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## PUBLIC HEALTH CONSULTATION

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Penobscot River,  
Maine

June 1, 2006

U.S. Department of Health and Human Services  
Agency for Toxic Substances and Disease Registry  
Division of Toxicology and Environmental Medicine  
Emergency Response Team  
Atlanta, GA 30333

## BACKGROUND AND STATEMENT OF ISSUES

The Agency for Toxic Substances and Disease Registry (ATSDR) provides public health support to Tribal Governments through a Memorandum of Understanding with the Bureau of Indian Affairs (BIA). Members of the Penobscot Tribe in Maine have expressed concerns that consumption of contaminated fish from the Penobscot River are causing elevated cancer rates among tribal members [1, 2]. The Tribe has requested the Office of Tribal Affairs (OTA) of the Agency for Toxic Substances and Disease Registry (ATSDR) to assist in evaluating the potential public health implications posed by these potential exposures. The OTA in turn requested the ATSDR Emergency Response (ER) Team of the Division of Toxicology and Environmental Medicine to review fish tissue sampling results, calculate fish consumption limits, and provide a public health opinion regarding the health implications associated with eating the fish.

The State of Maine conducted fish tissue sampling for the period 1988 through 2003. The ER Team has reviewed historical sampling results for a predatory (Small Mouth Bass) and bottom feeding (White Sucker) species from the Penobscot River. Other data reviewed included studies conducted on behalf of the Penobscot Nation and the US Geological Survey. The sampling data included data for chlorinated-dibenzo-p-dioxins (CDDs) such as 2,3,7,8 tetrachloro-dibenzo-p-dioxin (TCDD), chlorinated-dibenzofurans (CDFs) such as 2,3,7,8 tetrachlorodibenzofuran (TCDF), polychlorinated biphenyls (PCBs), and methyl mercury. Although Penobscot tribal members have historically subsisted on fish, fiddlehead ferns, and wildlife from along the banks of the Penobscot River, this public health consultation focuses on available fish sampling data. A review of health outcome data such as cancer rates is also beyond the scope of this consultation.

Furthermore, ATSDR examined additional data for other food chain entities (i.e., eel and muskrat) for this site and there is evidence of dioxin contamination, however, the data are over 10 years old and limited, and insufficient to characterize any potential health risks.

The Penobscot Nation currently extends from the Indian Island at Old Town, Maine, north along a series of islands in the middle of the River, and east and west into tributaries near the high country around the 5200 foot Mount Katahdin [1]. Upon detecting dioxins, mercury, and other contaminants in fish tissues collected in 1987, the US Environmental Protection Agency (EPA), the Penobscot Nation and the Maine Bureau of Health (BOH) issued fish consumption advisories for the Penobscot River to protect the public from potential health risks associated with consuming the fish [1].

Guidance for evaluating potential health threats associated with contaminated fish recommends that a minimum of two target species be sampled including one predatory and one bottom feeding species (e.g., Small Mouth Bass and White Sucker) [3,4]. Target species are chosen to meet several criteria [3,4]. They are known to accumulate high concentrations of target contaminants in their tissue [3]. They normally populate the freshwater system being studied and are routinely caught and consumed by anglers. Also, the target species should be non-migratory, pollutant-tolerant, easily identified, abundant and easy to collect, and of sufficient size to provide adequate tissue samples for analyses of contaminants [3].

## DISCUSSION

Fish advisories are issued for the general population, as well as for certain segments of the population that may be at higher risks such as pregnant females, nursing mothers, infants, and children. Fish advisories can vary somewhat by state, province, and target audience, but are generally issued for the following reasons: to (1) inform the public about the chemical contaminants in sport fish; (2) educate consumers as to how they can minimize their exposure to contaminants; (3) remind consumers of the health benefit of consuming fish; and (4) present advisory information in a manner conducive to maximal voluntary compliance [4].

### CHLORINATED DIBENZO-P-DIOXINS /CHLORINATED DIBENZOFURANS

Chlorinated dibenzo-p-dioxins are a family of 75 different compounds or congeners commonly referred to as dioxins. The 2,3,7,8 form of TCDD is one of the most toxic forms and is considered a human carcinogen by the US Department of Health and Human Services [5,6]. The International Agency for Research on Cancer (IARC) considers 2,3,7,8 TCDD a Class A carcinogen [5,6], which means that it is well established that it causes cancer in humans. EPA considers 2,3,7,8 TCDD a B-2 probable human carcinogen, which means that there is sufficient evidence in animal studies to indicate it is a carcinogen, but not in human studies [7]. Chlorinated dibenzofurans, or furans, are structurally and toxicologically related compounds [8]. There are 135 different congeners of furans. Dioxin/furan adversely affect the human reproductive system, and immune system and are associated with chloracne (an acne-like conditions associated with exposures to halogenated aromatic hydrocarbons) with exposure to high levels [5]. Appendix A discusses Dioxin/Furan toxicity in more detail.

Although all dioxin-like compounds including dibenzofurans are thought to act in the same way, they are not all equally toxic. Their different toxicities may be due to their unique properties of absorption, distribution, metabolism, and elimination in the body and/or strengths of binding to the aryl hydrocarbon (Ah) receptor. Therefore, the health risk of each congener is assessed by rating their toxicities relative to 2,3,7,8 TCDD, the most potent of the dioxins. 2,3,7,8 TCDD is assigned a value of "1" and each of the toxic dioxin/furan congeners is assigned a "toxicity factor" that estimates its toxicity relative to 2,3,7,8 TCDD [9]. The resulting estimates are called toxic equivalency factors (TEFs), which have been recently updated by the World Health Organization (WHO) [10]. The toxic equivalent quotients (TEQs) are determined by multiplying the concentration of a dioxin congener by its toxicity factor. The total TEQ in a sample is then derived by adding all of the TEQ values for each congener. About 90% of the total TEQ value results from dioxin-like compounds other than 2,3,7,8 TCDD. There is good experimental support for the assumptions that underlie the TEQ system. The TEQs make it possible to take toxicity data on 2,3,7,8 TCDD, a compound about which our knowledge is vast, and estimate toxicity for other compounds about which much less is known [9].

The Main Bureau of Health (BOH) collected fish for dioxin/furan analysis from 4 locations along the Penobscot River near Lincoln, Maine for the period 1988 through 2003 [11]. Fish tissue dioxin TEQs are summarized in tables 1A and 1B by species. The data indicate that the levels of dioxin/furan in fish tissues are slightly decreasing for the years reviewed. The reasons for the concentration spikes in 1994 are not known. The instrumentation method detection limit for dioxin/furan is  $1 \times 10^{-6}$  mg/kg.

## Summary of Fish Dioxin/Furan TEQ Data From 1988 Through 2003

Table 1A

Small Mouth Bass (TEQ Dioxin/Furan)			
Sampling Year	Max (ng/kg)	Min (ng/kg)	Average (ng/kg)
1988-1990	2.7	1.7	2.34
1991	1.7	1.2	1.48
1992	1.2	0.4	0.74
1993	2.46	0.27	1.22
1994	4.69	0.14	1.84
1995	1.9	0.2	0.69
1997	2.1	0.8	1.49
1999	3.68	0.35	1.61
2000	1.1	0.9	0.97
2001	0.72	0.03	0.35
2002	0.04	0	0.02
2003	1.40	0	0.17

Table 1B

White Suckers (TEQ Dioxin/Furan)			
Sampling Year	Max (ng/kg)	Min (ng/kg)	Average (ng/kg)
1988-1990	67.2	9.8	32.2
1991	5.0	4.9	4.95
1992	6.8	4.6	5.28
1993	6.4	2.7	3.6
1994	6.1	1.6	4.1
1995	2.5	0.8	1.7
1997	5.2	3.2	4.2
1999	2.25	1.26	1.65
2000	1.7	1.1	1.47
2001	1.72	.05	0.45
2002	2.29	.76	1.4
2003	1.42	0.04	0.39

Max        4.69        ng/kg  
 Min        0.0            ng/kg  
 Average    0.73         ng/kg

Max        67.2         ng/kg  
 Min        0.04         ng/kg  
 Average    2.95         ng/kg

ng/kg= nanogram per kilogram  
 max=maximum  
 min=minimum  
 TEQ=toxic equivalency quotients

ATSDR utilized EPA methodology for evaluating carcinogenic health effects related to fish consumption and dioxin/furan TEQ tissue levels to calculate fish consumption limits (See Appendix B). ATSDR has utilized an excess lifetime cancer risk rate of one in 1,000,000 to comment on the cancer risk [12]. Table 2 indicates the maximum number of fish meals per month that may be consumed which may not exceed dioxin/furan levels that may be of public health concern. Because of the lack of specific consumption rates for different individuals, the matrix in Table 2 indicates fish tissue contaminant levels and portion sizes. Portion sizes range from 32 grams (1.23 oz) to 453.5 grams (16 oz) and are expected to bracket actual meal sizes for different individuals.

## Dioxin/Furan Monthly Fish Consumption Limits

Table 2

Maximum Number of Fish Meals per Month					
Cancer Risk Level = 1 in 1,000,000					
32 grams of fish per meal (1.23 oz)	97 grams of fish per meal (3.42 oz)	227 grams of fish per meal (8oz)	340 grams of fish per meal (12oz)	453.5 grams of fish per meal (16oz)	Fish Tissue Dioxin/Furan Levels (ng/kg, TEQ wet weight)
>90	66	28	19	14	0 – 0.019
>90	33	14	9	7	0.020 – 0.038
76	25	11	7	5	0.039– 0.05
50	17	7	5	4	0.051 – 0.075
25	8	4	2	2	0.076 -0.15
20	6	3	2	1	0.16 – 0.2
13	4	2	1	1	0.21 – 0.3
6	2	1	0.5	0.5	0.31 – 0.6
3	0.5	0.5	None	None	0.61 – 1.2
1.5	None	None	None	None	1.2

Consumption Limits are based on adult body weight of 70 kg and a cancer potency factor of  $1.75 \times 10^4(\text{mg/kg/d})^{-1}$  derived from DHHS & FDA's risk specific dose for 2,3,7,8 TCDD of 0.057pg/kg/d [5]

ng/kg=nanogram per kilogram=parts per trillion

None = No consumption recommended

Cancer Risk Level = maximum acceptable individual lifetime risk level

TEQ = Toxic Equivalent

Oz = ounce

Tables 1A and 1B indicate that the maximum dioxin TEQ levels reported in 1999 fish tissue at 3.7 ng/kg for small mouth bass and at 2.3 ng/kg for white suckers.

ATSDR's oral chronic-duration (>365 days) Minimal Risk Level (MRL) for 2,3,7,8 TCDD is 1 picogram/kilogram body weight /day (pg/kg/d). An oral MRL is the amount of a substance that a person can be exposed to orally on a daily basis for a specified duration (intermediate duration is 15 days to 365 days) or (chronic duration is greater than 365 days) that is unlikely to result in non-carcinogenic adverse health effects. The Department of Health and Humans Services (DHHS) and the Food and Drug Administration's (FDA) risk specific dose for 2,3,7,8 TCDD and the risk specific dose for total toxic equivalents (TEQs) is 0.057picograms/kilogram body weight/day (pg/kg/d) [5]. WHO's total daily Intake for dioxins and related compounds such as dibenzofurans and dioxin like PCBs is 1 to 4 pg/kg/d [10].

In characterizing the risk posed by consumption of dioxin/furan contaminated fish from the Penobscot River, ATSDR assumed a worst case scenario, that a 70 kilogram adult consumed 227 grams or 8 ounces of small mouth bass daily for 365 days which contained the maximum level (4.69 ng/kg) of dioxin/furan detected in fish during 1994. The estimated exposure dose of dioxin/furan would be approximately 14 pg/kg/d. This estimated exposure dose exceeds ATSDR's oral MRL for dioxin of 1 pg/kg/d. Furthermore, this estimated exposure dose exceeds both the

HHS risk specific dose of 0.057 pg/kg/d, and WHO's daily intake rate of 1-4 pg/kg/d. Although the levels of dioxin/furan reported in fish caught from the Penobscot River appear to be decreasing, the maximum detected level of dioxin/furan in 2003 still remain at levels of public health concern. The maximum dioxin level detected in fish reported in 2003 was 1.4 ng/kg. If dioxin/furan fish tissue concentrations decline below 1.2 ng/kg Table 2 may be used to calculate the number of fish meals per month below which a concern for public health would not be expected.

### **POLYCHLORINATED BIPHENYLS**

US FDA has set a food tolerance level for PCBs in interstate commercial fish at 2 ppm. Food tolerance levels represent levels at or above which FDA may take legal action to remove adulterated products from the market. Although FDA has no statutory authority over intrastate fishing considerations, such as non-commercial fishing, it does provide advice to local, or state authorities when requested, and where no guidelines are tolerance values are available. FDA's advice to the state is the best scientific opinion FDA can give, but it is not enforceable per se [13]. The underlying assumptions used in the FDA methodology were never intended to be protective of recreational, ethnic, tribal, and subsistence fishers who typically consume larger quantities of fish than the general population and often harvest the fish and shellfish they consume from the same local body of waters repeatedly over many years [4].

ATSDR's oral chronic MRL for PCBs is .02 µg /kg/d. Fish tissue levels of PCBs detected in small mouth bass and white suckers for a period of 1993 – 2001 from the Penobscot River near Lincoln appears to be at levels of public health concern (i.e. levels detected 0.000005 to 0.63 mg/kg in small mouth bass and 0.0000002 to 0.003 mg/kg in white suckers).

### **METHYL MERCURY**

Mercury is present in fish caught in all inland waters of Maine, and the levels are among the highest reported in North America [14]. The unborn fetus and young children are especially sensitive to the toxic effects of mercury because they have actively developing nervous systems. Mercury's harmful effects may include brain damage, mental retardation, and loss of voluntary muscle control, blindness, seizures, and inability to speak. Mercury can be passed from the mother to the fetus or the child. Children poisoned by mercury may develop problems of their central and peripheral nervous systems, digestive system, and kidneys [15]. Appendix C discusses methyl mercury toxicity in more detail.

Maine has issued a consumption advisory to protect the unborn fetus and young children. A less restrictive advisory is issued for all other individuals (the general population). For both groups, separate advisories are issued regarding warm-water fish (e.g., bass, pickerel, perch, sunfish, and crappie) versus cold-water fish (e.g., trout, salmon, smelt, and cusk). Warm- water species tend to have higher levels of mercury than cold-water species [14].

The Maine BOH advisory recommends that:

“Pregnant women, nursing mothers, women who plan to become pregnant, and children less than 8 years of age, should not eat warm water fish species caught in any of Maine’s inland surface waters; consumption of cold water fish species should be limited to 1 meal per month; All other individuals should limit consumption of warm water species caught in Maine’s inland waters to 2 to 3 meals (8oz meal) per month. There are no limits for consumption of cold water species for the general population [14]”.

The Maine BOH collected fish for methyl mercury analysis from 4 locations along the Penobscot River for the period 1988 through 2000 [11]. The methyl mercury levels for fish tissue samples are summarized in Tables 3A and 3B by species. The data indicate that the levels of methyl mercury in fish tissues are slightly increasing for the years reviewed [11]. The instrumentation method detection limit for methyl mercury is  $1 \times 10^{-3}$  mg/kg.

### Summary of Fish Methyl Mercury Data From 1988 Through 2000

**Table 3A**

Small Mouth Bass Methyl mercury			
Sampling Year	Max (mg/kg)	Min (mg/kg)	Average (mg/kg)
1988	0.34	0.18	0.26
1993	0.56	0.23	0.36
1994	0.51	0.38	0.45
1996	1.12	0.53	0.76
1997	0.48	0.09	0.31
1998	0.34	0.18	0.26

**Table 3B**

White Suckers Methyl mercury			
Sampling Year	Max (mg/kg)	Min (mg/kg)	Average (mg/kg)
1988	0.1	0.04	.07
1993			
1994	0.16	0.13	0.15
1996	0.29	0.15	0.22
1997	0.42	0.11	0.22
2000	0.21	0.21	0.21

Max 0.92 mg/kg  
 Min 0.11 mg/kg  
 Average 0.51 mg/kg

Max 0.42 mg/kg  
 Min 0.03 mg/kg  
 Average 0.17 mg/kg

Max = Maximum

Min = Minimum

mg/kg = milligram per kilogram

ATSDR utilized EPA methodology for evaluating non-carcinogenic health effects related to fish consumption and methyl mercury fish tissue levels to calculate fish consumption limits (See Appendix B). Table 4 indicates the maximum number of fish meals per month that may be consumed without exceeding methyl mercury doses that may be of public health concern. Because of the lack of specific consumption rates for different individuals, the matrix in Table 4 indicates fish tissue contaminant levels and portion sizes. Portion sizes range from 32 grams (1.23 oz) to 453.5 grams (16 oz) and are expected to bracket actual meal sizes for different individuals.

**Table 4 Methyl Mercury Monthly Fish Consumption Limits**

Maximum Number of Fish Meals per Month (ATSDR Methyl Mercury MRL 0.3 µg/kg/day)					
32 grams of fish per meal (1.23 oz)	97 grams of fish per meal (3.42 oz)	227 grams of fish per meal (8oz)	340 grams of fish per meal (12oz)	453.5 grams of fish per meal (16oz)	Fish Tissue Methyl Mercury Concentration (µg /kg, wet weight)
90	90	90	64	48.5	0 – 0.029
90	90	47.5	32	24	30.0 – 59.0
90	84	36	24	18	60.0 – 78.0
90	55	23	15.5	11.5	79.0 – 120.0
86.5	28.5	12	8	6	121.0 – 230.0
64	21	9	6	4.5	231.0 – 310.0
42.5	14	6	4	3	311.0 – 470.0
21	7	3	2	1.5	471.0 – 940.0
10.5	3	1	1	.5	941.0 – 2,000
10	3	1	.5	None	> 2,000

Consumption Limits are based on adult body weight of 70 kg and a MRL 0.3 µg/kg/day.

None = No consumption recommended

Values are reported in milligram/kilogram (mg/kg).

MRL = ATSDR's Minimal Risk Level

ATSDR's oral chronic-duration MRL for methyl mercury is 0.3 micrograms per kilogram per day (µg/kg/day). The MRL was derived from a chronic-duration oral exposure study of neuro-developmental outcomes of children exposed during pregnancy via the mother's consumption of methyl mercury contaminated fish [15]. EPA's oral chronic-duration Reference Dose (RfD) for methyl mercury is 0.1µg/kg/day. An RfD is the amount of a substance that a person can be exposed to on a daily basis for a specified duration (intermediate duration of 15 to 365 days or chronic duration of greater than 365 days) which is unlikely to cause adverse non-carcinogenic human health effects. This RfD is derived from a developmental neurological study in children [15]. FDA has established an action level of 1 mg/kg for methyl mercury in fish. FDA recommends that regular consumption of fish with methyl mercury levels around 1 mg/kg be limited to approximately 7 ounces per week; for fish with levels averaging 0.5 mg/kg the limit is about 14 ounces per week [15]. Again, the underlying assumptions used in the FDA methodology were never intended to be protective of recreational, ethnic, tribal, and subsistence fishers who typically consume larger quantities of fish than the general population and often harvest the fish and shellfish they consume from the same local body of waters repeatedly over many years [4].

In characterizing the risk posed by consumption of methyl mercury contaminated fish from the Penobscot River, ATSDR assumed that a 70 kilogram adult consumed 227 grams or 8 ounces of white sucker daily for 365 days which contained the maximum level (0.42 mg/kg) detected in fish during 1997, the most recent year. The estimated exposure dose of methyl mercury would be approximately 1.3 µg/kg/day. This estimated exposure dose exceeds ATSDR's oral MRL for methyl mercury of 0.3µg/kg/day. Furthermore, this estimated exposure dose exceeds the EPA RfD of 0.1 µg/kg/day. The Penobscot Nation's advisory that pregnant women, nursing mothers,

women who plan to become pregnant, and children less than 8 years of age, should not eat warm water fish species caught in any of Maine's inland surface waters remains valid. If all other individuals limit consumption of warm water species caught in Maine's inland waters to 2 to 3 meals (8oz meal) per month there would be no concern for public health for concentrations of methyl mercury reported for 1997 for small mouth bass and for 2000 for white suckers. If methyl mercury levels have increased significantly above the levels reported in 1997 for small mouth bass and in 2000 for white suckers, the advisory may need to be modified.

## **CONCLUSIONS**

Based on the data reviewed, ATSDR concludes the following:

1. ATSDR concurs with the Penobscot Nations Natural Resource's Public Health Advisories for Fish Consumption.
2. Dioxin/furan TEQ levels reported for small mouth bass and white suckers in 2003 remain at levels of public health concern, and unless levels have declined significantly since 2003, these fish should not be consumed.
3. Methyl mercury levels reported for small mouth bass in 1997 and white suckers in 2000 remain at levels of public health concern for pregnant women, nursing mothers, women who plan to become pregnant, and children less than 8 years of age and these sensitive populations should not eat warm water fish species caught in any of Maine's inland surface waters. All other individuals should limit consumption of warm water species caught in Maine's inland waters to 2 to 3 meals (8oz meal) per month.
4. The analytical results of fish tissue samples obtained from the Penobscot River appear to indicate that Dioxin/Furans TEQ concentrations have slightly decreased since 1988.
5. The methyl mercury tissue levels of fish caught from the Penobscot River appear to have slightly increased since 1988.
6. Polychlorinated Biphenyls TEQ levels reported for small mouth bass caught from the Penobscot River are at levels of public health concern.

## **RECOMMENDATIONS**

ATSDR recommends the following;

1. Anyone consuming fish from the Penobscot River should follow the Penobscot Nation Natural Resource's dioxin/furan, PCBs and methyl mercury Public Health Advisories for the Penobscot River;
2. The State of Maine should continue monitoring of dioxin/furan, PCBs and methyl mercury in fish in the Penobscot River annually;
3. BIA and the Environmental Protection Agency should consider additional sampling of food chain entities and include other traditional subsistence foods that could potentially be adversely affected by contaminants in the Penobscot River;
4. BIA and US Environmental Protection Agency should ensure that the laboratory performing the sampling analysis has approved quality assurance and quality control procedures with an instrumentation method detection limit for dioxin/furan of  $1 \times 10^{-6}$  mg/kg and a method detection limit for methyl mercury of  $1 \times 10^{-3}$  mg/kg;

5. BIA, or US Environmental Protection Agency should provide culturally sensitive public health education to Penobscot tribal members to prevent, reduce, or eliminate the potential health risks associated with consuming dioxin/furan and methyl mercury contaminated fish caught from the Penobscot River.

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## APPENDIX A

### TOXICITY OF DIOXINS/FURANS/PCBS

Chlorinated dibenzo-p-dioxins are a family of 75 different compounds commonly referred to as dioxins [5]. The 2,3,7,8 TCDD congener is one of the most toxic chemicals known to man. Chlorinated dibenzofurans or furans, are structurally and toxicologically related compounds family of compounds with 135 different congeners [8]. Dioxins/furans have been reported to be formed during the chlorine bleaching process used by pulp and paper mills [5]. Dioxins and related compounds enter the environment as mixtures and tend to be associated with ash, soil, or any surface with a high organic content [16]. They are persistent in the environment; are resistant to degradation; and tend to adsorb to sediment and, therefore serve as a continuing source of contamination for bottom feeding fish. These compounds tend to accumulate in the organs of fish with less accumulation in the tissues [5].

The 2,3,7,8 TCDD congener is considered a human carcinogen by the US Department of Health and Human Services [5]. The International Agency for Research on Cancer (IARC) considers it a Class A carcinogen [6], which means that it is well established that it causes cancer in humans. EPA considers 2,3,7,8 TCDD as a B-2 probable human carcinogen, which means that there is sufficient evidence in animal studies to indicate that it is a carcinogen, but not in human studies. Dioxins, adversely affect the human reproductive and immune systems and are associated with chloracne with exposure to high levels [16].

A study of the general population reports that human adipose (fat) tissue levels of 2,3,7,8 TCDD ranged from non-detect to 20.2 nanograms per kilogram (ng/kg or parts per trillion) [5]. A similar study conducted in Canada reported that 2,3,7,8 TCDD levels in adipose tissues of the general population were between 5 and 10 ng/kg [5]. Due to the lipid solubility of these compounds, they tend to cross the placenta and blood brain barriers with ease. They accumulate in fat or lipid tissues within the human body, and are often detected in a nursing mother's breast milk. Therefore, dioxin compounds may adversely affect a nursing infant [16]. The biological half life of 2,3,7,8 TCDD has been reported to be 5.8 to 11.3 years in humans [6,16].

Toxicity of any chlorinated dibenzo-dioxin is assessed by the affinity that the compound has for a cytoplasmic intracellular receptor protein known as the aryl-hydrocarbon receptor (Ah). Following exposure, dioxin crosses the cell membrane and binds to the Ah receptor with-in the cytoplasm, and subsequently the dioxin Ah receptor complex is translocated to the nucleus via a translocating protein [17]. Once inside the nucleus, the Ah receptor-dioxin-translocating protein complex binds to regulatory DNA sequences known as dioxin responsive elements and enhances the translation of cytochrome P450 1A1 by messenger RNA (ribonucleic acid) [16,17]. The induction of cytochrome P450 1A1 is responsible for the bio-transformation of other carcinogens such as benzene [17] which otherwise may pass through the body and not be bio-transformed to its reactive or toxic metabolites.

Although all dioxin-like compounds including dibenzo-furans are thought to act in the same way they are not all equally toxic. Their different toxicities may be due to their unique properties of absorption, distribution, metabolism, and elimination in a body and/or strengths of binding to the Ah receptor. Therefore, the health risk of each congener is assessed by rating their toxicities relative

to 2,3,7,8 TCDD, the most potent of the dioxin/furan. 2,3,7,8 TCDD is assigned a value of "1" and each of the remaining toxic dioxin/furan and PCB congeners is assigned a "toxicity factor" that estimates its toxicity relative to 2,3,7,8 TCDD [6]. The resulting estimates are called toxic equivalency factors (TEFs), which have been recently updated by the World Health Organization. The toxic equivalent quotients (TEQs) are determined by multiplying the concentration of a dioxin/furan congener by its toxicity factor. The total TEQ in a sample is then derived by adding all of the TEQ values for each congener. While 2,3,7,8 TCDD is the most toxic form of dioxin/furans, 90% of the total TEQ value results from dioxin-like compounds other than 2,3,7,8 TCDD. There is good experimental support for the assumptions that underlie the TEQ system. The TEQs make it possible to take toxicity data on 2,3,7,8 TCDD, a compound about which our knowledge is vast, and estimate toxicity for other compounds about which much less is known [9].

Dioxin/furan and related compounds (e.g., PCBs) are also considered endocrine disruptors because they produce reversible, or irreversible biological effects in individuals by interfering with normal hormone function. They act through a number of mechanisms by temporarily, or permanently altering feedback loops involving the brain, pituitary, gonads, thyroid gland, or other organs. Their actions are attributed to mimicking, or interfering with the normal functioning of sex hormones such as estrogen, testosterone, and progesterone.

### Polychlorinated Biphenyls

Polychlorinated biphenyls are a group of man-made chemicals that contain 209 individual congeners or compounds. They are widely distributed in the environment and are considered as probable human carcinogens by US EPA. A probable human carcinogen is considered a chemical that induces cancer in animals, but the data is insufficient to establish that it will cause cancer to develop in humans. Polychlorinated biphenyls are persistent in the environment and are resistant to degradation. They are lipophilic (fat loving) and tend to adsorb strongly to soils, therefore, they are not expected to leach significantly into groundwater. Most exposures to PCBs were considered occupational or environmental without symptoms of toxicity upon initial exposure. Acute toxicity is low level, and because PCBs accumulate in animal and human tissue, chronic or delayed toxicity may occur. Chloracne is a dermatologic condition observed in some individuals who are exposed to PCBs. The lesions may include cysts that may become inflamed and infected. The rash may be found on the trunk, arms, face, neck, or back, and is quite resistant to treatment. Any route of exposure to PCBs may result in chloracne.

PCBs are unavoidable contaminants in certain foods, including fish and shellfish, because of previous widespread and uncontrolled PCBs use. US FDA has set a food tolerance level for PCBs in interstate commercial fish at 2 ppm. Food tolerance levels represent levels at or above which FDA may take legal action to remove adulterated products from the market. Although FDA has no statutory authority over intrastate fishing considerations, such as non-commercial fishing, it does provide advice to local or state authorities when requested, and where no guidelines are tolerance values are available. It is the best scientific opinion the agency can give, but it is not enforceable per se [13].

## APPENDIX B

### EQUATIONS USED TO DEVELOP RISK-BASED CONSUMPTION LIMITS FOR DIOXINS/FURANS, POLYCHLORINATED BIPHENYLS, AND METHYL MERCURY IN FISH

ATSDR utilized two of US EPA's equations [4] to derive meal consumption limits for carcinogenic and non-carcinogenic health effects for the contaminants reported i.e., dioxins/furans and methyl mercury. The carcinogenic health effects equation and non-carcinogenic health effects equation are used to calculate daily consumption limits in units of milligrams of edible fish per kilogram of human body weight per day (mg/kg/d); Meal consumption limit equation is used to convert daily consumption limits to meal consumption limits over a specified period of time (e.g., 1 month). Table 5 below provides the toxicological benchmark values for carcinogenic and non-carcinogenic health effects used in the calculation of risk-based consumption limits:

**Table 5**

Target Analyte	Chronic RfD <sup>a</sup> (mg/kg/d)	ATSDR's MRL (µg/kg/d) Oral Chronic	CPF <sup>b</sup> (mg/kg/d) <sup>-1</sup>
2,3,7,8 –TCDD	NA	1 x 10 <sup>-6</sup>	1.75 x 10 <sup>4</sup>
PCB (Aroclor 1254)	2 x 10 <sup>-5</sup>	0.02	2 x 10 <sup>-5a</sup>
Methyl Mercury	1 x 10 <sup>-4</sup>	0.3	NA

CPF = Cancer Potency Factor

MRL = Minimal Risk Level

RfD = Oral reference dose

NA = not available in EPA's Integrated Risk Information System

**a** Values are the most current oral RfDs and CSFs in EPA's IRIS Database [7].

**b** Derived from FDA's risk specific dose for 2,3,7,8 TCDD 0.057pg/kg/d [5].

#### **Calculations of Consumption Limits for Cancer Health Effects**

It is necessary to specify an "acceptable" lifetime risk level (ARL) in order to calculate consumption limits for cancer health effects. This document presents consumption limits that were calculated using a risk level of 1 in 1,000,000 (10<sup>-6</sup>) [12]. The cancer health equation and the meal consumption limit equation were used to calculate risk-based consumption limits for dioxins/furans with cancer slope factors based on an assumed 70-yr exposure. This is a standard value however, individuals may actually be exposed for greater or lesser periods of time depending on their lifespan, consumption habits, and residential location [4].

#### **Calculation of Daily Consumption Limits— Cancer**

Cancer Health Effects Equation calculates an allowable daily consumption of contaminated fish based on a contaminant's cancer potential expressed in kilograms of fish consumed per day:

## CANCER HEALTH EFFECTS EQUATION

$$\text{CRLim} = \frac{\text{ACRL} \cdot \text{BW}}{\text{CPF} \cdot \text{Cm}}$$

where

**CRLim** = maximum allowable fish consumption rate (kg/day)

**ACRL** = maximum acceptable individual lifetime cancer risk level (unit less)

**BW** = human body weight (kg);

**CPF** = cancer potency factor, derived from FDA's risk specific dose for 2,3,7,8 TCDD  
0.057pg/kg/d [5]

**Cm** = measured concentration of chemical contaminant *m* in a given species of fish  
(mg/kg).

The calculated daily consumption limit (CRLim) represents the amount of fish (in kilograms) expected to generate a risk no greater than the maximum ARL used based on a lifetime of daily consumption at that consumption limit.

### **Calculations of Meal Consumption Limits—**

Daily consumption limits may be more conveniently expressed as the allowable number of fish meals of a specified meal size that may be consumed over a given time period. The consumption limit is determined in part by the size of the meal consumed. An 8-oz (0.227-kg) meal size is commonly assumed and can be used to convert daily consumption limits, the number of allowable kilograms per day to the number of allowable meals per month.

## MEAL CONSUMPTION LIMIT EQUATION

$$\text{CRmm} = \frac{\text{CRLim} \cdot \text{Tap}}{\text{MS}}$$

Where

**CRmm** = maximum allowable fish consumption rate (meals/month)

**Crlim** = maximum allowable fish consumption rate (kg/day)

**MS** = meal size (0.227 kg fish/meal)

**Tap** = time averaging period (365.25 days/12 month = 30.44 days/month).

The meal consumption equation was used to convert daily consumption limits, in kilograms, to meal consumption limits over a given time period (month) as a function of meal size. Consumption rates, such as meals per week, could also be calculated using this equation by substituting, for example, 7 days/week for 30.44 days/month.

### **Calculations of Consumption Limits for Non-Cancer Health Effects**

Non-cancer health effects caused by consumption of contaminated fish include systemic effects such as liver, kidney, neurological, muscular, ocular, reproductive, respiratory, circulatory, or other organ toxicities and adverse developmental/reproductive effects from acute and chronic exposure. The non-carcinogenic health effects equation calculates an allowable daily consumption limit

(CRLim) of contaminated fish, based on a contaminant's non-carcinogenic health effects, and is expressed in kilograms of fish per day [4]:

### Non-Cancer Health Effects Equation

$$\text{CRLim} = \frac{\text{MRL} \cdot \text{BW}}{\text{Cm}}$$

Where

**CRLim** = maximum allowable fish consumption rate (kg/d)

**MRL** = Minimal Risk Level (0.3 µg/kg/d)

**BW** = human body weight (kg)

**Cm** = measured concentration of chemical contaminant *m* in a given species of fish (mg/kg).

The maximum allowable fish consumption rate represents the maximum lifetime daily consumption rate (in kilograms of fish) that would not be expected to cause adverse non-carcinogenic health effects. Most MRLs are based on chronic exposure studies. Because the contaminant concentrations required to produce chronic health effects are generally lower than those causing acute health effects, the use of chronic MRLs in developing consumption limits is expected to also protect consumers against acute health effects [4].

#### **Calculations of Meal Consumption Limits—**

Similarly, the meal consumption equation is used to convert daily consumption limits in kilograms to meal consumption limits over given time periods as a function of meal size. Various meal sizes were assumed (see Tables 4 and 5). Monthly consumption limits pertain to recreational fishers. Note that irrespective of the time-averaging period selected (e.g., 7-days, 10-days, 14-days, monthly), the same chronic systemic MRLs are applicable; the difference is in the averaging periods used in the meal consumption equation. This approach does not expressly limit the amount of fish that may be consumed in a given day during the specified time period, so care must be taken to inform subsistence fishermen of the dangers of eating large amounts of contaminated fish in one meal when certain acute or developmental toxicants are of concern [4].

## APPENDIX C

### TOXICITY OF METHYL MERCURY

Environmental methyl mercury arises from the methylation of inorganic or ionic mercury, degassing of the earth's crust, emissions from volcanoes, and evaporation from natural bodies of water. Where mercury is found in soil and in river sediment, methyl mercury may also be found since it is both produced and destroyed by microbial processes involving mercury compounds [16].

Methyl mercury is rapidly taken up by fish and other organisms either directly through water or through the food chain, and accumulates in their tissues where it is retained for relatively long periods of time (e.g., 1 to 3 years) [18,19]. Methyl mercury is neurotoxic to humans following acute, intermediate, or chronic oral exposure. Approximately 95% of methyl mercury in fish is absorbed from the human gastrointestinal (GI) tract. Approximately 1% to 10% of methyl mercury absorbed from the human GI tract is distributed to the blood, with approximately 5% being absorbed into the blood stream and distributed to all tissues within a few days [19]. Methyl mercury is much more bio-available and toxic than ionic and elemental mercury [15,19]. The biological half life of methyl mercury in humans is reported to be 44 to 80 days [15].

Methyl mercury is especially toxic to the central and peripheral nervous systems where it crosses cellular membranes with ease because of its lipid solubility. The major early neurotoxic effects observed include motor disturbances, such as ataxia (the inability to coordinate muscle activities), tremors, and signs of sensory dysfunction such as impaired vision [15]. The predominant mechanism for methyl mercury's neurotoxic effect is degenerative changes in the cerebellum and degradation (i.e., destruction) of the myelin sheath which covers or insulates nerve fibers. This is likely the mechanism involved in motor effects and peripheral neuropathy (decreased nerve conduction velocity) [15]. Small amounts of methyl mercury can harm the brain during its developmental stage; for this reason, unborn fetuses, nursing babies and young children are most at risk. Methyl mercury levels in fetal red blood cells are about 30% greater than in maternal (mother's) red blood cells [18]. Although a nursing mother's milk may contain only about 5% of the mercury concentration of maternal blood, an infant's exposure to mercury may be increased by nursing. For these reasons, public health consumption advisories are issued to protect the unborn fetus and young children.

Approximately 7% to 15% of ingested ionic mercury is rapidly distributed to the blood and organs in humans. Ionic mercury has an affinity for and binds to the sulfhydryl groups in the red blood cells and plasma. Because the kidney tissue proteins are rich in amino acids which contain sulfhydryl groups, mercury will accumulate in the kidneys. Less than 0.01% of elemental mercury is absorbed across the human GI tract (stomach-intestine) because of the very slow dissolution rate of elemental mercury [16]. For this reason, elemental mercury is not of public health concern following oral exposure. Elemental mercury and methyl mercury can be changed in humans to ionic mercury and result in brain accumulation of mercury for long periods of time [15].

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