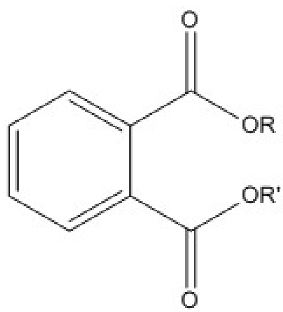
Potential Designated Chemicals:

***ortho*-Phthalates**

(1,2-Benzenedicarboxylic acid esters)



July 16, 2015 Meeting of the Scientific Guidance Panel
Biomonitoring California[1]

Introduction

o-Phthalates are esters of 1,2-benzenedicarboxylic acid, with the general structure as shown above. R and R´ are commonly alkyl groups, as in di-2-ethylhexyl phthalate (DEHP), for example. *o*-Phthalates are widely used as plasticizers to increase flexibility. They are also used in personal care products and cosmetics as solvents.

The *o*-phthalates currently on the list of designated chemicals for Biomonitoring California are shown below. These were designated based on their inclusion in the National Reports on Human Exposure to Environmental Chemicals program of the Centers for Disease Control and Prevention (CDC). The Scientific Guidance Panel recommended these *o*-phthalates as priority chemicals in March 2009.

o-Phthalates currently on the lists of designated and priority chemicals:

Benzylbutyl phthalate (BzBP)	Di-2-ethylhexyl phthalate (DEHP)
Di-*n*-butyl phthalate (DnBP)	Diisodecyl phthalate (DIDP)
Diisobutyl phthalate (DIBP)	Diisononyl phthalate (DINP)
Dicyclohexyl phthalate (DCHP)	Dimethyl phthalate (DMP)
Diethyl phthalate (DEP)	Di-*n*-octyl phthalate (DnOP)

[1] California Environmental Contaminant Biomonitoring Program, codified at Health and Safety Code section 105440 *et seq.*

Six *o*-phthalates are listed under Proposition 65 as known to the State of California to cause cancer and/or reproductive toxicity (OEHHA, 2015). Of these, di-*n*-hexyl phthalate (DnHxP) is not on the list of designated chemicals.

Proposition 65 listed *o*-phthalate	**Type of toxicity**
Benzylbutyl phthalate (BzBP)	developmental
Di-*n*-butyl phthalate (DnBP)	developmental, male, female
Di-2-ethylhexyl phthalate (DEHP)	cancer, developmental, male
Di-*n*-hexyl phthalate (DnHxP)	female, male
Di-isodecyl phthalate (DIDP)	developmental
Di-isononyl phthalate (DINP)	cancer

Restrictions on the use of a number of phthalates in the US, Canada, Europe, and Japan are leading to changing use patterns. In California, DEHP, DnBP, BzBP, DINP, DIDP, and DnOP were banned for use in children's toys and childcare articles at concentrations above 0.1%, effective January 2009 (California Health and Safety Code §108935-108939). The California legislation directed manufacturers to use the least toxic alternative in replacing phthalates and prohibited use of phthalates that are carcinogens or reproductive toxicants. Existing federal regulations on phthalates in children's toys are similar (Consumer Product Safety Improvement Act, 2008). The US Consumer Product Safety Commission (CPSC, 2014a) recently proposed a permanent federal ban on the use of DINP, DIBP, DCHP, di-*n*-pentyl phthalate (DPenP), and DnHxP in children's products at concentrations greater than 0.1%.

DEHP is being replaced in some applications with DINP and/or DIDP (Zota et al., 2014; Yen et al., 2011). Based on an analysis of NHANES[2] urinary metabolite data from 2001 to 2010, Zota et al. (2014) found decreasing exposures to DEHP, DnBP, and BzBP, and increasing exposures to DINP, DIBP, and DIDP.

There is an extensive body of literature on *o*-phthalates. This summary provides a brief overview of information relevant to the criteria for designated chemicals. We highlight available findings for *o*-phthalates not currently included on Biomonitoring California's list of designated chemicals.

If the Panel were to recommend adding the class of *o*-phthalates to the list of designated chemicals, the Program could include any member of this class in future biomonitoring studies. Listing the class would give the Program the flexibility to track changing exposures to *o*-phthalates as market shifts occur.

[2] National Health and Nutrition Examination Survey

Chemical identity and production/import volume

The following table (on page 4) lists selected *o*-phthalates and available US production/import volumes. An asterisk (*) denotes the *o*-phthalates not currently on the list of designated chemicals. Though alternatives are beginning to emerge, *o*-phthalates are still the most widely used plasticizers globally. Tullo (2015) estimated that worldwide consumption of plasticizers was 8 million metric tons (18 billion pounds), of which 70% was *o*-phthalates.

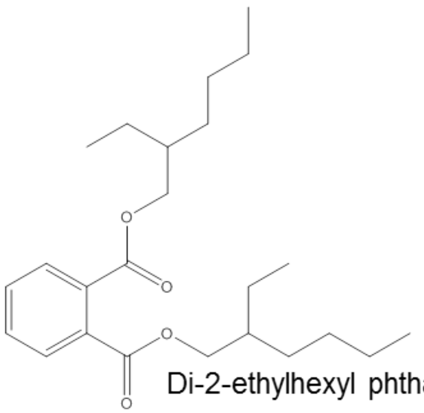
Selected phthalates[3]: US production/import volume for reporting years 2006 and 2012

Chemical (*in approximate order of alkyl chain length*)	**CASRN**	**Production/import volume (lbs)[4]**
Diethyl phthalate (DEP)	84-66-2	2006: 10M – < 50M 2012: 5.6M
Diallyl phthalate (DAP)*	131-17-9	2006: 1M – < 10M 2012: withheld[5]
Di-*n*-butyl phthalate (DnBP)	84-74-2	2006: 10M – < 50M 2012: 7M
Diisobutyl phthalate (DIBP)	84-69-5	2006: 500K – < 1M 2012: 454K
Benzylbutyl phthalate (BzBP)	85-68-7	2006: 50M – < 100M 2012: 50M – < 100M
Di-*n*-hexyl phthalate (DnHxP)*	84-75-3	2006: 500K – < 1M 2012: 48K
Diisoheptyl phthalate (DIHpP)*	71888-89-6	2006: 50M – <100M 2012: withheld
Di-2-ethylhexyl phthalate (DEHP)	117-81-7	2006: 100M – < 500M 2012: 153M
Di-*n*-octyl phthalate (DnOP)	117-84-0	2006: 10M – < 50M 2012: withheld
Diisononyl phthalate (DINP)	68515-48-0	2006: 100M – < 500M 2012: 100M – 250M
	28553-12-0	2006: 100M – < 500M 2012: 108M
Diisodecyl phthalate (DIDP)	26761-40-0	2006: 1M – < 10M 2012: 500K – < 1M
	68515-49-1	2006: 100M – < 500M 2012: 163M
Di-2-propylheptyl phthalate (DPHP)[6]	53306-54-0	2006: 1M – < 10M 2012: 50M – < 100M
Diundecyl phthalate (DUP)*	3648-20-2	2006: 10M – < 50M 2012: 10M – < 50M
Diisoundecyl phthalate (DIUP)*	85507-79-5	2006: 1M – < 10M 2012: 8M
Diisotridecyl phthalate (DTDP)*	68515-47-9	2006: 10M – < 50M 2012: 10M – < 50M

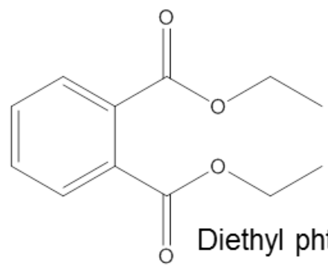
*Not currently on the list of designated chemicals for Biomonitoring California.

[3] Refer to the glossary on page 13 for a complete list of *o*-phthalates mentioned in this document.
[4] From US EPA (2006; 2012a).
[5] This information was withheld by the manufacturer (US EPA, 2012a).
[6] DPHP is a specific isomer of DIDP. DIDP is on the list of designated chemicals.

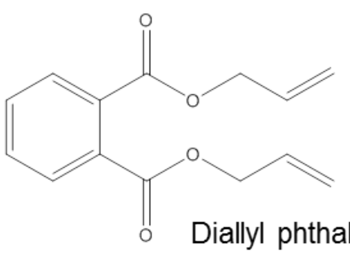
Below are some example structures of *o*-phthalates.



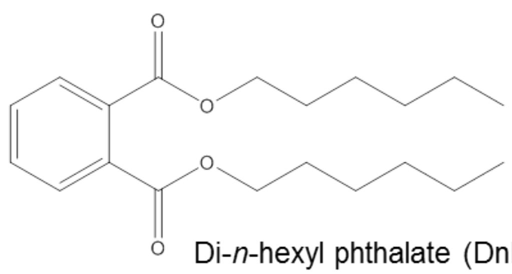
Di-2-ethylhexyl phthalate (DEHP)



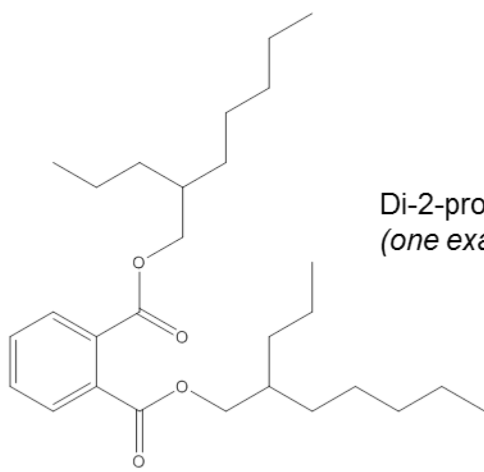
Diethyl phthalate (DEP)



Diallyl phthalate (DAP)



Di-*n*-hexyl phthalate (DnHxP)



Di-2-propylheptyl phthalate (DPHP)
(one example DIDP isomer)

Exposure or potential exposure to the public or specific subgroups

o-Phthalates are extensively used in a wide variety of applications. Example plastic products containing *o*-phthalates include shower curtains, children's toys, processing equipment for food, packaging materials, automotive plastics, and plastic medical supplies, such as tubing and bags for intravenous fluids or blood. *o*-Phthalates are used in a variety of building materials such as vinyl flooring, wires and cables, wallpaper, and carpet backing (Just et al., 2015; CPSC, 2010; ATSDR, 2002). They are found in paints, adhesives, and coatings for medications (CPSC, 2010; Just et al., 2015; Kelley et al., 2013). *o*-Phthalates are used in personal care products and cosmetics for many purposes including: fragrance carriers; to prevent brittleness and cracking in nail polish; as skin moisturizing, softening, and penetrating agents; and as antifoaming agents (Koo and Lee, 2004). Scented products like air fresheners can also contain *o*-phthalates.

The following sections summarize data on detections of selected *o*-phthalates in food, personal care products, consumer products, dust, and indoor air.

Diet:

Diet is considered to be a major route of exposure to high molecular weight *o*-phthalates, such as DEHP, DINP, and DIDP (Koch et al., 2013). *o*-Phthalates can migrate into food from food processing and handling equipment (like tubing, conveyor belts, and gloves), as well as food packaging materials (Kappenstein et al., 2012; Gallart-Ayala et al., 2013). *o*-Phthalates may also be in food due to widespread presence in the environment (Kappenstein et al., 2012). A number of *o*-phthalates[7] are approved for use in food contact surfaces and materials and as indirect food additives (US FDA, 2014a; 2014b; 2014c).

Bi et al. (2013) found diallyl phthalate (DAP) and DPenP each in over half of the vegetable oil samples purchased in Delaware supermarkets (n=21) at levels ranging from below the detection limit to 306 µg/kg (DAP) or 876 µg/kg (DPenP). Neither of these *o*-phthalates is currently on the list of designated chemicals. In comparison, DEHP was found in all samples, with levels ranging from 50.3 to 6,166 µg/kg. Three other *o*-phthalates not currently included on the list of designated chemicals, di-*n*-propyl phthalate (DnPP), DnHxP, and di-*n*-heptyl phthalate (DnHpP) were each detected in less than 15% of vegetable oil samples.

Schecter et al. (2013) found DnHxP in 15% of food samples (n=72) collected from Albany, New York in 2011. For example, DnHxP was found in two samples of ice cream (maximum=8.82 µg/kg wet weight [wt]), one sample of ground beef (4.83 µg/kg wet wt), and in one of two butter samples tested (1.58 µg/kg wet wt). For comparison, DEHP was detected in 74% of the samples at levels ranging from 3.71 to 1158 µg/kg wet wt.

---

[7] *o*-Phthalates approved by US FDA for use in food contact materials and/or as indirect food additives include: DMP, DAP, DEP, DnBP, DIBP, BzBP, DCHP, DEHP, DIDP, and DUP.

Personal care products:
o-Phthalates are directly added to many personal care products, but can also migrate into the products from packaging (Guo and Kannan, 2013). Routine use of personal care products may contribute to high levels of exposure to certain *o*-phthalates, such as DEP (Philippat et al., 2015a; Just et al., 2010; Guo and Kannan, 2013). DEP is commonly used in personal care products that contain fragrances (Philippat et al., 2015a; US FDA, 2014d).

Dodson et al. (2012) conducted a broad survey of *o*-phthalates and other chemicals in a variety of consumer products, which they categorized as “conventional” versus “alternative” based on specific criteria. They used a compositing approach, combining as many as seven conventional products of a particular type to create a single sample for analysis. Except for sunscreen, the alternative products were analyzed individually. DEP was one of the most frequently detected compounds in composite samples of conventional personal care products, such as soap, lotion, and shaving cream. It was also found in samples of alternative body lotion, conditioner, and sunscreen. DEHP was found in both conventional and alternative personal care products. DnHxP, not currently on the list of designated chemicals, was detected in the composite conventional lipstick sample. A single sample of an alternative shaving cream contained four phthalates (DEHP, DnBP, BzBP, and DINP), as well as the phthalate alternative di(2-ethylhexyl) adipate, illustrating the potential for multiple exposures. Dicyclohexyl phthalate (DCHP) and DINP were detected only in alternative personal care products, which the authors highlighted as possible evidence of substitution.

Guo and Kannan (2013) reported that DEHP was the most frequently detected phthalate in a survey of personal care products collected in Albany, New York in 2012. The detection frequency in “leave-on” and “rinse-off” products was 66% and 76%, respectively. The authors proposed that the DEHP in the products was coming from the plastic packaging. DEP, DIBP, and DnBP[8] were also found in leave-on products (DFs were 53%, 23%, and 39%, respectively) and rinse-off products (DFs were 24%, 27%, and 17%, respectively). With regard to concentrations, DEP was found at the highest levels, ranging up to a maximum of nearly 8000 µg/g wet wt in perfume. DMP and BzBP were found in about 10% of the leave-on and rinse-off products evaluated. DnHxP, not currently on the list of designated chemicals, was detected in 3% of leave-on products and 7% of rinse-off products. The highest concentrations of DnHxP were found in deodorant (mean, 2.69 µg/g wet wt; max, 37.7 µg/g wet wt).

[8]Guo and Kannan (2013) used the abbreviation “DBP” (dibutyl phthalate), which is assumed to be DnBP.

Bao et al. (2015) conducted a survey of personal care products in China, with samples collected in 2013. The authors indicated that DEP was the most frequently detected *o*-phthalate (DF=29.8%), and that most concentrations were above 20 µg/g. The authors also reported detections in less than 5% of products of some *o*-phthalates not currently on the list of designated chemicals: di(methoxyethyl) phthalate (DMEP), diphenyl phthalate (DPhP), and bis(4-methyl-2-pentyl)phthalate (one isomer of diisohexyl phthalate [DIHxP]).

In a small study of personal care products (n=26) from Spain, Llompart et al. (2013) reported that DEP levels were higher in "leave-on" products (DF=53%; range from below the limit of detection [<LOD] to 357 µg/g) compared to levels in "rinse-off" products (DF=29%; two detections at 2.5 and 0.72 µg/g). Several *o*-phthalates not currently on the list of designated chemicals were detected in leave-on products (n=19): DMEP (two detections, deodorant and hair product); DPhP (two detections, hand/skin lotion); DPenP (one detection, hair product), and diisopentyl phthalate (DIPenP) (one detection, hair product).

Children's toys and childcare products:
In a study of 72 PVC toys and other childcare products purchased from 17 countries, Stringer et al. (2000) reported that DINP was the most frequently found *o*-phthalate (DF= 64%), followed by DEHP (DF= 48%). Five of the six children's toys and products bought in the US were made in China; the sixth was made in the US. DINP concentrations in these toys and products ranged from <LOD to 37.2% by weight. DEHP was found in only one teether purchased in the US (made in China), at 0.06%. In the teether that was bought and also made in the US, neither DEHP nor DINP were detected.

In a German study, DPHP was identified in children's toys at concentrations ranging from approximately 10-48% by weight (Federal Institute for Risk Assessment, 2011).

CPSC (2014b) analyzed 1,125 children's toys and childcare articles for *o*-phthalates, as part of enforcement of Section 108 of the Consumer Product Safety Improvement Act of 2008. Seven hundred and twenty-five (725) samples were found to have at least one of six regulated phthalates (DEHP, DnBP, BzBP, DINP, DIDP, and DnOP) at levels above 0.1%. Most of the 725 samples contained DEHP (DF=96%). DINP and DnBP were detected much less frequently (DF=13% and 12%, respectively). In the remaining 400 children's toys and childcare articles that did not contain one of the regulated phthalates, CSPC reported results for unregulated *o*-phthalates. DIBP was found in 132 of the 400 samples, and DPHP was found in 16 of the 400 samples

Other consumer products:
Recent data on emerging *o*-phthalates in other consumer products were limited. The Dodson et al. (2012) survey discussed above included consumer products like vinyl products, household cleaners, laundry detergent, and car care products. DEHP was found at high concentrations in a vinyl pillow protector and a composite sample of two vinyl shower curtains. DEP was found in conventional laundry, cleaning and car care products, and was also detected in an alternative stain remover. DnPP, not currently on the list of designated chemicals, was not detected in any of the conventional products but was found in a sample of alternative laundry bleach, as well as samples of baking soda and borax.

Dust:
Dodson et al. (2015) studied phthalates in house dust samples collected in Richmond and Bolinas homes in 2006. Three phthalates not currently on the list of designated chemicals were detected: DnHxP (DF=96%), DPenP (DF=12%), and DnPP (DF=2%). The median level of DnHxP was 0.66 µg/g, with a maximum value of 110 µg/g. Median values for DPenP and DnPP in dust were <LOD. For comparison, DEHP was detected in 100% of samples, at a median level of 140 µg/g and a maximum of 800 µg/g.

DnHxP was measured in two other US studies of phthalates in dust. Guo and Kannan (2011) detected DnHxP in all indoor dust samples from Albany, New York at a median level of 0.6 µg/g. Rudel et al. (2003) found DnHxP in 76% of house dust samples collected from homes in Cape Cod, Massachusetts at a median level of 1.1 µg/g. For comparison, DEHP was detected in 100% of dust samples from these two studies (median levels of 304 and 77 µg/g, respectively).

Kubwabo et al. (2013) measured phthalate levels in Canadian house dust samples collected from 2007 to 2010. Some *o*-phthalates not currently on the list of designated chemicals were detected: DnHxP (DF=89%; median=0.47 µg/g), diisoheptyl phthalate (DIHpP) (DF = 98%, median=18.9 µg/g), diundecyl phthalate (DUP) (DF = 99%, median=3.9 µg/g), and a C7-C9 alkyl benzyl phthalate (DF= 95%; median=1.24 µg/g). For comparison, DEHP, DINP, and DIDP were found in 100% of samples at median levels of 462, 112, and 111 µg/g, respectively.

Air:
Rudel et al. (2010) studied phthalates in paired indoor and outdoor air samples collected in 2006 in Richmond (n=40) and Bolinas (n=10). DEP, DnBP, and DIBP were detected in 100% of indoor air samples from Richmond (median levels were 330, 140, and 140 ng/m^3, respectively) and in Bolinas (320, 140, and 81 ng/m^3, respectively). The detection frequency of DEHP was 90% in indoor air samples from Richmond

(median=69 ng/m^3) and 50% in indoor air samples from Bolinas (median=47 ng/m^3). Three *o*-phthalates not on the list of designated chemicals were each found in 2% of Richmond indoor air samples: DnHxP (maximum=52 ng/m^3), DPenP (maximum=4.0 ng/m^3), and DnPP (maximum= 2.3 ng/m^3). DnHxP was found in 6% of Richmond outdoor air samples (maximum=15 ng/m^3).

Known or suspected health effects

There is an extensive body of toxicological literature on some *o*-phthalates, including DEHP. A number of *o*-phthalates are identified as male reproductive toxicants (DEHP, DnBP, DnHxP), female reproductive toxicants (DnBP, DnHxP), and/or developmental toxicants (DEHP, DIDP, DnBP) (OEHHA, 2015). DEHP and DINP are carcinogens. For many other *o*-phthalates, only limited data are available.

In male rats, *in utero* exposure to anti-androgenic phthalates has been shown to result in abnormalities in reproductive tract development, the entire spectrum of which is termed the “phthalate syndrome” (Mylchreest et al., 1998, 2000; Gray et al., 2000; Foster, 2005; 2006). Some characteristics of phthalate syndrome include various malformations of male reproductive organs, including hypospadias, cryptorchidism (undescended testes), and reduced anogenital distance (AGD). Phthalate exposure in humans is linked with some of these conditions as well. Several studies have found that decreased AGD in baby boys was associated with higher maternal urinary phthalate levels (Swan et al., 2005; Suzuki et al., 2012; Bustamante-Montes et al., 2013; Bornehag et al., 2015; Swan et al., 2015).

The Chronic Health Advisory Panel (CHAP, 2014) on Phthalates and Phthalate Alternatives convened by CPSC reviewed limited studies on reproductive and developmental toxicity for many phthalates not yet on the list of designated chemicals, including DPenP, DnHxP, DIHpP, and DnHpP (see CPSC, 2011a; 2011b; 2011c; 2011d; 2010). CHAP identified the following *o*-phthalates as anti-androgenic phthalates capable of producing rat phthalate syndrome, in order of activity: DPenP > BzBP ~ DnBP ~ DIBP ~ DnHxP ~ DEHP ~ DCHP > DINP (see also Gray et al., 2000; National Research Council, 2008). DPenP and DnHxP are not currently on the list of designated chemicals.

In a recent review of the literature on effects of *o*-phthalates on the ovary, Hannon and Flaws (2015) reported that DEHP disrupts ovarian folliculogenesis at numerous points during development. DnBP and BzBP disrupted follicle development and DINP was found to decrease the number of corpora lutea in adult rats after perinatal exposure. Hannon and Flaws also summarized findings that *o*-phthalates can alter ovarian steroidogenesis at a number of steps in the estradiol synthesis pathway.

Phthalates have also been shown to affect neurodevelopment, and epidemiological studies have found associations between phthalate levels and differences in cognition and behavior (Miovodnik et al., 2014). In experimental studies, possible mechanisms for observed neurodevelopmental effects include changes in brain aromatase activity (DEHP), interference with calcium signaling (DEHP, BzBP, DnBP), effects on brain lipids (DEHP), effects on brain dopamine pathways (DEHP, DnBP, DCHP), changes in levels of certain neurotransmitters (DEHP, DCHP), and alterations in thyroid homeostasis (DEHP, BzBP, DnBP, DnOP, DINP) (Miovodnik et al., 2014).

Boas et al. (2012) also reviewed *o*-phthalate mediated disruption of thyroid homeostasis in experimental studies. BzBP, DnBP, and DnOP were found to interfere with the sodium/iodide symporter. Boas et al. (2012) summarized findings that DnBP and BzBP inhibited thyroid hormone uptake into cells. BzBP inhibited T3 binding to the thyroid hormone binding protein transthyretin. In epidemiological studies, urinary levels of DEHP and DnBP were negatively associated with serum thyroid hormone levels (Boas et al., 2012).

o-Phthalates have been implicated in the development of allergies and asthma in some studies (North et al., 2014). However, there have been mixed reports on the association of phthalates and allergic disease (North et al., 2014; Bornehag and Nanberg, 2010; Bekö et al., 2015). In a study in female BALB/cJ mice, Larsen and Nielsen (2008) concluded that sensitization depended on both the lipophilicity and stereochemistry of the phthalate. In a recent epidemiological study, Bekö et al. (2015) reported significant associations between non-dietary exposure (i.e., inhalation or dermal) to phthalates and allergic sensitization among children with asthma, rhinoconjunctivitis, or atopic dermatitis.

In utero exposure to low doses of MEHP was reported to induce obesity in male mice (Hao et al., 2012), and several other phthalates have been found to affect adipogenesis, possibly through activation of peroxisome proliferator activated receptors (PPARs) (Pereira-Fernandes et al., 2013; Hurst and Waxman, 2003). Disruption of thyroid homeostasis has also been discussed as another possible mechanism for o-phthalate induced obesity (Kim and Park, 2014). Goodman et al. (2014) conducted a systematic review of epidemiological studies that looked at potential associations between phthalate exposure and health endpoints related to obesity, type 2 diabetes, and cardiovascular disease, and found no consistent patterns.

Twenty *o*-phthalates[9] were evaluated in US EPA's high-throughput chemical Toxicity Forecaster (ToxCast™) program (Dix et al., 2007; Kavlock et al., 2012). ToxCast

[9] The *o*-phthalates and some metabolites evaluated in US EPA's ToxCast program were: DAP, DMP, monomethyl phthalate, DnBP, DIBP, monobutyl phthalate, BzBP, monobenzyl phthalate, DEP, DnHxP,

includes several hundred *in vitro* assays, including assays related to androgen, estrogen, and thyroid receptor pathways, gene expression and activity of PPARs, and cell proliferation. Most of the *o*-phthalates tested in ToxCast were active in assays targeting the estrogen receptor pathway and the PPAR subtypes, but few were active in assays targeting the androgen receptor pathway. *o*-Phthalates with four to six carbons in their alkyl side chain backbones were the phthalates active in the most ToxCast assays overall (US EPA, 2015).

Potential to biomonitor

Physical chemical properties:
o-Phthalates are not persistent or bioaccumulative. Log K_{OW} increases and vapor pressure declines with increasing alkyl chain length (National Industrial Chemicals Notification and Assessment Scheme [NICNAS], 2008).

Metabolism:
Phthalates are rapidly metabolized to their monoesters (Koch and Calafat, 2009). Oxidation of the monoester results in formation of the hydroxyl, oxo, and carboxyl secondary metabolites. For high molecular weight phthalates, the monoester is readily converted to these oxidized metabolites. The oxidized secondary metabolites are the main metabolites for long-chain phthalates (DEHP, DINP, and DPHP) and the monoesters are the main metabolites for short chain phthalates (Wittassek and Angerer, 2008). Both the monoester and the oxidized secondary metabolites are conjugated with glucuronic acid and excreted in the urine (Koch and Calafat, 2009).

Past biomonitoring studies:
Widespread exposure to many *o*-phthalates, including DEHP, DnBP, and DEP, has been demonstrated in biomonitoring studies worldwide (Philippat et al., 2015a; Zota et al., 2014; Calafat et al., 2011; Göen et al., 2011; Wittassek et al., 2007; Cutanda et al., 2015; Guo et al., 2011). Limited biomonitoring data for *o*-phthalates that are not currently on the list of designated chemicals were located, and are briefly discussed below.

Schütze et al. (2015) investigated time trends of DPHP metabolites in urine samples collected between 1999-2012 and stored in the German Environmental Specimen Bank. Mono-oxo-propylheptyl phthalate (oxo-MPHP) was detected in samples from 2009 (n=60, 3.3% > LOQ) and 2012 (n=60, 21.7% > LOQ) but was not detected in any samples from 1999, 2003, or 2006. oxo-MPHP concentrations ranged from less than the limit of quantitation (LOQ=0.25 µg/L) to 0.96 µg/L. Mono(propyl-6-hydroxyheptyl)

DnOP, DEHP, DINP, MEHP, DIUP, diisopropyl phthalate, DIPenP, DCHP, octyl decyl phthalate, and DIDP.

phthalate was also only detected in samples from 2009 (3.3% >LOQ; range <LOQ [0.3 µg/L] to 0.64 µg/L) and 2012 (3.3% >LOQ; range from <LOQ [0.3 µg/L] to 0.36 µg/L). Mono(propyl-6-carboxyhexyl) phthalate was not detected in any samples.

Silva et al. (2011) measured DPenP metabolites in 45 urine samples collected in 2009 from US adult residents. Mono(4-hydroxypentyl) phthalate (MHPP) was detected in 29% of adult urine samples (range from <LOD [0.7 µg/L] to 8 µg/L). Mono-*n*-pentyl phthalate (MPenP) was not detected (LOD=0.6 µg/L).

Hartmann et al. (2015) found the DPenP metabolite MPenP in urine samples from Austrian children and adults collected between 2010 and 2012 (range of DFs across all age groups was 4.1 to 6.5%; n=595). The levels ranged from <LOQ (0.55 µg/L) to 4.5 µg/L.

Kasper-Sonnenberg et al. (2011) detected MPenP above the LOQ in 2% of urine samples from German mothers (n=103) and children (n=104) collected from late 2007 to early 2009. The urinary levels for children (6 to 8 years old) were not quantifiable; in mothers' samples the values ranged from <LOQ (0.20 µg/L) to 1.3 µg/L (Kasper-Sonnenberg et al., 2011). Kasper-Sonnenberg et al. (2014) detected MPenP above the LOQ in 7.4% of urinary samples from school-aged children (8 to 10 years old; n=465). The unadjusted 95th percentile was below the LOQ (0.2 µg/L). When adjusted for creatinine, the median MPenP urinary level was 0.09 µg/g creatinine and the 95th percentile was 0.26 µg/g creatinine.

Zimmermann et al. (2012) detected DAP in breast milk samples (n=30) collected from German women (27% of values were >LOQ; median=2.0 ng/g). For comparison, DIBP was detected above the LOQ in 77% of samples (median=1.0 ng/g). DEHP and DnBP were detected above the LOQs in 43% of samples (median levels were 2.3 and 0.6 ng/g, respectively).

Analytical considerations

The Environmental Health Laboratory's (EHL's)[10] urinary phthalate metabolite method uses on-line solid phase extraction high performance liquid chromatography tandem mass spectrometry (SPE–HPLC-MS/MS). The current method can measure ten urinary phthalate metabolites with detection limits ranging from 0.1 to 0.9 µg/L. The on-line SPE–HPLC-MS/MS system allows rapid and simultaneous sample preparation and analysis of multiple phthalates in urine. EHL's method avoids the issues associated with a manual off-line approach, such as lack of repeatability and potential

[10] EHL is in the California Department of Public Health and is one of Biomonitoring California's laboratories.

contamination. Additional phthalate metabolites can easily be added to the method without loss of sensitivity, though further optimization and validation of the method might be required.

Incremental costs to expand the method will include the purchase of additional native and labeled standards, reagents, and other laboratory supplies.

Need to assess efficacy of public health action

Adding the entire class of *o*-phthalates as designated chemicals would allow Biomonitoring California to study whether emerging *o*-phthalates are found in California residents and at what levels. Listing these chemicals as a class would be a resource-efficient approach. For example, it would facilitate the use of non-targeted laboratory screening methods, allowing the state to determine which phthalates pose the highest exposure concerns in California. Using this approach, the most important phthalates could be tracked over time to monitor levels in urine.

Glossary of *o*-phthalates (alphabetical by acronym)

BzBP: Benzylbutyl phthalate
DAP: Diallyl phthalate
DCHP: Dicyclohexyl phthalate
DEP: Diethyl phthalate
DEHP: Di-2-ethylhexyl phthalate
DIBP: Diisobutyl phthalate
DIDP: Diisodecyl phthalate
DIHpP: Diisoheptyl phthalate
DIHxP: Diisohexyl phthalate
DINP: Diisononyl phthalate
DIPenP: Diisopentyl phthalate
DIUP: Diisoundecyl phthalate
DMEP: Dimethoxylethyl phthalate
DnBP: Di-*n*-butyl phthalate
DnHpP: Di-*n*-heptyl phthalate
DnHxP: Di-*n*-hexyl phthalate
DnOP: Di-*n*-octyl phthalate
DnPP: Di-*n*-propyl phthalate
DPenP: Di-*n*-pentyl phthalate
DPHP: Di-2-propylheptyl phthalate
DPhP: Diphenyl phthalate
DTDP: Diisotridecyl phthalate
DUP: Diundecyl phthalate

References consulted (not all references are cited in the text)

Agency for Toxic Substances and Disease Registry (ATSDR) (2002). Toxicological Profile for Di(2-ethylhexyl) Phthalate. Available online: http://www.atsdr.cdc.gov/toxprofiles/tp9.pdf

Aydoğan Ahbab M and Barlas N (2015). Influence of in utero di-*n*-hexyl phthalate and dicyclohexyl phthalate on fetal testicular development in rats. Toxicol Lett 233:125-37.

Bahadar H, Maqbool F, Abdollahi M (2014). Consumption of phthalates coated pharmaceutical tablets: An unnoticed threat. Int J Pharmacol 10:78-81.

Bao J, Wang M, Ning X, Zhou Y et al. (2015). Phthalate concentrations in personal care products andthe cumulative exposure to female adults and infants in Shanghai. J Toxicol Env Heal A 78:325-41.

Bekö G, Callesen M, Weschler CJ, Toftum J et al. (2015). Phthalate exposure through different pathways and allergic sensitization in preschool children with asthma, allergic rhinoconjunctivitis, and atopic dermatitis. Env Res 137:432-9.

Bekö G, Weschler CJ, Langer S, Callesen M et al. (2013). Children's phthalate intakes and resultant cumulative exposures estimated from urine compared with estimates from dust ingestion, inhalation and dermal absorption in their homes and daycare centers. PLoS ONE 8(4):e62442.

Bi X, Pan X, Yuan S, and Wang Q (2013). Plasticizer contamination in edible vegetable oil in a US retail market. J Agric Food Chem 61:9502-9.

Bradley EL, Burden RA, Leon I, Mortimer DN et al. (2013a). Determination of phthalate diesters in foods. Food Addit Contam A 30:722-34.

Bradley EL, Burden RA, Bentayeb K, Driffield M et al. (2013b). Exposure to phthalic acid, phthalate diesters and phthalate monoesters from foodstuffs: UK total diet study results. Food Addit Contam A 30:735-42.

Braun J, Sathyanarayana S, Hauser R (2013). Phthalate exposure and children's health. Curr Opin Pediatri 25:245-54.

Boas M, Feldt-Rasmussen U, Main KM (2012). Thyroid effects of endocrine disrupting chemicals. Mol Cell Endocrinol 355:240-8.

Bornehag CG, Carlstedt F, Jonsson BA, Lindh CH et al. (2015). Prenatal phthalate exposures and anogenital distance in Swedish boys. Environ Health Perspect 123:101-7.

Bornehag CG and Nanberg E (2010). Phthalate exposure and asthma in children. Int J Androl 33:333-45.

Bustamante-Montes LP, Hernandez-Valero MZ, Flores-Pimentel D, Garcia-Fabila M et al. (2013). Prenatal exposure to phthalates is associated with decreased anogenital distance and penile size in male newborns. J Dev Orig Health Dis 4:300-6.

Calafat AM, Wong L-Y, Silva MJ, Samander E et al. (2011). Selecting adequate exposure biomarkers of diisononyl and diisodecyl phthalates: Data from the 2005-2006 National Health and Nutrition Examination Survey. Environ Health Perspect 119:50-5.

California Health and Safety Code. Division 104 Environmental Health. Part 3 Product Safety. Chapter 11. Phthalates in products for young children. Sections 108935-108939. Available online: http://www.leginfo.ca.gov/cgi-bin/displaycode?section=hsc&group=108001-109000&file=108935-108939

Canada Consumer Product Safety Act (S.C. 2010, c21). Phthalates regulations SOR/2010-298. Available online: http://laws-lois.justice.gc.ca/PDF/SOR-2010-298.pdf

Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives (CHAP) (2014). Report to the US Consumer Product Safety Commission. Available online: https://www.cpsc.gov/PageFiles/169876/CHAP-REPORT-FINAL.pdf

Consumer Product Safety Commission (CPSC) (2014a). Prohibition of Children's Toys and Child Care Articles Containing Specified Phthalates. 16CFR Part 1307 Docket No. CPSC-2014-0033. Notice of Proposed Rulemaking. Available online: http://www.gpo.gov/fdsys/pkg/FR-2014-12-30/pdf/2014-29967.pdf

CPSC (2014b). Summary of Phthalates Testing Results and Potential Modifications to the Testing Method. Memorandum from M Dreyfus, via A Orland to M Babich (October 27, 2014). Available online as part of a briefing package (see pages 151-152): http://www.cpsc.gov//Global/Newsroom/FOIA/CommissionBriefingPackages/2015/ProposedRule-Phthalates-112514.pdf

CPSC (2011a). CPSC Staff Toxicity Review of Two Phthalates and One Phthalate Alternative for Consideration by the Chronic Hazard Advisory Panel. Memorandum from L Patton, via M Babich and L Saltzman, to MA Danello. Available online: http://www.cpsc.gov/PageFiles/125715/DMEP.pdf

CPSC (2011b). Toxicity Review of Di(2-propylheptyl) phthalate (DPHP). Staff memorandum from K Carlson and L Patton, via MA Danello and L Saltzman, to M Babich (October 30, 2010) and contractor report (Contract No. CPSC-D-06-0006, May 16, 2011). Available online: https://www.cpsc.gov/PageFiles/125788/dphp.pdf

CPSC (2011c). Toxicity Review of Diisoheptyl phthalate (DiHP). Staff memorandum from K Carlson and L Patton, via MA Danello and L Saltzman, to M Babich (October 30, 2010) and contractor report (Contract No. CPSC-D-06-0006, July 14, 2011). Available online: http://www.cpsc.gov/PageFiles/125776/dihp.pdf

CPSC (2011d). Toxicity Review of Diundecyl Phthalate (DUP). Staff memorandum from K Carlson and L Patton, via MA Danello and L Saltzman, to M Babich (October 25, 2010) and contractor report (Contract No. CPSC-D-06-0006, June 29, 2011). Available online: http://www.cpsc.gov/PageFiles/125795/dup.pdf

CPSC (2010). Overview of Phthalates Toxicity. Memorandum from M Babich, via L Saltzman, to MA Danello (April 12, 2010). Available online: https://www.cpsc.gov/PageFiles/126521/phthalover.pdf

Consumer Product Safety Improvement Act (2008). Available online: http://www.cpsc.gov/PageFiles/129663/cpsia.pdf

Cutanda F, Koch HM, Esteban M, Sanchez J et al. (2015). Urinary levels of eight phthalate metabolites and bisphenol A in mother–child pairs from two Spanish locations. Int J Hyg Envir Heal. 218:47-57.

Danish Environmental Protection Agency (EPA) (2013). Phthalate Strategy. Available online: http://www2.mst.dk/Udgiv/publications/2013/06/978-87-93026-22-3.pdf

Department of Toxic Substances Control (DTSC). Candidate Chemical Database. Available online: https://calsafer.dtsc.ca.gov/chemical/chemicalsearch.aspx

Dix D, Houck KA, Martin MT, Richard AM et al. (2007). The ToxCast Program for prioritizing toxicity testing of environmental chemicals. Tox Sci 95:5-12.

Dodson RE, Camann DE, Morello-Frosch R, Brody J et al. (2015). Semivolatile organic compounds in homes: Strategies for efficient and systematic exposure measurement based on empirical and theoretical factors. Environ Sci Technol 49: 113-22.

Dodson RE, Nishioka M, Standley L, Perovich LJ et al. (2012). Endocrine disruptors and asthma-associated chemicals in consumer products. Environ Health Perspect 120:935–43.

European Union (EU) (2005). Directive 2005/84/EC of the European Parliament and of the Council of 14 December 2005 amending for the 22nd time Council Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations (phthalates in toys and childcare articles). Available online: http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32005L0084

European Chemicals Agency (ECHA) (2011). Committee for Risk Assessment RAC Annex 1 Background document to the Opinion proposing harmonised classification and labelling at Community level of Di-*n*-hexyl phthalate (DnHP). Available online: http://echa.europa.eu/documents/10162/0fc1bf32-1cd4-4294-a7fc-7ba778f78f13

Federal Institute for Risk Assessment (Bundesinstitut fur Risikobewertung [BfR]) (2011). DPHP detected in toys: BfR assessing the risk of the softener. BfR Opinion No. 004/2012 of 28 June 2011. English Summary, full article in German. Available online: http://www.bfr.bund.de/cm/349/dphp-detected-in-toys-bfr-assessing-the-risk-of-the-softener.pdf

Fisher M, Arbuckle TE, Mallick R, LeBlanc R et al. (2015). Bisphenol A and phthalate metabolite urinary concentrations: Daily and across pregnancy variability. J Expo Sci Environ Epidemiol 25:231-9.

Frederikson H, Kuiri-Hanninen T, Main KM, Dunkel L et al. (2014). A longitudinal study of urinary phthalate excretion in 58 full-term and 67 preterm infants from birth through 14 months. Environ Health Perspect 122:998–1005.

Fromme H, Gruber L, Schlummer M, Wolz G 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 33:1012-20.

Fromme H, Lahrz T, Piloty M, Gebhart H et al. (2004). Occurrence of phthalates and musk fragrances in indoor air and dust from apartments and kindergartens in Berlin (Germany). Indoor Air 14:188-95.

Foster PMD (2005). Mode of action: Impaired fetal leydig cell function - Effects on male reproductive development produced by certain phthalate esters. Crit Rev Toxicol 35:713–9.

Foster PMD (2006). Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. Int J Androl 29:140-7.

Furr J, Lambright C, Wilson VS, Foster PM, Gray Jr. LE (2014). A short-term *in vivo* screen using fetal testosterone production, a key event in the phthalate adverse outcome pathway, to predict disruption of sexual differentiation. Tox Sci 140:403-24.

Gallart-Ayala H, Nunez O, Lucci P (2013). Recent advances in LC-MS analysis of food packaging contaminants. Trend Anal Chem 42:99-124.

Gaspar FW, Castorina R, Maddalena RL, Nishioka MG et al. (2015). Phthalate exposure and risk assessment in California child care facilities. Environ Sci Technol 48:7593-601.

Gao X, Yang B, Tang Z, Luo X et al. (2014). Determination of phthalates released from paper packaging materials by solid-phase extraction-high-performance liquid chromatography. J Chromatogr Sci 52:383-9.

Göen T, Dobler L, Koschorreck J, Müller J et al. (2011). Trends of the internal phthalate exposure of young adults in Germany—Follow-up of a retrospective human biomonitoring study. Int J Hyg Envir Heal 215:36-45.

Goodman M, LaKind J, Mattison DR (2014). Do phthalates act as obesogens in humans? A systematic review of the epidemiological literature. Crit Rev Toxicol 44:151-75.

Granholm T, Creasy DM, Pollanin P, Soder O (1992). Di-*n*-pentyl phthalate-induced inflammatory changes in the rat testis are accompanied by local production of a novel lymphocyte activating factor. J Reprod Immunol 21:1-14.

Gray Jr. LE, Ostby J, Furr J, Price M et al. (2000). Perinatal exposure to the phthalates DEHP, BBP, and DINP, but not DEP, DMP, or DOTP, alters sexual differentiation of the male rat. Toxicol Sci 58:350-65.

Gries W, Ellrich D, Küpper K, Ladermann B et al. (2012). Analytical method for the sensitive determination of major di-(2-propylheptyl)-phthalate metabolites in human urine. J Chromatogr B Analyt Technol Biomed Life Sci 908:128-36.

Guo Y and Kannan K (2013). A survey of phthalates and parabens in personal care products from the United States and implications for human exposure. Environ Sci Technol 47:14442-9.

Guo Y and Kannan K (2012). Challenges encountered in the analysis of phthalate esters in foodstuffs and other biological matrices. Anal Bioanal Chem 404:2539-54.

Guo Y and Kannan K (2011). Comparative assessment of human exposure to phthalate esters from house dust in China and the United States. Environ Sci Technol 45:3788-94.

Guo Y, Alomirah H, Cho H-S, Minh TB et al. (2011). Occurrence of phthalate metabolites in human urine from several Asian countries. Environ Sci Technol 45:3138-44.

Hannas BR, Furr J, Lambright CS, Wilson VS et al. (2011a). Dipentyl phthalate dosing during sexual differentiation disrupts fetal testis function and postnatal development of the male Sprague-Dawley rat with greater relative potency than other phthalates. Toxicol Sci 120:184-93.

Hannas BR, Lambright CS, Furr J, Howdeshell KL et al. (2011b). Dose-response assessment of fetal testosterone production and gene expression levels in rat testes following in utero exposure to diethylhexyl phthalate, diisobutyl phthalate, diisoheptyl phthalate, and diisononyl phthalate. Toxicol Sci 123:206-16.

Hannas BR, Lambright CS, Furr J, Evans N et al. (2011c). Genomic biomarkers of phthalate-induced male reproductive developmental toxicity: A targeted RT-PCR array approach for defining relative potency. Toxicol Sci 125:544-57.

Hannon PR and Flaws JA (2015). The effects of phthalates on the ovary. Front Endocrinol 6:8 doi: 10.3389/fendo.2015.00008.

Hao C, Cheng X, Xia H, Ma X (2012). The endocrine disruptor mono-(2-ethylhexyl) phthalate promotes adipocyte differentiation and induces obesity in mice. Biosci Rep 32:619-29.

Hartmann C, Uhl M, Weiss S, Koch HM et al. (2015). Human biomonitoring of phthalate exposure in Austrian children andadults and cumulative risk assessment. Int J Hyg Envir Heal. 218:489-99.

Hurst CH and Waxman DJ (2003). Activation of PPARalpha and PPARgamma by environmental phthalate monoesters. Toxicol Sci 74:297-308.

Just AC, Miller RL, Perzanowski MS, Rundle AG et al. (2015). Vinyl flooring in the home is associated with children's airborne butylbenzyl phthalate and urinary metabolite concentrations. J Expo Sci Environ Epidemiol doi: 10.1038/jes.2015.4

Just AC, Adibi JJ, Rundle AG, Calafat AM et al. (2010). Urinary and air phthalate concentrations and self-reported use of personal care products among minority pregnant women in New York City. J Expo Sci Environ Epidemiol 20:625–33.

Kambia N, Farce A, Belarbi K, Gressier B et al. (2015). Docking study: PPAR interaction with the selected alternative plasticizers to di(2-ethylhexyl) phthalate. J Enzym Inhib Med Chem Early Online 1-8.

Kappenstein O, Vieth B, Luch A, Pfaff K (2012). Toxicologically relevant phthalates in food. A. Luch (ed.), Molecular, Clinical and Environmental Toxicology, Experientia Supplementum 101:87-106. doi 10.1007/978-3-7643-8340-4_4, ©Springer Basel AG 2012.

Kasper-Sonnenberg M, Koch HM, Wittsiepe J, Bruning T et al. (2014). Phthalate metabolites and bisphenol A in urines from German school-aged children: Results of the Duisburg birth cohort and Bochum cohort studies. Int J Hyg Envir Health 217:830-8

Kasper-Sonnenberg M, Koch HM, Wittsiepe J, Wilhelm M (2011). Levels of phthalate metabolites in urine among mother–child-pairs – results from the Duisburg birth cohort study, Germany. Int J Hyg Envir Health 215:373-82.

Kavlock R, Chandler K, Houck K, Hunter S et al. (2012). Update on EPA’s ToxCast program: Providing high throughput decision support tools for chemical risk management. Chem Res Toxicol 25:1287−302.

Kelley KE, Hernandez-Diaz S, Chaplin EL, Hauser R et al. (2013). Identifcation of phthalate in medications and dietary supplement formulations in the United States and Canada. Environ Health Perspect 120:379-84.

Kim SH and Park MJ (2014). Phthalate exposure and childhood obesity. Ann Pediatr Endocrinol Metab 19:69-75.

Kim YJ and Ryu JC (2006). Evaluation of estrogenic effects of phthalate analogues using *in vitro* and *in vivo* screening assays. Mol Cell Toxicol 2:106-13.

Koch HM, Lorber M, Christensen KLY, Pälmke C et al. (2013). Identifying sources of phthalate exposure with human biomonitoring: Results of a 48h fasting study with urine collection and personal activity patterns. Int J Hyg Envir Health 216:672-81.

Koch HM and Calafat AM (2009). Human body burdens of chemicals used in plastics manufacture. Philos Trans R Soc Lond B Biol Sci 364:2063-78.

Koo HJ and Lee BM (2004). Estimated exposure to phthalates in cosmetics and risk assessment. J Toxicol Env Health A 67:1901-14.

Kozlowski RR and Storzum U (2005). Di(2-propylheptyl) phthalate: A new plasticizer choice for PVC compounders. J Vinyl Addit Technol 11:155-9.

Kubwabo C, Rasmussen PE, Fan X, Kosarac I et al. (2013). Analysis of selected phthalates in Canadian indoor dust collected using household vacuum and standardized sampling techniques. Indoor Air 23:506-14.

LaRocca J, Binder AM, McElrath TF, Michels KB (2015). First-trimester urine concentrations of phthalate metabolites and phenols and placenta miRNA expression in a cohort of US women. Environ Health Perspect doi:10.1289/ehp.1408409.

Larsen ST and Nielsen GD (2008). Structure-activity relationship of immunostimulatory effects of phthalates. BMC Immunology 9:61.

Leng G, Koch HM, Gries W, Schütze A et al. (2014). Urinary metabolite excretion after oral dosage of bis(2-propylheptyl) phthalate (DPHP) to five male volunteers--characterization of suitable biomarkers for human biomonitoring. Toxicol Lett 231:282-8.

Lioy PJ, Hauser R, Gennings C, Koch HM et al. (2015). Assessment of phthalates/phthalate alternatives in children's toys and childcare articles: Review of the report including conclusions and recommendation of the Chronic Hazard Advisory Panel of the Consumer Product Safety Commission. J Expo Sci Environ Epidemiol 25:343-53.

Llompart M, Celeiro M, Lamas JP, Sanchez-Prado L et al. (2013). Analysis of plasticizers and synthetic musks in cosmetic and personal care products by matrix solid-phase dispersion gas chromatography-mass spectrometry. J Chromatogr A 1293:10-9.

McKee RH, Pavkov KL, Trimmer GW, Keller LH et al. (2006). An assessment of the potential developmental and reproductive toxicity of di-isoheptyl phthalate in rodents. Reprod Toxicol 21:241-52.

Miovodnik A, Edwards A, Bellinger DC, Hauser R (2014). Developmental neurotoxicity of *ortho*-phthalate diesters: Review of human and experimental evidence. Neurotoxicology 41:112-22.

Mylchreest E, Cattley RC, Foster PM (1998). Male reproductive tract malformations in rats following gestational and lactational exposure to di(*n*-butyl) phthalate: an antiandrogenic mechanism? Toxicol Sci 43:47-60.

Mylchreest E, Wallace DG, Cattley RC, Foster PMD (2000). Dose-dependent alterations in androgen-regulated male reproductive development in rats exposed to di(*n*-butyl) phthalate during late gestation. Toxicol Sci 55:143-51.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013). Phthalate Hazard Assessment Reports. Australian Government, Department of Health and Ageing. Available online: http://www.nicnas.gov.au/chemical-information/other-assessment-reports/phthalates-hazard-assessment-reports

NICNAS (2008). Existing Chemical Hazard Assessment Report. Phthalates Hazard Compendium. A summary of physicochemical and human health hazard data for 24 *ortho*-phthalate chemicals. Available online: http://www.nicnas.gov.au/__data/assets/pdf_file/0008/4958/Phthalate-Hazard-Compendium.pdf

National Research Council (2008). Phthalates and Cumulative Risk Assessment: The Task Ahead. Washington, DC:National Academies Press. Available online: http://www.nap.edu/openbook.php?record_id=12528

National Toxicology Program-Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR, 2003). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-*n*-Hexyl Phthalate (DnHP). National Toxicology Program, US Department of Health and Human Services, Research Triangle Park, NC. Available online: http://ntp.niehs.nih.gov/ntp/ohat/phthalates/dnhp/dnhp_monograph_final.pdf

National Toxicology Program (NTP) (1983). Carcinogenesis bioassay of diallyl phthalate (CASRN 131-17-9) in B6C3F$_1$ mice (gavage study). Available online: http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr242.pdf

NTP (1985). NTP Technical Report on the toxicology and carcinogenesis studies of diallylphthalate (CAS No. 131-17-9) in F344/N rats (gavage studies). Available online: http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr284.pdf

North ML, Takaro TK, Diamond ML, Ellis AK (2014). Effects of phthalates on the development and expression of allergic disease and asthma. Ann Allergy Asthma Immunol 112:496-502.

Office of Environmental Health Hazard Assessment (OEHHA) (2015). Proposition 65 List of Chemicals. June 19, 2015 version. Available online: http://oehha.ca.gov/prop65/prop65_list/files/P65single061915.pdf

OEHHA (2013). Evidence on the Carcinogenicity of Diisononyl Phthalate (DINP). Available online: http://oehha.ca.gov/prop65/hazard_ident/pdf_zip/DINP_HID100413.pdf

OEHHA (2008). Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for Di-*n*-Hexyl Phthalate (DnHP). Available online: http://oehha.ca.gov/prop65/law/pdf_zip/DHPMADL051608.pdf

OEHHA (2001). No Significant Risk Level (NSRL) for the Proposition 65 Carcinogen Di(2-ethylhexyl) phthalate. Available online: http://www.oehha.ca.gov/prop65/law/pdf_zip/dehpnsrl.pdf

Pereira-Fernandes A, Demaegdt H, Vandermeiren K, Hectors TLM et al. (2013). Evaluation of a screening system for obesogenic compounds: Screening of endocrine disrupting compounds and evaluation of PPAR dependency of the effect. PLOS one 8(10):e77481.

Philippat C, Bennett D, Calafat AM, Hertz-Picciotto I (2015a). Exposure to select phthalates and phenols through use of personal care products among Californian adults and their children. Environ Res 140:369-76.

Philippat C, Bennett D, Krakowiak P, Rose M et al. (2015b). Phthalate concentrations in house dust in relation to autism spectrum disorder and developmental delay in the CHildhood Autism Risks from Genetics and the Environment (CHARGE) study. Environ Health 14:56.

Ritter EJ, Scott JR, Randall JL, Ritter JM (1985). Teratogenicity of dimethoxyethyl phthalate and its metabolites methoxyethanol and methoxyacetic acid in the rat. Teratology 32:25-31.

Rudel RA, Dodson RE, Perovich LJ, Morello-Frosch R et al. (2010). Semivolatile endocrine-disrupting compounds in paired indoor and outdoor air in two Northern California communities. Environ Sci Technol 44:6583-90.

Rudel RA, Camann DE, Spengler JD, Korn LR et al. (2003). Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. Environ Sci Technol 37:4543-53.

Saillenfait AM, Roudot AC, Gallissot F, Sabaté JP (2011a). Prenatal developmental toxicity studies on di-*n*-heptyl and di-*n*-octyl phthalates in Sprague–Dawley rats. Reprod Toxicol 32:268-76.

Saillenfait, AM, Roudot, AC, Gallissot F, Sabaté, JP et al. (2011b). Developmental toxic potential of di-*n*-propyl phthalate administered orally to rats. J Appl Toxicol 31:36-44.

Saillenfait AM, Gallissot F, Sabaté JP (2009a). Differential developmental toxicities of di-*n*-hexyl phthalate and dicyclohexyl phthalate administered orally to rats. J Appl Toxicol 29:510-21.

Saillenfait AM, Sabaté JP, Gallissot F (2009b). Effects of *in utero* exposure to di-*n*-hexyl phthalate on the reproductive development of the male rat. Reprod Toxicol 28:468-76.

Saillenfait AM, Gallissot F, Sabaté JP (2008). Evaluation of the developmental toxicity of diallyl phthalate administered orally to rats. Food Chem Toxicol 46:2150-6.

Schecter A, Lorber M, Guo Y, Wu Q et al. (2013). Phthalate concentrations and dietary exposure from food purchased in New York State. Environ Health Perspect 121:473-94.

Schütze A, Gries W., Kolossa-Gehring M, Apel P et al. (2015). Bis-(2-propylheptyl) phthalate (DPHP) metabolites emerging in 24h urine samples from the German Environmental Specimen Bank (1999–2012). Int J Hyg Environ Health pii: S1438-4639(15)00079-6.

Serrano SE, Braun J, Trasande L, Dills R et al. (2014). Phthalates and diet: a review of the food monitoring and epidemiology data. Environ Health 13:43.

Serrano SE, Karr CJ, Seixas NS, Nguyen RHN et al. (2014b). Dietary phthalate exposure in pregnant women and the impact of consumer practices. Int J Environ Res Public Health 11:6193-215.

Shin HM, McKone TE, Nishioka MG, Fallin MD et al. (2014). Determining source strength of semivolatile organic compounds using measured concentrations in indoor dust. Indoor Air 24:260-71.

Silva MJ, Furr J, Samandar E, Preau JL et al. (2011). Urinary and serum metabolites of di-*n*-pentyl phthalate in rats. Chemosphere 82:431-6.

Stringer R, Labunska I, Santille D, Johnston P et al. (2000). Concentrations of phthalate esters and identification of other additives in PVC children's toys. Environ Sci Pollut Res Int 7:27-36.

State of Washington Department of Ecology. Children's Safe Products Act. The Reporting List of Chemicals of High Concern to Children (CHCC). Available online: http://www.ecy.wa.gov/programs/swfa/cspa/chcc.html

Suzuki Y, Yoshinaga J, Mizumoto Y, Serizawa S et al. (2012). Foetal exposure to phthalate esters and anogenital distance in male newborns. Int J Androl 35:236-44.

Swan SH, Sathyanarayana S, Barrett ES, Janssen S et al. (2015). First trimester phthalate exposure and anogential distance in newborns. Human Reprod 30:963-72.

Swan SH (2008). Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. Environ Res 108:177-84.

Swan SH, Main KM, Liu F, Stewart SL et al. (2005). Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Perspect 113:1056-61.

Tran TM and Kannan K (2015). Occurrence of phthalate diesters in particulate and vapor phases in indoor air and implications for human exposure in Albany, New York, USA. Arch Environ Contam Toxicol 68:489-99.

Trasande L, Sathyanarayana S, Messito MJ, Gross RS et al. (2013). Phthalates and the diets of US children and adolescents. Environ Res 126:84-90.

Tullo AH (2015). Plasticizer makers want a piece of the phthalates pie. Chemical and Engineering News 93:16-8. Available online: http://cen.acs.org/articles/93/i25/Plasticizer-Makers-Want-Piece-Phthalates.html

US Department of Health and Human Services (DHHS). Household Product Database. Available online: http://householdproducts.nlm.nih.gov/cgi-bin/household/list?tbl=TblChemicals&alpha=D

US Environmental Protection Agency (EPA) (2015). Interactive Chemical Safety for Sustainability Dashboard. Available online: http://actor.epa.gov/dashboard/

US EPA (2014). TSCA Work Plan for Chemical Assessments: 2014 Update. Available online: http://www.epa.gov/oppt/existingchemicals/pubs/TSCA_Work_Plan_Chemicals_2014_Update-final.pdf

US EPA (2012a). Non-Confidential 2012 Chemical Data Reporting (CDR). Toxic Substances Control Act (TSCA) Inventory. Available online: http://www.epa.gov/oppt/cdr/index.html

US EPA (2012b). Phthalates Action Plan. Available online: http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/phthalates_actionplan_revised_2012-03-14.pdf

US EPA (2010). Screening-level hazard characterization. Phthalate esters category. Available online: http://www.epa.gov/hpvis/hazchar/Category_%20Phthalate%20Esters_March%202010.pdf

US EPA (2006). Non-Confidential 2006 Inventory Update Reporting Company/Chemical Records. Toxic Substances Control Act (TSCA) Inventory.

US FDA (2014a). Title 21. Food and Drugs. Chapter I. Food and Drug Administration, Department of Health and Human Services, SubChapter B –Food for Human Consumption. Subpart C--Substances for use as components of coatings. Part 175 Indirect food additives: Adhesives and components of coatings. Available online: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=175

US FDA (2014b). Title 21. Food and Drugs. Chapter I. Food and Drug Administration, Department of Health and Human Services, SubChapter B –Food for Human Consumption Subpart B--Substances for use only as components of paper and paperboard. Part 176 Indirect food additives: Paper and paperboard components. Available online: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=176

US FDA (2014c). Title 21. Food and Drugs. Chapter I. Food and Drug Administration, Department of Health and Human Services, SubChapter B –Food for Human Consumption Subpart B--Substances for use as basic components of single and repeated use food contact surfaces. Part 177 Indirect food additives: Polymers. Available online: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=177

US FDA (2014d). Fragrances in cosmetics. Available online http://www.fda.gov/Cosmetics/ProductsIngredients/Ingredients/ucm388821.htm

US FDA (2014e). Phthalates. Available online: http://www.fda.gov/Cosmetics/ProductsIngredients/Ingredients/ucm128250.htm

Wittassek M, Wiesmüller GA, Koch HM, Eckard R et al. (2007). Internal phthalate exposure over the last two decades – A retrospective human biomonitoring study. Int J Hyg Environ Health 210:319-33.

Wittassek M and Angerer J (2008). Phthalates: metabolism and exposure. Int J Androl 31:131-8.

Yen TH, Lin-Tan DT, Lin JL (2011). Food safety involving ingestion of foods and beverages prepared with phthalate-plasticizer containing clouding agents. J Formos Med Assoc 110:671-84.

Zimmermann S, Gruber L, Schlummer M, Smolic S et al. (2012). Determination of phthalic acid diesters in human milk at low ppb levels. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 29:1780-90.

Zota AR, Calafat AM, Woodruff TJ (2014). Temporal trends in phthalate exposures: findings from the National Health and Nutrition Examination Survey, 2001–2010. Environ Health Perspect 122:235-41.