

DRAFT RSET ISSUE PAPER #5 – TEF Methods for Wildlife

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QUESTION/ISSUE: Summarize existing information and recommendations for use of Dioxin-like TEFs for assessing risks to humans and wildlife from exposure to PCBs, PCDDs, and PCDFs. Are TEFs for wildlife ready for prime time?

DISCUSSION: A procedure for assessing the toxicity to humans of a mixture of dioxins and furans has been developed. This method utilizes “toxicity equivalency factors” (TEFs) for adjusting the potency values of individual dioxin/furan isomers and PCB congeners relative to 2,3,7,8-TCDD and derives a “summed” 2,3,7,8-TCDD equivalent concentration of these compounds. These compounds comprise a class of chemicals that include several hundred compounds in closely related families; the chlorinated dibenzo-p-dioxins (CDDs), chlorinated dibenzofurans (CDFs), and certain polychlorinated biphenyls (PCBs).

For the SEF, depending on the need for analyzing for dioxins/furans, the TEF methodology can be used for analytical data for these compounds collected in either bulk sediment or fish tissue to estimate exposure. The SEF will only recommend PCB Congener analysis for fish tissue and the discussion of PCB Congener TEFs are limited to this application.

Central to the use of the TEF methodology is that all the compounds that are summed to derive the 2,3,7,8-TCDD Equivalence must have the same mechanism of toxicity. For PCBs, dioxins, and furans, the common toxic mechanism of action is that all these compounds require the presence of a cytosolic aryl hydrocarbon receptor (Ah-R). All these compounds act as ligands to the Ah-R and this binding to the Ah-R is a necessary first step in initiating any dioxin-like toxic effects. Also central to the TEF approach is the concept of additivity. Not only does there need to be a clear understanding of the relative potencies of individual isomers/congeners relative to 2,3,7,8-TCDD, but it **MUST** be assumed that they all work through an additive model of toxicity to exert their dioxin-like effects (i.e., all toxicity is Ah-R mediated).

For human health, the TEFs that have been developed by the World Health Organization are currently being used to assess human health impacts from exposure to “dioxin-like” compounds (EPA, 1994). These TEFs currently are available for CDD and CDF isomers.

For wildlife, EPA has reviewed the use of TEFs and has proposed a draft set of TEFs for mammals, birds, and fish that include TEFs for CDDs, CDFs, and twelve dioxin-like PCB congeners (EPA, 1993 and EPA, 2003). The greatest challenge in the evaluating whether these TEFs are scientifically justified for use are the uncertainty associated with the derivation of these TEFs relative to the uncertainty associated with other aspects of the ecological risk assessment process (EPA, 2003).

It should be noted that the relative sensitivity to dioxin-like toxicity among species that possess the Ah-R varies greatly, even within taxonomic class (Eisler, 2000). For example, the sensitivity of bird species tested to date to TCDD-induced embryo mortality varies by about 200-fold, with domestic chickens generally more sensitive than wildlife species (EPA, 2003). Similar differences have been observed amongst mammals and fish. Therefore, there are relative potency issues within a particular species and inter-species differences in sensitivity to dioxin like toxicity.

The relative sensitivity of animal classes is not constant across chemical class either. For example, while fish are generally more sensitive to PCDDs and PCDFs relative to birds and mammals, they are much less sensitive to mono-ortho-substituted PCBs (EPA, 2003). Amphibians, reptiles, and primitive fish are relatively insensitive to dioxin-like chemicals. Although Ah-R homologs have been identified in amphibians and primitive fish, their toxicological significance is unknown. It has also been demonstrated that a wide variety of invertebrates including amphipods, cladocerans, midges, mosquito larvae, sandworms, oligochaete worms, snails, clams, and grass shrimp are insensitive to 2,3,7,8-TCDD induced toxicity (EPA, 2003).

Therefore, the application of TEFs for wildlife species presents additional complexities that were not encountered in the development of TEFs for a single species (Humans). In addition, the two fundamental assumptions in the use of TEFs have not been verified as being true for all wildlife species being considered; the assumption that all toxicity associated with the CDD, CDF, and PCBs are related to Ah-R interactions (there is some evidence of reproductive and other toxic endpoints that may be derived from other toxic mechanisms); and the assumption that the individual potencies of isomers/congeners are additive.

The potential development of appropriate TEFs for wildlife is an exciting opportunity for addressing potential risks from this complex class of persistent compounds. Additional data in the form of laboratory and field verification of some of the assumptions in the proposed EPA methodology over the next few years should help RSET assess the technical defensibility of this approach and whether it is ready for recommendation for use in the Pacific Northwest.

REFERENCES:

Eisler, R., 2000. Handbook of Chemical Risk Assessment: Health Hazards to Humans, Plants, and Animals. Volume 2; Organics. Lewis publishers.

EPA, 1987. Interim Procedures for estimating Risks Associated with Exposures to Mixtures of Chlorinated Dibenzo-*p*-dioxins and -dibenzofurans (CDDs and CDFs). Risk Assessment Forum. EPA/625/3-87/012 March 1987.

EPA, 1993. Interim Report on Data and Methods for Assessment of 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin Risks to Aquatic Life and Associated Wildlife. Office of Research and Development. EPA/600/R-93/055. March 1993.

EPA, 1994. Estimating Exposure to Dioxin-Like Compounds: Volume I: Executive Summary. Office of Research and Development. EPA/600/6-88/005Ca.

EPA, 2003. Framework for Application of the Toxicity Equivalence Methodology for Polychlorinated Dioxins, Furans, and Biphenyls in Ecological Risk assessment. External Review Draft. EPA/630/P-03/002A. June 2003.

Tillit, D.E., 1999. The Toxic Equivalents Approach for Fish and Wildlife. Human and Ecological Risk Assessment: Vol. 5 (1). Pp. 25-32.

RECOMMENDATION: Use of TEFs for assessing human health risks from CDDs and CDFs that interact with the cytosolic aryl hydrocarbon receptor (Ah-R) are well established and accepted. The EPA draft wildlife TEFs have only been recently developed and there are still considerable uncertainties in their application in ecological risk assessments. RSET can possibly present these approaches in an appendix with a discussion of uncertainties but wildlife TEFs are still a few years from being ready for general use. Additional field and laboratory validation studies need to be completed to ensure that the assumptions inherent in the Wildlife TEFs are acceptable and correct.

PROPOSED LANGUAGE: For risk assessment purposes, the use of TEFs for addressing human health impacts from exposure to “dioxin-like” compounds is relatively well established and have been approved by EPA as well as international organizations (e.g., World Health Organization). Recently, there have been attempts to develop similar TEFs for addressing ecological risks and draft TEFs for CDDs, CDFs, and twelve PCB congeners have been developed for mammals, birds, and fish (EPA, 2003). These are still draft values and with the uncertainty in the underlying toxicological principles for their use, it is recommended that they not be adopted by RSET at this time. These TEFs can be used a part of a weight-of-evidence approach for estimating ecological risk but should not be relied upon alone to make ecological risk decisions. There should be more information coming out with the review of this draft EPA document that may help address the uncertainties and provide a more technically defensible methodology for addressing ecological risks from these compounds. Additional field and laboratory validation studies need to be completed to ensure that the assumptions inherent in the Wildlife TEFs are acceptable and correct.

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