and Giesy, 2002). Because of this assumed similarity in the mechanism of action, concentrations of 17 PCDD and PCDF congeners substituted with chlorines at positions 2, 3, 7, and 8 (and a structurally related set of 12 PCB congeners) are often converted to TEQ using the 2005 World Health Organization (WHO) TEFs (Table 1, Van den Berg et al., 2006) (Eq. (1)). TEQ values reported herein were calculated using these 2005 TEF values. These calculated values may differ from those in the original studies because of different TEFs (such as 1998 TEFs; Van den Berg et al., 1998) formerly used in the calculation of TEQ. TEF values, such as those proposed by the WHO are not precise measures of relative potencies for PCDD, PCDF, and PCB congeners. Rather, they are consensus values that purposely overestimate the relative potency of congeners across a taxonomic class for the express purpose of risk assessment. TEF values are designed to be protective, rather than predictive of thresholds of effects. As such, they are uncertain and may vary among species, measurement endpoints, and relative proportions of chemicals in complex mixtures. Thus, relative potency factors (RPFs) from the scientific literature may be used in place of WHO TEFs in instances where related or same species data are available in order to reduce uncertainty (USEPA, 2003a). The TEFs are consensus values developed for use in risk assessments and are thus, intentional overestimates that provide a level of conservatism and safety, by resulting in overestimates of the relative potency of individual constituents in mixtures (Van den Berg et al.,