Evidence for the Role of Diet in the Exposure of Americans to Phthalates

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December 2, 2010

Chronic Hazard Advisory Panel (CHAP) on Phthalates

Consumer Product Safety Commission

December 15, 2010

Credit

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Outline

- Background for presentation

- First a word on Bisphenol A (BPA)

- Use of NHANES 2003/4 database to study the potential influence of diet on phthalate exposures

- Use of American Chemistry Council database in a "forward" approach to assessing exposure

- What's next

Background
Phthalate Intake Estimates in the Literature

- Wormuth et al. 2006. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? Risk Analysis 26: 803 – 824.

  "Forward-based" analysis combining contact rate and concentrations of phthalates in environmental and exposure media, including consumer products. Adult mean Exposures, µg/kg-day:

Food Dominated:		Non-food Dominated:	
DnBP	2.0	DMP	0.2
DiBP	0.7	DEP	1.0
DEHP	3.0	BBzP	0.3
		DiNP	0.005
		DiDP	0.007

- Many estimates in the literature on DEHP intake based on urine measurements and creatinine or urine volume correction; intakes on the order of 1 to 5 µg/kg-day for adult central tendency in North America and Europe.

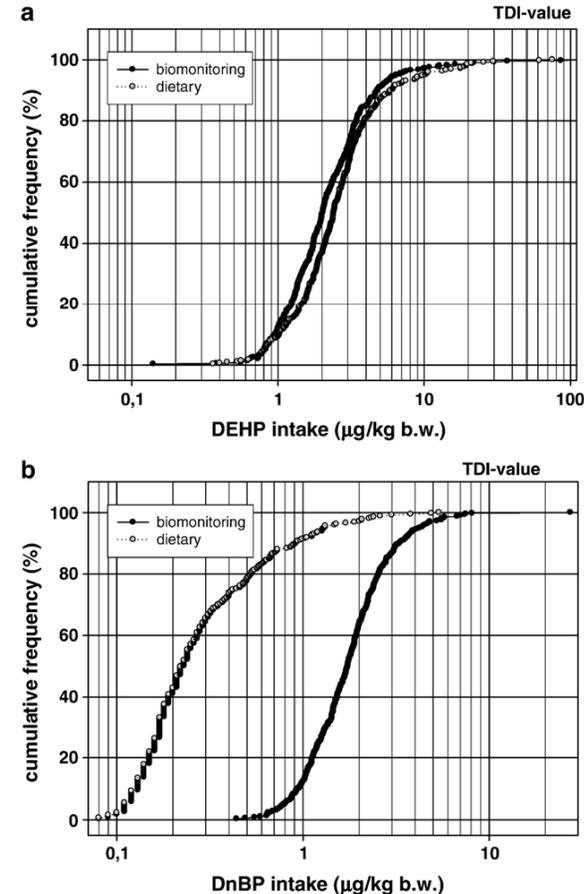**EPA** United States Environmental Protection Agency

Fromme et al. 2007. Intake of phthalates and di(2-ethylhexyl)adipate: Results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data. Env Int 33: 1012-1020.
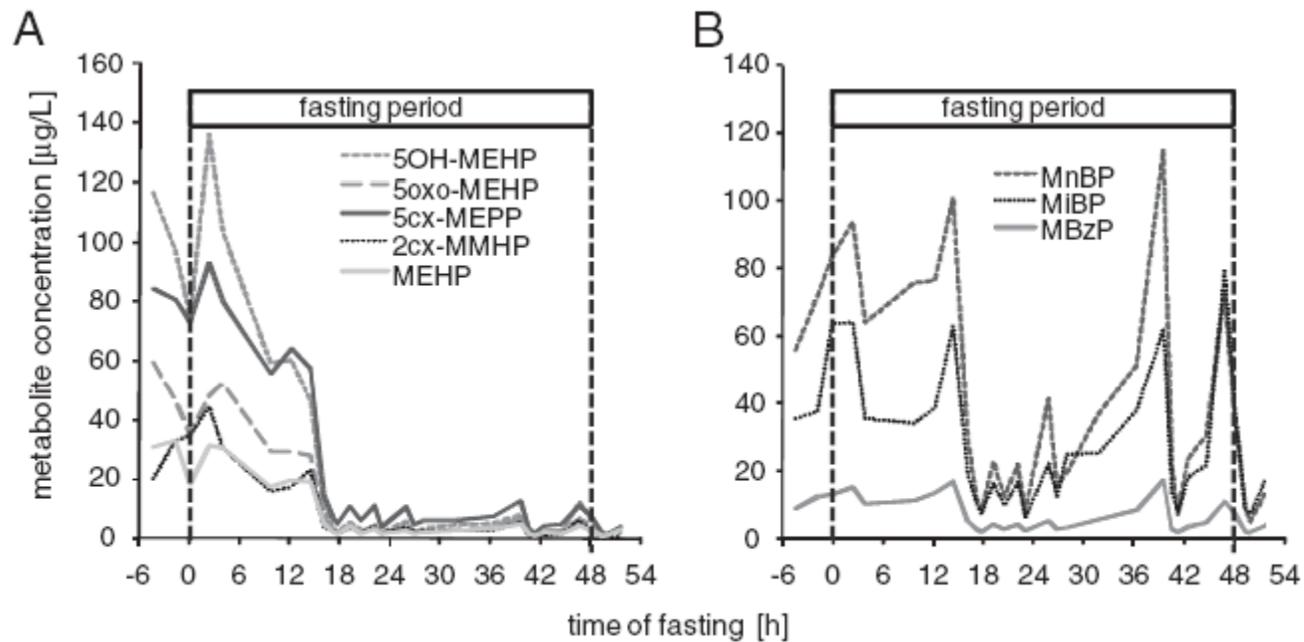
Duplicate diet samples from 50 individuals were measured for DEHP, DnBP, DiDP, and DEHA, allowing for dietary intakes in μg/kg-day. Urine measurements of mono ester metabolites were converted to a total daily intake of parent phthalate in similar units.

The charts compare the cumulative (over all participants/days) intakes inferred from daily diets and daily urine excretions. As seen, there is nearly a one-to-one correspondence with DEHP but no relation with DnBP. Other analyses also support the finding that diet predominates for DEHP.

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a — TDI-value — biomonitoring / dietary — cumulative frequency (%) vs. DEHP intake (μg/kg b.w.)

b — TDI-value — biomonitoring / dietary — cumulative frequency (%) vs. DnBP intake (μg/kg b.w.)

Background
Evidence for the Importance of Diet in Phthalate Exposure

A

metabolite concentration [µg/L]

fasting period

5OH-MEHP
5oxo-MEHP
5cx-MEPP
2cx-MMHP
MEHP

B

fasting period

MnBP
MiBP
MBzP

time of fasting [h]

Note: This supports the finding of Fromme et al that DnBP exposure is not diet-dominated. This contrasts the finding of Wormuth, who did find that DnBP exposure was dominated by diet

Koch fasting study in, Wittassek, et al, 2010. Assessing exposure to phthalates –
The human biomonitoring approach. Mol. Nutr. Food Res, advance online June, 2010

Background
The ratio of tertiary to secondary metabolites of DEHP

- In separate experiments including a self-dosing (blue diamonds) of a large amount of labelled-DEHP and an evaluation of DEHP metabolite levels following apheresis blood platelet donation (pink squares), it was found that the tertiary metabolite, 5cx-MEPP, eventually dominated the profile in urine samples and exceeded the concentration of the secondary metabolite, 5OH-MEHP, by a factor of 2 and more:
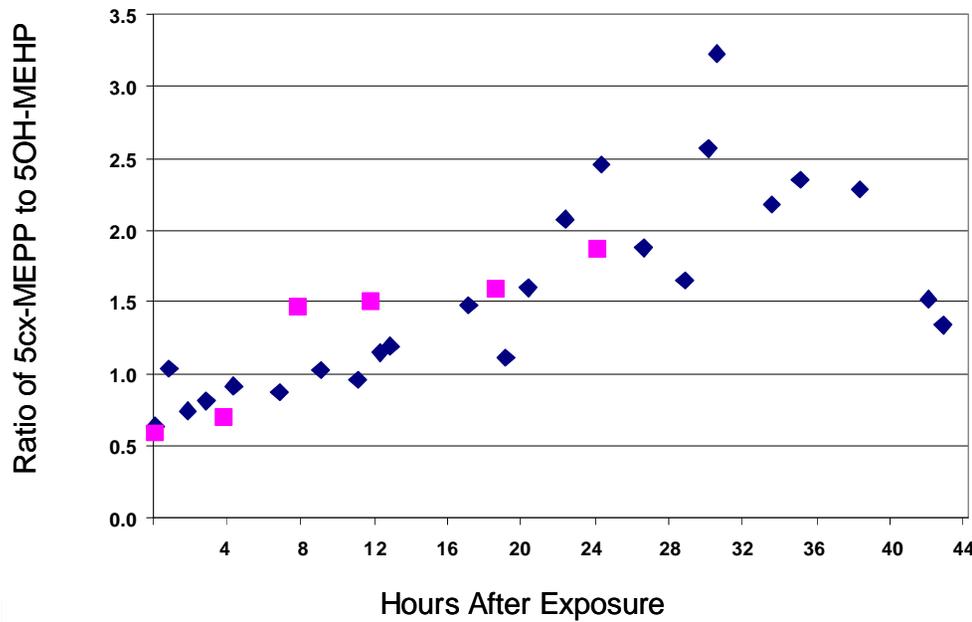
Source: Lorber, M., HM Koch, J Angerer. 2010. A critical evaluation of the creatinine correction approach: Can it underestimate intakes of phthalates? A case study with di-2-ethylhexyl phthalate. J. Expo. Sci. Environ. Epidemiol. Advance on-line September 8, 2010; doi:10.1038/jes.2010.43

Background
The "phafsthr" parameter in NHANES

- Defined as, "The time (in hours) between when the examinee last ate or drank anything other than water and the time of the venipuncture."

- Participants were told to "a) "not eat or drink anything except water" and b) have "no coffee, tea, food, dietary supplements, mints, cough drops, gum, snacks, or beverages, and no nicotine for at least 3 hours". However, they were all asked at time of sampling if they, in fact, had these consumptions and reported yes or no. The analysis in this evaluation did not separate out the "yes" group.

- Recall accuracy uncertain. Influence of other possible ingestion-related exposures such as brushing teeth on phthalate metabolite concentrations within reported "phafsthr" is unclear. Of course, non-ingestion exposures not known and expected to influence results.

But First a Word on Bisphenol A

- Stahlhut, et al. 2009. Bisphenol A Data in NHANES Suggest Longer than Expected Half-Life, Substantial Nonfood Exposure, or Both. Env Health Persp. 117: 784-789

- Analyzed NHANES 2003/4 data using phafsthr (and minutes) to find:

N	Fast time, hr	Median, ug/g creatinine
129	0 – 4.5	2.6
441	4.5 – 8.5	2.3
899	8.5 – 24.0	2.4

- n = 1469. Excluded individuals under 18 years old (34% of population), >85 years old (2%), and greater than 24 hr fast (1%)

But First a Word on Bisphenol A

- Did an independent analysis of NHANES 2003/4 and looked at: straight as well as creatinine-corrected concentrations, means and medians, different hourly intervals:

N	Fast time, hr	urine volume, ng/mL		urine creatinine, µg/g	
		mean	median	mean	median
341	0 – 4	6.1	4.0	5.7	3.6
634	4 – 8	4.9	2.7	4.2	2.6
527	8 – 12	5.5	3.1	3.9	2.5
685	12 – 16	4.6	2.8	3.6	2.3
228	16 – 20	5.3	3.3	3.6	2.3
36	20 – 24	6.1	3.7	3.4	2.3

- Creatinine corrected values show a more consistent picture: a slow decline with increasing fsthr. The variability brought in with hydration makes urine volume concentrations a poor metric

- Medians for creatinine-corrected consistent with Stahlhut except 0-4 hr. Is information on age < 18 important?

But First a Word on Bisphenol A

- Looked at NHANES 2003/4 BPA creatinine-corrected for ages < 18 and >= 18

		<18			>= 18	
Fast time, hr	n	mean	median	n	mean	median
0 – 4	194	**6.7**	**4.3**	147	4.3	2.6
4 – 8	187	**5.1**	**3.2**	462	3.8	2.3
8 – 12	141	4.5	2.8	386	3.7	2.5
12 – 16	220	4.3	2.5	466	3.3	2.3
16 – 20	80	4.5	2.7	148	3.1	2.2
20 – 24	20	3.8	3.2	37	3.1	2.1

Looks like a dietary signal for younger individuals, particularly in 0-4 versus other time periods:

- more food intake per body weight (?)
- more rapid metabolism leading to meaningful initial excretion (?)

Still a small signal for adults by looking at 0-4 mean versus other means

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DEHP Examination #1
Ratio of Tertiary and Secondary Metabolites

phafsthr	average ratio
0-4	1.72
4-8	1.77
8-12	1.77
12-16	1.85
16-20	1.91
20-24	2.05
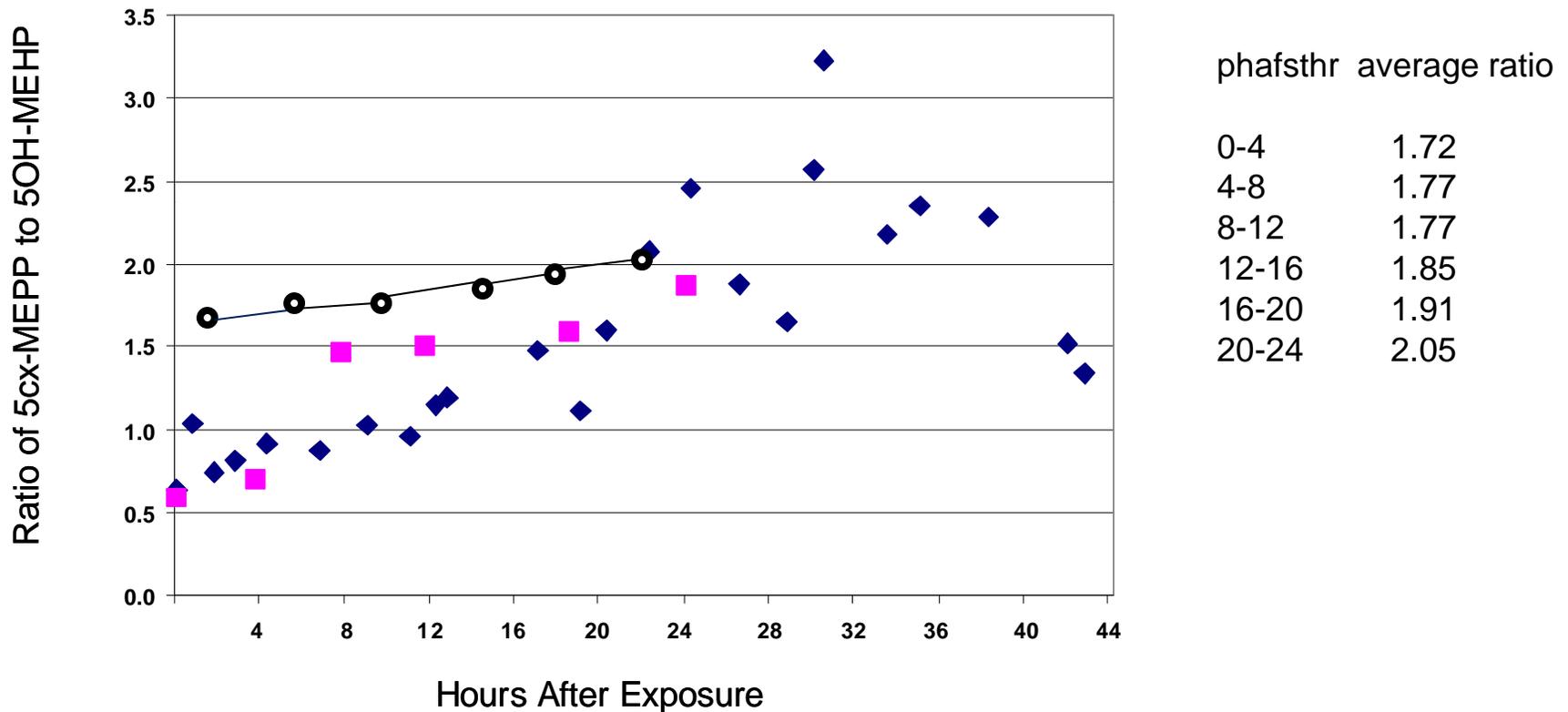
Maybe a signal here, but a weak signal compared to experimental data

DEHP Examination #2
Creatinine-corrected MEHP and phafsthr as a function of age

	<18			>= 18		
Fast time, hr	n	mean	median	n	mean	median
0 – 4	221	7	3	153	7	3
4 – 8	192	7	2	454	8	2
8 – 12	147	6	2	433	8	2
12 – 16	238	6	2	462	5	2
16 – 20	76	2	1	158	3	1
20 – 24	16	4	2	38	4	1

- Gently declining trends in medians similar by age category, but decline in means do not appear until after about 12 to 16 hr of fasting.

DEHP Examination #3
Creatinine-corrected 5cx-MEPP and phafsthr as a function of age

Fast time, hr	<18			>= 18		
	n	mean	median	n	mean	median
0 – 4	221	78	45	153	59	25
4 – 8	192	93	38	454	62	27
8 – 12	147	66	33	433	75	29
12 – 16	238	77	39	462	58	22
16 – 20	76	40	25	158	48	21
20 – 24	16	53	29	38	70	25

- Maybe a trend for <18 for median in 0-4 hr vs. other time periods, maybe a trend for declines by 16-20 hrs, but really not much there upon visual inspection

BBzP Examination – Nonfood exposures (?)
Creatinine-corrected MBzP and phafsthr as a function of age

Fast time, hr	<18			>= 18		
	n	mean	median	n	mean	median
0 – 4	221	46	27	153	19	11
4 – 8	192	36	19	454	17	10
8 – 12	147	35	20	433	20	13
12 – 16	238	40	22	462	18	11
16 – 20	76	33	22	158	19	12
20 – 24	16	19	14	38	25	12

- Clear difference as a function of age, but little evidence of a trend with phafsthr.
- Maybe something in the difference between 0-4 hr versus later exposures of individuals <18

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DnBP Examination – Food exposures (?)
Creatinine-corrected MnBP and phafsthr as a function of age

Fast time, hr	<18			>= 18		
	n	mean	median	n	mean	median
0 – 4	221	54	31	153	43	24
4 – 8	192	41	27	454	32	20
8 – 12	147	41	26	433	29	20
12 – 16	238	46	28	462	37	17
16 – 20	76	44	28	158	24	17
20 – 24	16	36	20	38	30	18

- Also a difference as a function of age, but little evidence of a trend with phafsthr.
- Maybe something in the difference in 0-4 hr vs. later exposures of both sets of individuals

DiBP Examination – Food exposures (?)
Creatinine-corrected MiBP and phafsthr as a function of age

Fast time, hr	<18			>= 18		
	n	mean	median	n	mean	median
0 – 4	221	9	7	153	6	4
4 – 8	192	8	5	454	6	3
8 – 12	147	6	5	433	5	3
12 – 16	238	10	6	462	5	4
16 – 20	76	7	5	158	5	4
20 – 24	16	10	4	38	6	4

- Also a difference as a function of age, but little evidence of a trend with phafsthr.

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- The previous slides showed that DEHP metabolites were consistent in the <18 and >=18 age groups, but that concentrations of metabolites of DiBP, DnBP, and BBzP were higher in the younger as compared to older groups.

- The daily creatinine excretion in children under 18 tend to range from an average of 0.5 g/day for children ages 5-11 to an average of 1.2 g/day for adolescents from 11-17. This compares to 1.5 g/day in adults. Therefore, on a mass basis, an NHANES finding that individuals less than 18 have a creatinine-based phthalate excretion twice that of adults (as in MBzP), the actual mass excreted may be more like the same:

$$2 \text{ ug MBzP/g} * 0.8 \text{ g/day} \sim 1 \text{ ug MBzP/g} * 1.5 \text{ g/day}.$$

- However, body weight of children in the 6 – 18 year old range from 20-70 kg, with an average of about 45 kg, whereas adult body weights range more narrowly between 70 and 80 kg. This implies that, on a body weight basis, the same amount of mass excreted by the two age ranges might translate back to a finding that, on a body weight basis, the lower range might be twice as high.

THEREFORE, creatinine-based concentrations might be a good first indicator for trends in body-weight based exposures.
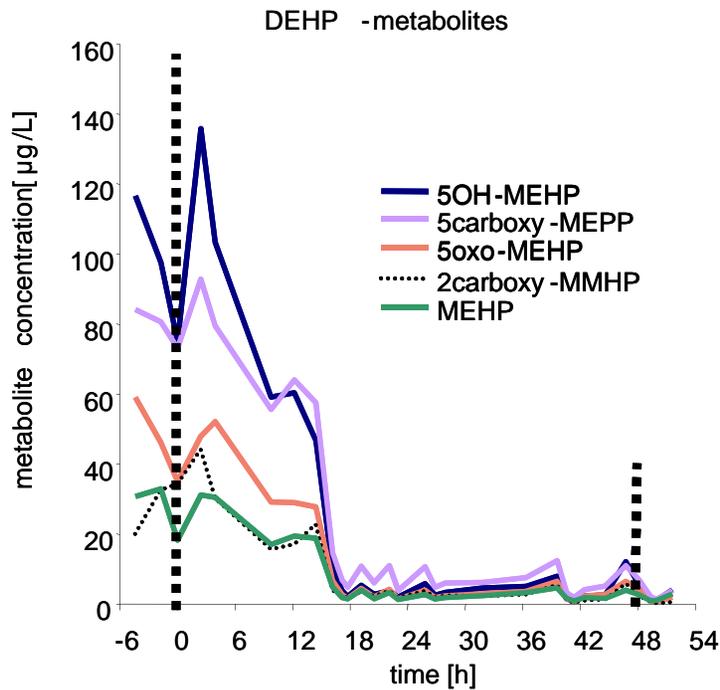
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Review of Observations from NHANES 2003/4 Examination

- Metrics generated from creatinine-corrected concentrations expected to be more stable than urine volume concentration (shown for BPA, not evaluated for phthalates but expected to also be true).

- Means and medians of creatinine-corrected phafsthr groupings of NHANES examined; remains unclear which metric is best descriptor for groupings. Other analyses, such as scatter plots and regression lines, need also to be developed.

- BPA showed what appears to be evidence for food-related exposures when looking at individuals < 18 years old, but not for individuals older than 18. For this reason, phthalate analysis also looked at this age breakout for all groupings of phafsthr, although same disparity did not seem to show up as clearly for phthalates.

- Ratio of tertiary to secondary DEHP metabolite showed upward trend with phafsthr, but not as steep as implied by experimental data; weak but supportive evidence for dietary effect.
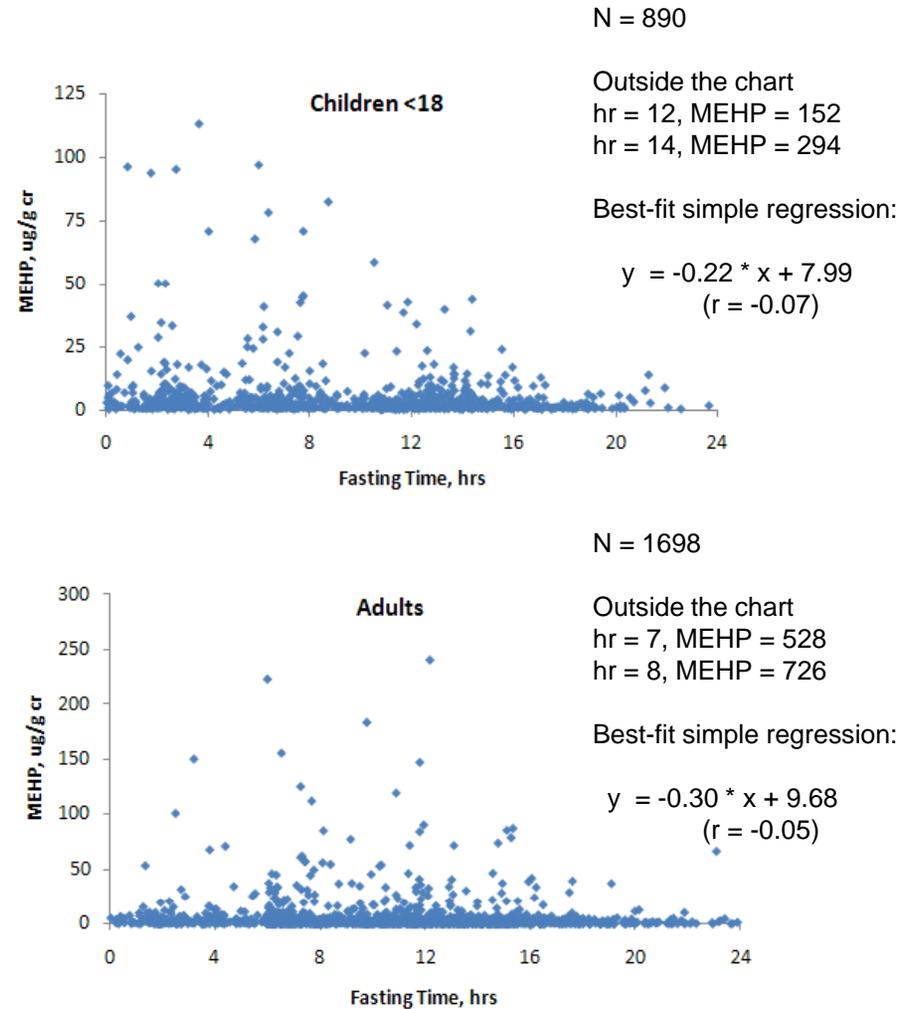
- HYPOTHESIS: If a relationship between phafsthr and DEHP metabolites is going to appear, it would most likely appear for MEHP because of: external evidence that DEHP exposures are food related, and MEHP has short half-life (5 hrs) compared to other DEHP metabolites, and maybe other phthalate monoester metabolites. In fact, of all phthalate metabolites examined, the most clear relationship is seen between phafsthr and MEHP:
  - Between both age groups
  - Not only between 0-4 and 4-8 hr, but continued declines as phafsthr increases

- Weak or non-existent relationship between fsthr and concentrations for 5cx-MEPP and other three phthalate monoester metabolites, despite Wormuth finding that diet explained exposures for 2 of 3 other phthalates. Maybe something to learn from differences in 0-4 hr, and subsequent time periods, but that's it.

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DEHP - metabolites

5OH-MEHP
5carboxy -MEPP
5oxo-MEHP
2carboxy -MMHP
MEHP

Does the NHANES data also show steep declines only after 14 hours from start of fast?

N = 890

Outside the chart
hr = 12, MEHP = 152
hr = 14, MEHP = 294

Best-fit simple regression:

$y = -0.22 * x + 7.99$
$(r = -0.07)$

N = 1698

Outside the chart
hr = 7, MEHP = 528
hr = 8, MEHP = 726

Best-fit simple regression:

$y = -0.30 * x + 9.68$
$(r = -0.05)$

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Discussion Point
Confounders With Study of "phafsthr"

- "phafsthr" only provides an indication, hopefully an accurate one, of the last possible dietary exposure. There is no information on last (or last few) urination event. The fasting experiments of Koch or the duplicate diet studies of Fromme, maybe on a broader scale (more individuals of varying ages, life styles, etc) would be optimally informative on the role of diet in the exposure to phthalates.

- The time during the day when the sample is taken could very well be critical in the interpretation of "phafsthr" trends:
    - Maybe not only the time of last dietary exposure, but magnitude of that last dietary exposure and other dietary exposures near in time to that last dietary exposure
    - Does the generation of creatinine vary over the course of a day? Is the muscle excretion the same during the night than after a day of activity?
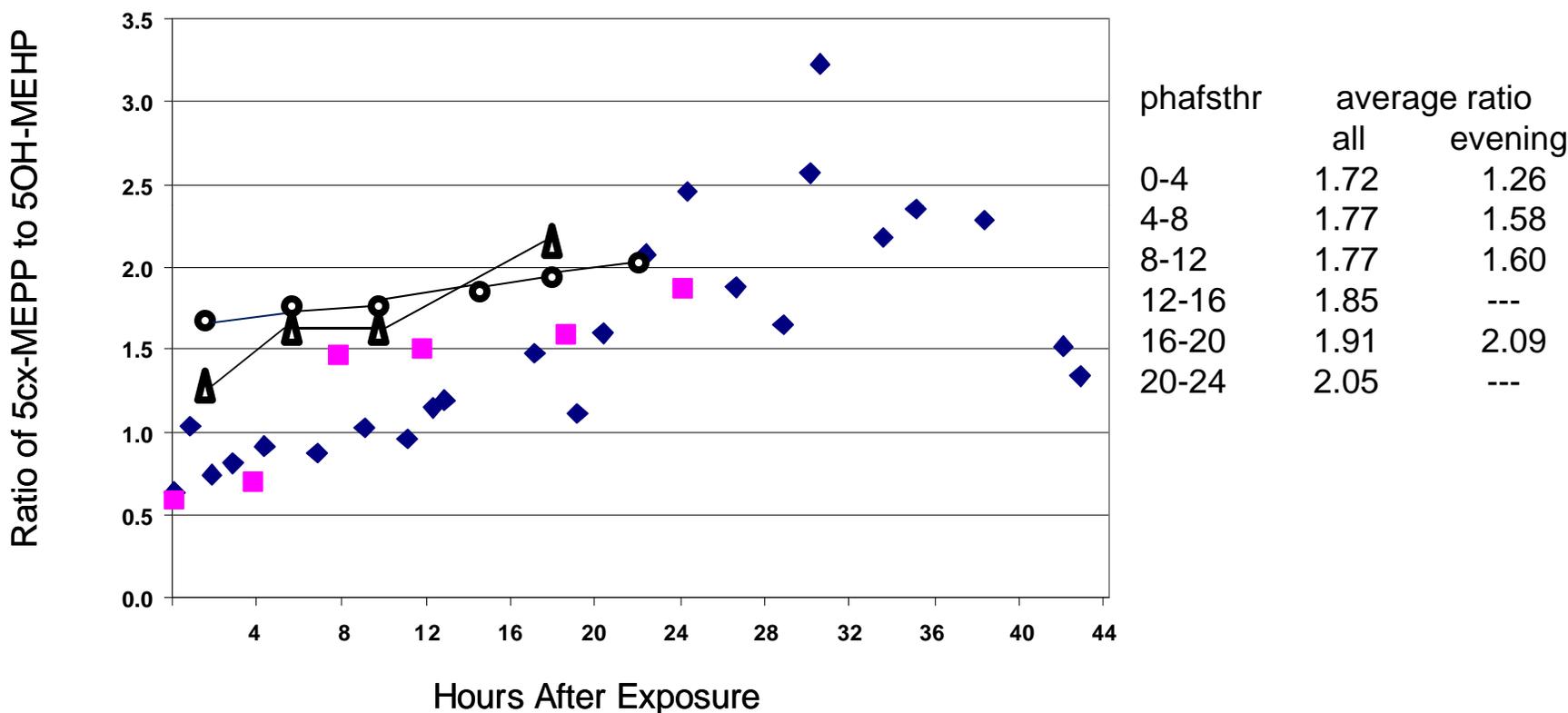
DEHP Exposure – Is Sample Time a Factor?
NHANES 2003/4 MEHP samples taken 3 different times, for adults

Fast time, hr	"morning" n	mean/median	"afternoon" n	mean/median	"evening" n	mean/median
0 – 4	59	4 / 3	60	4 / 2	34	*17 / 6*
4 – 8	14	6 / 3	280	7 / 2	161	*10 / 2*
8 – 12	292	7 / 2	92	12 / 2	49	*6 / 2*
12 – 16	399	5 / 2	60	3 / 1	3	1 / 1
16 – 20	48	5 / 2	107	3 / 1	3	3 / 3
20 – 24	9	9 / 2	18	3 / 1	11	2 / 1
TOTAL	821	6 / 2	617	6 / 2	261	*10 / 2*

HYPOTHESIS: The "evening" sampling time might be the best of the three to examine trends. This is because previous exposures include breakfast/lunch/snacks while previous exposures for "morning" and "afternoon" samplings might only have included breakfast.

DEHP Exposure – Is Sample Time a Factor?
Key Metabolite Ratio for Evening Samples, for adults

phafsthr	average ratio	
	all	evening
0-4	1.72	1.26
4-8	1.77	1.58
8-12	1.77	1.60
12-16	1.85	---
16-20	1.91	2.09
20-24	2.05	---

Y-axis: Ratio of 5cx-MEPP to 5OH-MEHP

X-axis: Hours After Exposure

▲ = Average ratios for each 4-hr time period; time periods 12-16 (n=3), 16-20 (n=3), and 20-24 (n=11) added to get a larger n of 17

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Modeling of MEHP Urine Concentration Over Time As a Function of Dose Regime and Urine Frequency
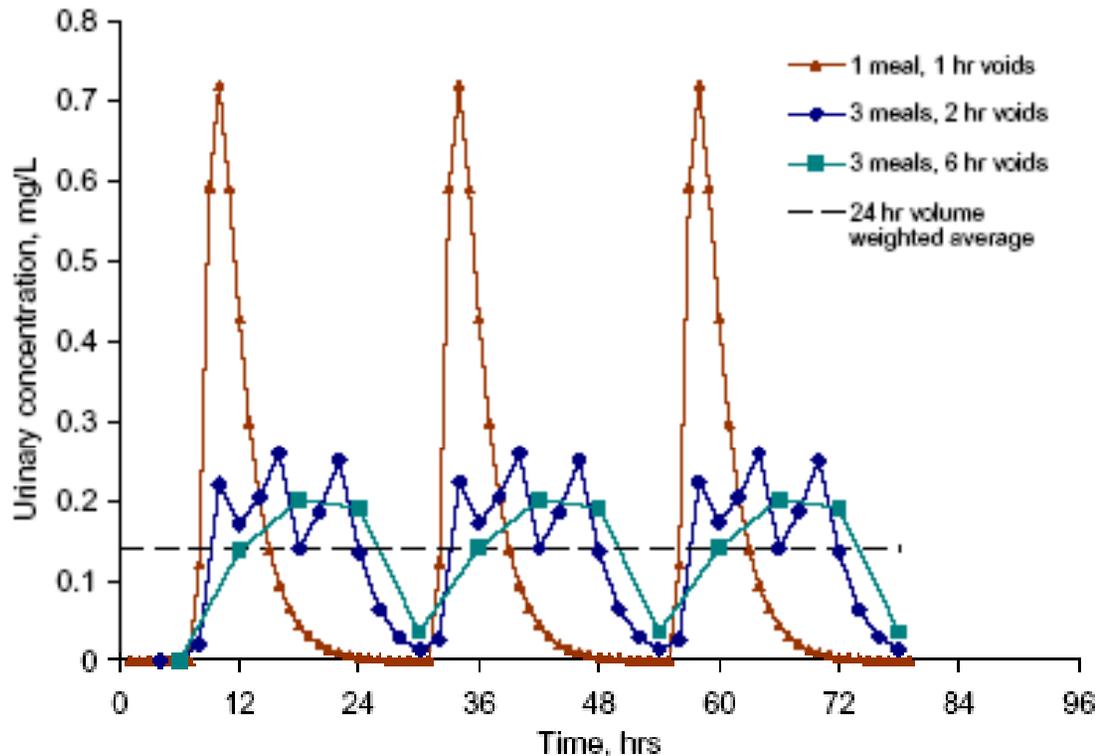
Looking at 3 meal scenarios, It is clear that concentrations of MEHP in the afternoon and evening are higher than in the morning (dose was 20 µg/kg-d DEHP)

Source: Aylward et al. 2009. Derivation of Biomonitoring Equivalents for di(2-ethylhexyl)phthalate (CAS No. 117-81-7). Reg Tox and Pharm, 55, 249-258

The American Chemistry Council Phthalate Ester Concentration Database

- A comprehensive compilation of data on parent phthalate and metabolites. The database includes measured concentrations in surface water, groundwater, landfill leachate, drinking water, sediment, suspended particulate matter, soil, air (outdoor and indoor), dust, precipitation, wastewater, sewage sludge, food, vegetation, wildlife, consumer products, and human milk, blood, and urine.

- The database is provided on Excel spreadsheets and includes generation of average concentrations for each chemical and matrix.

- This database was used to generate a "forward" estimate of intakes of DEHP. Average concentrations from this database were used in conjunction with exposure factors that were taken from EPA's draft 2009 Exposure Factors Handbook. This approach is similar to the one taken by: Clark et al. 2010. Modeling Human Exposure To Phthalate Esters: A comparison of indirect and biomonitoring estimation methods. In press in Human and Ecological Risk Assessment.

The ACC Database
Example – DEHP in Poultry

Type	Date	N	Average		SD	Median	Single Point	Range Low	Range High	Data Quality	Reference	Comments	
POULTRY													
Poultry	1986	1	2.6	2.6			2.6			1	Page and Lacroix, 1995		
Poultry	1993	2	0.7	1.4						2	MAFF Report #82, March, 1996	Prepared for consumption	
Poultry - Switzerland	1991-96	1	0.57	0.57			0.57			4	Kuchen, et al. 1999		
Chicken	N/A			0					1.8	4	Ishida, et al, 1981		
Chicken	95-96	1	1.1	1.1	0.1					4	Yin and Su, 1996		
Chicken, whole packaged frozen	87-89	1	0.05	0.05			<0.1			1	Page and Lacroix, 1995		
Processed Food-Japan	N/A			0				0.05	0.22	4	Yano, 1979		
Chicken (fried) -Japan, Osaka	2000	2	15	30				13.1	16.9	1	Tsumura et al., 2001b	Prepared for consumption	
		8	4.5	35.72				0.05	16.9				

- Straight averages with each sample having equal weight are calculated assuming half-detection for non-detects

- Note here the high concentration for fried chicken in Japan

The ACC Database
Example – DEHP intakes

Exposure Pathway	Contact Rates	Concentration	Intake µg/kg-d
NON-FOOD			
Dust ingestion	0.00071 g/kg-d	525 µg/g	0.38
Dust dermal	0.00017 g/kg-d	525 µg/g	0.09
Inhalation	0.019 m^3/kg-d	0.13 µg/m^3	0.03
Water ingestion	0.02 L/kg-d	0.17 µg/L	0.003
FOOD			
Fish	0.27 g/kg-d	0.26 µg/g	0.07
Total Dairy	3.30 g/kg-d	0.39 µg/g	1.29
Eggs	0.32 g/kg-d	0.29 µg/g	0.09
Beef	0.90 g/kg-d	0.34 µg/g	0.31
Pork	0.36 g/kg-d	0.39 µg/g	0.14
Poultry	0.58 g/kg-d	4.50 µg/g	2.61
Veg	3.00 g/kg-d	1.69 µg/g	5.07
Fruit	1.20 g/kg-d	0.035 µg/g	0.04
Grains	2.00 g/kg-d	2.60 µg/g	5.20
		TOTAL	**15.3**

- This is higher than the 1-5 µg/kg-d surmised from urine data

- Criteria for exclusion of studies:
  - Studies after 1980 only
  - Studies from Europe, North America only; not Far East
  - Exclude "CMA, 1986" Chemical Manufacturer's Association, lab report

Type	Date	N	Average		SD	Median	Single Point	Range Low	Range High	Data Quality	Reference	Comments
POULTRY												
Poultry	1986	1	2.6	2.6			2.6			1	Page and Lacroix, 1995	
Poultry	1993	2	0.7	1.4						2	MAFF Report #82, March, 1996	Prepared for consumpt
Poultry - Switzerland	1991-96	1	0.57	0.57			0.57			4	Kuchen, et al. 1999	
Chicken	N/A			0					1.8	4	Ishida, et al, 1981	
Chicken	95-96	1	1.1	1.1	0.1					4	Yin and Su, 1996	
Chicken, whole packaged frozen	87-89	1	0.05	0.05			<0.1			1	Page and Lacroix, 1995	
Processed Food-Japan	N/A			0				0.05	0.22	4	Yano, 1979	
Chicken (fried) -Japan, Osaka	2000	2	15	30				13.1	16.9	1	Tsumura et al., 2001b	Prepared for consumpt
		8	4.5	35.72				0.05	16.9			
		5	0.9	4.62								

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The ACC Database
Example – DEHP intakes

Exposure Pathway	Contact Rates	Concentration	Intake µg/kg-d
NON-FOOD			
Dust ingestion	0.00071 g/kg-d	525 µg/g	0.38
Dust dermal	0.00017 g/kg-d	525 µg/g	0.09
Inhalation	0.019 m^3/kg-d	0.13 µg/m^3	0.03
Water ingestion	0.02 L/kg-d	0.17 µg/L	0.003
FOOD			
Fish	0.27 g/kg-d	0.14 µg/g	0.04
Total Dairy	3.30 g/kg-d	0.29 µg/g	0.96
Eggs	0.32 g/kg-d	0.29 µg/g	0.09
Beef	0.90 g/kg-d	0.21 µg/g	0.19
Pork	0.36 g/kg-d	0.39 µg/g	0.14
Poultry	0.58 g/kg-d	0.90 µg/g	0.52
Veg	3.00 g/kg-d	0.30 µg/g	0.90
Fruit	1.20 g/kg-d	0.035 µg/g	0.04
Grains	2.00 g/kg-d	0.40 µg/g	0.80
		TOTAL	**4.2**

The ACC Database
Example – BBzP intakes

Exposure Pathway	Contact Rates	Concentration	Intake µg/kg-d
NON-FOOD			
Dust ingestion	0.00071 g/kg-d	110 µg/g	0.08
Dust dermal	0.00017 g/kg-d	110 µg/g	0.02
Inhalation	0.019 m³/kg-d	0.04 µg/m³	0.008
Water ingestion	0.02 L/kg-d	0.07 µg/L	0.001
FOOD			
Fish	0.27 g/kg-d	0.006 µg/g	0.002
Total Dairy	3.30 g/kg-d	0.05 µg/g	0.17
Eggs	0.32 g/kg-d	0.08 µg/g	0.03
Beef	0.90 g/kg-d	0.04 µg/g	0.04
Pork*	0.36 g/kg-d	0.00 µg/g	0.00
Poultry	0.58 g/kg-d	0.04 µg/g	0.02
Veg*	3.00 g/kg-d	0.00 µg/g	0.00
Fruit	1.20 g/kg-d	0.02 µg/g	0.02
Grains*	2.00 g/kg-d	0.00 µg/g	0.00
		TOTAL	**0.38**

* No data or very few data points with only non-detects, so 0 assumed for concentration.

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The American Chemistry Council
Phthalate Ester Concentration Database

- The values derived for DEHP and BBzP are consistent with what Wormuth found, and others found for DEHP based on urine measurements. There is probably merit in following through with similar intake estimations for other phthalates, as this database is likely as comprehensive as available regarding publicly available information (and some not easily available as well). Care must be taken, however, when selecting studies to represent exposures, and further thought might be in order for proper use of data – means, medians, weight, etc.

- Still a big need for data on consumer products. Only one reference with data provided for both DEHP and BBzP on consumer product concentrations, and this was for consumer products in Japan:

  Shen, H.-Y., H.-L. Jiang, H.-L. Mao, G. Pan, L. Zhou, and Y.-F. Cao. 2007. "Simultaneous determination of seven phthalates and four parabens in cosmetic products using HPLC-DAD and GC-MS methods".   J. Sep. Sci., 30(1):48-54.

Next Steps

United States Environmental Protection Agency

- …to be determined.

- The panel's input would be much appreciated and useful.

Disclaimer: The views expressed in this presentation are those of the author and do not necessarily reflect the views or policies of the US EPA

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DnBP Exposure – Is Sample Time a Factor?
NHANES 2003/4 MnBP samples taken 3 different times, for adults

Fast time, hr	"morning" n	mean/median	"afternoon" n	mean/median	"evening" n	mean/median
0 – 4	59	32 / 21	60	31 / 23	34	**85 / 27**
4 – 8	14	27 / 22	280	28 / 18	161	**40 / 21**
8 – 12	292	24 / 18	92	32 / 25	49	**52 / 18**
12 – 16	399	38 / 16	60	28 / 20	3	20 / 16
16 – 20	48	28 / 20	107	22 / 15	3	28 / 20
20 – 24	9	25 / 22	18	39 / 32	11	18 / 16
TOTAL	821	32 / 18	617	28 / 19	261	**47 / 22**

HYPOTHESIS: This pattern for DnBP looks similar to DEHP. The analysis by Wormuth suggested that DEHP, DnBP, and DiBP were dominated by food exposures. However, the studies of Fromme (duplicate diet, urine) and Koch (fasting) suggest that diet did not dominate for DnBP.

BBzP Exposure – Is Sample Time a Factor?
NHANES 2003/4 MBzP samples taken 3 different times, for adults

	"morning"			"afternoon"			"evening"	
Fast time, hr	n	mean/median	n	mean/median		n	mean/median	
0 – 4	59	17 / 9	60	14 / 11		34	*32 / 18*	
4 – 8	14	15 / 10	280	15 / 10		161	21 / 10	
8 – 12	292	20 / 13	92	18 / 12		49	21 / 10	
12 – 16	399	17 / 11	60	21 / 11		3	16 / 6	
16 – 20	48	21 / 14	107	18 / 10		3	23 / 11	
20 – 24	9	41 / 28	18	24 / 18		11	14 / 8	
TOTAL	821	19 / 12	617	17 / 11		261	22 / 10	

HYPOTHESIS: The analysis by Wormuth suggested that BBzP, DiNP, DiDP, DMP, and DEP were NOT dominated by food exposures. This pattern for BBzP suggests an influence of diet for evening samples for 0-4 hr, but not thereafter and not for whole "evening" sample as compared to other two times.

DiBP Exposure – Is Sample Time a Factor?
NHANES 2003/4 MiBP samples taken 3 different times, for adults

	"morning"		"afternoon"		"evening"	
Fast time, hr	n	mean/median	n	mean/median	n	mean/median
0 – 4	59	5 / 3	60	7 / 4	34	7 / 4
4 – 8	14	7 / 4	280	5 / 3	161	6 / 4
8 – 12	292	5 / 4	92	5 / 4	49	6 / 3
12 – 16	399	5 / 3	60	5 / 4	3	4 / 3
16 – 20	48	7 / 4	107	5 / 4	3	5 / 3
20 – 24	9	6 / 4	18	8 / 3	11	4 / 4
TOTAL	821	5 / 3	617	5 / 3	261	6 / 4

HYPOTHESIS: The analysis by Wormuth suggested that DEHP, DnBP, and DiBP were dominated by food exposures. This pattern for DiBP does not suggest a dietary exposure pattern, as did the data for DEHP and DnBP.