DOSE COMPARISON APPROACH FOR EVALUATING INGESTION OF PCDD/Fs AND DIOXIN-LIKE PCBs IN SEAFOOD VS. TYPICAL DIETARY INTAKES

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Abstract
Traditionally, the U.S. Environmental Protection Agency (USEPA) recommends using a dose-response equation to assess the probability of increased cancer risk for an individual. Because dioxin-like compounds are ubiquitous in the environment, and because of the magnitude of the USEPA dioxin cancer slope factor, even "background" dietary doses of dioxins can be associated with an "unacceptable" increased individual cancer risk (i.e., $> 1 \times 10^{-6}$). Obviously, this can complicate risk management decisions at dioxin-contaminated sites, particularly those that involve contaminated sediments and fish ingestion. Here, we present another approach to evaluating dietary dioxin risk. In this analysis, we compared the daily dioxin TEQ doses associated with the consumption of seafood from the Passaic River and fish from southern Mississippi to the dietary TEQ dose associated with other foods for adults and breast milk for children. We found that the daily dioxin TEQ intake associated with the consumption of catfish from southern Mississippi and fish and blue crab from the Passaic River was substantially lower than the amount typically ingested by a nursing infant and less than the amount ingested daily by adults as part of a typical U.S. diet that includes meat, dairy and fish.

Introduction
Polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and polychlorinated biphenyls (PCBs) are ubiquitous and persistent environmental contaminants that bioaccumulate in biological tissues. This class of compounds is frequently measured in the tissues of birds, fish, and mammals, including human adipose tissue and milk[1]. While humans may be exposed to these chemicals through various pathways, the diet serves as the primary route of exposure for the general population[2, 3].

Despite the presence of measurable levels in a variety of food products, regulatory agencies such as the U.S. Food and Drug Administration and the U.S. Department of Agriculture have not recommended that people avoid eating foods – such as meat, dairy, and fish – unless the levels exceed established regulatory thresholds. By assessing the intake associated with background levels in typical dietary foods, we were able to evaluate daily total TEQ intake resulting from consumption of wild-caught fish and seafood in the context of intake from other dietary sources for both infants and adults. Here we compare intake of PCDD/Fs and dioxin-like PCBs, reported as total TEQ, as a result of consuming fish and crab from the Passaic River and catfish from southern Mississippi to 1) the total TEQ dose that an adult ingests daily from typical dietary sources and 2) the total TEQ dose that an infant ingests daily from breast feeding.

Materials and Methods
Daily total TEQ intake from fish and crab consumption was determined using total TEQ tissue concentrations specific for fish and blue crab and daily ingestion rates derived by the USEPA[4] and Ray et al. (2007)[5]. Geometric mean total TEQ concentrations in fish filets and blue crab from the Passaic River were estimated using data from the Lower Passaic River Restoration Project website[6]. Median total TEQ concentrations in catfish were reported previously by Ferriby et al. (2006)[7] and the mean ingestion rates from the Mississippi River were determined using data from USEPA[4].

Comparison with Typical U.S. Diet
Adult daily intake of total TEQ associated with the consumption of beef, pork, poultry, eggs, dairy products (excluding milk but including table fats), milk, freshwater fish, shellfish, and marine fish was calculated from a mean total TEQ concentration and a mean ingestion rate for each food group. The concentrations and ingestion rates for these calculations were based on multiple sources from the scientific literature.

Comparison with Breast Milk

To calculate total TEQ intake from breast milk consumption, we used Lorber et al.'s (2002)[8] approach for estimating the daily dose of total TEQ received for a nursing infant. Their equation (Eq. 1) was based on the dioxin concentration in milk fat [C(t)], the fraction of fat in breast milk (f), the ingestion rate of breast milk (IR), and the body weight of the infant (BW).

$$D(t) = \frac{(C(t) * f * IR)}{BW} \quad (1)$$

To calculate the total TEQ body burden of a nursing mother, we utilized the NHANES 2003-2004 PCDD/F and dioxin-like PCB serum concentration data, adopting the same methodology to estimate total TEQ concentrations as described in Ferriby et al. (2006)[9] and Scott et al. (2008)[10]. Women between 20 and 44 years of age were assumed to represent nursing mothers. For this population, the geometric mean total TEQ concentration or C(t) was estimated to be 11.36 pg/g lipid. We assumed that, from birth to the first month of life, an infant had the same total TEQ concentration body burden as its mother. To estimate body burden over time, we used Lorber and colleagues' (2002)[8] assumption that the total TEQ concentration in breast milk decreases by 50% at six months of age and decreases another 50% at 12 months. Lorber et al. (2002)[8] also assumed that the total TEQ concentration in breast milk remained constant between year one and two of an infant's life. These assumptions were incorporated into the calculations as well.

The total fat in breast milk, f, varied between 3% and 5% based on our review of the literature[8, 11]. For this analysis, we adopted 4% as the fraction of fat content in breast milk.

Ingestion rates of breast milk were obtained from the USEPA Exposure Factors Handbook[4]. Drawing from five published breast milk intake studies, the USEPA calculated a weighted average of consumption rates for infants aged 1, 3, 6, 9 and 12 months[4]. For the remaining ages, an incremental average was calculated using statistical interpolation methods

Infant body weights for each month were also obtained from the USEPA Exposure Factors Handbook[4]. The USEPA, however, measured body weights for infant males and females separately[4]. Since the difference between infant male and female body weights was no greater than 0.69 kg, infant body weights for this analysis were averaged at months 1, 3, 6, 9, 12, 18, and 24. For the remaining months, incremental averages were calculated.

Results and Discussion

The estimated daily total TEQ intake or dose associated with consumption of fish and blue crab from the Passaic River and catfish from southern Mississippi is presented in Table 1. The daily total TEQ intake from Passaic fish and blue crab was estimated to be 0.22 and 0.07 pg/kg-day, respectively, while the daily total TEQ intake from consuming catfish from Mississippi was 0.04 pg/kg-day.

Table 1: Estimated Daily Intake of Total TEQ for Passaic River Fish and Crab and Southern Mississippi Catfish

River Biota	Geometric Mean Total TEQ (pg/g)	Consumption Rate (g/kg-day)	Daily Total TEQ Intake (pg/kg-day)	Reference For Geometric Mean	Reference Ingestion Rate
Passaic Fish (filet)	36.3	0.006[b]	0.22	LPRRP(2007)[6]	Ray et al. (2007)[5]
Passaic Blue Crab (muscle)	17.3	0.004[b]	0.07	LPRRP(2007)[6]	USEPA(1997)[4]
Mississippi Catfish (filet)	1.17[a]	0.03	0.04	Ferriby et al. (2006)[7]	USEPA(1997)[4]

[a] Median
[b] Central tendency estimates

Using mean ingestion rates, as determined by the USEPA and USDA, and mean total TEQ concentrations measured in various foods that are considered part of the normal U.S. diet, we calculated daily total TEQ intake for different food groups as well as a total daily TEQ dose. Beef and dairy products were associated with the highest daily total TEQ intake levels while the lowest intake levels were from consumption of poultry and eggs. Assuming an adult would consume food from each of these groups in a single day, the total daily TEQ intake was estimated to be 0.58 pg /kg-day for the general U.S. adult population (Table 2).

Table 2: Estimated Daily Intake of Total TEQ from Foods Typically Found in the U.S. Diet

Food Group	Mean Total TEQ (pg/g) Concentration	Mean Ingestion Rate (g/kg-day)	Daily TEQ Intake (pg/kg-day)	References for Mean TCDD	Reference for Ingestion Rate
Beef	0.18	0.825	0.15	Winters et al. (1996)[12]	USEPA (1997)[4]
Pork	0.28	0.261	0.07	Lorber et al. (1997)[13]	USEPA (1997)[4]
Poultry	0.068	0.598	0.04	Ferrario et al. (1997)[14]	USEPA (1997)[4]
Eggs	0.081	0.317	0.03	Hayward et al. (2000)[15]	USEPA (1997)[4]
Dairy Products	0.12	0.871	0.10	Lorber et al. (1998)[16]	USDA (1995)[17]
Milk	0.018	2.500	0.05	Lorber et al. (1998)[16]	USDA (1995)[17]
Freshwater Fish/ Shellfish	1.0	0.086	0.09	Fiedler et al. (1997a,b); Jensen et al. (2000, 2001)[18-21]	USEPA (1997)[4]
Marine Fish/Shellfish	0.26	0.201	0.05	Fiedler et al. (1997a,b); Jensen et al. (2000)[18-20]	USEPA (1997)[4]
U.S. Diet (Total)			**0.58**		

As presented in Table 2, the highest estimated daily total TEQ intake from breast milk was 77.14 pg/kg-day for breastfeeding infants one month of age. More notably, daily total TEQ intake steadily decreased as the age of the infant increased with the lowest level of intake (0.91 pg/kg-day) calculated for infants 18 months of age. Daily total TEQ intake from breast milk for children aged 24 months was assumed to be zero since the ingestion rate of breast milk for children this age was estimated to be zero.

Table 1: Daily Estimated Intake of Total TEQ from Breast Milk Over a 24 Month Period

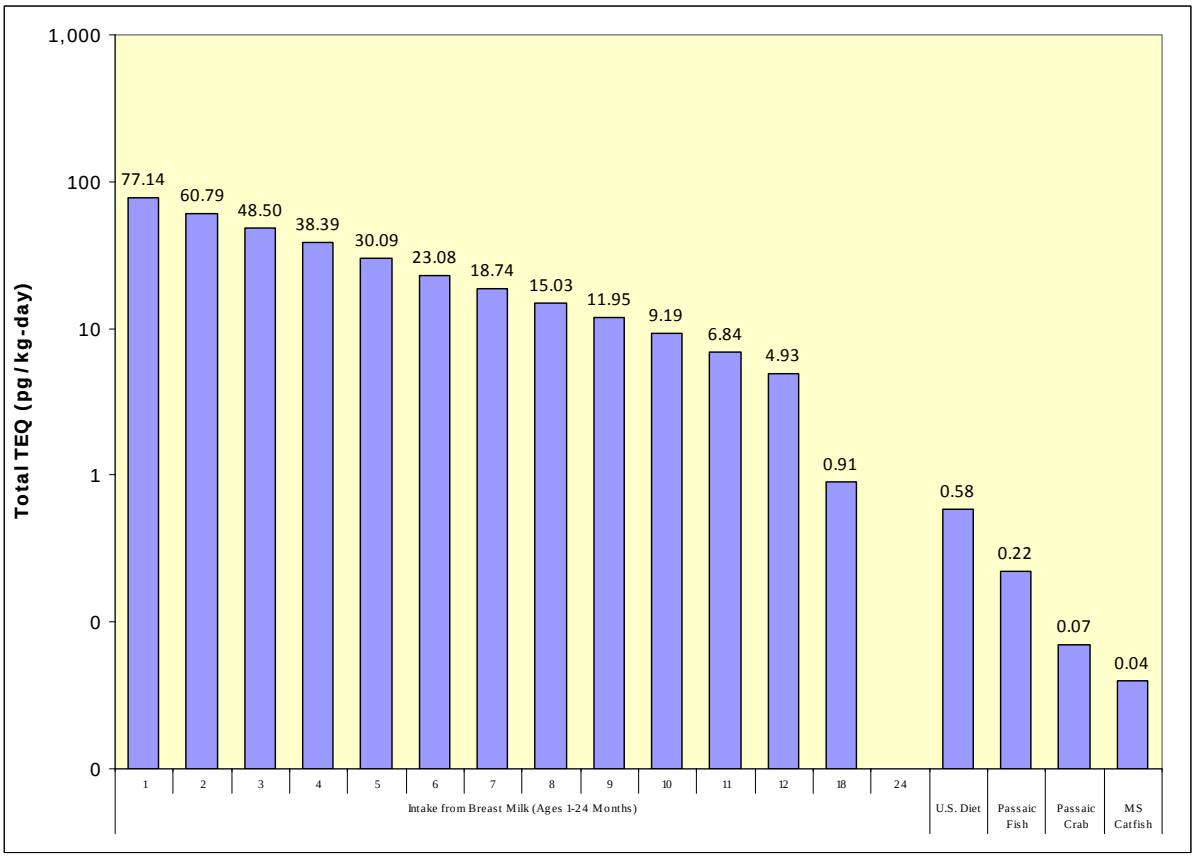
Age* (months)	C(t) (pg/g lipid)	*f*	IR (g/day)	Body Weight (kg)	D(t) (pg/kg-day)
1	11.36	0.04	702	4.14	77.14
2	10.22	0.04	731	4.91	60.79
3	9.09	0.04	759	5.69	48.50
4	7.95	0.04	761	6.30	38.39
5	6.82	0.04	763	6.91	30.09
6	5.68	0.04	765	7.53	28.08
7	5.21	0.04	717	7.98	18.74
8	4.73	0.04	669	8.42	15.03
9	4.26	0.04	622	8.87	11.95
10	3.79	0.04	557	9.19	9.19
11	3.31	0.04	492	9.52	6.84
12	2.84	0.04	427	9.84	4.93
18	2.84	0.04	89	11.15	0.91
24	2.84	0.04	0	12.25	0

*age is the equivalent of time, t

The total TEQ intake associated with consumption of breast milk (by age), adult consumption of typical foods that are part of the U.S. diet, and seafood from New Jersey and Mississippi is summarized in Figure 1. Interestingly, the total TEQ dose associated with the ingestion of breast milk for infants between the ages of 1 and 18 months was approximately 4 to 350 times greater than the dose associated with the ingestion of fish from the Passaic River, 13 to 1,100 times greater that the dose associated with the ingestion of Passaic River blue crab, 23 to 1,900 times greater than the intake associated with the ingestion of Mississippi catfish, and 2 to 130 times greater than the dose associated with a normal diet. Furthermore, comparison of the total TEQ intake associated with consumption of a typical adult diet with the intake calculated from consuming fish and crab showed that the total TEQ intake from a typical adult diet was approximately 2.6, 8.3, and 14.5 times greater than that of the total TEQ intake of fish and crab from the Passaic River and catfish from Mississippi, respectively.

Given these results, an individual will ingest,on average, 6.75% of their lifetime total TEQ dose from consuming breast milk in the first two years of life. Moreover, the estimated two-year total TEQ intake from breast milk consumption (67,475 picograms of total TEQ/ 70kg body weight/ 2 years) is substantially higher than a two-year dose resulting from the ingestion of Passaic River fish (11,242 picograms of total TEQ / 70kg body weight/ 2 years), Passaic River crab (3,577 picograms of total TEQ/ 70kg body weight/ 2 years), and Mississippi catfish (2,044 picograms of total TEQ/ 70kg body weight/ 2 years).

Figure 1: Total TEQ Intake Comparisons between Potential Sources of Exposure



In summary, the daily total TEQ intake associated with the consumption of catfish from Mississippi and Passaic River fish and blue crab is 1) less than the amount ingested daily by a nursing infant and 2) less than the amount ingested as a result of consuming a typical adult diet. It is therefore unlikely that TEQ levels measured in the biota from these areas (Passaic River and southern Mississippi) pose a significant health risk to most anglers. We believe the comparative analysis presented here should be considered in risk management decisions regarding intake of seafood from potentially contaminated sites.

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References
1. Safe, S. *Crit. Rev. Toxicology* 1990; 21: 51.
2. USEPA (U.S. Environmental Protection Agency) 2003.
3. ATSDR (Agency for Toxic Substances & Disease Registry) 1998.
4. USEPA (U.S. Environmental Protection Agency) *Exposure factors handbook* 1997; Volume II of III: Food ingestion factors.
5. Ray R., Craven V., Bingham M., Kinnell J., Hastings E., and Finley B. *J Toxicol Environ Health A* 2007; 70: 512.
6. LPRRP (Lower Passaic River Restoration Project 2000) Retrieved at http://www.ourpassaic.org/
7. Ferriby LL, Williams ES, Luksemburg WJ, Paustenbach DJ, Haws LC, Birnbaum LS, and Harris MA. *Organohalogen Compounds* 2006; 68: 612.
8. Lorber M. and Phillips L. *Environmental Health Perspective* 2002; 110: 325.

9. Ferriby L., Knutsen J., Harris M., Unice K., Scott P., Nony P., Haws L., and Paustenbach D. *Journal of Exposure Science and Environmental Epidemiology* 2006; 17: 358.
10. Scott LL, Unice KM, Scott P, Nguyen LM, Haws LC, Harris MA, and Paustenbach D. J Expo Sci Environ Epi 2008; 18: 524.
11. LaKind J. Wilkins A., and Berlin C. *Toxicology and Applied Pharmacology* 2004; 198: 184.
12. Winters D., Cleverly D., Meier K., Dupuy A., Byrne C., Deyrup C., Ellis R., Ferrario J., Harless R., Lesse W., Lorber M., McDaniel D., Schaum J., and Walcott J. *Organohalogen Compounds* 1996; 32: 469.
13. Lorber M., Saunders P., Ferrario J., Lesse W., Winters D., Cleverly D., Schaum J., Deyrup C., Ellis R., Walcott J., Dupuy A., Byrne C., and McDaniel D. *Organohalogen Compounds 1997;* 32: 238.
14. Ferrario J, Byrne C, Dupuy AE. *Chemosphere* 1997; 34: 2451.
15. Hayward DG. and Bolger PM. *Organohalogen Compounds* 2000; 47: 345.
16. Lorber M., Winters D., Griggs J., Cook R., Baker S., Ferrario J., Byrne C., Dupo A., and Schaum J. *Organohalogen Compounds* 1998; 38:125.
17. USDA (U.S. Department of Agricultural) 1995; NFS Report No. 91-2.
18. Fiedler H., Cooper K.R., Bergek S., Hjelt M., and Rappe C. *Chemosphere* 1997; 34: 1411.
19. Fiedler H., Cooper K., Rappe C., Bergek S., Hjelt M., Bonner M., and Howell F. *Organohalogen Compounds* 1997; 32: 311.
20. Jensen E., Canady R., and Bolger P. *Organohalogen Compounds* 2000; 47: 318.
21. Jensen E, Egan S, Canady R., and Bolger P. *Toxicol Ind Health* 2001; 17: 157.
22. Jensen E. and Bolger P. *Food Additives and Contaminants* 2000; 18: 395.

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