Research to Characterize Ecological Risks Associated with 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Related Chemicals in Aquatic Ecosystems

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In addition to establishing a research program for the reassessment of human health risks associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and other polyhalogenated aromatic hydrocarbons (PHAH) that are toxicologically-related through an Ah receptor mediated mode of action, the Office of Research and Development of the U.S. EPA has initiated research to characterize the ecological risks associated with these chemicals in aquatic environments. This research is intended to improve the state of scientific knowledge concerning TCDD toxicity to aquatic organisms and the wildlife species that prey on them and also to provide a basis for the derivation in 1993 of an EPA water quality criterion based on the effects of TCDD on aquatic organisms. As Figure 1 illustrates, these two objectives are quite compatible. Risk assessments for anthropogenic chemicals normally evaluate the impact of chemical loadings on a specific ecosystem (chemical source to exposure media to organism to population to community). Water and sediment quality criteria start with general ecological community protection objectives and proceed (community to population to organism to exposure media to source), through application of the criteria, to the determination of safe chemical loadings. Thus both ecological risk assessments and EPA water and sediment quality criteria for toxic, lipophilic organic chemicals utilize information on exposure, bioaccumulation, and toxicity hazards to protect aquatic populations and associated community structure.

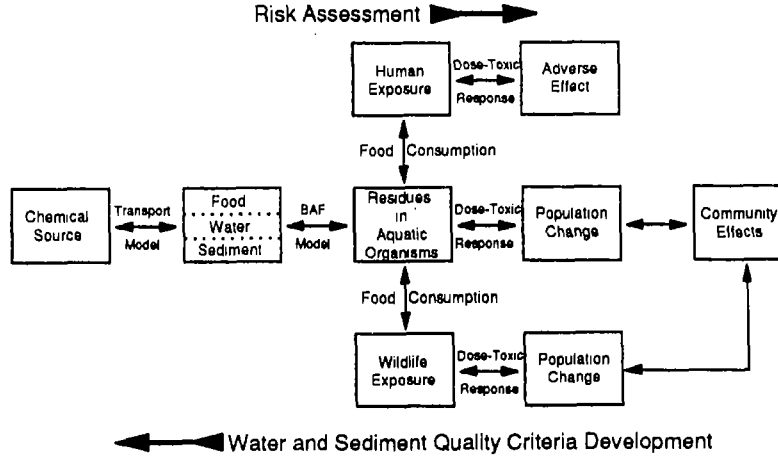

Figure 1. Components of risk assessments for lipophilic chemicals in aquatic ecosystems

Aquatic sediments and food chains are important components of the environmental distribution of PHAHs because of the persistence and hydrophobicity of these chemicals. The dioxin aquatic risk research in progress provides an important link to wildlife and human health risk assessments through the development of bioaccumulation factors for predicting residues of these chemicals in the tissues of aquatic organisms consumed as food by wildlife and humans. Bioaccumulation factors and physiologically-based kinetic models are needed in order to most effectively determine the concentrations of TCDD and related chemicals in sensitive tissues of fish and wildlife that cause toxic effects. Aquatic TCDD toxicity hazard assessment is complicated by the wide range of species exposed, a wide range of sensitivity among these species, complex exposure routes, multiple toxic effects and complex mixtures of chemicals that can exert biological effects through interaction with the Ah receptor.

Thus, three goals for determining toxicity hazards associated with TCDD and related chemicals in aquatic systems are: (1) Identify the most sensitive toxic effects of TCDD that are likely to result in population declines for organisms in aquatic food webs; (2) Provide dose-toxic effects data that are suitable for the development of water quality and sediment quality criteria for TCDD; and (3) Develop and validate dioxin toxicity equivalence factors (TEFs) for TCDD mode-of-action chemicals that are bioaccumulated by fish.

Table 1. Relative lethal doses for 2,3,7,8-TCDD: mammals and fish

Mammals[2]	LD_{50}(g/kg)	Fish	LR_{50}: 50% Lethality Accumulated Residue (g/kg)
Hamster	5000		
Dog	>300		
Mouse	114		
Rabbit	115		
Monkey	<70		
Rat (female)	45		
Rat (male)	22	Fathead minnow[1]	>10
		Medaka[3]	2-4
		Carp[1]	2-3
		Rainbow trout fry[4]	1
Guinea Pig	1	Rainbow trout sac fry[6]	0.35
		Lake trout sac fry[5]	0.06

Aquatic Toxicity Investigations

The EPA aquatic toxicity testing program for TCDD started in the fall of 1991 with the knowledge that fish are very sensitive[1]. Table 1 compares the lethality of TCDD to fish (on a tissue residue basis; LR_{50}) to mammals (on a total dose basis; LD_{50}). The most sensitive species and life stage known is lake trout (Salvelinus namaycush) sac fry[5] for which a no observable effect residue in embryos is approximately 30 pg TCDD/g wet tissue. Exposure of female lake trout has now been shown, through maternal transfer of TCDD to oocytes, to result in the same egg residue-response relationship[7]. Aquatic invertebrates, on the other hand, appear to not possess an Ah receptor[8] and thus should be much less sensitive to TCDD and related chemicals than fish. This is consistent with limited testing of invertebrates reported to date[9,10].

Features of TCDD toxicology to be considered in designing an aquatic toxicity testing plan suitable for risk characterization and criteria development are: slow uptake and elimination kinetics; delayed mortality following short term exposures regardless of dose; importance of the food route of exposure; influence of dissolved and particulate organic carbon on chemical bioavailability from water; suspected insensitivity of invertebrates; and the possibility that developmental endpoints may be more sensitive than early life stage mortality. Three fish species were chosen for reproductive effects testing involving TCDD exposure of males and females prior to spawning; brook trout (Salvelinus fontinalis) to be exposed through diet, medaka (Oryzias latipes) to be exposed through water and mummichog (Fundulus heteroclitus), a saltwater species to be exposed through diet at EPA's Research Laboratory at Narragansett, Rhode Island. Additional freshwater fish species may be tested via egg exposures. TCDD toxicity testing with invertebrates (a snail, a benthic crustacean, two insects, a worm and a planktonic crustacean) will involve 96 hour exposures via water to achieve the greatest whole body residue possible (> 10 ng/g). If no toxic effects are elicited after 30 days (or through emergence), full reproductive effects testing will be unnecessary for aquatic invertebrates as fish will have been demonstrated to be 10-1000 times more sensitive.

The exposures planned for fish will be the first investigations of the total potential for TCDD-induced reproductive failure. Previous studies have not examined reproductive effects due to male exposure; the influence of TCDD on gonadotropin hormone levels and consequent effects on vitellogenesis, ovulation, spermatogenesis, spermiogenesis or spawning success; or the relative TCDD residue distribution to the gonads over the time period for these events. Tissue residues associated with adverse effects will be the primary exposure index for characterizing TCDD toxicity associated with environmental exposures. The choice of toxicological endpoints for study of other Ah receptor active PHAHs will depend heavily on the results of these toxicity tests.

Aquatic Exposure and Toxicity Hazard Assessment for Complex Mixtures of TCDD Mode of Action Chemicals

TCDD, other 2,3,7,8-chlorinated dibenzo-p-dioxins, dibenzofurans and co-planar PCBs all have been shown through water and injection exposure of rainbow trout eggs to

produce early life stage lethality prior to swim-up, characterized by an edematous syndrome identical to blue-sac disease[6]. TCDD toxicity equivalency factors (TEFs) calculated on the basis of these whole organism response data[11] indicate that the relative PCB contribution to TCDD toxicity-associated impairment of fish reproduction is 10-100 fold less than predicted on the basis of TEFs derived from mammalian models[12].

TCDD TEFs of potentially Ah-active PHAH congeners will be measured with the fertilized trout egg injection exposure model of Walker and Peterson[6]. If more sensitive fish reproductive effects occur as a result of parental exposure, medaka exposures to individual congeners will be employed to determine TEFs on a multi-endpoint basis. The TCDD toxic equivalence additivity hypothesis will be tested with binary mixtures of congeners using trout egg and possibly medaka exposures. Validation of the resulting TCDD toxicity equivalence concentration (TEC) model will involve exposure of trout eggs and prespawning adult brook trout to complex, environmentally relevant mixtures of PHAHs. This validation will include additional comparisons of laboratory test results to observations from field monitoring[13] and epidemiological[14] investigations. Bioaccumulation factors and physiologically-based kinetic models for tissue distribution of bioaccumulative PHAHs will be further developed in order to relate tissue residues of these chemicals associated with TCDD toxic effects to hazardous environmental exposure levels in water, sediment or food.

Aquatic Environment TCDD Ecological Risk Characterization Reports

The primary goal of these studies is to integrate information concerning the exposure of aquatic organisms to TCDD and related PHAHs with toxicity hazard information in order to characterize ecological risks. A draft interim aquatic ecological risk characterization report for TCDD was completed in May, 1992. This report, after undergoing peer review, will provide EPA with the present state of knowledge and will establish a framework for an expanded final aquatic ecological risk characterization report to be completed in September, 1993. The final report will be the scientific basis for an aquatic effects based water quality criterion. The report will incorporate results of the new toxicity tests and an assessment of risks associated with exposures to complex PHAH mixtures. Both reports will have chapters on exposure and bioaccumulation, toxicity hazards including epidemiological data, and the ecological risk characterization.

EPA is not presently conducting additional tests on toxic effects of TCDD to wildlife. An analysis of risks to fish eating mammals and birds based on information from the literature and the proposed procedure for deriving criteria for the protection of wildlife in EPA's Great Lakes Water Quality Initiative (GLWQI), which included TCDD as a chemical of concern, will be included in the TCDD ecological risk characterization reports. The GLWQI interim TCDD wildlife values, expressed as the greatest water concentrations that would not cause significant reduction in growth, reproduction or viability of species recognized to have large exposures through aquatic food chains, are shown in Table 2.

Because of the magnitude of fish eating wildlife species' exposures to TCDD and other PHAHs and their estimated sensitivity for toxic effects, the estimated safe water concentrations are similar to the past 10^{-6} human cancer risk-derived water quality criterion.

Similar numbers may be required for protection of trout populations. As both human health and ecological risk characterizations near completion during the next year, risk managers will likely be concerned with how to incorporate such diverse information into environmental protection decisions.

Table 2. GLWQI calculations for proposed safe water concentrations of TCDD for great lakes wildlife compared to the existing EPA 10^{-6} human cancer risk based water quality criterion (WQC).

$$\text{Wildlife value (WV)} = \frac{\text{NOAEL} \times UF_s \times M}{F \times BAF}$$

NOAEL = Mammalian or avian no observable adverse reproductive effect level
UF_s = Interspecies uncertainty factor = 0.1
M = Mass of animal
F = Feeding rate
BAF = Bioaccumulation factor for food (fish) = 90,000

Species	NOAEL (g/kg/d)	F (kg/d)	M (kg)	WV (pg/l)
Mink	0.001	0.1500	1.00	0.0074
Otter	0.001	0.9000	8.00	0.0099
Kingfisher	0.014	0.0750	0.15	0.0310
Osprey	0.014	0.3000	1.50	0.0780
Eagle	0.014	0.5000	4.50	0.1400
Man	10^{-6} cancer risk (WQC)	0.0065	70.00	0.0130

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