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Estimated Phthalate Exposure and Risk to Women of Reproductive Age as Assessed Using 2013/2014 NHANES Biomonitoring Data

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Executive Summary

As directed by section 108 of the Consumer Product Safety Improvement Act of 2008 (CPSIA), the Consumer Product Safety Commission (Commission or CPSC) appointed a Chronic Hazard Advisory Panel (CHAP) "to study the effects on children's health of all phthalates and phthalate alternatives as used in children's toys and child care articles." On July 18, 2014, the CHAP submitted its report to the Commission. As part of its analysis, the CHAP used biomonitoring data from the 2005/2006 National Health and Nutrition Examination Survey (NHANES) cycle released by the Centers for Disease Control and Prevention (CDC). The CDC has released additional NHANES data sets since the 2005/2006 data set. In June 2015, CPSC staff released a report that evaluated subsequent NHANES data sets (2007/2008, 2009/2010, and 2011/2012) using the CHAP's methodology.

The CDC publicly released phthalate metabolite biomonitoring data from its 2013/2014 NHANES[1] data cycle in late December 2016. CPSC staff applied previously documented methods[2] to these current biomonitoring data. This report presents estimates of phthalate exposures and cumulative risk for women of reproductive age .

CPSC staff's risk analysis demonstrates that a number of women of reproductive age (WORA; ages 15-45 years) had phthalate hazard quotients (DEHP and DINP) and hazard indices that exceeded one in the 2013/2014 National Health and Nutrition Examination Survey (NHANES) data set. As many as one percent of WORA exceeded an HQ or HI of one. These estimates, however, are statistically unstable, meaning that there are too few cases used as the basis of this estimate to be confident in their magnitude.

[1] NHANES includes a health examination data survey that is nationally representative of the civilian, non-institutionalized U.S. Population. The biomonitoring data are found in one of three laboratory subsets of the NHANES survey structure, and weighted accordingly.

[2] CPSC, June 2015 "Estimated Phthalate Exposure and Risk to Pregnant Women and Women of Reproductive Age as Assessed Using Four NHANES Biomonitoring Data Sets (2005/2006, 2007/2008, 2009/2010, 2011/2012)".

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Abbreviations

ADI	Acceptable daily intake
BBP	Butyl benzyl phthalate
CDC	Centers for Disease Control and Prevention (U.S.)
CHAP	Chronic Hazard Advisory Panel
CI	Confidence interval
CPSC	Consumer Product Safety Commission (U.S)
CPSIA	Consumer Product Safety Improvement Act of 2008
DBP	Dibutyl phthalate
DIBP	Diisobutyl phthalate
DEHP	Di(2-ethylhexyl) phthalate
DI	Daily Intake
DINP	Diisononyl phthalate
DNOP	Di-*n*-octyl phthalate
FHSA	Federal Hazardous Substances Act
HI	Hazard Index
HQ	Hazard Quotient
Log_{10}	Logarithm to the base 10
MBP	Monobutyl phthalate
MBzP	Monobenzyl phthalate
MCPP	Mono-(3-carboxypropyl) phthalate
MEHHP	Mono-(2-ethyl-5-hydroxy-hexyl) phthalate
MEHP	Mono(2-ethylhexyl) phthalate
MEOHP	Mono-(2-ethyl-5-oxo-hexyl) phthalate
MEP	Monoethyl phthalate
MIBP	Monoisobutyl phthalate
MINP	Mono(isononyl) phthalate
MOE	Margin of Exposure
N/A	Not available or specified
NHANES	National Health and Nutrition Examination Survey
PEAA	Potency Estimates for Antiandrogenicity
P-value	Probability value
PW	Pregnant women
WORA	Women of reproductive age (15-45 years old; non-pregnant)

INTRODUCTION

Background

Section 108 of the Consumer Product Safety Improvement Act (CPSIA) of 2008 established requirements for CPSC regarding phthalates. As directed, the Commission appointed a Chronic Hazard Advisory Panel (CHAP) to "study the effects on children's health of all phthalates and phthalate alternatives as used in children's toys and child care articles." . The CHAP provided its report with recommendations to the Commission in July 2014.[3] In accordance with section 108(b)(3) of the CPSIA, the Commission reviewed the CHAP report, and issued a notice of proposed rulemaking (NPR), which published in the *Federal Register* on December 30, 2014. (79 FR 78324)

Consistent with the statutory directive, the CHAP's recommendations to the Commission were, in part, based on risk estimates from a cumulative assessment that considered exposures from selected phthalates. The CHAP estimated phthalate exposures using biomonitoring data (urinary metabolite levels) from the Centers for Disease Control and Prevention's (CDC) National Health and Nutrition Examination Survey (NHANES) 2005/2006 data cycle. The CHAP analyzed data for pregnant women (PW) from this data cycle to meet its charge to "consider the likely levels of children's, pregnant women's, and others" exposure to phthalates . . ." CPSIA § 108 (b)(2)(B).

At the Commission briefing on the NPR on December 5, 2014, the Chairman directed staff to evaluate the more recent NHANES data sets. Using the CHAP's methods, CPSC staff reproduced the CHAP's estimated cumulative exposures and hazard indices (using 2005/2006 NHANES data) and applied the same methods to estimate cumulative phthalate exposures and risk using later NHANES biomonitoring data (2007/2008, 2009/2010, and 2011/2012 data cycles).[4]

In late December 2016, the CDC released measurements of phthalate metabolites in urine for participants in the 2013/2014 NHANES data cycle. CPSC staff applied the previously documented methods to these biomonitoring data. Estimates of phthalate exposures and risk for WORA are presented in this report.[5]

[3] Available at: https://www.cpsc.gov/PageFiles/169876/CHAP-REPORT-FINAL.pdf.
[4] Ibid.
[5] Ibid.

METHODS

In late December 2016, the CDC released the measurements of phthalate metabolites in urine from participants in its 2013/2014 NHANES data cycle. CPSC staff applied the data conventions and estimation algorithms described in Section 2 of the previous report (CPSC, 2015) to generate Daily Intakes (DI), Hazard Quotients (HQ), and Hazard Indices (HI) for each Woman of Reproductive Age (WORA, 15 to 45 years old) with phthalate metabolite measurements in the 2013/2014 NHANES data set. Table 1 reports the NHANES data files used to generate estimated exposures and hazard indices.

Table 1. 2013/2014 NHANES Data Sets Used to Estimate WORA Exposure to Phthalates

Phthalates – Urine	Urinary albumin and urinary creatinine	Urine pregnancy test	Demographic variables and sample weights	Body measures
PHTHTE_H Data (December 2016)	ALB_CR_H Data (updated Sept. 2016)	UCPREG_H Data (October 2015)	DEMO_H Data (October 2015)	BMX_H Data (October 2015)

The 2013/2014 NHANES data set reports phthalate metabolites for 538 nonpregnant WORA. As in data sets after the 2005/2006 data cycle, the number of PW in the 2013/2014 NHANES data cycle was insufficient to support statistical estimates.[6]

[6] Ibid.

RESULTS

WORA Daily Intake of BBP, DEHP, DINP, DBP, and DIBP Estimated from 2013/2014 NHANES Data

Daily intakes estimates for WORA at the 50th and 95th percentiles are shown below (Table 2).

Table 2. Daily Intake Estimates (µg/kg-day) for Women of Reproductive Age (NHANES 2013/2014)

BBP	DEHP	DINP	DBP	DIBP
Median				
0.15	1.27	4.97	0.33	0.29
95th Percentile				
0.97	4.22	53.19	1.14	1.03

WORA Hazard Quotients for BBP, DEHP, DINP, DBP, and DIBP[7] Estimated from 2013/2014 NHANES Data

Median and 95th percentile hazard quotients (HQs) for WORA exposed to DEHP and DINP were all below 1. See Table 3 below.

Table 3. Hazard Quotient Estimates for Women of Reproductive Age (NHANES 2013/2014)

Phthalate	Percentile	PEAA Case	Hazard Quotients
DEHP	Median	Case 1	0.042
		Case 2	0.025
		Case 3	0.025
	95th Percentile	Case 1	0.141
		Case 2	0.084
		Case 3	0.084
DINP	Median	Case 1	0.003
		Case 2	0.043
		Case 3	0.010
	95th Percentile	Case 1	0.035
		Case 2	0.462
		Case 3	0.106

A number of WORA individuals had HQs greater than one when considering both DEHP and DINP (but not BBP, DBP, DIBP). The percentage of the population estimates are statistically

[7] BBP, DEHP, DINP, DBP, and DIBP are the 5 antiandrogenic phthalates for which NHANES has metabolite data across the cycles. The last year NHANES tested for DCHP was 2010; incidence and levels were very low. NHANES did not analyze for metabolites of the other four phthalates being recommended for prohibition.

unstable, however, meaning that there are too few cases used as the basis of this estimate to be confident in their magnitude. See Table 4 below.

Table 4. Estimated Percentage of Women of Reproductive Age with Hazard Quotient >1 by Phthalate and PEAA (NHANES 2013/2014)		
Phthalate	PEAA Case	2013-2014
DEHP	Case 1	<1%*
	Case 2	<1%*
	Case 3	<1%*
DINP	Case 1	--*
	Case 2	<1%*
	Case 3	--*
1% = 604,000		
*Marked estimates have a coefficient of variance that is considered high; these estimates are not considered stable.		

WORA Hazard Indices Estimated using BBP, DEHP, DINP, DBP, and DIBP from 2013/2014 NHANES Data

Median and 95th percentile hazard indices (HIs) were below 1 for all PEAA cases. See Table 5 below.

Table 5. Hazard Index Estimates for Women of Reproductive Age (NHANES 2013/2014)		
Percentile	PEAA Case	Hazard Indices
Median	Case 1	0.057
	Case 2	0.102
	Case 3	0.044
95th Percentile	Case 1	0.171
	Case 2	0.587
	Case 3	0.180

A number of WORA individuals had HIs greater than one. The percentage of the population estimates are statistically unstable, however, meaning that there are too few cases used as the basis of this estimate to be confident in their magnitude. See Table 6 below.

Table 6. Estimated Percentage of Women of Reproductive Age with

Hazard Index >1 by PEAA (NHANES 2013/2014)	
PEAA Case	2013-2014
Case 1	<1%*
Case 2	1.2%*
Case 3	<1%*
1% = 604,000	
*Marked estimates have a coefficient of variance that is considered high; these estimates are not considered stable.	

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