Food Packaging Containing Ortho-phthalates Decision Document

February 2021 (revised May 2021)

SAFER CONSUMER PRODUCTS PROGRAM

DEPARTMENT OF TOXIC SUBSTANCES CONTROL

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INTRODUCTION

In 2016 DTSC received a petition to designate food can linings containing bisphenol A (BPA) as a Priority Product under the SCP regulations.[1] The petition was denied, but it prompted DTSC to add food packaging to its 2018-2020 Priority Product Work Plan.[2] In implementing the 2018-2020 Work Plan DTSC has worked to evaluate a number of different food packaging products that may contain one or more Candidate Chemicals. One of those product categories included plastic food packaging and food packaging components containing ortho-phthalates (OPs).

DTSC conducted an extensive review of reliable information regarding OPs in food packaging in order to assess potential human exposures to OPs and their potential adverse impacts. DTSC also engaged stakeholders during the evaluation process. DTSC hosted a workshop on November 19, 2019, and a 30-day public comment period from November 19, 2019 until December 19, 2019. DTSC invited stakeholders to provide information to help answer specific questions and fill data gaps regarding OPs in the food packaging market. Based on the reliable information reviewed during the evaluation process, and the information received through stakeholder engagement, DTSC has determined that the available reliable information does not support identifying any food packaging containing OPs as a Priority Product at this time. This decision was made based on consideration of the following factors:

- NHANES biomonitoring data suggests that Human exposures to OPs in the U.S. have declined significantly since 2006.
- Several alternatives to the use of OPs are available and already in use.
- Manufacturers claim to have switched from the use of OPs to a variety of safer alternatives for many food packaging applications, and the limited test data that is available seems to support this.
- There is very little reliable information available that identifies food packaging that currently contains OPs. The only recent information DTSC could find showing the presence of OPs in food packaging is a single study that showed OPs in cap gaskets for some kinds of food and beverages. That study was limited in scope and cannot be used to estimate the prevalence of those cap gaskets in the market.
- DTSC's stakeholder engagement efforts failed to reveal any additional information that would support listing food packaging containing OPs as a Priority Product.
- Hazard data and toxicity endpoint information is limited or lacking for many OPs.

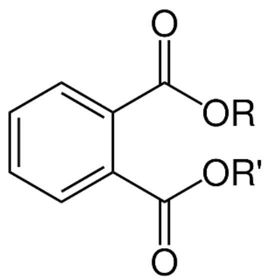
This document presents all the reliable information that DTSC relied on in making this decision. DTSC is providing this information to support transparency in its decision-making process, and to highlight the considerable effort that went into evaluating food packaging containing OPs. DTSC reserves the right to reevaluate OPs in food packaging at any time if additional information becomes available.

[1] Link to the petition for BPA in food can linings.
[2] Link to the 2018-2020 Priority Product Work Plan

In May of 2021 the American Chemistry Council (ACC) requested that this document be revised. DTSC made some, but not all, of the requested revisions. Sections 3.0, 4.0, and 5.4 of this document were revised in response to the ACC request.

1.0 WHAT ARE OPs AND WHAT ARE THEY USED FOR?

OPs are ortho isomers of phthalic acid esters having the general formula $C_8H_6O_4$:



OPs differ from one another only in the respective R-groups linked to phthalic acid by ester bonds.

There are 40 OPs on DTSC's informational Candidate Chemical (CC) List.[3] It is important to note that there are more than 40 known OPs, and all OPs are captured as a group on DTSC's official CC list, even if they are not specifically named on the informational list.

OPs are used primarily as "plasticizers" that are added to plastics such as polyvinyl chloride (PVC) to impart flexibility, pliability, and elasticity (Chou and Wright 2006). OPs are not covalently bound to the polymer matrix of the plastic, which makes them highly susceptible to leaching (Halden 2010). PVC plastics may contain as much as 50% by weight of plasticizers (Freire, Santana, and Reyes 2006; Kawakami, Isama, and Matsuoka 2011). According to the World Health Organization (WHO), OPs have been widely used as plastic additives in various industrial and consumer products, and exposure to OPs is inevitable (WHO 2012). In 2015 the production of plastics reached 380 million metric tons worldwide, and approximately 40% was used for various forms of packaging (PlasticsEurope, 2016; (Geyer, Jambeck, and Law 2017). OPs have historically comprised ~70% of the U.S. plasticizer market, although their use as plasticizers for some products has apparently decreased in recent years (Halden 2010).

OPs have been the most common plasticizer for products made of PVC, although the use of alternative plasticizers has been increasing. PVC is among the five polymers most commonly used in plastic packaging, along with polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), and polystyrene (PS) (Plastics Europe 2016) (Groh et al. 2019). OPs have been used in many products such as food wrap, plastic bottles, and bottle cap liners (Halden 2010). According to a statement by the American Plastics Council, food wraps and food containers manufactured in the United States no longer contained OPs as of 2006, and instead make use of alternative plasticizers such as di-(2-ethylhexyl) adipate (DEHA) (Enneking 2006).

[3] Link to DTSC's Informational Candidate Chemicals List

However, DTSC is unaware of any test data supporting this claim and many OPs are still approved for use by the U.S. Food and Drug Administration (FDA). In addition, a recent study reported finding OPs in bottle cap liners and other food contact materials sold in the U.S. (Carlos, de Jager, and Begley 2018).

The OP family includes higher molecular weight OPs having more than 7 carbon chain lengths such as di-isononyl phthalate, medium molecular weight OPs have between 3 and 6 carbon chain lengths such as di(2-ethylhexyl) phthalate, dibutyl phthalate, and butyl benzyl phthalate, and lower molecular weight OPs such as dimethyl phthalate and diethyl phthalate (Rudel et al. 2011; Babich 2010). All may be used in food packaging, but some are used more than others. The higher molecular weight OPs tend to be used primarily in food packaging, while medium and lower molecular weight OPs are mostly used in other products such as personal care products. Diethyl phthalate is commonly used as a solvent for fragrances.

2.0 HUMAN EXPOSURE TO OPS

Important routes of human exposure to OPs include:[4]

- Medical exposures caused by direct release of OPs into the human body (e.g., through dialysis and blood transfusions).
- Ingestion of contaminated materials, including contaminated food, house dust, or food that has been in contact with food packaging containing OPs.
- Dermal uptake of OPs from personal care products.
- Inhalation exposure from outdoor and indoor air containing OP off-gassing from paints, wall coverings, ceilings, and floors.

Widespread human exposure to OPs has previously been documented in the U.S. and in European countries, with some examples of unusually high exposures in certain populations (Rodgers, Rudel, and Just 2017). Diet is considered a primary route of exposure to OPs. In one study urinary phthalate excretion was monitored in individuals fasting for 48 hours (Koch et al. 2013). That study found that diet was the most significant pathway for exposures to several OPs including di(2-ethylhexyl) phthalate, while exposure to other OPs was primarily linked to non-food sources. Foods high in fat tend to be contaminated by higher weight OPs that are more lipophilic such as di(2-ethylhexyl) phthalate (Serrano et al. 2014). The primary source of di(2-ethylhexyl) phthalate and dibutyl phthalate exposure has also historically been diet, rather than cosmetics or personal care products (Hermann Fromme et al. 2007). A dietary intervention study confirmed the role that foods have played as a major source of phthalate exposure (Ji et al. 2010). In that study a group of 25 individuals participated in a five-day stay at a Buddhist temple in Korea and ate the vegetarian diet that was normally served to the resident monks.

[4] As reviewed in (Halden 2010), (Kamrin 2009), (Latini 2005), (Meeker John D., Sathyanarayana Sheela, and Swan Shanna H. 2009), (Sathyanarayana 2008b), (Sathyanarayana et al. 2008), and (Tickner et al. 2001).

Metabolites of four OPs were found in all participants before their stay. All metabolite levels dropped dramatically by the end of the stay. However, they did not disappear completely, indicating that not all sources of exposure (e.g., from personal care products) were eliminated by changing the diet. Diet is expected to be a very minor source of exposure to lower molecular weight OPs like dimethyl phthalate and diethyl phthalate (Rudel et al. 2011).

OPs can migrate into food from plasticized PVC materials such as tubing typically used in the milking process, lid gaskets, food-packaging, gloves used in the preparation of foods, and conveyor belts (Cao 2010). Some phthalate compounds are also found in printing inks and adhesives on food wrappers, as well as coatings on cookware that have been contaminated by packaging (Suciu et al. 2013) (Cao 2010). In a German study, the main source of phthalate exposure for individuals was house dust as opposed to diet, with the two highest OPs in dust being di(2-ethylhexyl) phthalate and di-isononyl phthalate (H. Fromme et al. 2004).

Exposure of the developing fetus to OPs may occur in utero from OPs crossing the placental barrier and from blood and amniotic fluid (Halden 2010; Sathyanarayana 2008b; Sathyanarayana et al. 2008; Meeker John D., Sathyanarayana Sheela, and Swan Shanna H. 2009). Infants can experience both prenatal (i.e., placental transfer) and postnatal exposure (e.g., from indoor dust, breastmilk, formula, and PVC-based toys and pacifiers) (K. Chou and Wright 2006).

In an effort to identify foods associated with increased risk of OP exposure, Serrano et al. conducted a review of food monitoring survey and epidemiological data (Serrano et al. 2014). They observed high di(2-ethylhexyl) phthalate concentrations in poultry, cooking oil and some dairy products consistently across food monitoring studies. Diethyl phthalate concentrations were low across all food groups evaluated. They also observed that epidemiological studies showed positive correlations between the consumption of meats, fat and some dairy products and di(2-ethylhexyl) phthalate exposure. Dairy was the largest contributor to di(2-ethylhexyl) phthalate exposure. Serrano et al. did not attempt to identify sources of OP contamination in the foods examined. However, two prior dietary intervention studies did look at food packaging as a potential source of OP contamination in foods.

In the first dietary intervention study a fresh foods “dietary intervention” was performed with volunteers from five families (Rudel et al. 2011). During a 3-day intervention the participants were required to eat only foods that were not canned or packaged in plastic. All participants ate the same foods. Urinary samples were collected before, during and after the intervention, and urinary concentrations of di(2-ethylhexyl) phthalate metabolites and bisphenol A (BPA) were measured. Geometric mean values of the di(2-ethylhexyl) phthalate metabolites fell by 53-56% while urinary BPA concentrations fell by 66% during the intervention. Participant surveys suggested that canned foods, beverages, and restaurant meals were the most likely sources of exposure to di(2-ethylhexyl) phthalate and BPA. The investigators suggested that PVC films that are commonly used in food storage may have been an important source of exposure. However, OPs are no longer used in PVC films (as discussed in section 4.0 of this document), and so it is unclear how well the study reflects the current market presence of OPs in food packaging. The investigators also identified food contamination from processing and the presence of BPA and OPs in the environment where the foods originated as other possible sources contamination.

In the second study Ten families participated in a randomized trial (Sathyanarayana et al. 2013). Half the participants were provided with a catered diet of fresh, organic foods. The other half were given written instructions on how to avoid OPs and BPA in their diet. The purpose of the study was to assess whether providing written instructions was as effective as actual dietary intervention in reducing exposure to OPs and BPA. Urinary samples were again collected before, during, and after the interventions and tested for BPA and di(2-ethylhexyl) phthalate metabolites. Surprisingly, all the individuals given the catered, organic fresh food diet exhibited a statistically significant increase in urinary di(2-ethylhexyl) phthalate metabolite concentrations. Subsequent testing of food ingredients revealed excessively high concentrations of di(2-ethylhexyl) phthalate in the ground coriander and milk provided for study participants. The investigators attributed this to possible contamination during food processing or packaging. Unfortunately, the results precluded any further assessment of dietary intervention in lowering OP exposure. The investigators concluded that the possibility of food contamination during processing or packaging highlights the need for government regulation.

The U.S. EPA evaluated data from the National Health and Nutrition Examination Survey (NHANES) and concluded that, while OP exposure has been widespread among women of child-bearing age and children in the U.S., exposures have decreased significantly since 2006 (OA US EPA 2015). A 67% decline in di-2-ethylhexyl phthalate exposure in the U.S. population between 2006 and 2012 has been reported (Zota, Calafat, and Woodruff 2014). In 2019 Wang et al. conducted an extensive survey of global biomonitoring data. They concluded that since 2001 there is clear evidence of a decline in diethyl phthalate, dibutyl phthalate, and di-2-ethylhexyl phthalate exposure in the U.S., but di-isononyl phthalate concentrations increased during this period (Wang, Zhu, and Kannan 2019). The exposure of children to OPs also decreased since 2006, but urinary levels are still higher in children than for adolescents or adults. A significant decline in OP exposure in Europe is also evident in biomonitoring data from 2011 to 2016 (Wang, Zhu, and Kannan 2019). Overall, exposure levels for OPs in the U.S. population appear to have declined significantly since 2006. This suggests that either manufacturers are phasing out the use of OPs in many consumer products, or that regulatory efforts have resulted in lower exposures from certain products (e.g., in children’s products), or both.

3.0 OP HAZARD TRAITS AND TOXICOLOGICAL ENDPOINTS

Exposure to OPs may be especially problematic for sensitive groups such as pregnant and nursing women, unborn fetuses, infants and children, and women of child-bearing age (Braun, Sathyanarayana, and Hauser 2013; Trasande et al. 2013; Sathyanarayana 2008a). The most widely used OPs have been characterized as endocrine disruptors, and there is growing concern over their potential developmental and reproductive toxicity (Fasano et al. 2012; Grün and Blumberg 2006). Some OPs have been recognized by various authoritative bodies as developmental and reproductive toxicants that may significantly and adversely impact the developing fetus. OPs may act in a dose-additive manner, and there is the potential for people to be exposed via multiple sources (Rodgers, Rudel, and Just 2017).

Some OPs have been evaluated more than others. Unfortunately, there is little to no toxicological data publicly available for many OPs. One evaluation of food additives and food contact materials used in food packaging concluded that almost two-thirds of OPs do not have any publicly available feeding data (Neltner et al. 2013). In addition to a lack of publicly available toxicological data, there is disagreement and controversy over the magnitude of the potential adverse effects of OPs on human health. Several authoritative bodies have conducted risk assessments for those OPs with available data and determined that they do not pose a public health risk (EFSA 2019; FSANZ 2018). However, in many cases they only evaluated a limited number of possible toxicological end-points and did not consider potential cumulative exposure effects. Other scientific panels and agencies have evaluated the safety of OPs and come to different conclusions (Kamrin 2009). Entities representing industry point to regulatory reviews that they claim show that the use of OPs having seven or more carbon backbones in food packaging is safe (American Chemistry Council 2019). The FDA and other regulatory bodies also presume that the use of certain OPs as plasticizers is safe so long as they are used as prescribed in regulation.[5] In contrast, governments have placed statutory restrictions on the use of some OPs in certain products, including children's products and consumer products due to concerns regarding their potential for adverse impacts on human health (Consumer Product Safety Commission 2017) (European Union 2018). The American Academy of Pediatrics recently published a policy statement on food additives and child health, and designated OPs as one of five chemical classes of emerging concern (Trasande et al. 2013; Elizabeth E. Hatch et al. 2008). They noted that there remain significant data gaps regarding the potential health effects of materials that may end up in food, including some OPs.

OP exposure has been associated with adverse developmental outcomes, obesity, metabolic disorders, cancer, increased rates of inattention and mood disorders, and cognitive problems in children. The adverse effects of OPs have been observed in children of both genders. In adults some OPs have been associated with increased weight, insulin resistance, asthma and allergies, uterine fibroids, and breast cancer (Crinnion 2010).

3.1 Endocrine Disruption Overview

Some OPs have endocrine disrupting properties on the developing reproductive system, especially in males (Rodgers, Rudel, and Just 2017). Recent epidemiological studies have demonstrated significant associations between increased maternal urinary concentrations of diethyl phthalate, diisobutyl phthalate, dibutyl phthalate, and di(2-ethylhexyl) phthalate, and shorter anogenital distance in male infants, a marker of feminization (Swan et al. 2005; (Swan 2008). Prenatal exposures are also related to changes in timing of labor, and infant hormone levels and infant and child neurobehavioral outcomes (Serrano et al. 2014).

[5] Link to FDA regulations for indirect food additives including plasticizers

In adult populations, various epidemiological studies suggest an association between OP exposure and decreased semen quality in men (Serrano et al. 2014). There is also evidence linking endometriosis in women with phthalate exposure (Serrano et al. 2014). Increases in waist circumference and body mass index (BMI) have been linked to exposure to several OPs in men, and in adolescent and adult females (Serrano et al. 2014).

In 2012 the World Health Organization (WHO) published a report on endocrine disrupters and child health (WHO 2012). WHO concluded that males are more susceptible to the adverse impacts of OP exposure but did note that there are also concerns related to the potential exposure of females. WHO noted that hypospadias[6] and cryptorchidism[7] in experimental animals can be induced by several endocrine disrupters that are either anti-androgenic or estrogenic (Toppari 2008). Examples of OPs with anti-androgenic activity are dibutyl phthalate and diethyl hexyl phthalate that disturb androgen biosynthesis (Mylchreest et al. 2002)(Fisher et al. 2003).

3.1.1 Effects on Male Reproduction and Development

Among the known and suspected adverse health effects of OPs are reproductive outcomes, including testicular dysgenesis syndrome comprising male genital abnormalities that can cause atypical sperm characteristics, and may later develop into testicular cancer (Skakkebaek, Rajpert-De Meyts, and Main 2001; Halden 2010). It is important to note that the higher molecular weight OPs, such as di(2-ethylhexyl) phthalate, dibutyl phthalate, and butyl benzyl phthalate, have been associated with endocrine disrupting effects on the male reproductive system whereas the lower molecular weight OPs, such as diethyl phthalate and dimethyl phthalate, do not exhibit these effects (Gray et al. 2000).

Laboratory studies in animals have shown that some OPs, including dibutyl phthalate, di(2-ethylhexyl) phthalate, and butylbenzyl phthalate, produce malformations of the male reproductive system, cryptorchidism, and testicular injury, together with permanent feminization evidenced by the retention of nipples/areolae and demasculinization of the growth of the perineum, resulting in a reduced anogenital distance (Foster 2006). A noteworthy human study of 85 mother/infant pairs demonstrated a relationship between increased maternal OP levels and reduced anogenital distance in male offspring, although this work is considered somewhat controversial (Swan et al. 2005)(Halden 2010)(McEwen and Renner 2006)(Swan et al. 2006). It has been observed that di(2-ethylhexyl) phthalate and dibutyl phthalate interfere with testosterone production, and therefore have potential anti-androgenic effects in developing rodents (Scott, Mason, and Sharpe 2009). In humans, OP levels in mothers' urine have been associated with the anogenital index (defined as the anogenital

[6] Hypospadias is a congenital disorder where the urinary opening is not at the usual location on the head of the penis, and instead is on the underside of the penis. It is the second-most common birth abnormality of the male reproductive system, affecting about one of every 250 males at birth.
[7] Cryptorchidism is a condition in which one or both of the testes fail to descend from the abdomen into the scrotum.

distance (AGD) divided by the weight of the boy at examination) of their sons, suggesting potential anti-androgenic effects (Swan et al. 2005). OP levels in breast milk have been positively correlated with increased luteinizing hormone/testosterone ratios, also compatible with an anti-androgenic effect (Main et al. 2006). However, in another study OP levels in mothers' breast milk were not directly associated with a risk of cryptorchidism in the offspring (Main et al. 2006). Different species and strains show varying susceptibility to the testicular effects of in utero OP exposure (Scott, Mason, and Sharpe 2009) (Johnson et al. 2008).

One study revealed a strongly significant association between DNA-damaged sperm and urinary levels of diethyl phthalate and di(2-ethylhexyl) phthalate metabolites in men (Hauser et al. 2007). Interestingly, the levels of monoethyl phthalate, a metabolite of diethyl phthalate, in this group of infertile males were similar to exposure levels found in CDC's National Health and Nutrition Examination Survey (NHANES), while the levels of di(2-ethylhexyl) phthalate metabolites were much higher (CDC 2019)(Crinnion 2010). The sperm DNA damage was significantly correlated to all three metabolites individually, not just cumulatively. These observations suggest that exposure to either diethyl phthalate or di(2-ethylhexyl) phthalate at levels commonly found in the U.S. population may damage sperm (Crinnion 2010).

OPs appear to have the most potential to damage male reproduction when the exposure occurs during fetal development (Crinnion 2010). Exposure to environmental endocrine disruptors during germ cell development appears to be the most opportune time for damage to occur (Crinnion 2010). In an animal study, prenatal exposure to OPs resulted in the male offspring developing testicular dysgenesis syndrome as a result of Leydig cell dysfunction (Hu et al. 2009). In vitro experimentation with human fetal testes revealed that mono-2-ethylhexyl (MEHP), a metabolite of di(2-ethylhexyl) phthalate, caused increased apoptosis of germ cells (Lambrot et al. 2009). Because those researchers only looked at MEHP, it cannot be determined whether other metabolites of diethyl phthalate and di(2-ethylhexyl) phthalate, or the metabolites of other OPs, would have had similar or more powerful effects.

A study of mother-infant pairs showed a clear association between maternal levels of certain urinary OP metabolites and reduced anogenital distances in their offspring (Marsee et al. 2006). The anogenital distance was measured in this study as a sensitive marker for in utero anti-androgen exposure. An association was also found between OP metabolite levels in maternal breast milk and sex hormone levels and ratios in male offspring (Main et al. 2006). Maternal OP exposure has also been positively associated with hypospadias in their offspring, which also reflects anti-androgenic effects during fetal sexual development (Nassar et al. 2010).

3.1.2 Effects on Female Development

Young girls with exposure to OPs appear to have problems with premature sexual development, especially thelarche(Chou et al. 2009).[8] An epidemic of early breast development in Puerto Rico was followed by many studies on putative endocrine disrupters, including OPs

[8] Thelarche is the onset of breast development.

(Colón et al. 2000). OPs were linked to premature thelarche because two thirds of 41 girls with premature thelarche had measurable OP levels in their serum. However, the OP measurements in these studies were criticized for technical inconsistencies and serious concerns were raised about possible sample contamination and other technical problems (Meeker John D., Sathyanarayana Sheela, and Swan Shanna H. 2009; WHO 2012).

3.1.3 Effects on the Thyroid

Studies of the thyroid-disrupting effects of OPs and their monoester metabolites have suggested the potential for adverse effects (WHO 2012). The basic synthesis of thyroid hormones may be compromised by substances interfering with processes in the thyroid gland, such as the uptake of iodine by the sodium iodide symporter, and the function of thyroid peroxidase. Di-isodecyl phthalate, butylbenzyl phthalate, and Di-n-octylphthalate have been shown to interfere with the activity of the sodium iodide symporter (Breous, Wenzel, and Loos 2005). In rats, dibutyl phthalate decreased T3 and T4 hormone levels in a dose-dependent manner (O'Connor, Frame, and Ladics 2002), and several studies have shown histopathological changes in the thyroid after exposure to OPs (Howarth et al. 2001) (Poon et al. 1997). In vitro studies have suggested that dibutyl phthalate and di(2-ethylhexyl) phthalate have antagonistic and thyroid system-disrupting properties in frogs and in vitro (Shen 2005) (Sugiyama et al. 2005). One study examined the associations between urinary levels of OPs in 76 pregnant women and thyroid function, and found a significant negative association between dibutyl phthalate-levels and T4 and free T4 hormone levels (Huang et al. 2007). Likewise, negative associations between di(2-ethylhexyl) phthalate exposure and free T4 and T3 hormone levels have been reported in adult men (Meeker, Calafat, and Hauser 2007), but studies of smaller populations did not find any relationships (WHO 2012) (Janjua et al. 2007) (Rais-Bahrami et al. 2004).

3.1.4 Obesogenicity

Adipose tissue was once considered an inert storage depot. However, the discovery of the hormone leptin in the 1990s led to the recognition that adipose is an active endocrine organ, secreting various hormones and adipokines and expressing many receptors (Kershaw and Flier 2004) (Ahima and Flier 2000) (Newbold, Padilla-Banks, and Jefferson 2009) (E. E. Hatch et al. 2010). Evidence also emerged supporting 'the developmental basis of adult disease,' which suggests that exposures in utero could lead to chronic diseases later in life (Heindel 2003) (Oken and Gillman 2003) (E. E. Hatch et al. 2010). The term 'obesogens' was coined in 2006, and defined as 'molecules that inappropriately regulate lipid metabolism and adipogenesis to promote obesity' (Grün and Blumberg 2006). As noted in a review by Hatch et al., others have recently proposed identifying a subclass of endocrine disrupting compounds that broadly affect metabolic signaling, such as weight homeostasis, and calling these chemicals 'metabolic disruptors'(E. E. Hatch et al. 2010) (Casals-Casas, Feige, and Desvergne 2008).

Some OPs appear to act as metabolic disruptors or obesogens, and it has been suggested that exposures early in development may have significant effects on human health later in life (E. E. Hatch et al. 2010). Some OPs are peroxisome proliferator activated receptor (PPAR) agonists (Hurst and Waxman 2003). PPAR-gamma agonists in particular have been linked to weight gain in animal studies (E. E. Hatch et al. 2010). Sex hormones also influence fat quantity and distribution (Pasquali 2006) (Lovejoy and Sainsbury 2009) . For example, in adulthood androgens are related to lower BMI in men, whereas estrogen levels tend to be inversely correlated with obesity and waist-to-hip ratio in women (Gapstur et al. 2002) (Björntorp 1996). Several OPs are suspected anti-androgens and thyroid disruptors in humans, and thus may have adverse effects on BMI (Swan 2008) (Main et al. 2006) (Pan et al. 2006).

One study evaluated the relationship between OP metabolites and waist circumference and homeostasis in adult males using cross-sectional data from NHANES (Stahlhut et al. 2007). The investigators observed positive associations between waste circumference, homeostasis model assessment, and exposure to several OPs. They did not report results for females. Hatch et al. analyzed associations between OP metabolites measured in urine, BMI, and waist circumference in 1999-2002 NHANES participants aged 6-80 (Elizabeth E. Hatch et al. 2008). They analyzed OP metabolites detectable in at least 80% of the NHANES study population. The metabolites included mono-ethyl (MEP), mono-2-ethylhexyl (MEHP), mono-n-butyl (MBP), and mono-benzyl (MBzP) phthalate. Associations between phthalate metabolite exposures, BMI, and WC differed markedly by gender (Elizabeth E. Hatch et al. 2008) (E. E. Hatch et al. 2010). For MBzP, there was a strong positive relationship with BMI and waste circumference among adult males aged 20–59, but no discernible trends among females. Similarly, for MBP, the patterns in adult males and females were different, with suggestive positive trends among males for both BMI and waste circumference, but inverse trends among females. While MEHP was inversely related to BMI and waste circumference in adolescent and adult females, there were no major trends between MEHP and either BMI or waste circumference among males. A positive relationship between MEP and BMI was apparent for adult males (20–59 and 60–80), and for adolescent and adult females (20–59). In general, there were few associations of note among children aged 6 to 11 for any of the metabolites. It was suggested that the contrast in results between males and females, particularly between the ages of 20 and 59, is biologically plausible because several OPs are anti-androgens, and the observed effects may differ according to levels of endogenous hormones. As noted previously, higher androgen levels are associated with smaller waste circumference in males, whereas higher androgen levels in females are associated with higher BMI, greater risk for metabolic syndrome, and conditions such as polycystic ovarian disease (E. E. Hatch et al. 2010) (Barber et al. 2006) (Sam 2007). Hatch et al. suggested that their results appear consistent with an anti-androgenic action for certain OPs, and not with action on PPAR-gamma or thyroid hormones which might be expected to have similar effects in males and females (E. E. Hatch et al. 2010). However, they noted that other explanations for the associations may be involved, particularly for MEP.

3.2 Other hazard characteristics

3.2.1 Carcinogenicity

Di(2-ethylhexyl) phthalate is listed as "possibly carcinogenic" by the International Agency for Research on Cancer (IARC) and is included on California's Prop 65 list of chemicals known to cause cancer. The observed development of liver tumors in adult rodents following dosing with high concentrations of di(2-ethylhexyl) phthalate initially led the IARC to classify di(2-ethylhexyl) phthalate as a "probable carcinogen". However, in 2000 IARC downgraded the designation to "cannot be classified as to its carcinogenicity in humans" (IARC 2000) (Sathyanarayana 2008). Then in 2013 IARC reversed course again and concluded that there is now enough evidence in animals to say that di(2-ethylhexyl) phthalate is "possibly carcinogenic" to humans.

Urinary OP metabolite levels have been positively associated with increased rates of breast cancer (Crinnion 2010). Women with the highest levels of a particular OP metabolite were 2.2 times more likely to develop breast cancer than those with the lowest levels(Crinnion 2010). For premenopausal women the odds ratio was even higher at 4.13. The levels of OPs that may lead to cancer were similar to the levels found in most U.S. residents. In a 2017 meta-analysis and bioinformatics study certain OP metabolites were associated with an increased risk of breast cancer(Fu et al. 2017). However, the authors noted that additional work is necessary to confirm the link between urinary OP metabolite levels and breast cancer. In what has been referred to as the largest study of its kind, no statistically significant positive associations between phthalates and breast cancer were observed (Reeves et al. 2019). The investigators concluded that phthalate biomarker concentrations did not result in an increased risk of developing invasive breast cancer.

3.2.2 Neurotoxicity

Fetal exposure to maternal OPs has been associated with behavior and mental affects (Crinnion 2010). Urine OP metabolites were tested in pregnant women in New York City during their third trimester, and their offspring were assessed within five days of birth and again between the ages of four and nine years (Colón et al. 2000) (Engel et al. 2009). Within days after birth children whose mothers had higher levels of OPs exhibited more problems with alertness and orientation. Unfortunately, when they were tested again between the ages of four and nine, the neurological problems had persisted and even increased. Children with higher exposure to OPs in utero had more problems with aggression, conduct, attention, and depression. They also exhibited poorer executive functioning and emotion control.

3.2.3 Respiratory and Dermal Toxicity

In a Swedish study, high levels of butylbenzyl phthalate in house dust were associated with higher rates of rhinitis and eczema, while dust-borne di(2-ethylhexyl) phthalate was associated with increased rates of asthma (Engel et al. 2010).

4.0 FOOD PACKAGING PRODUCTS THAT CONTAIN OPS

Food packaging technology appears to evolve very rapidly, and studies identifying chemicals used in food packaging become outdated after a short time. A recent report provides the only contemporary evaluation that DTSC could find regarding the use of OPs in food packaging sold in the U.S. (Carlos, de Jager, and Begley 2018). As noted in that report, there have not been any published reports regarding occurrences of OPs in food packaging in the U.S. for several years. To obtain OP occurrence data for food packaging products sold on the U.S. market, 56 food contact materials were purchased and analyzed (Carlos, de Jager, and Begley 2018). The manufacturers of the food packaging products were not identified in the published study. Both domestic and imported food packaging (from 14 countries), along with some tubing and conveyor belt material for food processing equipment, were included in the study. The products were divided in to five categories:

- tubing and belts for food processing equipment;
- non-alcoholic bottled beverages;
- bottled beer;
- food wraps; and
- jarred food products.

Three OPs were found among the products at concentrations ranging from 6 to 53%.

All five conveyor belt samples tested in the study contained diisononyl phthalate. There were two grades of flexibility for the conveyor belts and this was reflected in the concentrations of the diisononyl phthalate: The two more rigid belts had concentrations around 6%, while the three more flexible belts had concentrations near 30%. There was more variability in plasticizer type observed in the tubing samples. Three of the samples contained di(2-ethylhexyl) phthalate, and another contained diisodecyl phthalate at a concentration of approximately 40%. The final sample did not contain an OP. Food processing equipment was not included in the 2018-2020 Priority Product Work Plan and may not be considered for possible listing as a Priority Product unless it is added to a future Work Plan.

Three domestic and three international non-alcoholic bottled beverage products were tested. The gaskets of the caps for these products were found to contain a broad range of plasticizers. Three contained an OP (di(2-ethylhexyl) phthalate, diisodecyl phthalate, or diisononyl phthalate). The OP concentration was approximately 40% in all three cases. Although 50% of the cap gaskets tested contained an OP, the sample size (6 total) was so small that it is unclear how it reflects the presence of cap gaskets with OPs on the California market.

Nine bottled beer samples were also evaluated. The beers were selected based on U.S. consumption rates in order to get data representing potential exposure for a typical consumer. Again, the brands and manufacturers were not identified. Seven of the beer bottles had gaskets that contained PVC and two had non-PVC gaskets. The two with non-PVC gaskets were imported beers. Six of the PVC gaskets contained di(2-ethylhexyl) phthalate, and one brand did not contain any OP. The concentration of di(2-ethylhexyl) phthalate in the six PVC gaskets was about 45%. Again, although 50% of the cap gaskets tested contained an OP, the sample size (9) was so small that it is unclear how closely it reflects the presence of cap gaskets with OPs in bottled beer sold on the California market. Also, since it is recommended that pregnant women not consume any alcohol during pregnancy, and individuals under 21 years of age cannot legally purchase and consume alcoholic beverages in California, it appears that the presence of OPs in cap gaskets for alcoholic beverages would pose very little exposure risk to children. Finally, market data suggests that while bottles are still the dominant package chosen to bottle most beers, can sales for craft brewers have recently increased much faster than bottle sales (Watson 2017) (Market Watch 2018).

Of four food service wraps investigated, one was determined to be low-density polyethylene and the other three were PVC. Of three commercial wraps tested it was determined that only one was made of PVC. No OPs were found in any of the PVC food wraps. Similarly, in a 2014 Canadian study 118 commercial food wrap samples were tested, and none of the commercial wraps were found to contain OPs.

The largest category investigated in the FDA study was jarred food products, such as sauces, honeys and jarred vegetables. There were 11 domestic and 14 international products analyzed. Only four products had cap gaskets plasticized with OPs: Di(2-ethylhexyl) phthalate in two international products and diisodecyl phthalate in two domestic products, respectively. A large 1995 survey of products available for purchase in Canada covered numerous types of plasticized PVC products including jar lid gaskets collected from products purchased between 1985 and 1989 (Page and Lacroix 1995). In contrast to what was seen in the study by Carlos et al., all but 19 of the 80 gaskets investigated contained di(2-ethylhexyl) phthalate as their primary plasticizer. As Carlos et al. noted, later studies in Canada and elsewhere have shown a decrease in the frequency of products found containing OPs, suggesting that manufacturers are switching from OPs to alternatives.

The results of the study by Carlos et al. show that a wide variety of plasticizers are in use in products available for purchase in the United States. Conveyor belts for food processing equipment were the only category where 100% of the products tested contained an OP plasticizer. In summary:

- 100% of conveyor belts tested contained in OP plasticizer,
- 60% of the food processing tubing tested contained an OP plasticizer,
- 50% of the cap gaskets for non-alcoholic bottled beverages that were tested contained an OP plasticizer,
- 67% of the cap gaskets for bottle beers contained an OP plasticizer,
- 17% of food jar cap gaskets contained an OP plasticizer; two from the U.S., one from Mexico, and one from India,
- 0% of food wraps tested contained an OP plasticizer.

Carlos et al. noted that US occurrence data presented in their study, along with other published market surveys over the years, seem to suggest that manufacturers have been removing OPs from jar gaskets and replacing them with alternatives. Carlos et al. also noted that this trend may be reflected in NHANES data where there was a sharp decline in OP exposures starting in the survey year 2005–2006 that has continued in all years surveyed since 2006. Unfortunately, the sample size in the study by Carlos et al. was so small, it is unclear how well the data reflects the presence of OPs in cap gaskets sold in California.

In an earlier study of Korean and Japanese beverages di(2-ethylhexyl) phthalate and di-methyl phthalate were the two OPs most frequently found and in highest concentrations (Yano et al. 2002). The highest levels of these compounds were found in beer, wine, and "nutritive drink" samples.

5.0 DATA GAPS AND STAKEHOLDER ENGAGEMENT

Many data gaps precluded DTSC from fully evaluating the current market presence of food packaging containing OPs being sold or offered for sale in California. To help fill some of these gaps DTSC held a public workshop on November 19, 2019, and then held a public comment period from November 19, 2019 until December 19, 2019. DTSC asked stakeholders for any relevant information to help DTSC to further evaluate the use of OPs in food packaging sold in California, as well as information regarding the following specific questions:

- What food packaging sold in California currently contains OPs?
- Who are the major purchasers/users of food packaging in California?
- Who manufactures the food packaging sold or offered for sale in California?
- What is the market for various food packaging products containing OPs that are sold in California? i.e., how much is on the market?
- Do bottle or jar cap gaskets used in CA contain OPs and how much is sold in California?
- What percentage of the jar and bottle cap gaskets sold in California contain OPs?
- What are the alternatives to OPs that are used in food packaging?

DTSC received three public comments and hosted a meeting with one industry trade association. The input received is summarized below.

5.1 Comment from BASF[9]

Patrick Harmon with BASF, a manufacturer of OPs, provided some information identifying possible alternatives to the use of OPs in food packaging. Of the 10 alternatives he identified, only two, DEHA and DEHTP, are on DTSC’s Candidate Chemical (CC) list.

[9] Link to three public comments received regarding OPs in food packaging

There are no associated hazard traits listed in the CC list for DEHTP. The CC list identifies DEHTP hazard traits as "Hazard Trait Under Review". It was included on the CC list only because NHANES monitors for it. At this point, there is insufficient hazard data to suggest that the use of DEHTP in food packaging is something that requires further evaluation by DTSC.

The other alternative, DEHA, was listed on the CC list solely because it's a 303d water contaminant. DTSC reviewed the hazard trait and toxicological endpoints for DEHA, and concluded that the human hazard potential of DEHA is very low based on available reliable information (Department of Environmental Health 2018). This is not due to a lack of information but rather to numerous studies that demonstrate the relatively low toxicity associated with DEHA. DTSC concluded that DEHA also does not require further evaluation at this time.

Of all the alternatives to the use of OPs in food packaging that DTSC is aware of, none seem to be of concern with respect to hazards or toxicological endpoints. It appears that the alternatives being used are in fact "safer alternatives" to the use of some OPs.

5.2 Comment from the Flexible Vinyl Alliance (FVA)

Keven Ott stated that FVA conducted extensive outreach and surveyed their members. He stated that "almost all clearances for OPs in food packaging are not currently utilized by industry," though he did not identify those that are still in use. He then discussed the FVA petition to the FDA, that would delist certain OP uses (FDA 2018). He indicated that uses for OPs in food packaging that would still be allowed by the FDA even if they accepted the petition include:

- DINP in liners and beverage enclosures and dry food film wrap,
- DIDP and DEHP in beverage cap liners and seals for metal enclosures, and
- DCHP in adhesives for labels.

Kevin Ott also argues that hazard data for OPs is weak, or that exposure doses from food packaging applications are low.

5.3 Comment from Breast Cancer Prevention Partners

Lisette van Vliet with Breast Cancer Prevention Partners stated that OP exposure has been directly linked to breast cancer, and that OPs are still being used in paper and paperboard packaging, but she did not provide any references supporting this. DTSC contacted Lisette and asked her to provide references regarding the link between OP exposure and cancer, and the presence of OPs in paper and paperboard. Lisette provided one meta-data study that seemed to suggest a link between certain OP metabolites and breast cancer that was cited by DTSC in analyzing the potential hazards of OPs. However, the findings in the paper are not conclusive and the authors admit that much more work needs to be done to confirm a link. Moreover, a recent study concluded that phthalate biomarker concentrations do not result in an increased risk of developing invasive breast cancer (Reeves et al. 2019).

Lisette also provided two references related to the use of OPs in paper and paperboard. One of the references discussed the fact that recycling streams may inadvertently lead to the introduction of toxins into food packaging that is manufactured from recycled materials. It was not helpful for establishing that paper and paperboard food packaging contain OPs. The other paper did test paper and paperboard food packaging, and found OPs associated with some labels and adhesives on paper and paperboard. The actual products tested were not identified. Lisette acknowledged that a lack of data makes it hard to identify which packaging may still carry some OP uses. Lisette recommended that DTSC evaluated food processing equipment, which is out of the scope of the 2018-2020 Priority Product Work Plan. Lisette also acknowledged that the Carlos et al. paper regarding the testing of certain products for the presence of OPs, and cited by DTSC, does suggest that food packaging manufacturers are moving away from OPs.

5.4 Meeting with the ACC High Phthalates Panel

On January 22, 2020 representatives from the American Chemistry Council (ACC) High Phthalates Panel met with DTSC to give a presentation on their perspective of OPs in food packaging. This group represents the high-molecular weight OPs, which are those with a carbon backbone greater than 7. This class includes diisononyl phthalate (DINP) and diisodecyl phthalate (DIDP), which are two of the OPs that are authorized in food contact materials, and would still be allowed for use in food packaging by the FDA if the FVA petition discussed in section 7.1 of this report was accepted. The other two OPs that would still be allowed in food packaging are di(2-ethylhexyl) phthalate (DEHP) and dicyclohexyl phthalate (DCHP), both of which are low-molecular weight OPs and not represented by the High Phthalates Panel. The ACC asserted that it is the low-molecular weight OPs with a carbon backbone of between 3 and 6 carbons that are associated with reproductive effects in animals. The ACC highlighted that the approved uses for DINP and DIDP in food packaging is limited to sealing gaskets on bottlecaps for non-fatty food/low alcohol, food contact materials include conveyer belts and industrial tubing for non-fatty foods, and that the very low dietary exposure poses “no” risk. The ACC panel asserted that OPs are not used in food wraps and films. The panel indicated that in their opinion some of the studies cited by DTSC are flawed or misleading in their representation of the toxicity of DINP and DIDP.

6.0 RECENT LEGISLATIVE AND REGULATORY ACTIONS

6.1 The Food and Drug Administration

The FDA received a petition from the Flexible Vinyl Alliance asking that authorization for certain OP uses be rescinded because those uses have been abandoned(FDA 2018). In November of 2018 the FDA proposed a rule rescinding those uses. A public comment period regarding the rule closed on January 14, 2019. As of March 2019 the FDA has not taken action. It is unknown when or if the FDA may adopt the rule. The rule would remove many, but not all, currently authorized uses of OPs in food packaging and food contact material applications. It is DTSC's understanding that the specific uses of OPs that would still be allowed even if the FDA promulgated its rule include:

- Diisooctyl phthalate use as a plasticizer only for foods with high water content.
- Di(2-ethylhexyl) phthalate (DEHP) use as a plasticizer only for foods with high water content.
- Diethyl phthalate (DEP) use as a plasticizer.
- Ethoxycarbonylmethyl ethyl phthalate (Ethyl phthalyl ethyl glycolate) use as a plasticizer.

Moreover, there are other authorized OP uses not within the scope of the petition, and those applications would also continue to be permitted according to the FDA because the Flexible Vinyl Alliance has not made any claim that those uses have been abandoned. In particular, OPs that will remain authorized for certain uses in food contact materials, in addition to the prior sanctioned uses described above, include:

6.1.1 Di(2-ethylhexyl) phthalate (DEHP)

- Part 175: Use in adhesives intended for use in packaging, transporting, or holding food so long as the adhesive is either separated from the food by a functional barrier or used subject to the any additional limitations.

- Part 176: Permitted to be used in the formulation of defoaming agents.

- Part 177: May be used in the formulation of the semi rigid and rigid acrylic and modified acrylic plastics, or in the formulation of acrylic and modified acrylic components of article. At least 50 weight-percent of the polymer content of the acrylic and modified acrylic materials used as finished articles or as components of articles shall consist of polymer units derived from one or more of the acrylic or methacrylic monomers listed in the regulation.

- Part 177: May be safely used in cellophane for packaging food in accordance with the following prescribed conditions: Cellophane consists of a base sheet made from regenerated cellulose to which have been added certain optional substances of a grade of purity suitable for use in food packaging as constituents of the base sheet or as coatings applied to impart desired technological properties.

- Part 178: May be used in surface lubricants used in the rolling of metallic foil or sheet stock provided that total residual lubricant remaining on the metallic article in the form in which it contacts food does not exceed 0.015 milligram per square inch of metallic food-contact surface.

6.1.2 Di-isodecyl phthalate (DiDP)

- Part 175: Use in adhesives intended for use in packaging, transporting, or holding food so long as the adhesive is either separated from the food by a functional barrier or used subject to the any additional limitations. Also for use as plasticizer inside seam cements for containers intended for use in contact with food only of the types identified in paragraph (d) of this section, table 1, under Categories I, II, and VI:
  - Nonacid (pH above 5.0), aqueous products; may contain salt or sugar or both, and including oil-in-water emulsions of low- or high-fat content.
  - Acidic (pH 5.0 or below), aqueous products; may contain salt or sugar or both, and including oil-in-water emulsions of low- or high-fat content.
  - Beverages:
    - Containing alcohol.
    - Nonalcoholic.

- Part 177: May be used in closures with sealing gaskets for containers intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food. No limitation on amount that may be used for non-fatty foods containing <8% alcohol. Also may be used in rubber articles intended for repeated for producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food, provided that the total concentration does not exceed 30% by weight of the rubber product.

- Part 178: May be used in surface lubricants used in the rolling of metallic foil or sheet stock provided that total residual lubricant remaining on the metallic article in the form in which it contacts food does not exceed 0.015 milligram per square inch of metallic food-contact surface.

6.1.3 Dicyclohexyl phthalate (DCHP)

- Part 175: Use in adhesives intended for use in packaging, transporting, or holding food so long as the adhesive is either separated from the food by a functional barrier or used subject to the any additional limitations.

- Part 176: May be safely used as components of the uncoated or coated food-contact surface of paper and paperboard intended for use in producing, manufacturing, packaging, processing, preparing, treating, packing, transporting, or holding aqueous and fatty foods, subject to the provisions of this section. Not allowed as components of certain types of paper and paperboard in contact with dry food.

- Part 177: May be safely used in cellophane for packaging food in accordance with the following prescribed conditions: Cellophane consists of a base sheet made from regenerated cellulose to which have been added certain optional substances of a grade of purity suitable for use in food packaging as constituents of the base sheet or as coatings applied to impart desired technological properties.

- Part 178: May be safely used as plasticizers in polymeric substances used in the manufacture of articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food. My be used alone or in combination with other OPs, in plastic film or sheet prepared from polyvinyl acetate, polyvinyl chloride, and/or vinyl chloride copolymers complying with §177.1980 (in Vinyl chloride-propylene copolymers) of this chapter. Such plastic film or sheet shall be used in contact with food at temperatures not to exceed room temperature and shall contain no more than 10 % by weight of total OPs, calculated as phthalic acid.

6.1.4 Diisononyl Phthalate

- Part 178: May be safely used as plasticizers in polymeric substances used in the manufacture of articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food. For use only at levels not exceeding 43 % by weight of permitted vinyl chloride homo- and/or copolymers used in contact with food only of the types identified in §176.170(c) of this chapter (components of paper and paperboard in contact with aqueous and fatty foods), table 1, under Categories I, II, IV-B, and VIII, at temperatures not exceeding room temperature. The average thickness of such polymers in the form in which they contact food shall not exceed 0.005 inch.

    - Section 176.170(c) The food-contact surface of the paper and paperboard in the finished form in which it is to contact food, when extracted with the solvent or solvents characterizing the type of food, and under conditions of time and temperature characterizing the conditions of its intended use as determined from table 1 of this paragraph, shall yield net chloroform-soluble extractives (corrected for wax, petrolatum, mineral oil and zinc extractives as zinc oleate) not to exceed 0.5 milligram per square inch of food-contact surface as determined by the methods described in paragraph (d) of this section.

      Table 1 categories:

I. Nonacid, aqueous products; may contain salt or sugar or both (pH above 5.0).

II. Acid, aqueous products; may contain salt or sugar or both, and including oil-in-water emulsions of low- or high-fat content.

III. Dairy products and modifications:

   a. Oil-in-water emulsions, high- or low-fat.

IV. Dry solids with the surface containing no free fat or oil (no end test required).

A recent regulation set forth by the European Food Safety Authority (EFSA) to prevent phthalate contamination in food limits the specific migration limit (SML) for DBP of 300 µg/kg were considered high (Petersen and Jensen 2010). FDA does not have such a threshold.

6.2 U.S. EPA TSCA Prioritization

Under TSCA, the U.S. EPA must conduct a prioritization process to determine if chemicals are a high or low risk for prioritization (U.S. EPA 2019). Prioritization is the first step in evaluating the safety of chemicals under TSCA. The purpose of the prioritization process is to identify chemicals that are a high priority for further risk evaluation. Chemicals identified as low priority during this process would not be subject to additional risk evaluation.

On March 20, 2019 the U.S. EPA issued a list of 40 chemicals to begin the prioritization process (US EPA 2019). The list was divided into 20 candidates for evaluation as potential high priority chemicals, and 20 candidates for evaluation as potential low priority chemicals. The list of high priority candidates includes the following five OPs:

- Butylbenzyl phthalate (BBP)
- Di(2-ethylhexyl) phthalate (DEHP)
- Dibutyl phthalate (DBP)
- Dicyclohexyl phthalate (DCHP)
- Diisobutyl phthalate (DIBP)

These OPs are on DTSC's Candidate Chemical list. Of these five, only di(2-ethylhexyl) phthalate is authorized by the FDA for use as a plasticizer in food packaging. The other four OPs in this list are approved for various other minor uses, such as in adhesives and coatings or as adjuvants, aids and sanitizers.

A public comment on the proposed list of chemicals for prioritization closed on June 19, 2019. At some point after considering the comments received, the U.S. EPA will conduct a screening review and propose priority designations for the chemicals under evaluation, and then open another 90-day public comment period regarding the proposed priority designations, followed by final priority designation. Federal Statute requires the entire prioritization process to be completed in a minimum of 9 months, and a maximum of 12 months. Therefore, the U.S. EPA has until March 2020 to finalize any proposed priority designations. After the priority designations are complete, the U.S. EPA must initiate a risk evaluation for high priority chemicals. It is unclear how much time the U.S. EPA has before it must initiate the risk evaluation process.

7.0 DISCUSSION

7.1 Decreasing Human Exposures to OPs

NHANES biomonitoring data suggests that Human exposures to OPs in the U.S. have declined significantly since 2006. The U.S. EPA evaluated data from the National Health and Nutrition Examination Survey (NHANES) and concluded that exposures have decreased significantly since 2006 (OA US EPA 2015). A 67% decline in di-2-ethylhexyl phthalate exposure in the U.S. population between 2006 and 2012 has been reported (Zota, Calafat, and Woodruff 2014). In 2019 Wang et al. conducted an extensive survey of global biomonitoring data. They concluded that since 2001 there is clear evidence of a decline in diethyl phthalate, dibutyl phthalate, and di-2-ethylhexyl phthalate exposure in the U.S., but di-isononyl phthalate concentrations increased during this period (Wang, Zhu, and Kannan 2019). The exposure of children to OPs also decreased since 2006. A significant decline in OP exposure in Europe is also evident in biomonitoring data from 2011 to 2016 (Wang, Zhu, and Kannan 2019). Overall, exposure levels for OPs in the U.S. population appear to have declined significantly since 2006. This suggests that either manufacturers are phasing out the use of OPs in many consumer products, or that regulatory efforts have resulted in lower exposures from certain products (e.g., in children's products), or both.

7.2 Safer Plasticizer Alternatives to OPs are Available

The purpose of the SCP regulations is to encourage the identification and use of safer alternatives to the toxic chemicals used in some consumer products. While many alternative plasticizers to OPs have not been well studied with regard to their potential for adverse effects on human health, several alternatives are already available that appear to be less toxic than OPs (Lowell Center for Sustainable Production 2011)(Department of Environmental Health 2018). The limited test data that is available seems to suggest that manufacturers are switching to these safer plasticizer alternatives (Carlos, de Jager, and Begley 2018).

7.3 Limited Market and Product Information

In evaluating exposures, the SCP regulations require that DTSC consider a variety of factors including the market presence of the product and statewide sales by volume. It is important to note that DTSC may only consider listing as a Priority Product food packaging that is sold or offered to sale to food packagers in California. DTSC is not authorized to regulate any packaged food products. For example, DTSC may designate plastic bags that are sold to a food packager for the purpose of packaging a product. However, DTSC cannot regulate the package after food is placed into the bag and sold from the food packager to a distributor or retailer. Therefore, DTSC requires specific information identifying food packaging containing OPs that is sold or offered to sale to food packagers located in California, and how much OPs that specific packaging contains. Such information is not readily available. DTSC tried accessing information from a variety of databases and was unable to locate useful information. DTSC also asked stakeholders to provide such information during a workshop and subsequent public comment period held in 2019. DTSC did not receive any related information from stakeholders. In fact, one stakeholder acknowledged that the Carlos et al. paper regarding the testing of certain products for the presence of OPs does suggest that food packaging manufacturers are moving away from the use of OPs.

The only recent information DTSC could find showing the presence of OPs in food packaging is a single, limited study that showed OPs in the cap sealing gaskets for some kinds of food and beverages (Carlos, de Jager, and Begley 2018). That study was limited in scope and did not identify any manufacturers for the packaging products that were tested. DTSC is unable to use the study to estimate the market presence of any food packaging containing OPs that may be sold or offered for sale in California. That study did show that not all food packaging contains OPs and suggested that manufacturers are switching to alternatives.

7.4 Limited Hazard Trait Data

There are 40 OPs on DTSC's informational Candidate Chemical list. There are additional OPs that are captured on the Candidate Chemical list, but not specifically included on the informational list. Very few of these OPs have been evaluated for hazard and toxicity endpoints. The hazard trait of highest concern is potential adverse reproductive and developmental effects on children. However, there seems to be significant differences in this hazard trait for various OPs based on molecular weight. Higher molecular weight OPs appear to be more closely associated with endocrine disrupting effects that may adversely impact the reproductive system during development, while lower molecular weight OPs do not appear to exhibit these same effects (Gray et al. 2000).

Carcinogenicity is another hazard trait of concern. There is also considerable uncertainty associated with the potential carcinogenicity of OPs. As noted in section 4.2.1 of this report di(2-ethylhexyl) phthalate is currently listed as "possibly carcinogenic" by the International Agency for Research on Cancer (IARC). However, IARC previously had classified di(2-ethylhexyl) phthalate as a "probable carcinogen," and then downgraded the designation to "cannot be classified as to its carcinogenicity in humans" in 2000 (IARC 2000) (Sathyanarayana 2008). In 2013 IARC reversed course and concluded that there is enough evidence in animals to say that di(2-ethylhexyl) phthalate is "possibly carcinogenic" to humans. Urinary OP metabolite levels have been positively associated with increased rates of breast cancer (Crinnion 2010). A 2017 meta-analysis and bioinformatics study also suggested that certain OP metabolites were associated with an increased risk of breast cancer, although the authors noted that additional work would be necessary to confirm the link (Fu et al. 2017). However, in a recent study that has been referred to as the largest of its kind, no statistically significant positive associations between phthalates and breast cancer were observed (Reeves et al. 2019). These investigators concluded that phthalate biomarker concentrations did not result in an increased risk of developing invasive breast cancer.

8.0 CONCLUSION

DTSC has determined that the available reliable information cited in this document does not support identifying any food packaging containing OPs as a Priority Product at this time. This determination was made based on consideration of the following factors:

- NHANES biomonitoring data suggests that Human exposures to OPs in the U.S. have declined significantly since 2006. In fact, exposures also appear to have decreased in Europe during the same period. This suggest that manufacturers are switching to the use of alternatives to OPs, or that regulatory efforts to limit the use of certain OPs in some products are working, or both.
- The purpose of the Safer Consumer Product regulations is to encourage the identification and use of safer alternatives to the toxic chemicals used in some products. However, several alternatives to the use of OPs plasticizers are available and already in use. While there are some concerns about the potential hazards of these alternatives, many appear to be less toxic than the OPs they are intended to replace. The limited test data that is available seems to suggest that manufacturers have indeed switched to these alternatives in various applications.
- DTSC cannot adequately evaluate the market for food packaging containing OPs in California. There is very little reliable information available that identifies food packaging that currently contains OPs and that is sold or offered for sale in California. The only recent information DTSC could find showing the presence of OPs in food packaging is a single, limited study that showed OPs in cap gaskets for some kinds of food and beverages. That study was limited in scope and cannot be used to estimate the prevalence of those cap gaskets in the market. That study also did not identify specific products tested, or the manufacturers of the food packaging included in the study.
- DTSC's stakeholder engagement efforts failed to reveal any additional information that would support listing food packaging containing OPs as a Priority Product.
- Hazard data and toxicity endpoint information is limited or lacking for many OPs. The hazard and toxicity endpoint information that is available is limited for many OPs and suggests that hazard traits may differ significantly between OPs based on molecular weight. Unfortunately, much work remains to definitively establish hazard traits for most of the OPs captured on the Candidate Chemical list.

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