HEALTH IMPLICATIONS OF TCDD AND TCDF CONCENTRATIONS REPORTED FROM LAKE ROOSEVELT SPORT FISH

A report prepared by
Environmental Health Programs
Washington State Department of Health

APRIL 1991

Washington State Department of Health

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April 11, 1991

TO: Interested Persons

FROM: Kristine Gebbie
Secretary
Department of Health

SUBJECT: Department of Health Report--Health Implications of TCDD and TCDF Concentrations Reported From Lake Roosevelt Sport Fish

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The Department of Health has prepared a report that addresses health implications associated with consumption of sport fish contaminated with polychlorinated dibenzo-dioxins and furans in Lake Roosevelt and Rufus Lake. This report analyses data from a comprehensive sampling and analysis of Lake Roosevelt sport fish conducted by Department of Ecology between May and October 1990. Last August, based on preliminary information, the Department of Health (DOH) issued an advisory suggesting that young children should not eat lake whitefish from Lake Roosevelt. This interim advisory was issued in order to be protective of public health pending completion of Ecology's study and thorough review and analysis of the data.

In order to estimate possible health risks, a thorough review was made of the recent literature,including studies of dioxin exposed workers, animal experiments and other laboratory investigations. Because evidence has been insufficient for scientific consensus about human risk, DOH has chosen to establish policy intended to provide an extra margin of safety and confidence.

Now that final results are available, DOH is more confident about exposure levels and can comfortably recommend a more modest set of protective measures than the advisory issued last August. The advice now is that children or adults may eat fish, but in order to reduce exposure the following steps may be taken:

- Remove fat and skin from fish before eating.
- Allow fat to drip off during cooking.
- Use smaller and younger fish, which are less contaminated.
- Reduce the size of the portions consumed.
- Reduce the number of fish meals consumed per month.

It is further recommended that the Department of Ecology continue to monitor contamination levels in the lake and that all involved agencies evaluate and incorporate new relevant scientific data as appropriate.

ABSTRACT

Washington State Department of Health has analyzed information on 2,3,7,8-tetrachlorodibenzodioxin- and 2,3,7,8-tetrachloro dibenzofuran (TCDD and TCDF)-contaminated sport fish from Lake Roosevelt and Lake Rufus Woods in order to address human health effects. Two hundred and fifty-three fish, including walleye,rainbow trout, white sturgeon and lake whitefish, caught at several sites in the two lakes, were analyzed for these contaminants by Washington State Department of Ecology. Through evaluation of the recent scientific literature, which includes end-point specific experiments, as well as mechanistic studies, DOH has identified a range of values within which there is insufficient evidence to conclude that adverse effects occur. The lower limit of the range is a level below which no biological effects occur. The upper limit does not establish an adverse effect level, but indicates the limit for which there is insufficient evidence that adverse effect occurs. The biological response level, converted to human dose, was then applied in a paradigm using fish concentrations, together with exposure parameters, to determine an exposure dose for humans from consumed fish. Exposure parameters used were those for subsistence fishermen, who derive most of their dietary protein from fish, with appropriate meal frequency and portion size assumptions for such a group, including separate dose calculations for men, women and infants. The most exposed population in this group is the infant since for a given ingested concentration of contaminant, he gets a larger dose. If this most exposed population, as well as the most sensitive, is protected, all other populations, such as sport fishermen, and adult subsistence fishermen are also protected.

Results of the health analysis show that toxic equivalents of TCDD and TCDF in sport fish from Lake Roosevelt and Lake Rufus Woods do not constitute levels for restricting consumption in infants, nor in any other population exposed to these levels at the fish consumption amounts used. The previous cautionary advisory, based on preliminary analysis, is no longer necessary as a result of this new analysis. The levels of dioxin in these sport fish are still cause for concern because other sources of these contaminants contribute to human body contamination, and if concentrations in fish were to increase, resulting doses could have human health consequences. Also, ecological effects may be occurring at contaminant levels presently found, and these ecosystem effects have not been addressed.

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INTRODUCTION

Lake Roosevelt is located in the northeast corner of Washington State and is part of the Columbia River, (see Figure 1). Formed by Grand Coulee Dam in 1941, Lake Roosevelt extends approximately 150 miles, at full-pool, nearly reaching the Canadian border. The lake and shoreline comprise the Coulee Dam National Recreation Area, which was visited by more than 1.5 million people in 1990.

The Celgar pulp mill, located in Castlegar, British Columbia, thirty miles upstream of Lake Roosevelt, is the primary source of polychlorinated dibenzo-dioxins (PCDD) and -furans (PCDF) detected in Lake Roosevelt. In operation since the early 1960s, the Celgar pulp mill employs the bleached kraft process, discharging approximately 26 million gallons of untreated effluent into the Columbia River each day.

Contamination of lake whitefish, below the Celgar mill, was initially identified by Environment Canada during the spring of 1988 (Mah et al., 1989). 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) were detected in sufficiently elevated concentrations, relative to the Canadian standard, that a health advisory was issued recommending that consumption of lake whitefish within 7 kilometers downstream of the mill be limited to no more than 40 grams per week (Kirkpatrick, 1989). A subsequent investigation in November 1989, by the B.C. Ministry of Environment, resulted in a similar health advisory for mountain whitefish (B.C. Ministry of Environment, 1990).

In response to the Canadian findings of PCDD and PCDF in whitefish below the Celgar mill, the Washington State Department of Ecology (Ecology) conducted a preliminary survey in upper Lake Roosevelt during the summer of 1989 (Johnson, 1990). Muscle tissue samples from two walleye and from two white sturgeon were collected and analyzed. The results indicated the presence of elevated levels of PCDDs and PCDFs. Due to small sample size and the range of concentrations, the results were considered inconclusive.

In May 1990, Ecology initiated a comprehensive sampling and analysis plan to determine the extent and degree of PCDD and PCDF contamination of Lake Roosevelt sport fish. Major sport fish species from popular fishing locations were collected and analyzed to determine the mean concentrations of TCDD and TCDF in edible muscle tissue. One composite sample each of liver and eggs was collected from lake whitefish. Fish tissue samples were also collected from Rufus Woods Lake, the reservoir below Grand Coulee Dam. The Washington State Department of Health (DOH) issued a limited health advisory for Lake Roosevelt whitefish in August, 1990. Based on preliminary results, children under four years old, or weighing less than 40 pounds, were advised not to eat whitefish from Lake Roosevelt (Gebbie, 1990). On January 20, 1991, the final data set from the analysis of Lake Roosevelt sport fish was received from Ecology. The Office of Toxic Substances (OTS) reviewed the fish tissue data and conducted a comprehensive review of existing PCDD and PCDF scientific literature. This report addresses the human health implications associated with the consumption of TCDD and TCDF contaminated sport fish species from Lake Roosevelt and Rufus Woods Lake.

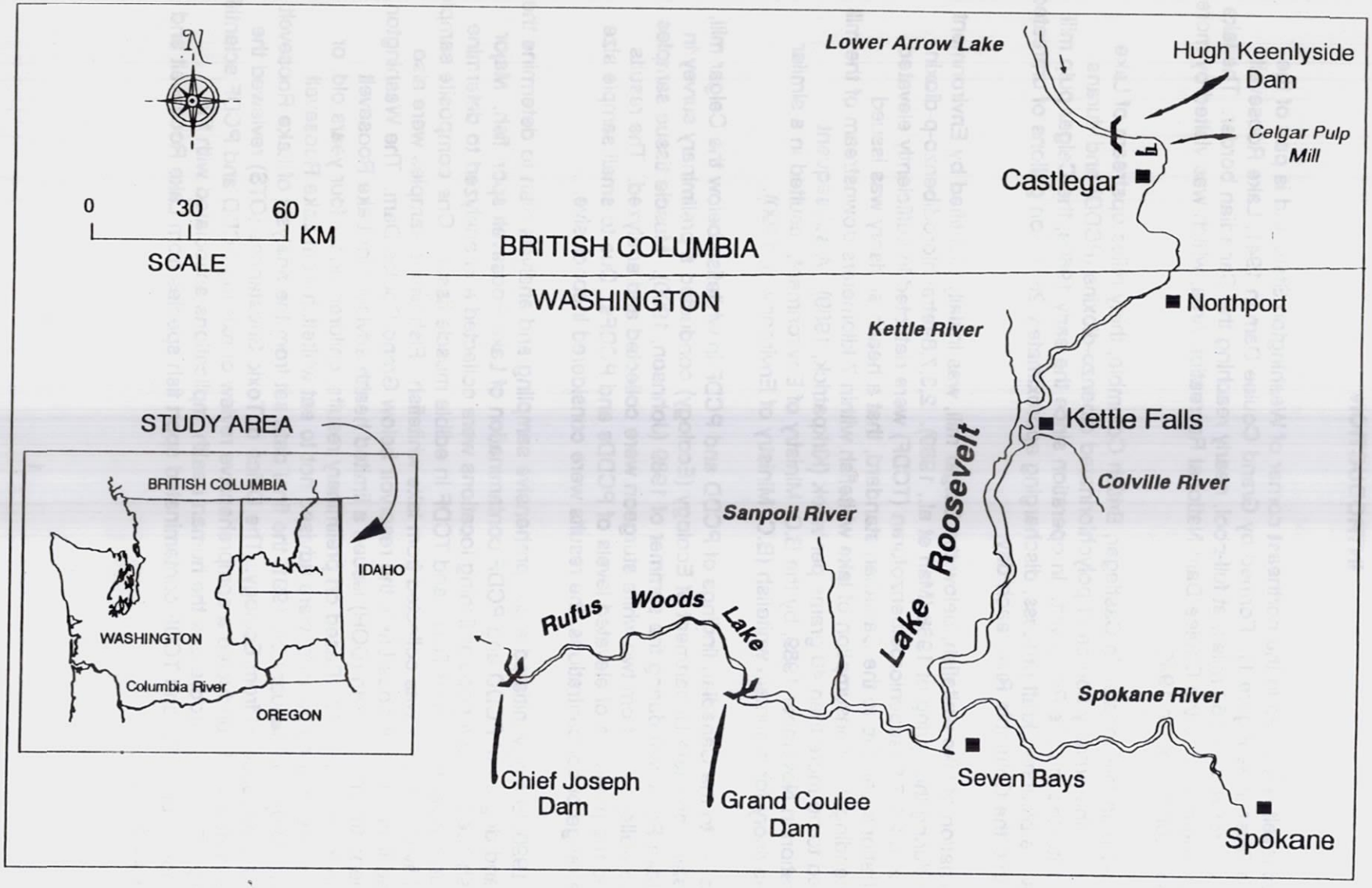

Figure 1. Study Area for Ecology 1990 Survey of PCDDs and PCDFs in Lake Roosevelt Sportfish

BACKGROUND ON PCDD AND PCDF

Polychlorinated dibenzo-p-dioxins and -furans are groups of synthetic compounds commonly referred to as dioxins and furans. Seventy-five possible congeners are possible for the dibenzo-p-dioxin structure. The one congener with chlorine atoms located at the 2, 3, 7 and 8 position, 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD or TCDD), is the most toxic of all possible congeners. PCDFs are similar to the PCDDs in structure, yet are less toxic than the TCDD molecule. The toxicity of individual PCDD and PCDF congeners are described relative to the toxicity of the TCDD molecule in terms of a toxicity equivalency factor (TEF). The TCDF molecule has a TEF of 0.1, which means that it is estimated to be 1/10th as toxic as TCDD (Barnes et al., 1989). TEFs are then added together to derive the TCDD toxicity equivalent (TEQ).

PCDDs and PCDFs are produced inadvertently as impurities in a variety of industrial processes and everyday activities. Major sources include the production of chlorophenol herbicides, the incineration of municipal and industrial wastes, fires involving polychlorinated biphenyls (PCBs), and paper production employing chlorine bleached pulp. Minor sources include motor vehicle exhaust, forest fires and residential wood burning (EPA, 1987, 1988; ATSDR, 1989).

In the environment, PCDDs and PCDFs are always found as mixtures and are minimally soluble in water. TCDD is soluble to 19.3 ± 3.7 ng/L (ppt) at 22 °C (Marple et al., 1986). When PCDDs and PCDFs are discharged to aquatic environments, their primary fate is sorbtion to particles and subsequent deposition in sediments. The ultimate environmental sink of airborne particulate PCDDs and PCDFs is also likely to be the sediments of surface and marine waters (Miller et al., 1987; Podoll et al., 1986). In lake sediments, the half-life of TCDD has been estimated to be greater than 1.5 years (ATSDR, 1989), and may be ten years or more (Eisler, 1986).

PCDD AND PCDF EXPOSURE

PCDDs and PCDFs are ubiquitous, and have been measured in virtually every aspect of the environment, including soil, air and food. Beef and dairy cattle accumulate PCDDs and PCDFs from their diet and from the ingestion of contaminated soils. This is the major route of uptake for cattle (USEPA, 1988). Jensen et al., (1981) reported a beef fat to diet ratio of 4:1 and a cream butter fat to diet ratio of 1.6 - 2.2:1. Fish selectively bioaccumulate PCDDs and PCDFs substituted at the 2,3,7 and 8 positions (Rappe et al., 1981; Kuehl et al., 1985, 1987a, b). Some fish species even demonstrate a preferential affinity for 2,3,7,8-TCDD (Kuehl et al., 1987b). The concentrations of PCDDs and PCDFs in fish varies with species, lipid content, weight, surface area-to-weight ratio, feeding habits, food intake rate, density of suspended particulate matter, sediment organic carbon concentration, and PCDD and PCDF concentrations in the sediment. These findings clearly indicate that PCDDs and PCDFs bioaccumulate in food chains, and that ingestion of contaminated organisms is a route of exposure for human beings.

The estimated average daily nonoccupational human intake of PCDDs and PCDFs in the United States from air, water, and food ranges from 0.04 to 0.51 picograms per kilogram of

body weight per day (pg/kg/day) and the upper bound estimate of 2,3,7,8-TCDD in human adipose tissue is estimated to be 6.7 parts per trillion (EPA, 1988). Food, particularly fish, milk, and beef, is the major source of nonoccupational human exposure to PCDDs and PCDFs. Because these chemicals accumulate in the body, the dose from all sources is additive. Since there are no known beneficial health effects associated with PCDDs and PCDFs, it is prudent to minimize exposure.

TISSUE SAMPLING AND ANALYTICAL RESULTS

Between May and October, 1990, comprehensive sampling and analysis of Lake Roosevelt sport fish was conducted by Ecology. Sampling focused on four species - walleye (*Stizostedion vitreum*), rainbow trout (*Oncorhyncus mykiss*), white sturgeon (*Acipenser transmontanus*), and lake whitefish (*Coregonus clupeaformis*). A limited number of kokanee (*Oncorhyncus nerka*) and burbot (*Lota lota*) were also collected. The species selected reflect the sports catch from Lake Roosevelt, with walleye and rainbow trout being the most popular species (Peone et al., 1991). A total of 253 fish were analyzed during the course of this survey.

Fish were collected by electroshocking, gill net and hook-and-line methods. Individual fish samples were generally within the legal size limit, with the exception of walleye. Of the 70 individual walleye caught, 53 percent were between 16 and 20 inches in length, which represents an illegal catch for Lake Roosevelt. These fish were estimated to be three to four years old and representative of TCDD/TCDF contamination in consumed walleye (Johnson et al., 1991).

A total of 51 composite fish tissue samples were collected. Each composite sample, except for burbot, consisted of muscle tissue from five individual fish; only four burbot were collected for each composite. Ideally, six composites for each species from both upper and lower Lake Roosevelt were desired; due to a lack of species availability, only five composite samples were collected.

A skinless rectangular piece of muscle of approximately 40 grams was excised from above the lateral line and forward of the dorsal fin on each fish. Excess fat was removed from the sturgeon samples. In addition, one sample each of liver and egg tissue was composited from each of three lake whitefish.

Standardized sample handling procedures were followed prior to analysis (Johnson et al., 1991). Tissue samples were submitted to Triangle Laboratories, Inc., Research Triangle Park, North Carolina for homogenation and chemical analysis for TCDD, TCDF, and percent lipids. Select samples were analyzed for PCDDs and PCDFs substituted at the 2,3,7,8 and other positions. All analytical data were reviewed for qualitative and quantitative accuracy by an independent consultant (Johnson et al., 1991).

A summary of the TCDD and TCDF analysis of muscle tissue from fish caught in Lake Roosevelt, and Rufus Woods Lake is contained in Table 1 and 2 respectively. Data from the analysis of liver and egg tissue are contained in Table 3. Yet, due to an insufficient number of samples, representative concentrations of TCDD and TCDF in liver and egg tissue could not

Table 1. TCDD and TCDF Concentrations in Muscle Tissue of Lake Roosevelt Sportfish Species Collected May - October, 1990 and Background Concentrations From Lake Wenatchee (Composites Consist of five fish each)

Sample Location	Fish Species	# Comp.	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)
Upper Lake Roosevelt					
Kettle Falls	Walleye	6	ND	3	0.5
	L. Whitefish	6	1.9	126	15
Kettle Falls/ Northport	Rainbow Trout	6	1.2	38	5.1
Kettle Falls/ Gifford	Burbot #	2	ND	2.8	0.3
Marcus Island	W. Sturgeon	4	2.4	147	17
Lower Lake Roosevelt					
Seven Bays	Walleye	6	ND	2	0.4
	L. Whitefish	6	1.7	145	16
Seven Bays/ Sanpoil	Rainbow Trout	6	ND	12	1.6
Spring Canyon/ Seven Bays	Kokanee	2	0.8	53	0.6
Lake Wenatchee					
	Mt. Whitefish	3	ND	0.3	0.1

TEQ - 2,3,7,8-TCDD Toxic Equivalents (TCDD + 0.1 X TCDF)

ND - not detected

- four fish composite

NOTE: 1/2 detection limit used to calculate means and TEQs for non-detected values (see Johnson et al., 1991)

Table 2. TCDD and TCDF Concentrations in Muscle Tisse of Rufus Woods Lake Sportfish Collected August, 1990 and Background Concentrations From Lake Wenatchee (Composites consist of five fish each)

Sample Location	Fish Species	# Comp.	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)
Rufus Woods Lake					
Bridgeport Park	Walleye	2	ND	2.6	0.8
	Rainbow Trout	3	0.2	4.3	0.6
	L. Whitefish	2	2.2	142	16
Lake Wenatchee					
	Mt. Whitefish	3	ND	0.3	0.1

TEQ - 2,3,7,8-TCDD Toxic Equivalents (TCDD + 0.1 X TCDF)

ND - not detected

NOTE: 1/2 detection limit used to calculate means and TEQs for non-detected values (see Johnson et al., 1991)

Table 3. TCDD and TCDF Concentrations in Liver and Egg Tisse of Lake Whitefish Collected Near Kettle Falls, October, 1990 (Composites consist of three fish each)

Sample Location	Fish Species	Tissue	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)
Upper Lake Roosevelt					
Kettle Falls Park	L. Whitefish	Liver	3.1	289	32
		Egg	8.5	787	87

TEQ - 2,3,7,8-TCDD Toxic Equivalents (TCDD + 0.1 X TCDF)

ND - not detected

NOTE: 1/2 detection limit used to calculate means and TEQs for non-detected values (see Johnson et al., 1991)

not be determined. Also, representative portion size and frequency of consumption is unknown. Therefore, these values were not included in the evaluation for health effects. In addition to the above analysis, four fish (two lake whitefish and two white sturgeon) were analyzed for PCDDs and PCDFs substituted at the 2,3,7,8 and other positions. The fraction of the TEQ contributed by these congeners was estimated to be one to five percent, which includes one-half the detection limit for nondetects (ND). Because of this limited amount of data and the low toxicity of these congeners relative to TCDD, only the data for TCDD and TCDF were considered in this evaluation.

White sturgeon were found to contain the highest concentration of both TCDD and TCDF. The results for lake whitefish were similar to those for sturgeon in both upper and lower Lake Roosevelt, and Rufus Woods Lake. No TCDD was detected in walleye in either the upper or lower Lake, burbot in the upper, and rainbow trout in the lower. Relatively little TCDF was reported for rainbow trout, burbot, walleye or kokanee. However, all the species analyzed contained TCDF above the background concentration of 0.3 ng/kg (i.e., Lake Wenatchee data). It is important to note that the TEQ reported for lake whitefish and white sturgeon in Lake Roosevelt and Rufus Woods Lake is primarily a result of TCDF concentrations and not TCDD, the most toxic congener. For a more thorough presentation and discussion of the analytical data, see Johnson et al., (1991).

EXPOSURE ASSESSMENT METHODOLOGY

To assess the health impacts of a particular toxicant, exposure must first be demonstrated. The consumption of fish caught from Lake Roosevelt and Rufus Woods Lake represents the primary route of exposure to TCDD and TCDF discharged from the Celgar pulp mill in Castlegar, B.C. To calculate exposure, (i.e., a daily dose) a mathematical model was used. Daily doses of both TCDD and the TEQ from the consumption of Lake Roosevelt fish are calculated in Table 4. The following assumptions were used in these calculations:

- Body Weight
  - child: 10 kg
  - adult female: 60 kg
  - adult male: 70 kg
- Meal Serving Size
  - child: 100 g
  - adult female: 200 g
  - adult male: 200 g
- Meal Frequency (meals/month): 20
- No Changes Occur To TCDD and TCDF During Cooking

Table 4. Daily Dose of TCDD and TCDF Calculated From Mean Muscle Tissue Concentrations in Lake Roosevelt, Rufus Woods Lake and Lake Wenatchee Sportfish, and Exposure Assumptions

Sample Location	Fish Species	# Comp.	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)	Absorb. Coef.	Body Wt.(kg)	Serving Size (g)	Meals / Month	Daily Dose 2,3,7,8-TCDD (pg/kg/day)	Daily Dose TEQ (pg/kg/day)
Upper Lake Roosevelt											
Kettle Falls	Walleye	6	ND	3	0.5	0.68	10	100	20	0.0	2.2
			ND	3	0.5	0.68	60	200	20	0.0	0.7
			ND	3	0.5	0.68	70	200	20	0.0	0.6
	L. Whitefish	6	1.9	126	15	0.68	10	100	20	8.5	67.1
			1.9	126	15	0.68	60	200	20	2.8	22.4
			1.9	126	15	0.68	70	200	20	2.4	19.2
Kettle Falls/ Northport	Rainbow Trout	6	1.2	38	5.1	0.68	10	100	20	5.4	22.8
			1.2	38	5.1	0.68	60	200	20	1.8	7.6
			1.2	38	5.1	0.68	70	200	20	1.5	6.5
Kettle Falls/ Gifford	Burbot #	2	ND	2.8	0.3	0.68	10	100	20	0.0	1.3
			ND	2.8	0.3	0.68	60	200	20	0.0	0.4
			ND	2.8	0.3	0.68	70	200	20	0.0	0.4
Marcus Island	W. Sturgeon	4	2.4	147	17	0.68	10	100	20	10.7	76.0
			2.4	147	17	0.68	60	200	20	3.6	25.3
			2.4	147	17	0.68	70	200	20	3.1	21.7

Table 4. (Continued)

Sample Location	Fish Species	# Comp.	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)	Absorb. Coef.	Body Wt.(kg)	Serving Size (g)	Meals / Month	Daily Dose 2,3,7,8-TCDD (pg/kg/day)	Daily Dose TEQ (pg/kg/day)
Lower Lake Roosevelt											
Seven Bays	Walleye	6	ND	2	0.4	0.68	10	100	20	0.0	1.8
			ND	2	0.4	0.68	60	200	20	0.0	0.6
			ND	2	0.4	0.68	70	200	20	0.0	0.5
	L. Whitefish	6	1.7	145	16	0.68	10	100	20	7.6	71.5
			1.7	145	16	0.68	60	200	20	2.5	23.8
			1.7	145	16	0.68	70	200	20	2.2	20.4
Seven Bays/ Sanpoil	Rainbow Trout	6	ND	12	1.6	0.68	10	100	20	0.0	7.2
			ND	12	1.6	0.68	60	200	20	0.0	2.4
			ND	12	1.6	0.68	70	200	20	0.0	2.0
Spring Canyon/ Seven Bays	Kokanee	2	0.8	53	0.6	0.68	10	100	20	3.6	2.7
			0.8	53	0.6	0.68	60	200	20	1.2	0.9
			0.8	53	0.6	0.68	70	200	20	1.0	0.8
Rufus Woods Lake											
Bridgeport Park	Walleye	2	ND	2.6	0.8	0.68	10	100	20	0.0	3.6
			ND	2.6	0.8	0.68	60	200	20	0.0	1.2
			ND	2.6	0.8	0.68	70	200	20	0.0	1.0
	Rainbow Trout	3	0.2	4.3	0.6	0.68	10	100	20	0.9	2.7
			0.2	4.3	0.6	0.68	60	200	20	0.3	0.9
			0.2	4.3	0.6	0.68	70	200	20	0.3	0.8
	L. Whitefish	2	2.2	142	16	0.68	10	100	20	9.8	71.5
			2.2	142	16	0.68	60	200	20	3.3	23.8
			2.2	142	16	0.68	70	200	20	2.8	20.4

Table 4. (Continued)

Sample Location	Fish Species	# Comp.	Mean 2,3,7,8-TCDD (ng/kg)	Mean 2,3,7,8-TCDF (ng/kg)	Mean TEQ (ng/kg)	Absorb. Coef.	Body Wt.(kg)	Serving Size (g)	Meals / Month	Daily Dose 2,3,7,8-TCDD (pg/kg/day)	Daily Dose TEQ (pg/kg/day)
Lake Wenatchee											
	Mt. Whitefish	3	ND	0.3	0.1	0.68	10	100	20	0.0	0.4
			ND	0.3	0.1	0.68	60	200	20	0.0	0.1
			ND	0.3	0.1	0.68	70	200	20	0.0	0.1

- four fish composites

ND - not detected

TEQ - 2,3,7,8-TCDD Toxic Equivalents (TCDD + 0.1 x TCDF)

NOTE: 1/2 detection limit used to calculate means and TEQs for non-detected values (see Johnson et al., 1991)

Average body weights of 10, 60, and 70 kilograms for infants, adult females and males, respectively, were used. Children of this weight range were placed in a distinct category so that the physiological differences that exist between infants and adults could be taken into account.

Residents along Lake Roosevelt include the Colville and the Spokane Indian Tribes. Fish consumption by these populations is for subsistence purposes, which differs significantly from that of the sport fisherman. Given a lack of site-specific consumption data, a serving size of 200 grams and a meal frequency of 20 times per month was assumed. Although the exact fish consumption rate for Indian Tribes along Lake Roosevelt and Rufus Woods Lake is unknown at this time, the values assumed for this report exceed the 95th percentile for the consumption of fish by U.S. consumers (EPA, 1989). A fish consumption survey of Indian Tribes along the Columbia River is currently being organized. These data will be incorporated as they become available.

MECHANISM OF TCDD RESPONSES

Since the early 1970s, the scientific community has attempted to determine if TCDD causes cancer in humans. While TCDD has been shown to play a potent role in carcinogenesis in animal studies, epidemiological studies have provided only ambiguous results, due in large part to sample size limitations or inadequate exposure data. A recently published epidemiological study indicates that there may be a link between workers occupationally exposed to TCDD and the occurrence of soft tissue sarcomas (STS) (Fingerhut et al., 1991). Although the association between increased STS incidence and TCDD exposure is weak, this is the first indication that TCDD exposure may have human health consequences beyond the already well-documented effect of chloracne. Since the concentrations these workers were exposed to were disproportionately high when compared with public exposure levels, the significance of this study, with respect to public health, is unclear. Although this research endeavor is of high quality and merit, further research will be required if an answer regarding TCDD's carcinogenic potential, especially at ambient concentrations, is to be determined.

DOH used the best available data to determine an exposure level for TCDD which would constitute a level of concern for this contaminant. A level of concern determined from the presently available animal data for TCDD is a dose level below which no biological effects will occur. This is not to indicate that at concentrations above this level adverse effects will result, since there is insufficient evidence to conclude that any adverse effects will follow at dose levels even four fold higher.

The lack of definitive human evidence precludes determining a particular level of concern without also considering the animal data. The animal data consist of past cancer, mutagenicity, immunotoxicity, and reproductive studies, along with significant new research endeavors that have recently been completed. The results of a recent study on reproductive effects of TCDD, using rhesus monkeys, show that reproductive toxicity occurs at concentrations equivalent to those causing an increase in tumor incidence in rodents (Bowman et al., 1989; Kociba et al., 1976 & 78). Many of the animal studies done to date provide data that pertain to a precise set of pathological endpoints only (Murray et al., 1979; Kociba et al., 1976 & 78, Bowman et al., 1989). These types of experiments do not attempt to

address the mechanisms by which TCDD produces its toxic effects. Understanding biological mechanisms is imperative for determining the means by which a particular compound exerts toxic effects. By considering the mechanisms through which adverse effects occur concommitantly with animal data that focus on a single toxicologic endpoint, conclusions regarding levels of human health concern can be more adequately derived.

An example of mechanistic data which needs to be integrated with endpoint specific information is that of TCDD liver-to-adipose tissue concentration ratios. Data from mice studies show that doses producing hepatoxoic effects have TCDD liver-to-adipose tissue ratios greater than 1.0 and as high as 6.1 (Leung et al., 1990b; Allen et al., 1975; Gasiewicz et al., 1983; Olson et al., 1980; Olson, 1986). In the control animals, this ratio was consistently less than 1.0 (0.17-0.38), and this correlates well with ratios reported for humans that had been environmentally exposed to low levels of TCDD (Leung, et al., 1990c; Faccetti, et al., 1990; Ryan et al., 1985). The information gleaned from these ratios is that hepatotoxic effects are only observed in animals that have liver to adipose tissue ratios greater than 1.0. It can be concluded that previous experimental efforts have used doses sufficiently greater than those to which humans are ambiently exposed, that their results are of questionable value when attempting to address the human health impact of TCDD exposure.

In determining a level of concern, DOH has relied heavily, but not solely, on the mechanistic studies performed with TCDD. Information obtained from mechanistic studies including mutagenicity studies, indicate that TCDD does not bind directly and irreversibly to DNA, and thus does not cause cancer via mechanisms associated with genotoxins (Safe, 1986; Shu et al., 1988). The data do suggest however, that TCDD produces its effects epigenetically, either by being cytotoxic, or as a promotor. Cytotoxins produce their effect by poisoning cells. Promoters are agents that increase the tumorigenic response to a genotoxic carcinogen when exposure follows initial carcinogen exposure. This implies a two stage model for carcinogenesis, initiation and then promotion. As with other promoters, there may be a threshold level below which no adverse effect(s) will occur (Greenlee et al., 1990). The evidence indicates that TCDD produces its effects via receptor mediated toxicity. This means that a certain number, or a percentage of the total number, of cellular receptors available for TCDD interaction must be occupied before a biological response is observed. To further support this claim, the Kociba et al. (1976 & 78; PWG, 1990a & 90b) and Bowman et al. (1989) studies have data that demonstrate levels below which a biological response was not observed after chronic exposure to TCDD. These experiments support the hypothesis that a biological response is associated with a receptor-mediated event.

Studies which were designed to elucidate the cellular mechanisms by which TCDD produces toxic effects can, when used in context with available human and animal data, provide a means for evaluating the level at which this receptor-mediated process manifests a biological response. TCDD first binds and occupies a cytosolic receptor referred to as the Ah-receptor (Poland et al., 1976). The occupancy of this receptor by TCDD induces arylhydrocarbon hydroxylase (AHH) activity and the synthesis of a microsomal binding protein in the liver (Grieg and Dematties, 1973; Nebert and Jensen, 1979). The biological responses that stem from the actions of this receptor-ligand complex on DNA are believed to be associated with TCDD's promotional ability (Poland and Knutson, 1982; Silbergeld and Gasiewicz, 1989). Yet, for TCDD to produce any of the myriad of observed adverse effects, TCDD must first bind to and activate the Ah-receptor (Roberts, 1991). Although the exact number of receptors

required to produce a biological response can only be elucidated through further research, a receptor occupancy level of approximately five percent is considered by many researchers to be a valid and conservative level. A physiologically based pharmacokinetic model has been established for rats which predicts the occupancy level of the cytosolic receptor at a given dose (Leung et al., 1988, 90a & 90b). This model has been applied to the Kociba data, and a five percent receptor occupancy has been determined by DOH to occur at a dose level of approximately 0.002 µg/kg/day (Kociba et al., 1976 & 78, Leung et al., 1990b).

From this value of 0.002 µg/kg/day determined in rats, a level of concern must be established that protects human health. There is variation in the degree of response to which experimental species, and humans, respond to toxic agents. This variation between species, as well as the variation of sensitivity within the human population, must be taken into consideration if levels of human health concern are to be determined. Such consideration is applied by using a protective factor. Usually the experimentally determined level in animals is divided by a factor of ten for interspecies variation, and again by a factor of ten for intraspecies (human) variation. The total modifying factor by which experimental levels are divided is 100, and this renders a value of 20 pg/kg/day as a human dose level of concern.

It must be noted that several important studies, including one dealing with the promotional mechanism(s) of TCDD are still ongoing. As this new scientific information becomes available, DOH will re-examine its conclusions, and if necessary, will alter the value(s) now considered to be levels of concern. The Department feels that this is both essential and prudent. It is the intention of this agency to stay abreast of the relevant scientific information as it becomes available, in order to provide the best and most plausible recommendations to the public on this as well as other issues.

Along with the human health implications of TCDD exposure, the ecological implications of environmental TCDD contamination should be examined. There is adequate evidence characterizing the effects of TCDD on fish, larvae, and eggs. Symptoms of chronic/sublethal TCDD intoxication are many, and include pathological changes in the liver, such as focal necrosis and nuclear enlargement, as well as decrease in food consumption and weight, and increase in the incidence of diseased fins (Dewse, 1976; Hawkes and Norris, 1977). Pathological changes, along with the induction of AHH activity, in fish, are similar to those observed in mammals (Dewse, 1976). It is apparent that TCDD can have an effect on members of the ecosystem and in doing so, these effects can have both direct and indirect human health consequences.

DISCUSSION/CONCLUSIONS

The underlying premise of all toxicologic evaluations is that toxicity is dose-dependent, and that there exists a level of exposure, below which a specific chemical does no harm. Noncarcinogens are characterized as having a threshold, below which adverse human health effects are unlikely, whereas carcinogens have in the past been characterized as having a nonthreshold dose-response relationship. There is little doubt that a sufficient dose of a particular carcinogen can induce a cancerous state. The argument that a single molecule can produce a cancer, however, is a more tenuous position. Research in the field of cancer initation indicates that multiple hits, rather than a single hit by a cancer-causing chemical, are

required to induce a tumorigenic state. This suggests that there are levels for such compounds below which no toxic human health effects ensue. DOH has derived a level for TCDD below which no biological effects are believed to occur. As previously discussed, present research suggests that TCDD must first produce a biological response prior to initiating any toxicological effect. The biological response is associated with a receptor-mediated event for TCDD and thus all toxicological endpoints, cancerous or noncancerous, result from this biochemical event. Thus, by addressing the biological response, all toxicological effects will be included.

The exposure scenarios developed by DOH use fish consumption levels that represent an approximation of those for subsistence fishermen. This assumes that most of the dietary protein required by this population is derived from eating fish. The size of portions and number of meals for men, women, and children is derived from this assumption, and states that this group eats fish frequently and in large portions. For instance, children approximately 10 kilograms in body weight are considered to eat 20 meals of fish per month (each meal = 100 grams of fish). Because of the small body size of infants, they receive a proportionately larger dose than adults when exposed to the same concentration. They are thus the most exposed, as well as the most sensitive group considered. Doses which are protective of this group are protective of all less exposed and less sensitive groups.

The dose data expressed in Table 4 show that TCDD concentrations in all species of fish, from all locations sampled, are so low that they, when considered alone, are not at levels of health concern for any population exposed. This includes children, women and men from subsistence populations, as well as all sport fishermen eating fish from Lake Roosevelt, and Lake Rufus Woods. Concentrations of TCDF seen in these fish are at higher levels than TCDD. Doses for TCDD and TCDF are expressed as a TEQ which adds the toxicity of TCDD to that of TCDF. The elevated TEQs seen in Table 4 are predominantly based on high levels of TCDF.

For infants eating large amounts of fish from these locations, the TEQs exceed 20 pg/kg/day for consumption of lake whitefish caught near Kettle Falls, Seven Bays, and in Rufus Woods Lake near Bridgeport Park. Sturgeon caught at this last location also show doses to infants above 20 pg/kg/day TEQ.

Data for the toxicity of 2,3,7,8-TCDF are less definitive than those for 2,3,7,8-TCDD. This is why toxic equivalent factors (TEFs) are used to estimate the toxicity of this compound relative to the toxicity of TCDD, which is expressed as a TEQ. 2,3,7,8-TCDF is assigned a TEF value of 0.1, indicating that it is ten times less toxic than 2,3,7,8-TCDD. Recent evidence indicates that this may, in fact, be a high estimate, and that a TEF value of 0.03 to 0.05 should be considered.

Because of the uncertainty inherent in the TEF for 2,3,7,8-TCDF, and because of the uncertainty about where adverse effects from exposure doses begin, DOH judges that TEQ's in the range from 20 to 80 pg/kg/day do not constitute levels for restricting the consumption of lake whitefish and sturgeon for infants. The 20 pg/kg/day exposure dose indicates a level below which no biological effects are believed to occur. Biological effects include those by which individuals compensate and adapt to environmental challenge. Adverse effects occur when such ability to adapt or compensate is exceeded. There is insufficient evidence to

conclude that adverse effects occur even at dose levels four fold higher then 20 pg/kg/day.

The uncertainty regarding these two parameters does, however, indicate that some caution be exercised in relation to the exposure of infants eating lake whitefish in subsistence amounts (sturgeon are not eaten frequently enough to represent a significant exposure). The previous advisory restricting consumption of lake whitefish for children of less than 40 pounds or 4 years of age was a prudent measure based on preliminary analysis. This new analysis makes the restriction on consumption of lake whitefish for children unnecessary.

There are no known beneficial health effects associated with PCDDs and PCDFs and therefore it is prudent to minimize exposure. Options for reducing exposure, can be considered general recommendations for more healthful living. Since TCDD and TCDF accumulate in fish over time, older fish tend to be more contaminated than younger fish from a specific location. Age of fish is reflected in size, so one means of reducing exposure to contaminants is to prepare smaller fish for consumption by infants. TCDDs and TCDFs also tend to concentrate in fatty tissue. Food preparation which removes fat and skin, or allows fat to drip off during cooking, will also reduce exposure. Finally, reducing the size of portions below 100 g, or decreasing the frequency of fish meals for infants below 20 meals a month, also reduces exposure.

Uncertainty regarding the point above the indicator level where adverse effects actually begin, and the uncertainty regarding TEQs, requires that caution be exercised regarding ongoing contaminant levels in fish in Lake Roosevelt. Although no restrictions are presently being placed on whitefish and sturgeon consumption, DOH believes that the present levels of TCDD and TCDF are still cause for concern. Even though there is insufficient evidence to conclude that adverse effects occur at these dose levels, were concentrations to increase further, the resulting doses could have adverse human health consequences. Also, ecological effects may occur at contaminent levels found in Lake Roosevelt, and these ecosystem effects have not been addressed. At present, there is no control on contaminant effluents from Celgar mill. Control technology and change in processes producing TCDD and TCDF from this facility, will probably take two to three years to complete. While this should decrease the dioxin contribution from this source to the lake, continuing contamination needs to be monitored. Existing contamination of the lake should decrease over time, as the source is limited. It seems prudent to continue periodic surveillance of dioxin and furan concentrations in sport fish, to determine whether contamination is increasing or decreasing.

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