APPARENT HALF-LIVES OF DIOXINS, FURANS, AND PCBS IN ADULTS AND CHILDREN

Milbrath M O[1], Wenger Y[1], Gillespie B[2], Jolliet O[1]
[1]Department of Environmental Health Sciences, University of Michigan School of Public Health, 109 S Observatory, Ann Arbor, MI 48109; [2]Department of Biostatistics, University of Michigan School of Public Health, 109 S Observatory, Ann Arbor, MI 48109

Abstract
It is necessary to know the half-life of each congener of polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurnans (PCDFs), and dioxin-like polychlorinated biphenyls (PCBs) in the body to estimate the contribution of past exposures on current serum concentrations. A literature search was conducted for measured and modeled kinetic values for 29 congeners. The mean or median age of each exposed cohort was recorded, and best available data and models were examined to determine a mean half-life for each congener. Sources that provide consistent data for numerous congeners and that are within the range of reported values are used to determine reference half-life values for an infant and for a middle age male. These values can serve as points of departure for determining individual variations of half-life with age and body fat[1] and to adjust past intakes to present values[2].

Introduction
A central goal of the University of Michigan Dioxin Exposure Study (UMDES) is to determine the factors that explain variation in serum congener levels of polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and polychlorinated biphenyls (PCBs). To account for historical intake in current serum concentration levels of persistent congeners, it is necessary to decay past concentrations over time as a function of their half-lives. Different dioxin, furan, and dioxin-like PCB congeners have different persistence in the human body. This study examines the half-life data for 29 congeners from the literature. Based on the available information, a value for each congener is defined that approximatesthe half-life for an infant and for a hypothetical adult male nonsmoker with a normal body weight for an exposure to dioxins, furans, and dioxin-like PCBs, at a range relevant to the UMDES cohort (below 700 ppt TEQ). These values can be used as reference half-lives, and can be further adjusted for individual variation with known modifiers such as age, sex, percent body fat, and smoking status[1].

Materials and Methods
An extensive literature search was conducted for studies with half-life or decay values for dioxins and furans (table 1) and dioxin-like PCBs (table 2) in humans. When information on age was not directly available, a mean age during the time of sampling was estimated. Secondly, a subset of data representative of a middle aged adult was selected (white cells in tables) based on the following criteria: a) the blood serum concentration at the time of sampling was below <700 ppt, b) the subjects were adults, and c) the measurements were not later refined or reported as inaccurate in later studies. Half-life values that were measured in assumed steady state conditions were only retained if they were less than 10 years, because of large historical changes in intake levels. Values for children were also excluded, as the effect of dilution due to rapid growth in the first years results in a much shorter apparent half-life[3]. The mean half-lives were calculated for the retained subset to define a typical level for a moderately exposed adult. In the final part, reference values for a male adult and for an infant were selected based on the best available data. Sources that provided consistent data across congeners within the range of all measured data were chosen. Values reported by Hon-Wing et al. for breastfed infants were used as a point of departure at young ages[25].

Results and Discussion
The results of the literature search for dioxins and furans are presented in table 1. There is large variation in half-life values between congeners. For example, the mean half-lives for octa-chlorinated dibenzofuran (OCDF), tetra-chlorinated dibenzofuran (TCDF), and 1,2,3,7,8-pentachlorinated dibenzofuran are less than three years, whereas the mean half-lives for some of the hexa-chlorinated dibenzodioxins are over a decade.

Study	2378 TCDD	12378 PeCDD	123478 HxCDD	123678 HxCDD	123789 HxCDD	1234678 HpCDD	OCDD	2378 TCDF	12378 PeCDF	23478 PeCDF	123478 HxCDF	123678 HxCDF	123789 HxCDF	234678 HxCDF	1234678 HpCDF	1234789 HpCDF	OCDF	N	Age	Concentration Range	Cohort
Flesch-Janys1996[4]	7.2	11	8.4	9.9	4.9	3.7	6.7				6.2	6		5.8	3	3.2		43	48.7	15.6-300.2	Herbicide Plant Workers Š median value
Flesch-Janys1996[4]	6.1	11.2	9.76	13.1	5.1	4.9	6.7				6.4	7.2			3.1				48.7	15.6-300.2	Herbicide Plant Workers Š Regression
Van der Molen 2000[5]	6.3	8.3	7.8	10	4.6	3.2	4.6	2.4	3.9	7.8	5.6	7.1		3.1	2.8	5.2	1.6		48.7		Regression of Flesh Janys 1996 (Ogura 2004)
Van der Molen 2000[5]	7.8	11	12	12	6.8	8.8	5.7	1.4	2.9	10	7.7	24		3.6	5	10	0.7		48.7		Regression of Liem 1997 (Ogura 2004)
Liem 1997[6]	6.2	8.6	19	**13**	8.5	6.5	5.6	0.4	0.9	9.9	5.7	6.2	**6.2**	2.4	2.6	2.6	0.2				Population of Netherlands
Ogura 2004 blood[7]		6.7		42		5.8	22			4.9	9.9	17			4.8				42.5		General Japanese Population
Ogura 2004 adipose[7]	6.7	6.6		24	9.2	1.4	5	0.2	0.4	5	3.7	5.8		2.1	1.4		2.1		54.5		General Japanese Population
Pirkle 1989[8]	7.1																	36	44.7	16.9-423	Operation Ranch Hand
Wolfe 1994[9]	12																	337	44.7	16.9-422	Operation Ranch Hand
Michalek 1996[10]	8.7																	213	47.1	11.5-422.7	Operation Ranch Hand
Michalek 1999[11]	7.6																	97	49.6	11.5-422.7	Operation Ranch Hand
Michalek 2002[12]	7.5																	97	49.6		Operation Ranch Hand
Needham 1997[13]	8.2																	27		130-3830	Explosion in Seveso
Michalek 2002[12]	6.9																	54			Explosion in Seveso
Geusau 2002a[14]	1.5																	1	30	144000-35900	Austrian Female TCDD poisoning
Geusau 2002b[14]	2.9																	1	27	26000-9500	Austrian Female TCDD poisoning
Poiger 1986[15]	5.8																	1	42		Male Volunteer - one time
Schlatter 1991[16]	9.7																	1	45		Male Volunteer - one time
Rohde1999[17]	7.9	13.0	13.9	11.6	7.7	3.5	9.2			13.9	9	6		10	4	7.9	13	6	57	84-505	Former chemical plant employees
Schecter1990 b.[18]										4.7	2.9	3.5			6.5			1	60		Binghamton, NY Office building fire
Schecter1990 a.[18]										7.2	4.4	4.3			4.1			1	60		Binghamton, NY Office building fire
Schecter1990 comb.[18]										4.5	4	4.9			6.8			1	60		Binghamton, NY Office building fire
Iida 1995[19]										9.1	8.6							17			Yu-Cheng
Ryan 1991[20]										5	5										Yu-Cheng
Kashimoto 1983[21]										1.5	1.5							30			Yu-Cheng
Leung 2005[22]										1.1	2.3				1.5			22	53		Yu-Cheng/Yusho
Ryan1989[20]										1.7	2.4				2.4						Yu-Cheng
Ryan1991[23]										2.5	2.5				2.5			3			Yusho
Gorski1984[24]				3.5		3.2	5.7								1.7		1.8		1		Child Exposed from Wood in Home
HonWing 2006[25]	0.4	0.32		0.39		0.3	0.5			0.27									2	1	Breast Milk Fed Infants
Mean Value	7.5	9.87	12.6	11.6	6.7	4.7	6.7	1.1	2	5.92	5.1	7.5	6.2	4.5	3.5	5.8	3.2				
Adult Reference Value	7.2	11.2	9.82	13.1	5.1	4.9	6.7	2.1	3.5	7.03	6.4	7.2	6.2	2.7	3.1	4.6	1.4				
Infant Reference Value	0.4	0.32	0.5	0.39	0.3	0.3	0.5	0.1	0.2	0.27	0.4	0.4	0.3	0.2	0.2	0.3	0.1				
Reference Value Source	1	2	2	2	2	2	2	3	3	3	2	2	3	3	2	3	3				

Table 1. Measured and modeled half-lives for dioxins and furans reported in the literature. N is the number of subjects in the study. Concentrations are expressed as ppt. Values in gray were excluded from this analysis. Underlined values are estimates based on similar chemical structure.
Reference value sources: 1) Flesh-Janys reported median 2) Flesh-Janys Regression line 3) Van der Molen et al. model with Flesh-Janys data

The range and mean of reported values is for adults of both sexes with mixed smoking status and a range of percent body fat. The reference values were selected to represent a 48.7 year-old non-smoking male at a moderate level of exposure with a percent body fat of 21.86, the median age and percent body in the cohort studied by Flesh-Janys. The reference value was chosen to allow for adjustments based on known modifiers such as sex, smoking status, and percent body fat. The regression data of Flesch-Janys[4] was used preferentially because it examines a broad range of chemicals in a consistent way; contains information for percent body fat, sex, and smoking status; and the resulting value is within the range of the other studies. In the case of TCDD, the single median value given in the table of Flesh-Janys was used as the reference value, because it better fit with the reported data. For congeners not reported in the Flesch-Janys study, the model given by Van Der Molen et al. was used,[5] and a reference value was determined using the median age and percent body fat from Flesh-Janys (48.7, 21.9, respectively).

There is a dearth of information in the literature regarding the kinetics of PCBs. Half-life values reported in the literature are shown in table 2. To determine the point of departure for ten of the twelve PCB congeners, values given by Ogura et al. for blood were used[7]. The value given by Ogura for adipose was used for PCB 77 and PCB 81, because there was no blood data available. These values correspond to the half-lives of the general Japanese population assuming steady state conditions. Because of the large decrease in dioxin, furan, and PCB concentrations in the environment in the last 30 years, the steady state assumption is only appropriate for congeners with very short half-lives, and congeners with longer half-lives could be over estimated.

Study	PCB 77	PCB 81	PCB 126	PCB 169	PCB 105	PCB 114	PCB 118	PCB 123	PCB 156	PCB 157	PCB 167	PCB 189	N	Age	cohort
Liem 1997[6]	0.1	**0.1**	2.7	13	**2.7**	**2.7**	**2.7**	**2.7**	**13**	**13**	**13**	**13**			Population of Netherlands
Ogura 2004 blood[7]			1.6	7.3	2.4	10	3.8	7.4	16	18	12	22		42.5	General Japanese Population
Ogura 2004 adipose[7]	0.07	0.73	2.7	13	2.7	25	4.2	12	38	27	10	41		54.5	General Japanese Population
Ryan1991[23]					10.4								3		Yusho
Ryan 1993[26]					10.4			1.1		1.62			3		Yusho
Chen 1982[27]						0.58		0.83		**100**			17		Yu-Cheng
Chen 1982[27]						0.51		0.77		100			17		Yu-Cheng
Ryan 1993[26]					10.4			1.1		1.62			3		Yu-Cheng
Brown1989[28]						3.9		5.8					39	42.5	Occupational Exposure
Buhler1988[29]								0.5					1	50	Male Volunteer
Wolff 1991[30]										4.6				4	
Wolff 1992[31]								9.6						45	
HonWing 2006					100								2	1	Breast Milk Fed Infants
Mean Value	0.085	0.42	2.33	11.1	6.5	7.12	3.6	4.18	22.3	9.0075	11.67	25.33			
Adult Reference Value	1.43	0.14	0.74	1.65	7.35	2.45	105	3.85	7.45	165	185	125			
Infant Reference Value	0.004	0.04	0.09	0.46	0.13	0.56	0.2	0.41	0.89	1	0.67	1.222			
Reference Value Source	4	4	5	5	5	5	5	5	5	5	5	5			

Table 2. Measured and modeled half-lives for PCBs reported in the literature. N is the number of subjects in the study. Values in gray were excluded from analysis.
Reference values: 4) Ogura et al. blood (mean age = 49.5) 5) Ogura et al. adipose (mean age = 42.5)

Full understanding of the half-lives of different congeners in the body requires continued study of the kinetics of these compounds in humans, especially for PCBs. The mean values and reference values provided above reflect well the current available data in the literature. These half-life values can be further adjusted to reflect individual characteristics that affect the persistence of the different congeners in the body, and can then be used to determine the effect of past intake on current body concentrations.

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