A COMPARISON OF THE PCDD/PCDF TEQ FOR THE US POPULATION IN 2001-2002 AND A PHARMACOKINETIC MODEL FOR ESTIMATING EXPOSURE

Patterson DG Jr[1], Lorber M[2], Turner WE[1], and Needham LL[1]

[1]Organic Analytical Toxicology Branch, Division of Environmental Health Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, GA 30333; [2]National Center for Environmental Assessment, Office of Research and Development, US Environmental Protection Agency, 1200 Pennsylvania Ave, NW, Washington, DC

Introduction

A pharmacokinetic model for estimating the exposure of Americans to dioxin-like compounds in the past, present, and future was proposed by Lorber[1] in 2002. A national reference range for TEQ in the US population was recently established using samples collected as part of the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention. The Lorber paper made certain predictions of the future levels of TEQ and these predictions could be tested by the NHANES 2001-2002 data.

Materials and Methods

We first attempted to duplicate the PK modeling of the 2002 paper by Lorber[1] where the simulations were done using an object-oriented model called "Modelmaker". This "baseline" model (Table 1) produced results very close to the 2002 paper (see Table 6 in reference 1). Two additional models were constructed (Tables 2 and 3) with a steeper decline in the body burden TEQ. The organochlorine compounds in serum were measured by high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry (HRGC/ID-HRMS) in the dioxin laboratory at the Centers for Disease Control and Prevention.[2,3] The 1998 World Health Organization's Toxic Equivalency Factors (WHO-TEF) were used to report PCDD, and PCDF Toxic Equivalents (TEQs) since the TEQs in the Lorber[1] paper were calculated using the 1998 WHO-TEFs. For levels measured below the limit of detection, the limit of detection for the congener divided by the square root of 2 was substituted.

Results and Discussion

We summarize the predicted body burdens for the years 1990, 1995, 2000, and 2005; the focus is on predictions for the years 1995 and 2000. The primary data upon which to compare model predictions for purposes of this paper are the EPA Dioxin Reassessment assignment of body burdens and the 2001/2002 NHANES data. The EPA Dioxin Reassessment used CDC data from 1995-1997; it was a compilation of 316 individuals from about 6 studies, age range of 20-70 years.[1] The mean WHO98-PCDD/PCDF TEQ concentration was 20.1 pg/g lipid for 1995-1997 data. The 2001/2002 NHANES geometric mean WHO98-PCDD/PCDF TEQ as the average of four age ranges, 12 to 60+ years, males/females, race/ethnicity is 11.9 pg/g lipid. The observed data is, therefore:

Year	WHO98-PCDD/PCDF TEQ, pg/g lipid
1995-1997	20.1
2001/2002	11.9

In redoing the PK modeling, we found that the constructed dose for the second half of the 20th century was too high to adequately reproduce these numbers. Therefore, we created two additional models:

Baseline Model (Table 1): Peak reached in 1965 of 6.5 pg/kg-day, to linearly decline to 1.1 pg/kg-day in 1980, to then linearly decline to 0.5 pg/kg-day by the year 2000, and then stay constant at 0.5 pg/kg-day past 2000.[1]

More Steep Decline Model (MSD) (Table 2): peak reached in 1965 of 6.5 pg/kg-day, to linearly decline to 0.5 by 1980, and then to stay constant at 0.5 pg/kg-day into the future.

Even More Steep Decline Model (EMSD) (Table 3): peak reached in 1965 of 6.5 pg/kg-day, to linearly decline to 0.5 by 1980, to then continue to gradually decline to 0.25 pg/kg-day by 2000, to then stay constant at 0.25 pg/kg-day past 2000.

The predicted population averages for these models are (note: predictions are the average of ages 15, 20,….,70).

	Population predictions for			
Model	1990	1995	2000	2005
Baseline	33.2	25.1	19.1	14.9
MSD	27.8	20.5	15.8	12.8
EMSD	27.1	19.2	13.7	9.9

It would appear that the results for EMSD, 19.2 and 13.7 pg/g lipid for 1995 and 2000 provide the best match for the EPA Reassessment/NHANES results of 20.1 and 11.9 pg/g lipid, respectively.

We also looked at age differentiation, comparing NHANES to the 2000 predictions for the three models. If we consider the 12-19 age range to be represented by the average simulated for ages 15 and 20, for 20-39 years to be represented by the average of 20, 25, 30, 35, 40 (n=5), 40-59 years to be represented by the average of 40, 45, 50, 55, 60 (n=5), and >60 years to be represented by 60, 65, 70 (n=3), then the following Table results:

Age range	NHANES	Baseline	MSD	EMSD
12-19	4.3	8.5	6.7	4.3
20-39	6.0	12.5	9.7	7.5
40-59	12.8	22.6	18.9	16.8
60+	24.5	30.0	25.9	23.9

Clearly this shows that the model established for the 2002 manuscript[1], while effective in capturing broad trends of the 20th century, overestimated the exposures starting from near 1980. The two models devised had lower exposures from 1965 to 1980, and then lower from 1980 to the present. These lower exposures, particularly the lowest exposure, appear to better match the Dioxin Reassessment data for the mid-1990s and the NHANES data for the early part of this century.

Table 1. The “Baseline” Model

AGE	1990	1995	2000	2005
15	13.11	10.60	8.82	7.61
20	15.36	10.12	8.20	7.09
25	20.70	13.75	9.66	8.17
30	25.73	17.47	12.17	9.21
35	29.51	21.17	14.87	11.01
40	33.01	24.18	17.69	13.04
45	36.34	27.10	20.13	15.24
50	39.40	29.99	22.60	17.25
55	42.27	32.77	25.11	19.35
60	45.03	35.47	27.62	21.55
65	47.50	37.96	29.98	23.69
70	50.20	40.65	32.53	26.00
Av, 15-70	33.18	25.10	19.11	14.93
Av, 20-70	35.00	26.42	20.05	15.60

Table 2. The “More Steep Decline” (MSD) Model

AGE	1990	1995	2000	2005
15	7.47	7.06	7.05	7.05
20	10.53	6.44	6.24	6.24
25	15.58	9.66	7.04	6.92
30	20.44	13.12	9.21	7.48
35	24.08	16.64	11.66	9.00
40	27.53	19.48	14.27	10.80
45	30.83	22.29	16.52	12.80
50	33.89	25.09	18.83	14.61
55	36.75	27.80	21.22	16.53
60	39.51	30.44	23.60	18.58
65	42.01	32.90	25.87	20.58
70	44.70	35.52	28.31	22.74
AV, 15-70	27.78	20.54	15.82	12.78
AV, 20-70	29.62	21.76	16.62	13.30

Table 3. The "Even More Steep Decline" (EMSD) Model

AGE	1990	1995	2000	2005
15	6.58	5.30	4.41	3.81
20	9.81	5.07	4.10	3.55
25	14.83	8.24	4.84	4.08
30	19.71	11.70	6.98	4.61
35	23.37	15.24	9.45	6.12
40	26.84	18.11	12.10	7.93
45	30.16	20.95	14.38	9.95
50	33.23	23.78	16.72	11.79
55	36.11	26.52	19.14	13.73
60	38.89	29.18	21.55	15.80
65	41.40	31.66	23.85	17.84
70	44.70	34.31	26.31	20.02
Av, 15-70	27.14	19.17	13.65	9.93
Av, 20-70	29.00	20.43	14.49	10.49

References

1. Lorber M. *The Science of the Total Environment* 2002; 288: 81.
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