Environmental Health Perspectives doi:10.1289/ehp.1306681

Supplemental Material
Temporal Trends in Phthalate Exposures: Findings from the National Health and Nutrition Examination Survey, 2001–2010

Ami R. Zota, Antonia M. Calafat, and Tracey J. Woodruff

Table of Contents

Supplemental Material, Table S1. Limits of detection (LOD) for urinary phthalate metabolites by NHANES cycle.

Parent compound: ***Phthalate metabolite***	**2001-02 (ng/mL)**	**2003-04 (ng/mL)**	**2005-06 (ng/mL)**	**2007-08 (ng/mL)**	**2009-10 (ng/mL)**	**Maximum LOD (ng/mL)**
Dimethyl phthalate (DMP)						
Monomethyl phthalate (MMP)	0.2	1.0	1.1	1.1	0.5	1.1
Diethyl phthalate (DEP)						
Monoethyl phthalate (MEP)[a]	0.6	0.3	0.5	0.5	0.5	0.6
Di-*n*-butyl phthalate (DnBP)						
Mono-n-*butyl phthalate (MnBP)*[a]	1.1	0.4	0.6	0.6	0.4	1.1
Di-iso-butyl phthalate (DiBP)						
Monoisobutyl phthalate (MiBP)[a]	1.0	0.3	0.3	0.3	0.2	1.0
Butylbenzyl phthalate (BBzP)						
Monobenzyl phthalate (MBzP)[a]	0.2	0.1	0.2	0.2	0.2	0.2
Dicyclohexyl phthalate (DCHP)						
Monocyclohexyl phthalate (MCHP)	0.6	0.4	0.6	0.6	0.4	0.6
Di (2-ethylhexyl) phthalate (DEHP)						
Mono(2-ethylhexyl) phthalate (MEHP)[a]	1.0	0.9	1.2	1.1	0.5	1.2
Mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)[a]	1.0	0.3	0.7	0.7	0.2	1.0
Mono(2-ethyl-5-oxohexyl) phthalate (MEOHP) [a]	1.1	0.5	0.7	0.6	0.2	1.1
Mono(2-ethyl-5-carboxypentyl) phthalate (MECPP)[a]	--	0.3	0.6	0.5	0.2	0.6
Di-*n*-octyl phthalate (DnOP)						
Mono(3-carboxypropyl) phthalate (MCPP)[a]	0.4	0.2	0.2	0.2	0.2	0.4
Monooctyl phthalate (MOP)	1.7	1.7	1.9	1.9	0.8	1.9
Di-iso-nonyl phthalate (DiNP)						
Monoisononyl phthalate (MiNP)	1.2	1.5	1.2	1.2	0.8	1.5
Monocarboxyoctyl phthalate (MCOP)[a]	--	--	0.7	0.7	0.2	0.7
Di-iso-decyl phthalates (DiDP)						
Monocarboxynonyl phthalate (MCNP)[a]	--	--	0.6	0.5	0.2	0.6

[a]Indicates phthalate metabolites included in the present study.

Supplemental Material, Table S2. Detection frequency (%) of phthalate metabolites by NHANES sampling cycle using maximal LODs (N = 11071).

Parent compound: *Phthalate metabolite*	**2001-02 (n = 2418)**	**2003-04 (n = 2278)**	**2005-06 (n = 2243)**	**2007-08 (n = 2040)**	**2009-10 (n = 2092)**	**P-value[a]**
Dimethyl phthalate (DMP)						
Monomethyl phthalate (MMP)	60	54	37	38	45	< 0.0001
Diethyl phthalate (DEP)						
Monoethyl phthalate (MEP)[b]	100	100	100	100	100	0.17
Di-*n*-butyl phthalate (DnBP)						
*Mono-*n*-butyl phthalate (MnBP)*[b]	98	98	99	98	98	0.73
Di-iso-butyl phthalate (DiBP)						
Monoisobutyl phthalate (MiBP)[b]	72	88	89	94	96	< 0.0001
Butylbenzyl phthalate (BBzP)						
Monobenzyl phthalate (MBzP)[b]	99	99	98	98	99	0.06
Dicyclohexyl phthalate (DCHP)						
Monocyclohexyl phthalate (MCHP)	15	6	2	4	2	< 0.0001
Di (2-ethylhexyl) phthalate (DEHP)						
Mono(2-ethylhexyl) phthalate (MEHP)[b]	78	61	67	66	56	< 0.0001
Mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)[b]	98	98	99	99	98	0.04
Mono(2-ethyl-5-oxohexyl) phthalate (MEOHP)[b]	96	97	98	96	96	0.01
Mono(2-ethyl-5-carboxypentyl) phthalate (MECPP)	--	100	100	100	100	0.36
Di-*n*-octyl phthalate (DnOP)						
Mono(3-carboxypropyl) phthalate (MCPP)[b]	93	96	93	95	95	0.0008
Monooctyl phthalate (MOP)	2	1	1	1	1	0.05
Di-iso-nonyl phthalate (DiNP)						
Monoisononyl phthalate (MiNP)	4	5	11	10	28	< 0.0001
Monocarboxyoctyl phthalate (MCOP)[b]	--	--	96	96	98	0.007
Di-iso-decyl phthalates (DiDP)						
Monocarboxynonyl phthalate (MCNP)[b]	--	--	89	90	94	0.004

[a]P-value for overall comparison of groups evaluated by chi-square test of independence. [b]Indicates phthalate metabolites included in the present study.

Supplemental Material, Table S3. Association between phthalate metabolites concentrations (ng/ml) and NHANES cycle in the US general population after adjustment for urinary creatinine concentrations, calculated from multivariable regression models (N = 11071).[a]

Metabolite		2001-2002 (n = 2418)	2003-2004 (n = 2278)	2005-2006 (n = 2243)	2007-2008 (n = 2040)	2009-2010 (n = 2092)	P-value[b]
MEP	% change (95% CI)	*(ref)*	6 (-9, 23)	-5 (-17, 9)	-20 (-30, -9)	-42 (-49, -34)	< 0.0001
	LSGM (95% CI)	115.4 (106.0, 125.7)	122.2 (108.4, 137.8)	109.4 (98.1, 122)	91.9 (83.3, 101.4)	66.8 (61.0, 73.0)	
MnBP	% change (95% CI)	*(ref)*	7 (-1, 16)	5 (-3,13)	5 (-3,14)	-17 (-23, -9)	< 0.0001
	LSGM (95% CI)	18.4 (17.4, 19.5)	19.7 (18.5, 20.9)	19.2 (18.2, 20.3)	19.4 (18.3, 20.6)	15.3 (14.4, 16.3)	
MiBP	% change (95% CI)	*(ref)*	43 (27, 62)	106 (87, 127)	188 (163, 216)	206 (178, 236)	< 0.0001
	LSGM (95% CI)	2.6 (2.4, 2.7)	3.7 (3.3, 4.1)	5.3 (4.9, 5.7)	7.4 (6.9, 7.9)	7.8 (7.3, 8.4)	
MBzP	% change (95% CI)	*(ref)*	-9 (-17, -1)	-20 (-29, -9)	-27 (-34, -20)	-32 (-39, -23)	< 0.0001
	LSGM (95% CI)	10.4 (9.7, 11.1)	9.4 (8.9, 10.0)	8.3 (7.5, 9.2)	7.6 (7.1, 8.1)	7.1 (6.5, 7.8)	
MEHP	% change (95% CI)	*(ref)*	-42 (-49, -34)	-29 (-37,-20)	-36 (-45, -25)	-53 (-59, -45)	< 0.0001
	LSGM (95% CI)	4.1 (3.7, 4.6)	2.4 (2.2, 2.6)	3.0 (2.8, 3.2)	2.6 (2.4, 3.0)	2.0 (1.7, 2.2)	
MEHHP	% change (95% CI)	*(ref)*	5 (-7, 18)	31 (15, 50)	16 (-1, 35)	-29 (-40, -15)	< 0.0001
	LSGM (95% CI)	19.5 (17.8, 21.3)	20.4 (18.8, 22.1)	25.6 (23.2, 28.2)	22.5 (19.9, 25.6)	13.8 (11.9, 16.1)	
MEOHP	% change (95% CI)	*(ref)*	4 (-8, 17)	25 (10, 42)	-4 (-17, 12)	-34 (-43, -22)	< 0.0001
	LSGM (95% CI)	13.1 (12.0, 14.2)	13.6 (12.5, 14.9)	16.4 (14.9, 18.0)	12.6 (11.1, 14.2)	8.7 (7.6, 10.0)	
MECPP[c]	% change (95% CI)	--	*(ref)*	-14 (-1, 31)	-2 (-17, 17)	-40 (-48, -30)	< 0.0001
	LSGM (95% CI)	--	33.9 (30.6, 37.5)	38.6 (34.9, 42.6)	33.2 (28.9, 38.2)	20.4 (18.1, 23.0)	
∑DEHP metabolites[d]	% change (95% CI)	*(ref)*	-6 (-16, 6)	16 (2, 30)	-3 (-16, 13)	-37 (-46, -26)	< 0.0001
	LSGM (95% CI)	39.3 (36.3, 42.5)	37.0 (34.1, 40.2)	45.4 (41.4, 49.7)	38.3 (33.9, 43.3)	24.8 (21.5, 28.5)	
MCPP	% change (95% CI)	*(ref)*	9 (-2, 21)	-20 (-29, -10)	11 (0, 24)	25 (8, 45)	< 0.0001
	LSGM (95% CI)	2.7 (2.4, 2.9)	2.9 (2.7, 3.1)	2.1 (2.0, 2.3)	3.0 (2.8, 3.1)	3.3 (3.0, 3.7)	
MCOP[e]	% change (95% CI)	--	--	*(ref)*	31 (8, 58)	149 (102, 207)	< 0.0001
	LSGM (95% CI)	--	--	5.3 (4.6, 6.1)	7.0 (6.1, 8.0)	13.3 (11.4, 15.5)	
MCNP[e]	% change (95% CI)	--	--	*(ref)*	-7 (-18, 5)	15 (1, 30)	0.004
	LSGM (95% CI)	--	--	2.7 (2.4, 2.9)	2.5 (2.3, 2.7)	3.1 (2.8, 3.3)	

[a]The percent changes and least square geometric means (LSGMs) were calculated from multivariate regression models where the dependent variables were natural log-transformed phthalate metabolite concentrations and the independent variables were NHANES cycle (using four indicator terms and 2001-2002 participants as the reference group) and natural log-transformed urinary creatinine concentrations. We estimated the percent change in phthalate metabolite concentrations by NHANES cycle as $(e^{(\beta)} -1) * 100\%$ with 95% confidence intervals (CIs) estimated

as $(e^{(\beta \pm 1.99 * SE)} - 1)$ where β and SE are the estimated regression coefficient and standard error, respectively. We estimated least squares geometric means (LSGMs) of phthalate metabolites concentrations by NHANES cycle as $e^{(\text{least squares means})}$ with 95% CIs as $e^{(\text{least squares mean} \pm 1.99 * SE)}$ where the least squares means are the cycle-specific means of phthalate metabolite concentrations after adjustment for covariates. We used a critical value of ±1.99 from the t distribution for the calculation of all confidence intervals. [b]P-value for the overall comparison between groups assessed by the Wald Test. [c]Not measured in NHANES 2001-2002. [d]∑DEHP metabolites (expressed as ng/mL) is the molar sum of MEHP (MW = 278), MEHHP (MW = 294), and MEOHP (MW = 292) multiplied by the average MW of the three metabolites (MW = 288). [e]Not measured in NHANES 2001-2002 or 2003-2004.

Supplemental Material, Table S4. Association (LSGM (95% CI) between phthalate metabolites and NHANES sampling cycle in the US general population by age in the US general population (N = 11071)[a].

		2001-2002 (n = 2418)	**2003-2004 (n = 2278)**	**2005-2006 (n = 2243)**	**2007-2008 (n = 2040)**	**2009-2010 (n = 2092)**	**$P_{interaction}$[b]**
MEP							0.04
Children	% change (95% CI)	*(ref)*	2 (-14, 21)	-4 (-24, 20)	-7 (-21, 9)	-32 (-42, -20)	
	LSGM (95% CI)	62.8 (55.7, 70.1)	63.4 (56.3, 72.2)	59.7 (49.4, 72.2)	58.6 (52.5, 64.7)	42.5 (42.1, 62.2)	
Adolescents	% change (95% CI)	*(ref)*	8 (-14, 38)	-6 (-25, 19)	-27 (-43, -6)	-51 (-62, -36)	
	LSGM (95% CI)	103.5 (86.5, 124.0)	113.3 (96.5, 131.6)	97.5 (84.8, 113.3)	75.2 (62.8, 90.9)	50.9 (42.1, 62.2)	
Adults	% change (95% CI)	*(ref)*	5 (-10, 22)	-6 (-17, 6)	-22 (-30, -13)	-43 (-49, -36)	
	LSGM (95% CI)	127.7 (117.9, 137.0)	134.3 (117.9, 151.4)	119.1 (108.9, 131.6)	99.5 (91.8, 107.8)	72.2 (66.0, 79.0)	
∑DEHP metabolites[c]							0.002
Children	% change (95% CI)	*(ref)*	0 (-21, 26)	-7 (-19, 8)	-13 (-29, 6)	-51 (-59, -42)	
	LSGM (95% CI)	73.0 (66.7, 79.8)	73.0 (59.1, 90.9)	68.7 (61.6, 76.7)	63.4 (53.0,75.9)	35.5 (30.9, 41.3)	
Adolescents	% change (95% CI)	*(ref)*	-1 (-16, 16)	19 (-4, 48)	2 (-23, 35)	-39 (-55, -20)	
	LSGM (95% CI)	39.3 (34.8, 43.8)	38.5 (34.1, 43.4)	46.5 (38.5, 56.3)	40.0 (31.2, 51.4)	23.6 (18.2, 30.9)	
Adults	% change (95% CI)	*(ref)*	-7 (-17, 6)	19 (4, 36)	-1 (-15, 16)	-34 (-45, -21)	
	LSGM (95% CI)	36.2 (32.8, 40.0)	33.8 (31.5, 36.6)	42.9 (39.3, 47.0)	36.2 (32.1, 40.4)	24.0 (20.9, 27.7)	
MCPP							0.0004
Children	% change (95% CI)	*(ref)*	5 (-9, 21)	-25 (-36, -11)	11 (-10, 38)	-14 (-27, 2)	
	LSGM (95% CI)	7.3 (6.8, 7.9)	7.7 (6.9, 8.6)	5.5 (4.7, 6.4)	8.2 (6.6, 10.0)	6.3 (5.4, 7.3)	
Adolescents	% change (95% CI)	*(ref)*	-2 (-14, 11)	-22 (-33, -9)	4 (-12, 22)	12 (-9, 35)	
	LSGM (95% CI)	3.0 (2.7, 3.4)	3.0 (2.7, 3.2)	2.4 (2.1, 2.7)	3.2 (2.8, 3.6)	3.4 (2.9, 4.0)	
Adults	% change (95% CI)	*(ref)*	12 (0, 26)	-18 (-27, -8)	15 (3, 28)	36 (19, 57)	
	LSGM (95% CI)	2.3 (2.1, 2.5)	2.6 (2.4, 2.7)	1.9 (1.7, 2.0)	2.6 (2.5, 2.8)	3.1 (2.8, 3.5)	
MCNP[d]							0.009
Children	% change (95% CI)	--	--	*(ref)*	-19 (-33, -2)	-8 (-23, 9)	
	LSGM (95% CI)	--	--	5.0 (4.3, 5.6)	4.0 (3.5, 4.6)	4.5 (4.0, 5.2)	
Adolescents	% change (95% CI)	--	--	*(ref)*	-7 (-21, 9)	2 (-16, 25)	
	LSGM (95% CI)	--	--	2.6 (2.2, 3.0)	2.4 (2.2, 2.6)	2.6 (2.3, 3.0)	
Adults	% change (95% CI)	--	--	*(ref)*	-4 (-16, 9)	21 (6, 38)	
	LSGM (95% CI)	--	--	2.5 (2.3, 2.7)	2.4 (2.2, 2.6)	3.0 (2.8, 3.3)	

[a]Estimates are from linear regression models of interactions between NHANES sampling cycles and age adjusted for urinary creatinine, sex, race/ethnicity, and PIR. The least square geometric means (LSGMs) were calculated from multivariate regression models where the dependent variables were natural log-

transformed phthalate metabolite concentrations and the independent variables were NHANES cycle (using four indicator terms and 2001-2002 participants as the reference group) and natural log-transformed urinary creatinine concentrations. We estimated the percent change in phthalate metabolite concentrations by NHANES cycle as $(e^{(\beta)} - 1) * 100\%$ with 95% confidence intervals (CIs) estimated as $(e^{(\beta \pm 1.99 * SE)} - 1)$ where β and SE are the estimated regression coefficient and standard error, respectively. We estimated least squares geometric means (LSGMs) of phthalate metabolites concentrations by NHANES cycle as $e^{(\text{least squares means})}$ with 95% CIs as $e^{(\text{least squares mean} \pm 1.99 * SE)}$ where the least squares means are the cycle-specific means of phthalate metabolite concentrations after adjustment for covariates. We used a critical value of ±1.99 from the t distribution for the calculation of all confidence intervals. [b]P-value for the overall comparison between groups assessed by the Wald Test. [c]∑DEHP metabolites (expressed as ng/mL) is the molar sum of MEHP (MW = 278), MEHHP (MW = 294), and MEOHP (MW = 292) multiplied by the average MW of the three metabolites (MW = 288). [d]Not measured in NHANES 2001-2002 or 2003-2004.

Supplemental Material, Table S5. Association (LSGM (95% CI) between phthalate metabolites and NHANES sampling cycle in the US general population by sex in the US general population (N = 11071).[a]

		2001-2002 (n = 2418)	2003-2004 (n = 2278)	2005-2006 (n = 2243)	2007-2008 (n = 2040)	2009-2010 (n = 2092)	$P_{interaction}$[b]
MnBP							0.03
Males	% change (95% CI)	*(ref)*	4 (-6, 15)	9 (1, 20)	7 (-3, 19)	-10 (-17, 0)	
	LSGM (95% CI)	14.6 (13.6, 15.6)	15.2 (14.2, 16.1)	16.0 (15.3, 16.8)	15.6 (14.6, 16.8)	13.2 (12.4, 14.2)	
Females	% change (95% CI)	*(ref)*	11 (-2, 23)	3 (-9, 16)	6 (-7, 20)	-21 (-30, -12)	
	LSGM (95% CI)	22.6 (20.9, 24.5)	25.0 (22.9, 27.1)	23.3 (21.3, 25.5)	24.0 (21.8, 26.3)	17.8 (16.4, 19.3)	
∑DEHP metabolites[c]							0.0001
Males	% change (95% CI)	*(ref)*	8 (-18, 4)	20 (4, 36)	-6 (21, 12)	-31 (-41, -19)	
	LSGM (95% CI)	36.2 (32.8, 39.6)	33.1 (30.9, 35.9)	42.9 (38.9, 47.5)	33.8 (29.7, 38.9)	25.0 (22.0, 28.5)	
Females	% change (95% CI)	*(ref)*	-2 (-15, 14)	14 (0, 31)	4 (-10, 21)	-41 (-51, -27)	
	LSGM (95% CI)	41.7 (38.1, 46.1)	41.3 (36.6, 46.1)	47.9 (43.4, 52.5)	43.4 (38.5, 48.9)	25.0 (21.1, 29.4)	

[a]Estimates are from linear regression models of interactions between NHANES sampling cycles and sex adjusted for urinary creatinine, age (continuous), race/ethnicity, and PIR. The least square geometric means (LSGMs) were calculated from multivariate regression models where the dependent variables were natural log-transformed phthalate metabolite concentrations and the independent variables were NHANES cycle (using four indicator terms and 2001-2002 participants as the reference group) and natural log-transformed urinary creatinine concentrations. We estimated the percent change in phthalate metabolite concentrations by NHANES cycle as $(e^{(\beta)} - 1) * 100\%$ with 95% confidence intervals (CIs) estimated as $(e^{(\beta \pm 1.99 * SE)} - 1)$ where β and SE are the estimated regression coefficient and standard error, respectively. We estimated least squares geometric means (LSGMs) of phthalate metabolites concentrations by NHANES cycle as $e^{(\text{least squares means})}$ with 95% CIs as $e^{(\text{least squares mean} \pm 1.99 * SE)}$ where the least squares means are the cycle-specific means of phthalate metabolite concentrations after adjustment for covariates. We used a critical value of ±1.99 from the t distribution for the calculation of all confidence intervals. [b]P-value for the overall comparison between groups assessed by the Wald Test. [c]∑DEHP metabolites (expressed as ng/mL) is the molar sum of MEHP (MW =278), MEHHP (MW = 294), and MEOHP (MW = 292) multiplied by the average MW of the three metabolites (MW = 288).

Supplemental Material, Table S6. US chemical production data (pounds per year) by reporting year as provided by the US EPA.[a]

Species	Cas No.	1990	1994	1998	2002	2006	2012
BBzP	85-68-7	100 – 500 M	50 – 100 M	100 – 500 M	50 – 100 M	50 – 100 M	50 – 100 M
DEHP	117-81-7	100 – 500 M	100 – 500 M	100 – 500 M	100 – 500 M	100 – 500 M	153 M
DnBP	84-74-2	10 – 50 M	10 – 50 M	10 – 50 M	10 – 50 M	10 – 50 M	7 M
DiBP	84-69-5	1 – 10 M	1 – 10 M	1 – 10 M	0.5 – 1 M	0.5 – 1 M	0.5 M
DEP	84-66-2	10 – 50 M	10 – 50 M	10 – 50 M	10 – 50 M	10 – 50 M	6 M
DNOP	117-84-0	1 – 10 M	1 – 10 M	1 – 10 M	1 – 10 M	10 – 50 M	Confidential
DINP 1	68515-48-0	> 1B	100 – 500 M	100 – 500 M	100 – 500 M	100 – 500 M	100 – 250 M
DINP 2	28553-12-0	10 – 50 M	10 – 50 M	10 – 50 M	10 – 50 M	100 – 500 M	N/A
DIDP 1	26761-40-0	50 – 100 M	50 – 100 M	10 – 50 M	1 – 10 M	1 – 10 M	50 – 100 M
DIDP 2	68515-49-1	100 – 500 M	100 – 500 M	100 – 500 M	100 – 500 M	100 – 500 M	163 M

[a]Data obtained through the non-confidential US EPA Chemical Data Reporting Program. M = million, B = billion.

More information at http://epa.gov/cdr/