Review of Exposure Data and Assessments for Select Dialkyl *Ortho*-Phthalates*

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* This document represents the views of the CPSC staff. It has not been reviewed or approved by, and may not necessarily represent the views of, the Commission.

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1. INTRODUCTION

The objective of this report is to present existing data for human exposure to phthalates, focusing on the six dialkyl ortho-phthalates that were either permanently or temporarily prohibited (pending further study) in children's toys or child care articles under Section 108 of the Consumer Product Safety Improvement Act (CPSIA) on February 10, 2009. The three phthalates that have been permanently prohibited are di-(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and benzyl butyl phthalate (BBP). The three phthalates that have been temporary prohibited are diisodecyl phthalate (DIDP), diisononyl phthalate (DINP), and di-n-octyl phthalate (DnOP).

Phthalic acid esters (phthalates) are synthetic (Sathyanarayana, 2008) additives that are produced in high volume primarily to provide flexibility and durability to polyvinyl chloride (PVC) products (Shea, 2003). Phthalates are used as plasticizers in numerous commodities, including many building materials (Wormuth et al., 2006). They are also used in a vast range of consumer products. Given this extensive use, there is a high probability for general population exposure (Calafat and McKee, 2006). High concentrations of phthalates have been found in air and dust in residential and occupational environments. Phthalates are also ubiquitous contaminants in food (Wormuth et al., 2006). Human exposure to phthalates is therefore extensive, including exposure to special subpopulations (e.g., infants, toddlers, children), however, quantifying human exposures is both impressive and subject to error (Shea, 2003). Because phthalates are not covalently bound to PVC, they may be released when children place PVC products in their mouths. The use of phthalates in children's products has been under scrutiny, because some phthalates cause developmental effects in animals following perinatal exposure (Gray et al., 2000).

This report presents background information such as production volumes and uses of phthalates (Section 2), key physico-chemical properties, as well as general environmental fate properties such as distribution, degradation, and bioaccumulation (Section 3). It also presents concentrations of these six phthalates, measured (or estimated), in environmental media and consumer products and food to which humans may be exposed (Section 4). Environmental media examined include water, soil, sediment, sludge, solid waste, air, dust, and a variety of biota. Consumer product concentrations, including food and food related uses, have been provided where available, with the majority of the data retrieved from Asian, European, and North American literature. In general, maximum concentrations of phthalates are presented in Section 4.

Human exposures to phthalates are presented in Section 5 and include summaries of biomonitoring studies (Section 5.2) conducted in the United States (U.S.), Europe, and Asia over the past ten years for general populations and specific populations (i.e., children, women, and men). These data are representative of "ambient" exposures. Biomonitoring data associated with specific exposure scenarios are provided in Section 5.4 of this report. Summaries of occupational exposure studies are presented in Section 5.3. Section 5.4 details ten different scenarios for consumer exposures: toys and baby

equipment; medical devices; personal care products; clothing, gloves and footwear; car and public transportation interiors; building materials and furniture (house dust); food and food-related uses; pharmaceuticals; adult toys and gels; and miscellaneous. For each of these scenarios, summaries of available studies evaluating exposures to specific phthalates, assumptions used to calculate exposure, and the estimated human exposures are presented. Section 5.5 presents human exposures via the environment. Available studies that present cumulative exposure estimates are summarized in Section 5.6. Cumulative exposure estimates are provided for banned, interim banned, and other phthalates.

Other sections of the report discuss available literature on populations with potentially high exposures to phthalates (Section 5.7) and address the uncertainty and variability associated with estimating exposure (Section 5.8). The populations with the highest phthalate exposures were workers in occupational settings, women of child-bearing age, newborns, infants and children, dialysis patients, and patients receiving regular blood transfusions.

2. PRODUCTION AND USE OF PHTHALATES

2.1. PRODUCTION OF PHTHALATES

This section provides a summary of the literature review that was performed to obtain information on production of the phthalates DEHP, DBP, BBP, DINP, DIDP and DnOP. The units of tonnes per annum discussed in the European Union (EU) references are equivalent to 1,000 kg per year.

2.1.1. Production of DEHP

The Toxics Use Reduction Institute (TURI) (2006) stated that DEHP is the most commonly used phthalate plasticizer with an estimated annual production in Western Europe of 1.1 billion pounds per year and an estimated global annual production of between 2,205 and 8,818 billion pounds per year. According to TURI, the U.S. production of DEHP was 265 million pounds in 2002 which accounts for 18% of the total U.S. consumption of phthalate plasticizers. Thornton (2002) stated that the U.S. production of DEHP is approximately 4 billion pounds per year. The Agency for Toxic Substances and Disease Registry (ATSDR) (2002) report stated that production volumes for DEHP in the U.S. are not available, but estimated production information is available for a group of phthalate esters referred to as the dioctyl phthalates (DOP) which include diethylhexyl phthalate, diisooctyl phthalate, and DnOP. Production of DOP in the U.S. in 1998 was 285 million pounds. Previous years showed domestic production volumes of:

- 309 million pounds in 1990
- 258 million pounds in 1994
- 280 million pounds in 1995
- 280 million pounds in 1996
- 287 million pounds in 1997

The report stated that there may be a decreasing demand (production volume) for DEHP due to concern over health effects.

The European Chemicals Bureau (ECB) DEHP Summary (2008) and ECB DEHP (2008) reports stated that the global production of DEHP in 1994 in the EU was estimated to be between 2.2 and 8.8 billion pounds per year. The production volume of DEHP in Western Europe was 1.3 billion pounds in 1997. Information received from industry in 2005 showed that the use of DEHP in the EU decreased to 487 million pounds in 2004, and the use of the phthalates DINP and DIDP increased during the same period. Approximately 800 plants in EU use DEHP or preparations that contain DEHP. The amount of DEHP consumed in Europe was 1.0 billion pounds per year. According to industry, the amount of DEHP exported from the EU in 1997 was 410 million pounds and the amount of DEHP imported to the EU was 148 million pounds per year. Japan produced 769 million pounds of DEHP in 1993.

The European Chemicals Agency (ECHA) DEHP (2009) report stated that 750 million pounds per year of DEHP was manufactured in the EU in 2007. The manufacture of DEHP has decreased dramatically over the last 10 years from 1.3 billion pounds per year in 1997. The

report estimated a net export of pure DEHP at 110 million pounds per year in 2007, which is a slight decrease since 2005. In addition, the report estimates a net export of DEHP in preparations of approximately 22 million pounds per year in 2007. Therefore, the net use of DEHP in the EU was estimated to be approximately 617 million pounds per year in 2007.

2.1.2. Production of DBP

The ECHA DBP (2009) report indicated the total manufactured poundage of DBP in 2005, 2006 and 2007 is confidential, but in 2005 it was more than 22 million pounds per year and in 2007 it was less than 22 million pounds per year. A significant part of the manufactured tonnage is exported to countries outside the EU. In Western Europe, approximately 2.2 billion pounds of phthalates are produced each year, of which, approximately 2 billion pounds are used to plasticize PVC. DBP seems to represent less than 1% of the production. The market for DBP has been decreasing over the last decade. In 1994, approximately 108 million pounds per year were produced. In 1998, the production volume of DBP in the EU was estimated at 57 million pounds, of which 18 million pounds was thought to be exported outside the EU.

The ATSDR (2001) reported that during the 1980s there was an increase in the production of phthalate esters (including DBP) with a world-wide production volume of 4 billion pounds per year. The majority of phthalate esters are produced in Europe with the U.S. and Asia and Pacific Rim countries producing about the same amounts each. According to ATSDR (2001), DBP was produced at two manufacturing facilities in the U.S. (i.e., Eastman Chemical Company in Kingsport, Tennessee, and Unitex Chemical Corporation in Greensboro, North Carolina). Production volume records for DBP for the U.S. only provided combined production volumes for DBP and di-iso-butyl phthalate (DIBP). The combined production volume was highest in 1988, with a production volume of 26 million pounds per year, decreasing to 17 million pounds per year in 1994.

The ECB DBP (2003-04) report stated that the production volume of DBP in the EU was estimated to be 57 million pounds per year with 18 million pounds being exported from the EU. Therefore, approximately 40 million pounds per year are used within the EU. No DBP is imported to the EU. The production volume of DBP has been decreasing (i.e., 108 million pounds per year in 1994; 82 million pounds in 1997; and 57 million pounds in 1998).

2.1.3. Production of BBP

The ECHA BBP (2009) report stated that the total manufactured poundage of BBP in 2007 was below 40 million pounds and that a significant part of the manufactured poundage is exported to countries outside the EU. In Western Europe, about 2.2 billion pounds of phthalates are produced each year, of which, approximately 2 billion pounds are used to plasticize PVC. BBP seems to represent less than 1% of the production.

The market for BBP has been decreasing over the last decade. The ECB BBP Summary (2008) and ECB BBP (2007) reports stated that during the period between 1994 and 1997 there were 3 producers of BBP in the EU. The production of BBP reported during this period was 99 million

pounds per year, with approximately 20 million pounds per year being exported from the EU. It was estimated that approximately 79 million pounds per year of BBP were used in the EU. For 2004, industry estimated a use volume of 43 million pounds per year in the EU

2.1.4. Production of DINP

Thornton (2002) stated that the U.S. production of DINP is approximately 356 million pounds per year.

The ECB DINP Summary (2003) and ECB DINP (2003) reports stated that there were four producers of DINP in the EU. The reports stated that based on data provided by the producers of DINP, the total production volume in the EU was 408 million pounds per year for 1994. An estimated import volume of 12 million pounds per year was obtained from existing inventories from the previous year and approximately 184 million pounds per year were exported outside the EU. Therefore, the estimated consumption volume in 1994 was approximately 236 million pounds per year. The reports also stated that, based on estimates by the producers, the consumption volumes of DINP in Western Europe over past decades were as follows:

- 66 million pounds per year in 1964
- 88 million pounds per year in 1970
- 110 million pounds per year in 1975
- 154 million pounds per year in 1980
- 176 million pounds per year in 1985
- 220 million pounds per year in 1990
- 236 million pounds per year in 1994

A further increase in consumption of DINP was expected during subsequent years.

2.1.5. Production of DIDP

Thornton (2002) stated that the U.S. production of DIDP is approximately 270 million pounds per year.

The ECB DIDP Summary (2003) and ECB DIDP (2003) reports stated that there are currently four producers of DIDP in the EU. The reports stated that in 1994 the production volume of DIDP in the European Community was estimated to be approximately 616 million pounds per year. There were 5 major production companies located in Europe. Three companies have provided export data outside Europe of approximately 84 million pounds per year. The mean DIDP plasticizer consumption in Western Europe was reported to be approximately 441 million pounds per year. The reports also stated that, based on estimates by the producers, the consumption volumes of DIDP in Western Europe over past decades were as follows:

- 110 million pounds per year in 1964
- 110 million pounds per year in 1970
- 132 million pounds per year in 1975

- 198 million pounds per year in 1980
- 265 million pounds per year in 1985
- 309 million pounds per year in 1990
- 441 million pounds per year in 1994

A further increase in consumption of DIDP was expected during subsequent years.

2.1.6. Production of DnOP

The ATSDR (1997) report stated that the annual production of DnOP is difficult to estimate because of confusion in nomenclature regarding the octylphthalate isomers and reported data describing only the entire group of dioctyl orthophthalates. A total of 270 million pounds of total dioctylphthalates were produced in 1992. The amount of DnOP included in this group was not reported because of the possible revelation of confidential business information. A total of 10 million pounds of DnOP was produced in 1994 in the U.S. (NTP-CERHR DnOP, 2003; Silva, 2005).

The Non-confidential 2006 Inventory Update Reporting (IUR) database provides production importation values of 10 to less than 50 million pounds of liquid DnOP (purity >90%) (IUR, 2006).

2.2. USE OF PHTHALATES

Dialkyl *ortho*-phthalates (*o*-DAPs) are a group of chemicals that are used primarily as plasticizers in PVC and as solvents. *o*-DAPs are mainly used to soften and increase the flexibility of plastic consumer products such as shower curtains, medical devices, upholstery, raincoats, and soft squeeze toys (NTP-CERHR DBP, 2003). They can also be found in food wrappings, wood finishes, and upholstery (Hubinger and Havery, 2006). Additional applications include floor and wall coverings, windows and siding, solvents in inks, waxes and polishes, and coatings. Since, phthalates have such wide-ranging applications in industry; they have become highly prevalent in the environment and can now be found in food, water, and air. Plastic products (containing phthalates) disposed of as solid waste degrade over time when exposed to weather conditions, releasing phthalates into the environment. These released phthalates may eventually migrate to groundwater, including water intended for human use (Bosnir et al., 2007). Consequently, exposure to animals and human beings is a cause of concern. Human exposures to phthalates may occur via several routes, including oral (ingestion), dermal, inhalation, and intravenous (Blount et al., 2000). Most of the studies that have been conducted with phthalates in the last few years suggest that phthalate metabolites have been detected in virtually all humans tested (Fromme et al., 2007a).

There has been considerable debate about the use of phthalates in children's articles over the last decade. Because plasticizers are not chemically bound to PVC, they may be released when children place PVC products in their mouths. Until about 1985, DEHP was the predominant *o*-DAP in PVC children's products such as teethers, rattles, and soft toys. However, DEHP was found to be carcinogenic in laboratory animals (NTP, 1982). DEHP was replaced with another phthalate, DINP. In 1998, the U.S. Consumer Product Safety Commission (CPSC) staff began

investigating the potential chronic hazards from DINP in children's products (CPSC, 1998a). Subsequently, the National Environmental Trust and 11 other organizations petitioned the CPSC to ban the use of PVC in toys and other products intended for use by children five years of age and under, citing concerns about the adverse effects of phthalates, lead, and cadmium additives in PVC. Eventually, the CPSC concluded that DINP in toys is not harmful to children (Wind, 2002). Then in 2005, the European Commission banned BBP, DBP, and DEHP in all children's toys and related articles and also banned DIDP, DINP, and DnOP from those children's articles that would be put in their mouth (EUROPA, 2005). Finally, per Section 108 of the CPSIA enacted in February 2009, CPSC has implemented a new ban on certain phthalates in children's toys and related products (http://www.cpsc.gov/ABOUT/Cpsia/108rfc.pdf). The new law prohibits the manufacture, import, distribution, or sale of children's toys and child care articles that contain more than 0.1% (mass) of BBP, DBP, and DEHP. Moreover, it has also placed an interim ban on the manufacture, import, distribution, or sale of those children's toys, that can be placed in a child's mouth and child care articles that contain more than 0.1% (mass) of DIDP, DINP, and DnOP.

3. PHYSICO-CHEMICAL AND ENVIRONMENTAL FATE PROPERTIES OF PHTHALATES

3.1. PHYSICO-CHEMICAL PROPERTIES OF PHTHALATES

This section highlights the key physico-chemical properties of each of the six phthalates.

3.1.1. Benzyl butyl phthalate (BBP)

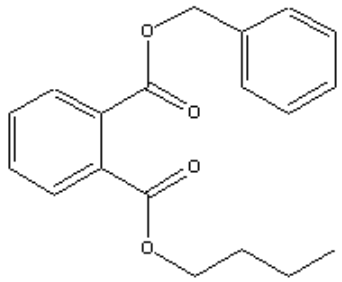

Figure 1. Structure of BBP

BBP (as shown in Figure 1) is a clear and slightly viscous liquid (man-made phthalate ester) that is mostly used in vinyl tile (NTP-CERHR BBP, 2003). It is also used in other products like conveyor belts, automotive trims, carpet, weather stripping and traffic cones. BBP is produced by the sequential reaction of butanol and benzyl chloride with phthalic anhydride (NTP-CERHR BBP, 2003). BBP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of BBP are tabulated in Table 3.1-1.

3.1.2. Di-n-butyl phthalate (DBP)

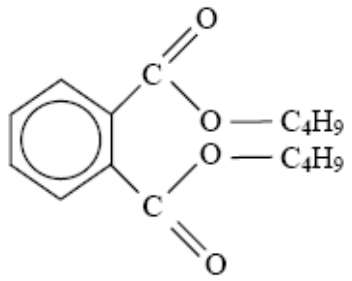

Figure 2. Structure of DBP

DBP (Figure 2) is an odorless and colorless (manmade phthalic ester) oily liquid that is produced when *n*-butanol reacts with phthalic anhydride. DBP is added to hard plastics to make them softer, such as cellulose and some PVC plastics. It is also used in products

like adhesives, dyes, lacquers, personal care products, and cosmetics (ATSDR, 2001). The major metabolite for DBP is monobutyl phthalate (MBP). DBP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of DBP are tabulated in Table 3.1-2.

3.1.3. Bis(2-ethylhexyl) phthalate (DEHP)

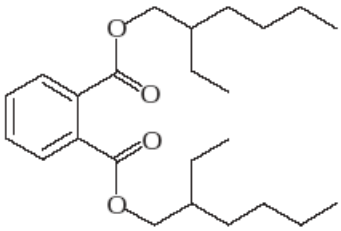

Figure 3. Structure of DEHP

DEHP (Figure 3) is a light color to colorless, oily liquid that is produced when 2-ethylhexanol reacts with phthalic anhydride (NTP-CERHR DEHP, 2006). DEHP is used in large quantities as a plasticizer for PVC in several products like building materials, clothing, car products, food packaging, and medical products. Vinyl materials can contain up to 40% of DEHP (ATSDR, 2002). The high usage of this product in the industry often leads to many possible scenarios of human and environmental exposure (ECB DEHP, 2008). DEHP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of DEHP are tabulated in Table 3.1-3.

3.1.4. Di-isodecyl phthalate (DIDP)

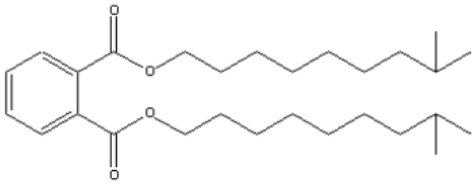

Figure 4. Structure of DIDP
(One of many possible isomers)

DIDP (Figure 4) is a complex substance, consisting of many isomers. It is an oily liquid. DIDP is manufactured by the reaction of phthalic anhydride and isodecyl alcohol in the presence of a catalyst (NTP-CERHR DIDP, 2003). It is used as a plasticizer in a wide

variety of PVC plastic products that include wire coverings, artificial leather, toys, carpet backing, and pool liners. The National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) (NTP-CERHR DIDP, 2003) study also indicates that DIDP has only limited use in food packaging or handling and is not used in medical devices. However, the use of DIDP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of DIDP are tabulated in Table 3.1-4.

3.1.5. Di-isononyl phthalate (DINP)

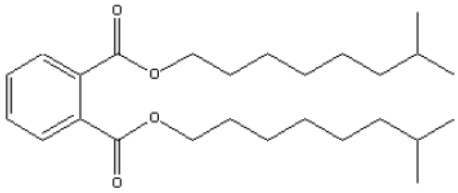

Figure 5. Structure of DINP
(One of many possible isomers)

DINP is an oily viscous liquid (NTP-CERHR DINP, 2003). It is a complex substance consisting of many isomers. DINP is available in two forms made by two different processes, which differ slightly in their isomeric composition. DINP is used to manufacture a broad range of consumer products such as garden hoses, pool liners, flooring tiles, tarps, and toys. The NTP-CERHR DINP (2003) study also indicates that DINP is not used in medical devices and finds only limited use in food packaging. However, the use of DINP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of DINP are tabulated in Table 3.1-5.

3.1.6. Di-n-octyl phthalate (DnOP)

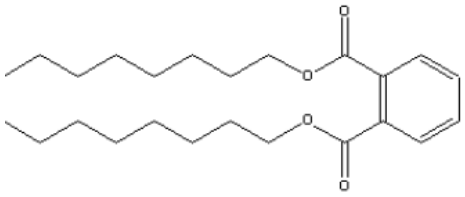

Figure 6. Structure of DnOP

DnOP (Figure 6) is an oily substance manufactured by reaction of phthalic anhydride and n-octanol in the presence of a catalyst (NTP-CERHR DnOP, 2003). DnOP is one of a

variety of plasticizers used in the production of PVC plastics. It has also been approved by the U.S. Food and Drug Administration (FDA) as an indirect food additive and is used in seam cements, bottle cap liners, and conveyor belts. The NTP-CERHR DnOP (2003) study also mentions that DnOP is also used in other commercial products like flooring, carpet tiles, tarps, and garden hoses. DnOP is not used in medical devices. The use of DINP is currently banned in children's toys in the U.S. if present in more than 0.1% of the mass of the toy. The EU prohibits the concentration of three phthalates (DEHP, DBP, and BBP or DnOP, DIDP, and DINP) combined in toys and childcare articles if they can be placed in the mouth by children. The physico-chemical properties of DnOP are tabulated in Table 3.1-6.

3.2. ENVIRONMENTAL FATE PROPERTIES OF PHTHALATES

This section discusses the key environmental fate properties of each of the phthalates and how they affect the environmental distribution and bioaccumulation of the phthalates.

3.2.1. Benzyl butyl phthalate (BBP)

Distribution and Degradation

Emissions to water and air are expected to be the most important entry routes of BBP into the environment (ECB BBP, 2007). The metabolic pathway of aerobic and anaerobic biodegradation of phthalates is a two-step process. First, the di-ester is hydrolyzed into the mono-esters (monobutyl phthalate and monobenzyl phthalate) by esterases, and next, the mono-esters are converted into phthalic acid. If released to air, BBP will exist in both the vapor and particulate phases in the atmosphere (HSDB BBP, 2009). In its vapor-phase, BBP will degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals (half-life of 1.5 days). In its particulate-phase, it will be removed from the atmosphere by wet or dry deposition. However, long distance transport is unlikely due to low volatility and short half life in the atmosphere.

The contribution of hydrolysis and photolysis in water to the overall environmental degradation of phthalate esters, including BBP, is expected to be low (ECB BBP, 2008, HSDB BBP, 2009). An atmospheric half-life of about 1.5 days has been estimated for the photo-oxidation reaction. BBP is readily biodegradable under aerobic conditions. Anaerobic test indicate that biodegradation of BBP is slower in the anaerobic environment (e.g., sediments or deeper soil or groundwater layers). A relatively low volatilization rate BBP indicates that it is not likely to volatilize from surface waters. A high octanol/water partition coefficient (K_{ow}) of DBP is responsible for greater soil adsorption. In addition, a relatively high partition coefficient (K_{oc}) indicates low to no mobility. Its volatilization from moist soil surfaces is expected to be an important fate process (HSDB BBP, 2009). However, adsorption to soil is expected to reduce the effects of volatilization. Similarly, volatilization from water surfaces is also expected to be an important fate process. However, volatilization from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column.

Table 3.1-1. Physico-Chemical Properties of BBP

Property	Value	Source
Chemical Name	Benzyl butyl phthalate	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a
CAS Number	85-68-7	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a
Chemical Formula	$C_{19}H_{20}O_4$	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a
Molecular Weight	312.35	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a
Physical State	Oily liquid	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a
Melting Point	-40.5°C -35°C <25°C	NTP-CERHR BBP, 2003 ECB BBP, 2008; NICNAS, 2008a NIH ChemIDPlus-BBP, 2009
Boiling Point	370°C	NTP-CERHR BBP, 2003; ECB BBP, 2008; NICNAS, 2008a; ChemIDPlus-BBP
Density	1.116 g/cm^3 at 25°C 1.114-1.122 g/cm^3 at 25°C	ECB BBP, 2008 NICNAS, 2008a
Vapor Pressure	8.0x10^{-5} Pa at 25°C 1.12x10^{-3} Pa at 20°C 2.49x10^{-3} Pa at 25°C 1.1x10^{-3} Pa at 25°C	NTP-CERHR BBP, 2003; NICNAS, 2008a ECB BBP, 2008 Cousins and Mackay, 2000 NIH ChemIDPlus-BBP, 2009
Surface Tension	NA	
Water Solubility	2.7 mg/L 2.8 mg/L 3.8 mg/L	NTP-CERHR BBP, 2003; NIH ChemIDPlus-BBP, 2009 ECB BBP, 2008; NICNAS, 2008a Cousins and Mackay, 2000
Henry's Law Constant	0.176 Pa-m^3 /mol (calculated) 0.205 Pa-m^3 /mol 0.128 Pa-m^3 /mol	ECB BBP, 2008 Cousins and Mackay, 2000 NIH ChemIDPlus-BBP, 2009
Air-Water Partition Coefficient (Log K_{aw})	-4.08	Cousins and Mackay, 2000
Octanol-Water Partition Coefficient (Log K_{ow})	4.59 4.84 4.7	NTP-CERHR BBP, 2003 ECB BBP, 2008; NICNAS, 2008a Cousins and Mackay, 2000; NIH ChemIDPlus-BBP, 2009
Octanol-Air Partition Coefficient (Log K_{oa})	8.78	Cousins and Mackay, 2000
Flash Point	198°C	ECB BBP, 2008; NICNAS, 2008a
Viscosity	NA	

Table 3.1-2. Physico-Chemical Properties of DBP

Property	Value	Source
Chemical Name	Di-n-butyl phthalate	ATSDR, 2001; ECB DBP, 2003-04; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009
CAS Number	84-74-2	ATSDR, 2001; ECB DBP, 2003-04; NIH ChemIDPlus-DBP, 2009
Chemical Formula	$C_{16}H_{22}O_4$	ATSDR, 2001; ECB DBP, 2003-04; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000
Molecular Weight	278.34	ATSDR, 2001; ECB DBP, 2003-04; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000
Physical State	Oily liquid	ATSDR, 2001; ECB DBP, 2003-04; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009
Melting Point	-35°C -69°C	ATSDR, 2001; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000 ECB DBP, 2003-04
Boiling Point	340°C	ATSDR, 2001; ECB DBP, 2003-04; NICNAS, 2008b; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000
Density	1.04 kg/L	ATSDR, 2001; NICNAS, 2008b
Vapor Pressure	$(2.68\text{-}3.0)\times10^{-3}$ Pa $9.7 \pm 3.3\times10^{-3}$ Pa at 25°C 3.6×10^{-3} Pa at 25°C	ATSDR, 2001; NIH ChemIDPlus-DBP, 2009 ECB DBP, 2003-04; NICNAS, 2008b NTP-CERHR DBP, 2000
Surface Tension	NA	
Water Solubility	11.2 mg/L 10 mg/L at 25°C	ATSDR, 2001; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000 ECB DBP, 2003-04; NICNAS, 2008b
Henry's Law Constant	$(8.94 – 45)\times10^{5}$ Pa-m^3/mole 0.183 Pa-m^3/mole at 23°C	ATSDR, 2001; NICNAS, 2008b NIH ChemIDPlus-DBP, 2009
Air-Water Partition Coefficient (Log K_{aw})	NA	
Octanol-Water Partition Coefficient (Log K_{ow})	4.45-4.72 4.57	ATSDR, 2001; NIH ChemIDPlus-DBP, 2009; NTP-CERHR DBP, 2000 ECB DBP, 2003-04; NICNAS, 2008b
Octanol-Air Partition Coefficient (Log K_{oa})	NA	
Flash Point	NA	
Viscosity	NA	

Table 3.1-3. Physico-Chemical Properties of DEHP

Property	Value	Source
Chemical Name	Bis(2-ethylhexyl) phthalate	ATSDR, 2002; NIH ChemIDPlus-DEHP, 2009; ECB DEHP, 2008
CAS Number	117-81-7	ATSDR, 2002; NIH ChemIDPlus-DEHP, 2009; ECB DEHP, 2008
Chemical Formula	$C_{24}H_{38}O_4$	ATSDR, 2002; NIH ChemIDPlus-DEHP, 2009; ECB DEHP, 2008; NTP-CERHR DEHP, 2006
Molecular Weight	390.6	ATSDR, 2002; Cousins and Mackay, 2000; NTP-CERHR DEHP, 2006
Physical State	Colorless oily liquid	ATSDR, 2002; ECB DEHP, 2008
Melting Point	-55°C -47°C	NIH ChemIDPlus-DEHP, 2009; ECB DEHP, 2008 ATSDR, 2002; NTP-CERHR DEHP, 2006
Boiling Point	384°C; 385°C; 386°C; 387°C	NIH ChemIDPlus-DEHP, 2009; ATSDR, 2002; ECB DEHP, 2008; NTP-CERHR DEHP, 2006; CPSC DEHP, 2009
Density	0.984 g/mL at 20°C 0.986	ATSDR, 2002; ECB DEHP, 2008 NTP-CERHR DEHP, 2006
Vapor Pressure	$2.52x10^{-5}$ Pa; $1.89x10^{-5}$ Pa; $1.33x10^{-5}$ Pa; $3.4x10^{-5}$ Pa; $1x10^{-7}$ mmHg at 25°C, $1.42x10^{7}$ mmHg at 25°C, $1.33x10^{-5}$ Pa at 25°C, $4.8x10^{-8}$ to $1.4x10^{-4}$	Cousins and Mackay, 2000; NIH ChemIDPlus-DEHP, 2009; ATSDR, 2002; NTP-CERHR DEHP, 2006; ECB DEHP, 2008; CPSC DEHP, 2009
Surface Tension	NA	
Water Solubility	$2.49x10^{-3}$ mg/L 0.27 mg/L $4.1x10^{-2}$ mg/L $3.0x10^{-3}$ mg/L	Cousins and Mackay, 2000 NIH ChemIDPlus-DEHP, 2009 ATSDR, 2002 ECB DEHP, 2008; NTP-CERHR DEHP, 2006
Henry's Law Constant	3.95 Pa-m^3/mole $2.74x10^{-2}$ Pa-m^3/mole 1.72 Pa-m^3/mole 4.43 Pa-m^3/mole	Cousins and Mackay, 2000 NIH ChemIDPlus-DEHP, 2009 ATSDR, 2002 ECB DEHP, 2008
Air-Water Partition Coefficient (Log K_{aw})	-2.80	Cousins and Mackay, 2000
Octanol-Water Partition Coefficient (Log K_{ow})	7.73; 7.6; 7.5; 9.64, 4.2-8.39	Cousins and Mackay, 2000; NIH ChemIDPlus-DEHP, 2009; ATSDR, 2002; ECB DEHP, 2008; NTP-CERHR DEHP, 2006; CPSC DEHP, 2009
Octanol-Air Partition Coefficient (Log K_{oa})	10.53	Cousins and Mackay, 2000
Flash Point	196°C 200°C	ATSDR, 2002; CPSC DEHP, 2009 ECB DEHP, 2008
Viscosity	81 mPa-s at 20°C 58 mPa-s at 25°C	ECB DEHP, 2008

Table 3.1-4. Physico-Chemical Properties of DIDP

Property	Value	Source
Chemical Name	Di-isodecyl phthalate	ECB DIDP, 2003
CAS Number	68515-49-1	ECB DIDP, 2003
Chemical Formula	$C_{28}H_{46}O_4$	ECB DIDP, 2003; NTP-CERHR DIDP, 2003
Molecular Weight	446.7	ECB DIDP, 2003; Cousins and Mackay, 2000; NTP-CERHR DIDP, 2003
Physical State	Oily viscous liquid	ECB DIDP, 2003
Melting Point	-45°C -48°C	ECB DIDP, 2003; NIH ChemIDPlus-DIDP, 2009 NTP-CERHR DIDP, 2003
Boiling Point	>400°C 370°C	ECB DIDP, 2003 NTP-CERHR DIDP, 2003
Density	0.966 at 20°C	ECB DIDP, 2003; NTP-CERHR DIDP, 2003
Vapor Pressure	$7.04x10^{-5}$ Pa at 25°C $5.10x10^{-5}$ Pa at 25°C $1.84x10^{-6}$ Pa at 25°C	NIH ChemIDPlus-DIDP, 2009 ECB DIDP, 2003 Cousins and Mackay, 2000
Surface Tension	NA	
Water Solubility	$2.0x10^{-4}$ mg/L 0.28 mg/L $3.81x10^{-5}$ mg/L <0.001 mg/L	ECB DIDP, 2003 NIH ChemIDPlus-DIDP, 2009 Cousins and Mackay, 2000 NTP-CERHR DIDP, 2003
Henry's Law Constant	$1.12x10^{-1}$ Pa-m^3/mole at 25°C 114 Pa-m^3/mole 21.6 Pa-m^3/mole at 25°C	NIH ChemIDPlus-DIDP, 2009 ECB DIDP, 2003 Cousins and Mackay, 2000
Air-Water Partition Coefficient (Log K_{aw})	-2.06	Cousins and Mackay, 2000
Octanol-Water Partition Coefficient (Log K_{ow})	10.36 8.8 9.46 ~10	NIH ChemIDPlus-DIDP, 2009 ECB DIDP, 2003 Cousins and Mackay, 2000 NTP-CERHR DIDP, 2003
Octanol-Air Partition Coefficient (Log K_{oa})	11.52	Cousins and Mackay, 2000
Flash Point	>200°C	ECB DIDP, 2003
Viscosity	130 mPa-s	ECB DIDP, 2003

Table 3.1-5. Physico-Chemical Properties of DINP

Property	Value	Source
Chemical Name	Di isononyl phthalate	NIH ChemIDPlus-DINP, 2009; NTP-CERHR DINP, 2003; NICNAS, 2008c
CAS Number	28553-12-0	NIH ChemIDPlus-DINP, 2009; NTP-CERHR DINP, 2003; NICNAS, 2008c
Chemical Formula	$C_{26}H42O_4$	NIH ChemIDPlus-DINP, 2009; NTP-CERHR DINP, 2003; NICNAS, 2008c
Molecular Weight	418.6 419 420.6	Cousins and Mackay, 2000 NTP-CERHR DINP, 2003 NICNAS, 2008c
Physical State	Oily viscous liquid	ECB DINP, 2003; NICNAS, 2008c
Melting Point	-48°C -50°C	NTP-CERHR DINP, 2003 ECB DINP, 2003; NICNAS, 2008c
Boiling Point	370°C >400°C	NTP-CERHR DINP, 2003 ECB DINP, 2003; NICNAS, 2008c
Density	975 kg/m^3 at 20°C	ECB DINP, 2003; NICNAS, 2008c
Vapor Pressure	$7.2x10^{-5}$ Pa at 25°C $6.0x10^{-5}$ Pa at 20°C $6.81x10^{-6}$ Pa at 25°C	NIH ChemIDPlus-DINP, 2009 ECB DINP, 2003; NICNAS, 2008c Cousins and Mackay, 2000
Surface Tension	NA	
Water Solubility	0.2 mg/L at 20°C <0.001 mg/L $6.0x10^{-4}$ mg/L at 20°C $3.08x10^{-4}$ mg/L at 25°C	NIH ChemIDPlus-DINP, 2009 NTP-CERHR DINP, 2003 ECB DINP, 2003; NICNAS, 2008c Cousins and Mackay, 2000
Henry's Law Constant	0.151 Pa-m^3/mole at 25°C 41.4 Pa-m^3/mole at 25°C 9.26 Pa-m^3/mole at 25°C	NIH ChemIDPlus-DINP, 2009 ECB DINP, 2003; NICNAS, 2008c Cousins and Mackay, 2000
Air-Water Partition Coefficient (Log K_{aw})	-2.43	Cousins and Mackay, 2000
Octanol-Water Partition Coefficient (Log K_{ow})	9.37 ~9 8.8 8.6	NIH ChemIDPlus-DINP, 2009 NTP-CERHR DINP, 2003 ECB DINP, 2003; NICNAS, 2008c Cousins and Mackay, 2000
Octanol-Air Partition Coefficient (Log K_{oa})	11.03	Cousins and Mackay, 2000
Flash Point	>200°C	ECB DINP, 2003; NICNAS, 2008c
Viscosity	100-150 mPa-s	ECB DINP, 2003

Table 3.1-6. Physico-Chemical Properties of DnOP

Property	Value	Source
Chemical Name	Di-n-octyl phthalate	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000
CAS Number	117-84-0	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000
Chemical Formula	$C_{24}H_{38}O_4$	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000
Molecular Weight	390.6	ATSDR, 1997; NICNAS, 2008d; Cousins and Mackay, 2000; NTP-CERHR DnOP, 2003
Physical State	Organic liquid	ATSDR, 1997; NICNAS, 2008d
Melting Point	-25°C	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000; NTP-CERHR DnOP, 2003
Boiling Point	390°C at 101325 Pa	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000; NTP-CERHR DnOP, 2003
Density	0.978 g/mL at 25°C	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000; NTP-CERHR DnOP, 2003
Vapor Pressure	$1.92x10^{-2}$ Pa at 25°C; $1.33x10^{-5}$ Pa at 25°C; $2.52x10^{-5}$ Pa at 25°C; $1x10^{-7}$ mmHg at 25°C, $1.44x10^{-4}$ mmHg at 25°C, $2.2x10^{-7}$ to $1.9x10^{-4}$	ATSDR, 1997; NICNAS, 2008d; NTP-CERHR DnOP, 2003; NIH ChemIDPlus-DnOP, 2009 ; Cousins and Mackay, 2000; CPSC DnOP, 2009
Surface Tension	NA	
Water Solubility	0.2-3.0 mg/L at 25°C; 0.02 mg/L at 25°C; 3.0 mg/L at 25°C; $2.49x10^{-3}$ mg/L at 25°C; $5.0x10^{-3}$ mg/L; 0.0005 mg/L; 0.00046-3 mg/L	ATSDR, 1997; NIH ChemIDPlus-DnOP, 2009; NICNAS, 2008d; Cousins and Mackay, 2000; NTP-CERHR DnOP, 2003; CPSC DnOP, 2009
Henry's Law Constant	0.55 - 6.67 Pa-m^3/mole; 0.26 Pa-m^3/mole at 25°C; 3.95 Pa-m^3/mole at 25°C; $1.03x10^{-4}$ atm-m^3/mole; $2.57x10^{-6}$ atm-m^3/mole at 25°C; 0.55 atm-m^3/mole; $6.68x10^{-3}$ atm-m^3/mole; $5.5x10^{-6}$ to $6.68x10^{-5}$ H atm-m^3/mole	ATSDR, 1997; NICNAS, 2008d NIH ChemIDPlus-DnOP, 2009 Cousins and Mackay, 2000 CPSC DnOP, 2009
Air-Water Partition Coefficient (Log K_{aw})	-2.80	Cousins and Mackay, 2000
Octanol-Water Partition Coefficient (Log K_{ow})	5.22; 8.1;7.73; 8.06; 8.16-8.18; 5.22-8.54	ATSDR, 1997; NICNAS, 2008d; NIH ChemIDPlus-DnOP, 2009 Cousins and Mackay, 2000; CPSC DnOP, 2009
Octanol-Air Partition Coefficient (Log K_{oa})	10.53	Cousins and Mackay, 2000
Flash Point	219°C	ATSDR, 1997; NICNAS, 2008d
Viscosity	NA	

Bioaccumulation

BBP is considered to have a high potential for bioaccumulation, based on a high K_{ow} value and a molecular weight < 700. Measured bioconcentration factors (BCF) based on total radioactivity range from 135 to 663 liters per kilogram (L/kg). The Good Laboratory Practice study performed by Carr in 1992 (ECB BBP, 2007) shows that BBP is rapidly metabolized and excreted by fish after exposure at 22°C. However, chronic exposure would lead to chronic levels of monoesters that may have harmful effects. The BCF value based on the evaluation of the BCF-tests regarding carbon-14 (^{14}C) method is 449 L/kg for fish. Studies summarized in Hazardous Substances Data Bank (HSDB) for BBP (2009) indicate half-lives of approximately 0.32 to 13 days, suggesting that biodegradation may be an important environmental fate process in water.

3.2.2. Di-n-butyl phthalate (DBP)

Distribution and Degradation

Emissions to water and air are expected to be the most important entry routes of DBP (ECB DBP, 2003-04) into the environment. The metabolic pathway of aerobic and anaerobic biodegradation of phthalates is a two-step process. First, the di-ester is hydrolyzed into the mono-ester by esterases, and next, the mono-ester is converted into phthalic acid. If released to air, DBP will exist in both the vapor and particulate phases in the atmosphere (HSDB DBP, 2009). In its vapor-phase, DBP will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals (half-life of 42 days). In its particulate-phase, it will be removed from the atmosphere by wet or dry deposition.

The contribution of hydrolysis to the overall environmental degradation of phthalate esters, including DBP, is usually low (ECB DBP, 2003-04, HSDB DBP, 2009). DBP has a half-life of about 68.5 hours (hrs) at pH 9 and is stable at pH 5 and pH 7. An atmospheric half-life of about 1.8 days has been estimated for the photo-oxidation reaction. DBP is readily biodegradable under aerobic conditions and its degradation is slower in anaerobic environments like sediments, deeper soil, and groundwater layers. A relatively low volatilization rate of DBP indicates that most of it will remain in the water phase at equilibrium. Nevertheless, DBP has been reported as a particulate and as a vapor in the atmosphere. The HSDB DBP (2009) report suggests that volatilization from moist soil surfaces, as well as water surfaces, is expected to be an important fate process. A high K_{ow} for DBP is responsible for greater soil adsorption. In the air, DBP is transported and removed by both wet and dry deposition.

Bioaccumulation

For phthalates it is known that an important biotransformation pathway is the formation of the mono-ester and the subsequent formation of phthalic acid. The high K_{ow} of DBP indicates that DBP has a potential for bioaccumulation. The available BCF data demonstrates a relatively low bioconcentration, but also indicates that higher BCF values are obtained when the BCF is calculated for the total amount of metabolites using ^{14}C-labelled material. The experimental BCF of 1.8 L/kg for DBP was shown in the study conducted by Hüls (1996). Studies summarized in

the HSDB DBP (2009) report suggest that bioconcentration in aquatic organisms is low to high. However, bioconcentration studies on compounds which are structurally similar to DBP suggest that bioconcentration may be lower than that indicated by the regression-derived equations due to the ability of aquatic organisms to metabolize readily this class of compounds.

3.2.3. Bis(2-ethylhexyl) phthalate (DEHP)

Distribution and Degradation

The photodegradation of DEHP (with a half-life of about one day) is important in the atmosphere but is of little importance in water and soil (ECB DEHP, 2008). DEHP does not hydrolyze in water. The biodegradation rates of DEHP vary among different studies. Based on the results of standard biodegradation test, DEHP is readily biodegradable. Experimental data indicates that DEHP readily biodegrades with a half-life of 50 days in surface water and 300 days in aerobic sediment. The degradation rates are inhibited by anaerobic conditions and low temperature.

Degradation studies (summarized by ECB DEHP, 2008) in agricultural soil (though variable) indicate moderate to low biodegradation rates. MEHP is the primary biodegradation product of DEHP. In contrast, studies summarized in the HSDB DEHP (2009) report indicate that biodegradation is expected to be an important process in both water and soil under aerobic conditions. River die-away tests report half-lives of 2 to 3 weeks. DEHP has a relatively high K_{ow} and is expected to be strongly adsorbed to organic matter. It is therefore expected to be found in the solid organic phase in the environment. Additionally, a high K_{oc} value causes it to be strongly adsorbed to the sludge in sewage treatment plants. A relatively low vapor pressure value indicates a low evaporation rate from its pure state, and a low Henry's law constant indicates a moderate evaporation from a pure water solution, making it semi-volatile (ECB DEHP, 2008).

Bioaccumulation

The bioaccumulation of DEHP is prevalent in aquatic organisms with the highest BCF values observed in invertebrates. This indicates that uptake via the food chain might be an important exposure route. Based on monitoring data and BCF values, DEHP does not bio-magnify. This may in part be due to a more effective metabolism rate in higher organisms. Due to its high affinity to organic matter, only a limited bioaccumulation of DEHP in plants is expected. Environmental studies conducted for DEHP indicate BCF values ranging between 0.01 and 5.9. Due to the large amount of DEHP accumulated in the technosphere, there is considerable potential for DEHP release and subsequent formation and distribution of MEHP. However, the formation rate and fate of MEHP in the environment is unknown. MEHP causes reproductive toxicity in studies on mammals. Studies summarized by HSDB DEHP (2009) indicate that most of DEHP did not reach the systemic circulation of the fish, but was present in the exposure water as metabolites as a result of presystemic branchial metabolism of this compound.

3.2.4. Di-isodecyl phthalate (DIDP)

Distribution and Degradation

The fate and transport behavior of DIDP (an isomeric mixture) is difficult to determine with accuracy. This is because each and every component of the mixture will exhibit different fate and transport properties in the environment (ECB DIDP, 2003). In general, if released to air, DIDP will exist in both the vapor and particulate phases in the atmosphere (HSDB DIDP, 2009). In its vapor-phase, DIDP will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals (half-life of 15 hrs). In its particulate phase, it will be removed from the atmosphere by wet or dry deposition. Although, DIDP does not hydrolyze in water, it is readily degradable (ECB DIDP, 2003, HSDB DIDP, 2009).

Representative half-lives of DIDP in surface water, soil, and sediment are 50, 300, and 3,000 days, respectively. In addition, DIDP has an estimated atmospheric half-life of 0.6 days. Studies summarized in the HSDB for DIDP (2009) suggest that biodegradation may be an important environmental fate process in soil. A high K_{ow} of DIDP indicates a high potential for bioaccumulation, strong sorption to sewage sludge, soils and sediments and very low mobility in soil (relatively high K_{oc}). Its volatilization from moist soil surfaces is expected to be an important fate process (HSDB BBP, 2009). However, adsorption to soil is expected to reduce the effects of volatilization. Similarly, volatilization from water surfaces is also expected to be an important fate process. However, volatilization from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column.

Bioaccumulation

BCFs (whole body values ranging from <14.4 to 4,000) have been reported with certain freshwater organisms. No results are available regarding bioaccumulation of DIDP in plants. Results of the model SIMPLETREAT indicate that 84.8% of any discharged DIDP in sewage treatment plants will be adsorbed on to sludge, 3.9% will be degraded, and 3.2% will be stripped to air, with the remaining 8.1% being released with the aqueous effluent (ECB DIDP, 2003).

3.2.5. Di-isononyl phthalate (DINP)

Distribution and Degradation

The fate and transport behavior of DINP (an isomeric mixture) is difficult to determine with accuracy. This is because each and every component of the mixture is expected to exhibit different fate and transport properties in the environment (ECB DINP, 2003). In general, if released to air, DINP will exist in both the vapor and particulate phases in the atmosphere (HSDB DINP, 2009). In its vapor-phase, DINP will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals (half-life of 16 hrs). In its particulate-phase, DINP will be removed from the atmosphere by wet or dry deposition. DINP does not hydrolyze in water (ECB DINP, 2003, HSDB DINP, 2009). Based on results from simulation tests performed with DEHP, DIDP is considered to be readily degradable.

Representative half-lives of DINP in surface water, soil, and sediment are 50, 300, and 3,000 days, respectively. In addition, it has an estimated atmospheric half-life of 0.7 days. A high K_{ow} of DINP indicates a high potential for bioaccumulation, strong sorption to sewage sludge, soils and sediments and very low mobility in soil (relatively high K_{oc}). Its volatilization from moist soil surfaces is expected to be an important fate process (HSDB BBP, 2009). However, adsorption to soil is expected to reduce the effects of volatilization. Similarly, volatilization from water surfaces is also expected to be an important fate process. However, volatilization from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column.

Bioaccumulation

BCFs (whole body values ranging from 800 to 4,000 L/kg) have been reported with certain freshwater organisms. Results of the model SIMPLETREAT indicate that 82% of any discharged DINP in sewage treatment plants will be adsorbed on to sludge, 10% will be degraded and 1% will be stripped to air, with the remaining 7% being released with the aqueous effluent (ECB DINP, 2003).

3.2.6. Di-n-octyl phthalate (DnOP)

Distribution and Degradation

The use of DnOP as a plasticizer may result in its release to the environment through various waste streams (HSDB DnOP, 2009). If released to air, DnOP will exist in both the vapor and particulate phases in the ambient atmosphere. In its vapor-phase, DnOP will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals (half-life of 19 hrs). In its particulate-phase DnOP will be physically removed from the atmosphere by wet and dry deposition. DnOP does not hydrolyze in water. DnOP will be relatively immobile in the soil given its high K_{ow} value. Its volatilization from wet and dry soil surfaces, as well as water surfaces, is not expected to be an important fate process. One of the studies in the HSDB for DnOP (2009) suggests that biodegradation in soil may be important following acclimation of the resident microbial population. Based on a relatively high K_{oc} value, DnOP will adsorb to suspended solids and sediment in the water column.

Bioaccumulation

Measured BCFs ranging from 1.1 to 9332 L/kg suggest bioconcentration of DnOP in aquatic organisms is low to high (HSDB DnOP, 2009).

4. ENVIRONMENTAL AND CONSUMER PRODUCTS CONCENTRATIONS

This chapter provides a brief summary of the concentrations of six phthalates of interest (BBP, DBP, DEHP, DINP, DnOP and DIDP) found in environmental media, consumer products, and food, to which humans might be exposed. The environmental media include water, soil, sediment, sludge, solid waste, air, dust, and a variety of biota (plants and animals). Consumer products and food will be discussed in greater detail within each exposure scenario section presented in Section 5.0 of this report. The literature from which the concentration data were extracted represents a variety of countries around the world with concentration data dated as far back as 1971.

Some assumptions were necessary prior to converting concentration data points into uniform units within each media type. First, data that were not identified as estimated values were assumed to be measured values and second, data not identified as either a minimum, median or mean value were treated as maximum values. Concentrations were reported from the U.S, Canada, the EU, and some in Asia. The remaining concentrations collected from other known countries were categorized as "Other" and the rest were categorized as "Unknown." Unknown does not necessarily mean that data were collected from an unknown location, rather, the location of the data point was not recorded when the value was extracted from the literature.

Next, all concentrations were manually entered in a spreadsheet (Microsoft Excel®) along with other details that included phthalate type, media, location, and source. Such spreadsheets were created for all the six phthalates that were identified in all media categories (environment, biota, food and consumer products). Finally, all the data was transferred to a relational database (Microsoft Access®) such that the entire data could be queried to generate specific and valuable information about the interactions of phthalates with the environment and consumer products. For this report, we summarize the maximum concentrations reported in the literature of each of the six phthalates within each specific media category. Maximums were selected as a representation of the relative magnitude of these chemicals in various media to which humans may be exposed. However, the phthalate database that has been created for this report can be used to generate a wide spectrum of summary statistics about phthalates. Some examples are (1) statistical measures (standard deviations, percentiles, and ranges) of maximum concentrations; (2) range of concentrations (minimum, maximum, mean, and average) for specific phthalate-media combinations; and (3) graphical representations (box plots, histograms, graphs, and other charts) of concentrations.

4.1. ENVIRONMENTAL MEDIA CONCENTRATIONS

A total of 53 documents were reviewed for environmental concentration data with a little more than 1,300 values extracted from the literature and then converted (if required) in order to compare maximum concentrations found for each media type. The majority of the environmental concentration data were retrieved from European and North American literature.

4.1.1. Water

Water media were categorized as surface water, groundwater/ leachates, drinking water, precipitation/storm water runoff, and wastewater. DIDP was the only phthalate of interest not detected in any of the water media. Of all the water media concentrations reviewed, wastewater effluents contained the highest detected phthalate concentration. Table 4.1-1 provides a summary of the maximum measured and estimated phthalate concentrations found in each of the water media.

Surface water samples were collected from various estuaries, streams, rivers, and bays near industrial, agricultural, and urban areas all over the world. BBP, DBP, and DEHP were all detected in surface waters with DBP having the highest measured concentration at 4.80 mg/L from estuaries in the United Kingdom (U.K.) (HSDB DBP, 2008). The EU estimated a DINP concentration of 0.0074 mg/L in local European surface waters near paint processing facilities (ECB DINP, 2003).

Table 4.1-1. Maximum Phthalate Concentrations Found in Water Media

Phthalate	Water Media Category	Maximum Concentration	Units	Location[a]	Reference
BBP	Surface water	0.0139	mg/L	Unknown	ECB BBP, 2008
DBP		4.80	mg/L	EU	HSDB DBP, 2008
DEHP		0.560	mg/L	Unknown	ECB DEHP, 2008
DINP[2]		0.0074	mg/L	EU	ECB DINP, 2003
DnOP		0.15	mg/L	U.S.	HSDB DnOP, 2009
BBP	Groundwater/Leachate	0.091	mg/L	U.S.	HSDB BBP, 2009
DBP		0.035	mg/L	Unknown	HSDB DBP, 2009
DEHP		0.51	mg/L	Unknown	ECB DEHP, 2008
DnOP[b]		0.0024	mg/L	U.S.	HSDB DnOP, 2009
BBP	Drinking water	0.038	mg/L	U.S.	HSDB BBP, 2009
DBP		0.47	mg/L	U.S.	HSDB DBP, 2009
DEHP		0.17	mg/L	U.S.	HSDB DEHP, 2009
DnOP		0.0005	mg/L	Unknown	NTP-CERHR DnOP, 2003
BBP	Precipitation/Storm water runoff	0.13	mg/L	U.S.	HSDB BBP, 2009
DBP		1.03	mg/L	Unknown	HSDB DBP, 2009
DEHP		0.00982	mg/L	Unknown	HSDB DEHP, 2009
DnOP		1.30×10^{-5}	mg/L	U.S.	HSDB DnOP, 2009
BBP	Wastewater - Influent	0.56	mg/L	Unknown	ECB BBP, 2007
DBP		0.20	mg/L	Unknown	ECB DBP, 2003-04
DEHP		1.80	mg/L	Unknown	ECB DEHP, 2008
BBP	Wastewater – Effluent	344	mg/L	Unknown	HSDB BBP, 2009
DBP		0.428	mg/L	Unknown	HSDB DBP, 2009
DEHP		3000	mg/L	U.S.	HSDB DEHP, 2009
DnOP		1090	mg/L	EU	HSDB DnOP, 2009

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Estimated value.

BBP, DBP, and DEHP were detected in groundwater/leachate samples with DEHP having the highest concentration at 0.51 mg/L measured after an application of sewage treatment plant sludge was applied to agricultural soil (ECB DEHP, 2008). HSDB reported an estimated DnOP concentration of 0.0024 mg/L for groundwater from a landfill well in Oklahoma, U.S. (HSDB DnOP, 2008).

BBP, DBP, DEHP and DnOP were all detected in drinking water samples with DBP having the highest measured concentration at 0.47 mg/L from New York, U.S. (HSDB DBP, 2008).

BBP, DBP, DEHP and DnOP were detected in precipitation/runoff samples which were collected from rain, snow and storm water runoff sampling. The highest phthalate concentration was DBP at 1.03 mg/L in storm water runoff from domestic sewers (HSDB DBP, 2008). The location of the sewers was not reported.

Wastewater influent and effluent samples contained BBP, DBP, DEHP and DnOP with DEHP having the highest concentration in both influent and effluent samples at 1.80 mg/L (ECB DEHP, 2008) and 3,000 mg/L (HSDB DEHP, 2008), respectively. The DEHP concentration in the wastewater effluent was located at a hazardous waste site in Louisiana, U.S.

4.1.2. Soil/Sediments/Sludge/Solid Waste

Soil, sediment, suspended matter, sludge, and solid waste concentrations were collected for all six phthalates of interest. Of the environmental media listed here, DEHP was detected at the highest concentration in sludge. Table 4.1-2 provides a summary of the maximum measured and estimated phthalate concentrations found in each of the media.

Soil samples were collected from agricultural plots, plots after sludge applications, plots after the use of artificial fertilizer, meadows receiving runoff from sludge storage, and plots near phthalate emitting plant sites in the U.S., Canada, and the EU. BBP, DBP, and DEHP were all detected in soil with DBP having the highest measured concentration at 10,600 mg/kg from an abandoned strip mine in Pennsylvania (HSDB DBP, 2008). The HSDB did not provide any information concerning the source of this phthalate at this location. The EU (ECB DINP, 2003) estimated a DINP concentration of 10 mg/kg in local European soils.

River sediments from the U.S. and EU were analyzed and BBP, DBP, DIDP, DEHP, and DnOP were all detected with DBP having the highest measured concentration at 2,100 mg/kg in a sediment sample from a river in the Netherlands (HSDB DBP, 2008). The highest concentration in suspended matter was DEHP at 282 mg/kg (ECB DEHP, 2008).

Sludge samples were collected from sewage treatment plants, household wastewater treatment plants, and industrial/municipal wastewater treatment plants primarily from the EU and Canada. BBP, DBP, DEHP and DINP were detected in the sludge samples. The maximum measured phthalate concentration in sludge was DEHP at 58,300 mg/kg in the U.S. (NTP-CERHR DEHP, 2006).

Solid waste samples included incinerator refuse, household waste, and compost. Of the solid waste data found in the literature reviewed for this effort, only DBP and DEHP were detected. The maximum measured phthalate detected in solid waste was DBP at 1,470 mg/kg found in household waste (HSDB DBP, 2008). The EU (ECB DEHP, 2008) provided both measured and estimated maximum concentrations of 139 mg/kg in compost and 0.07 mg/kg for generic waste incineration.

Table 4.1-2. Maximum Phthalate Concentrations Found in Soil, Sediment, Sludge and Solid Waste Media

Phthalate	Media Subcategory	Maximum Concentration	Units	Location[a]	Reference
BBP	Soil	0.94	mg/kg	EU	HSDB BBP, 2009
DBP		10,600	mg/kg	US	HSDB DBP, 2009
DEHP		55	mg/kg	US	HSDB DEHP, 2009
DINP[2]		10	mg/kg	EU	ECB DINP, 2003
BBP	Sediment	190	mg/kg	Unknown	ECB BBP, 2007
DBP		2,100	mg/kg	EU	HSDB DBP, 2009
DEHP		1,480	mg/kg	Unknown	ECB DEHP, 2008
DIDP		6.16	mg/kg	Unknown	ECB DIDP, 2003
DnOP		25.0	mg/kg	US	HSDB DnOP, 2009
BBP	Suspended matter	0.003	mg/kg	Unknown	ECB BBP, 2007
DEHP		282	mg/kg	Unknown	ECB DEHP, 2008
BBP	Sludge	210	mg/kg	Unknown	ECB BBP, 2007
DBP		100	mg/kg	Unknown	ECB DBP, 2003-04
DEHP		58,300	mg/kg	US	NTP-CERHR DEHP, 2006
DINP		72.0	mg/kg	EU	ECB DINP, 2003
DBP	Solid waste	1,470	mg/kg	Unknown	HSDB DBP, 2009
DEHP		139	mg/kg	Unknown	ECB DEHP, 2008
DEHP[b]		0.070	mg/kg	EU	ECB DEHP, 2008

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Estimated value.

4.1.3. Air/Dust/Indoor Surfaces

Atmospheric and dust-related samples were collected for each phthalate of interest. The atmospheric data included outdoor and indoor air concentrations. Dust-related samples included dust samples taken from floor surfaces and collected from vacuum cleaners. Concentrations from indoor surface wipes were also summarized to represent phthalate concentrations available for transfer from surfaces which can collect dust. DIDP was the only phthalate of interest not detected in any of the air, dust, or interior surface media. Table 4.1-3 provides a summary of the maximum measured and estimated phthalate concentrations found in indoor/outdoor air, dust, and indoor surface media.

Table 4.1-3. Maximum Phthalate Concentrations Found in Air, Dust and Indoor Surface Media

Phthalate	Media Subcategory	Maximum Concentration	Units	Location[a]	Reference
BBP	Outdoor air	0.63	mg/m^3	US	Adibi et al., 2003
DBP		14.8		EU	Adibi et al., 2003
DEHP		1.08		EU	Adibi et al., 2003
DINP		0.000462		EU	HSDB DINP, 2009
DINP[b]		0.00050		EU	ECB DINP, 2003
DnOP		$2.00x10^{-6}$		EU	HSDB DnOP, 2009
BBP	Indoor air	0.000465	mg/m^3	EU	HSDB BBP, 2009
DBP		0.00618		Asian	Otake et al., 2004
DEHP		0.00313		Asian	Otake et al., 2004
DEHP[b]		0.021		N/A	ECB DEHP, 2008
DINP		0.00066		Unknown	ECB DINP, 2003
BBP	Dust	319	mg/kg	EU	Bornehag et al., 2004
DBP		678		EU	HSDB DBP, 2009
DEHP		1,760		EU	NTP-CERHR DEHP, 2006
DINP		639		EU	Bornehag et al., 2004
DnOP		40.0		EU	NTP-CERHR DnOP, 2003
BBP	Indoor surfaces	1.33	mg/wipe	US	Wilson et al., 2003
DBP		0.605		US	Wilson et al., 2003

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Estimated value.

Air samples were collected from locations all over the world with most of the monitoring occurring in the U.S. BBP, DBP, DEHP, DINP, and DnOP were all detected in air samples. The highest measured concentration of phthalate in outdoor air was DBP at 14.8 milligrams per cubic meter (mg/m^3) collected in Krakow, Poland, for a prenatal exposure study (Adibi et al., 2003). The maximum estimated outdoor air concentration was provided by the EU (ECB DINP, 2003), which estimated an outdoor air concentration of DINP at 0.0005 mg/m^3. The highest measured concentration of phthalate in indoor air was DBP at 0.00618 mg/m^3 (Otake et al., 2004) reported in a study of 27 homes in Tokyo, Japan. The maximum estimated DEHP indoor air concentration was provided by the ECB DEHP (2008) at 0.021 mg/m^3.

Dust samples were collected from office buildings, residences, daycare centers, and directly from a vacuum cleaner. Concentrations were primarily from countries within the EU. BBP, DBP, DEHP, DINP, and DnOP were all detected in the dust samples. In effort to compare dust concentrations, when only mean and/or median values were provided in a document without a maximum concentration, the larger of the two values was treated as the maximum concentration. The highest measured concentration of phthalate in dust was DEHP at 1,760 mg/kg from

samples collected at 59 apartments in Berlin, Germany (NTP-CERHR DEHP, 2006). There were no estimated phthalate concentrations for dust. Two documents, in particular, provided phthalate concentrations in dust found in environments where children are most likely to be exposed (bedroom and day care center) (Bornehag et al., 2004, and EPA, 2008). According to these documents, the maximum measured concentrations of BBP, DEHP, and DINP found in dust from children's bedrooms in Europe were 319 mg/kg, 1,310 mg/kg, and 639 mg/kg, respectively. The maximum measured concentration of DBP was 678 mg/kg found in dust collected from a day care center in the U.S. (EPA, 2008).

Two documents provided measured phthalate concentrations from indoor surface wipes of homes and day care centers in the U.S. (Wilson et al., 2003, and EPA, 2008). BBP and DBP were the only phthalates of interest detected in the surface wipe samples. The maximum BBP concentration was 1.33 mg/wipe and the maximum DBP concentration was 0.61 mg/wipe (Wilson et al., 2003).

4.1.4. Biota

Phthalate concentrations were measured in biota were categorized as animals, birds, crops, fish, and shellfish. An "Others" category was created to include biota not covered in the other biota categories. DnOP was not reported in any of the collected biota concentration data. BBP, DBP, DEHP, DIDP, and DINP concentrations were found in one or more of the biota categories. Of the six biota categories, the one with the highest phthalate concentration was fish. Although, concentrations of phthalates in biota were measured from all over the world, the exact sampling locations for most of the data are not known. For the sampling locations which were recorded, most of the data came from Canada and then the EU. There were no estimated phthalate concentrations for biota. Table 4.1-4 provides a summary of the maximum measured phthalate concentrations found in each of the biota categories.

Animal samples consisted of seal, non-processed meats in general, cow heart, dog heart, rabbit heart, and rat heart. BBP, DBP, and DEHP were detected in the animal samples. The highest measured concentration of phthalate in animals was DEHP at 16 mg/kg in seal pup blubber from Canada (HSDB DEHP, 2008).

Bird samples consisted of surf scoters, gulls, and poultry. BBP, DBP, DEHP, DIDP, and DINP were detected in the bird samples. The highest measured concentration of phthalate in birds was DBP at 19 mg/kg in herring gulls (HSDB DBP, 2008). The location of the gulls was not provided in the HSDB report.

Crop samples consisted of fruit, grains, nuts, beans, and vegetables. BBP, DBP, and DEHP were detected in the crop samples. The highest measured concentration of phthalate in crops was DBP at >50 mg/kg in carrots from the St. David Coal Refuse Pile Reclamation site in the state of Illinois (U.S.) (HSDB DBP, 2008).

Table 4.1-4. Maximum Phthalate Concentrations Found in Biota

Phthalate	Biota Subcategory	Maximum Concentration	Units	Location[a]	Reference
BBP	Animals	0.13	mg/kg	Unknown	HSDB BBP, 2009
DBP		4.4	mg/kg	EU	ATSDR, 2001
DEHP		16.0	mg/kg	Unknown	HSDB DEHP, 2009
BBP	Birds	0.04	mg/kg	Unknown	HSDB BBP, 2009
DBP		19.0	mg/kg	Unknown	HSDB DBP, 2009
DEHP		2.6	mg/kg	Unknown	NTP-CERHR DEHP, 2006
DIDP		0.00315	mg/kg	Unknown	HSDB DIDP, 2009
DINP		0.00241	mg/kg	Canada	HSDB DINP, 2009
BBP	Crops	0.005	mg/kg	Unknown	HSDB BBP, 2009
DBP		50.0	mg/kg	Unknown	HSDB DBP, 2009
DEHP		2.2	mg/kg	Unknown	NTP-CERHR DEHP, 2006
BBP	Fish	0.71	mg/kg	U.S.	HSDB BBP, 2009
DBP		35.0	mg/kg	Unknown	HSDB DBP, 2009
DEHP		8060	mg/kg	Other	HSDB DEHP, 2009
DIDP		0.00414	mg/kg	Unknown	HSDB DIDP, 2009
DINP		0.00289	mg/kg	Canada	HSDB DINP, 2009
BBP	Shellfish	0.022	mg/kg	Unknown	ECB BBP, 2007
DBP		0.10	mg/kg	Unknown	HSDB DBP, 2009
DEHP		4.30	mg/kg	EU	ECB DINP, 2003
DIDP		0.00339	mg/kg	Unknown	HSDB DIDP, 2009
DINP		0.81	mg/kg	Unknown	ECB DINP, 2003
BBP	Other[b]	0.063	mg/kg	Unknown	ECB BBP, 2007
DBP		0.80	mg/kg	Unknown	ECB DBP, 2003-04
DEHP		63.0	mg/kg	Asian	ECB DINP, 2003
DIDP		3.87E-03	mg/kg	Unknown	HSDB DIDP, 2009
DINP		0.10	mg/kg	Unknown	ECB DINP, 2003

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Biota in the "Other" category include aquatic invertebrates and plankton.

Fish samples consisted of general fish and a large variety of different fish species from Asia, Canada, the EU, and the U.S., predominantly. BBP, DBP, DEHP, DIDP, and DINP were detected in the fish samples. The highest measured concentration of phthalate in fish was DEHP at 8,060 mg/kg in various fish from Mexico (HSDB DEHP, 2008).

Shellfish samples consisted of different crab, clam, mussel and oyster species from Canada and the EU, predominantly. BBP, DBP, DEHP, DIDP, and DINP were detected in the shellfish samples. The highest measured concentration of phthalate in shellfish was DEHP at 4.3 mg/kg in various river mollusks from the Elbe River in Germany (ECB DINP, 2003).

The last biota category included all biota media not covered in the previously discussed biota categories. Examples of biota included in the "Other" biota category were aquatic invertebrates, plankton, aquatic plants, lichen, and terrestrial invertebrates. BBP, DBP, DEHP, DIDP, and DINP were detected in the "Other" biota samples. The highest measured concentration of phthalate in the "Other" biota category was DEHP at 63 mg/kg in plankton collected from industrialized areas in Japan (ECB DINP, 2003).

4.2. CONSUMER PRODUCT RESIDUE CONCENTRATIONS

This report discusses nine different consumer product related exposure scenarios. Approximately 150 documents were reviewed for consumer product residue concentrations resulting in a little more than 340 values extracted and converted (if required) in order to compare maximum concentrations for each product type. Little to no residue concentration data were found for some of the consumer product categories. The consumer product category containing the most phthalate concentration data was Toys and Baby Equipment The majority of the consumer products residue concentration data were retrieved from Asian, European, and North American literature. Residue concentration values provided in this section were for products in general. Specific product manufacturers and brand names were not considered for this report.

4.2.1. Scenario 1: Children's Toys and Baby Equipment

This section covers concentrations of phthalates found in children's toys and baby equipment which have been defined in Subsection 108(e) of CPSIA. Children's toys are defined as "a consumer product designed or intended by the manufacturer for a child 12 years of age or younger for use by the child when the child plays." Toys are further defined as those items "that can be placed in a child's mouth"…"if any part of the toy can actually be brought to the mouth and kept in the mouth by a child so that it can be sucked and chewed. If the children's product can only be licked, it is not regarded as able to be placed in the mouth. If a toy or part of a toy in one dimension is smaller than 5 centimeters, it can be placed in the mouth." Child care articles are defined as "a consumer product designed or intended by the manufacturer to facilitate sleep or the feeding of children age 3 and younger, or to help such children with sucking or teething."

DEHP, DIDP, and DINP were found to be present historically in toys and teethers. BBP and DBP were also found to be present in these products, but only in trace amounts, probably as byproducts or impurities present during manufacture (Stringer et al., 2000). DnOP was found to be present in some children's toys, but at much lower concentrations than DEHP, DIDP, and DINP. Details for phthalate concentrations in children's toys and baby equipment are provided in Table 4.1-5.

The highest phthalate level for toys, 73% DINP, was found in a toy octopus during testing completed in 2008 by the California Department of Toxic Substances Control (CDTSC, 2008) (http://www.sfenvironment.org/our_programs/interests.html?ssi=2&ti=3&ii=135). The maximum DEHP concentration, 44%, was found in a toy from Europe (Bouma and Schakel, 2002). The maximum DIDP concentration, 20.1%, was found in a toy from Argentina (Stringer et al., 2000). Teethers were found to contain maximum phthalate concentrations of DEHP (22.4%, NTP–CERHR DEHP, 2000), DIDP (40%, CPSC, 2001) and DINP (40%, CPSC, 2001).

Table 4.1-5. Maximum Phthalate Concentrations Found in Children's Toys and Baby Equipment

Phthalate	Product Subcategory	Product Description	Maximum Concentration	Units	Location[a]	Reference
BBP	Toys and Baby Equipment	Toys	0.02	%	Asia	Stringer et al., 2000
DBP			0.18	%	EU	Stringer et al., 2000
DEHP			44.0	%	EU	Bouma et al., 2002
DIDP			20.1	%	Other	Stringer et al., 2000
DINP			73.0	%	U.S.	SFED, 2008
DnOP			6.70	%	U.S.	SFED, 2008
DEHP	Toys and Baby Equipment	Teethers	22.4	%	Unknown	NTP-CERHR DEHP, 2000
DIDP			10.1	%	Unknown	NTP-CERHR DIDP, 2003
DINP			40.0	%	Unknown	HSDB DINP, 2009

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.

4.2.2. Scenario 2: Medical Devices

Phthalates are used in a wide variety of medical devices. These devices include various types of tubing, storage bags, catheters, syringes and examination gloves. After reviewing the literature, it was evident that there is very little phthalate concentration data reported for medical devices. There were three documents that addressed medical devices specifically. The first was a U.S. Food and Drug Administration (FDA) (FDA, 2001) report measuring the migration of DEHP from PVC intravenous bags to the contents of the bags which contained drug solutions, frozen plasma, platelet concentrate, and red blood cells. These results are discussed in Section 5.4.2. The report also provided a maximum DEHP air concentration value of 21,200 mg/m^3 for air passing through PVC respirator tubing. The second article, by Sathyanarayana (2008), reported that PVC-containing medical devices may contain up to 40% DEHP by weight. This was reiterated in the third report by Health Canada (2002), where they reported that PVC-based medical devices generally contain a maximum of 40% DEHP by weight and that for a 500 mL blood bag, this would represent approximately 10 g of DEHP.

4.2.3. Scenario 3: Personal Care Products

BBP, DBP, DEHP, DIDP, and DINP concentrations were found in personal care products. Personal care products included cosmetics, deodorant, hair products, nail products, and perfume. Of the products reviewed, the personal care products with the highest phthalate concentrations were nail care products and perfume. Products with the highest concentrations found in the literature were predominantly from Europe and Asia. Table 4.1-6 provides a summary of the maximum measured phthalate concentrations found in each type of personal care product.

Cosmetics were found to contain DBP. Wormuth et al. (2006) reported a maximum DBP concentration of 10,000 mg/kg for cosmetics and, according to the ASTDR (2001), cosmetics contain up to 25% DBP. All of the deodorants mentioned in the literature contained DBP and

DEHP. The highest reported phthalate concentration in deodorants was DBP at 200 mg/kg (Wormuth et al., 2006).

Table 4.1-6. Maximum Phthalate Concentrations Found in Personal Care Products

Phthalate	Product Subcategory	Product Description	Maximum Concentration	Units	Location[a]	Reference
DBP	Cosmetics	General	25	%	N/A	ATSDR, 2001
DBP			10,000	mg/kg	EU	Wormuth et al., 2006
DBP	Deodorants	General	200	mg/kg	EU	Wormuth et al., 2006
DEHP			8.60		EU	Wormuth et al., 2006
DBP	Hair products	Hair styling products	160	mg/kg	EU	Wormuth et al., 2006
DEHP			41.0		EU	Wormuth et al., 2006
BBP		Hair spray	43.0	mg/kg	U.S.	Hubinger and Havery, 2006
DBP			54.0		U.S.	Hubinger and Havery, 2006
DBP		Shampoo	70.0	mg/kg	EU	Wormuth et al., 2006
DBP	Nail care products	General	150,000	mg/kg	EU	Wormuth et al., 2006
BBP		Enamels	107	mg/kg	U.S.	Hubinger and Havery, 2006
DBP			59,800		U.S.	Hubinger and Havery, 2006
DBP		Nail polish	3,900	mg/L	Asia	Koo and Lee, 2004
DEHP			25.1		Asia	NTP-CERHR DEHP, 2006
BBP	Perfumes	General	62.8	mg/L	Asia	Koo and Lee, 2004
DBP			5,050		Asia	Koo and Lee, 2004
DEHP			18.3		Asia	Koo and Lee, 2004
BBP			29.0	mg/kg	EU	Wormuth et al., 2006
DBP			890		EU	Wormuth et al., 2006
DEHP			130		EU	Wormuth et al., 2006

a. Data locations include U.S., EU countries; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.

Hair products include hair styling products, hairspray, and shampoos. The Wormuth et al. (2006) study reported maximum concentrations for general hair styling products and shampoos. Hair styling products were reported to contain both DBP and DEHP with the DBP having the highest concentration at 160 mg/kg. The shampoos contained DBP at a maximum concentration of 70.0 mg/kg (Wormuth et al., 2006). The Hubinger and Havery (2006) study reported that hairspray contained BBP and DBP. The highest concentration of phthalates in hairspray was DBP at 54.0 mg/kg.

Nail care products include nail enamels and nail polishes. Nail care products from the literature contained BBP, DBP, and DEHP. According to Wormuth et al. (2006), nail care products in general contain a maximum DBP concentration of 150,000 mg/kg. The highest phthalate concentration reported in the literature for nail enamel was DBP at 59,800 mg/kg (Hubinger and Havery, 2006) and the highest phthalate concentration in nail polish was 3,900 mg/L for DBP (Koo and Lee, 2004). Perfumes contained BBP, DBP, and DEHP. The maximum phthalate concentration found in perfumes was for DBP at 5,050 mg/L (Koo and Lee, 2004).

4.2.4. Scenario 4: Clothing, Gloves and Footwear

Phthalates can be found in clothing, gloves and footwear. After reviewing the literature, however, it was evident that there is very little phthalate concentration data reported for these items. The only clothing items found with phthalate concentration data were disposable diapers, plastic gloves, and boots for a Halloween costume. Disposable diapers were reported to contain a maximum DEHP concentration of 74.1 mg/kg (ATSDR DEHP, 2002). Gloves were found to contain BBP, DEHP, DIDP, and DINP. The highest phthalate concentration in gloves was DINP at 429,000 mg/kg (Wormuth et al., 2006). The maximum reported BBP, DEHP, and DIDP concentrations in gloves were 33,000 mg/kg, 420,000 mg/kg, and 171,000 mg/kg, respectively. The California Department of Toxic Substances Control (CDTSC, 2008) in partnership with the California State government conducted children product testing and found a maximum DnOP concentration of 6.7%, in the boots for a child's Halloween costume. DEHP was detected in textile fabrics. A maximum DEHP concentration of 8 mg/kg was reported for a variety of textiles which included cotton, wool, flax, polyethylene terephthalate (PET), and viscose (Jensen and Knudsen, 2006).

4.2.5 Scenario 5: Cars and Related Products

The literature reviewed indicated that there were limited concentrations of phthalates reported in cars and car related products. Fujii et al. (2003) estimated very high concentrations of phthalates from vehicle emission test chambers. They estimated a DBP concentration of 7,700 mg/m^3 and a DEHP concentration of $2.0x10^6$ mg/m^3 based on their tests. In contrast, DINP was detected at a very low concentration of $2.00x10^{-5}$ mg/m^3 based on the ECB report (ECB DINP, 2003). Besides car interiors, phthalates were also detected in wastewater from car washes and disposable wastes from cars. The EU Risk Assessment on BBP (ECB BBP, 2007) reported a BBP concentration of 0.15 mg/L from car wash wastewater. Additionally, the ECB report on DEHP, (ECB DEHP, 2008) reported a DEHP concentration of 0.07 mg/m^3 from waste volume collected from car shredders. Details of all phthalate concentrations detected in cars and related products are shown in Table 4.1-7.

Table 4.1-7. Maximum Phthalate Concentrations Found in Cars and Related Products

Phthalate	Product Subcategory	Product Description	Maximum Concentration	Units	Location[a]	Reference
DBP	Car	Interior air	7,700	mg/m^3	Unknown	Fujii et al., 2004
DEHP			$2.00x10^6$		Unknown	Fujii et al., 2004
DINP			$2.00x10^{-5}$		Unknown	ECB DINP, 2003
DEHP	Car	Solid shredder waste	0.07	mg/m^3	Unknown	ECB DEHP, 2008
BBP	Car	Car wash effluent	0.15	mg/L	Unknown	ECB BBP, 2007

a. Data locations include U.S., E.U. countries; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.

4.2.6 Scenario 6: Building Materials

This section of consumer products discusses phthalate concentrations in building materials. Items identified as building materials include floorings, paint, PVC-coated wall paper, adhesives, glues and other sealing compounds. In general, all six phthalates were detected at relatively high concentrations in various building materials from studies conducted mainly in European countries (ECB DINP, 2003; Clausen et al., 2004; NTP-CERHR DnOP, 2003). BBP had the highest concentration of 67,900 mg/kg for paints. Both DEHP and DBP had relatively high concentrations within this sub-group, at 18,200 mg/kg and 10,000 mg/kg, respectively. All concentrations for this sub-group were obtained from the study conducted by Wormuth et al. (2006). Details of all phthalate concentrations detected in building materials are shown in Table 4.1-8.

This study also indicated that within adhesives, glues, and sealants, all phthalates except DnOP had a consistent concentration of 55,000 mg/kg. It should be noted here that the authors of the study conducted by Wormuth et al. (2006) mention that their estimates were worst case scenarios and these numbers were used in models to calculate exposure estimates for phthalates. Fujii et al. (2003) estimated concentrations of DBP (5,100 mg/m^3) and DEHP (940 mg/m^3) in PVC-coated wall paper based on emission test chambers. This study was conducted to determine the emissions of phthalates from surfaces over time. A passive-type sampler was used to measure phthalate fluxes over time.

Table 4.1-8. Maximum Phthalate Concentrations Found in Building Materials

Phthalate	Product Subcategory	Product Description	Maximum Conc.	Units	Location[a]	Reference
BBP	Building materials	Paints	55,000	mg/kg	EU	Wormuth et al., 2006
DBP			55,000	mg/kg	EU	Wormuth et al., 2006
DEHP			55,000	mg/kg	EU	Wormuth et al., 2006
DIDP			55,000	mg/kg	EU	Wormuth et al., 2006
DINP			55,000	mg/kg	EU	Wormuth et al., 2006
BBP	Building materials	Adhesives, glues and sealing compounds	67,900	mg/kg	Europe	Wormuth et al., 2006
DBP			10,000	mg/kg	Europe	Wormuth et al., 2006
DEHP			18,200	mg/kg	Europe	Wormuth et al., 2006
DIDP			3,030	mg/kg	Europe	Wormuth et al., 2006
DINP			5,460	mg/kg	Europe	Wormuth et al., 2006
DBP	Building materials	PVC-coated wall paper[2]	5,100	mg/m^3	Unknown	Fujii et al., 2003
DEHP			940	mg/m^3	Unknown	Fujii et al., 2003
DEHP[b, c]	Building materials	Flooring	2.30	mg	Unknown	Clausen et al., 2004
DnOP			0.08	mg/kg	EU	NTP-CERHR DnOP, 2003

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Values represent interior air concentrations from test chamber with PVC-coated wall paper.
c. Estimated value.

The phthalate concentrations in floorings were much lower than the other sub-groups. Only DEHP and DnOP were detected. Clausen et al. (2004) reported that about 2.3 mg of DEHP was sorbed in floorings based on laboratory tests. Finally, DnOP was detected at a concentration of 0.08 mg/kg in floorings in Germany (NTP-CERHR DnOP, 2003).

4.2.7. Scenario 7: Pharmaceuticals

Many site-specific dosage medications have enteric coatings which generally consist of various polymers that contain plasticizers, including phthalates such as DBP (Hauser et al., 2004). Studies have been conducted to measure urinary concentrations of metabolites of the phthalate diesters that might be present as inactive ingredients in the medications. These studies (Hauser et al., 2004 and Hernández-Díaz et al., 2009) do not, however, provide phthalate concentrations for the medications taken prior to the collection of urine samples. Therefore, there are no phthalate concentration data points available at this time to report. The results from these studies are discussed in more detail in Section 5.0 of this report.

4.2.8. Scenario 8: Adult Toys and Gels

Two surveys were conducted by the DEPA to investigate the presence of chemicals, including phthalates, in adult toys and pleasure gels (Nilsson et al., 2006; Tønnig et al., 2006). Nilsson et al. (2006) measured DEHP, DINP and DnOP concentrations in 15 different sex toys made of soft vinyl, natural latex, rubber, and thermoplastic rubber. DEHP was detected in 8 of the 15 samples with a maximum concentration at 702,000 mg/kg. DINP and DnOP were detected in two samples each at maximum concentrations at 600,000 mg/kg and 239,000 mg/kg, respectively. Migration testing was also performed in this study and the results are discussed in Section 5.4.9.

Tønnig et al. (2006) conducted a survey and health assessment of chemicals substances in adult pleasure gels for the Danish Ministry of the Environment. As part of the study 15 gels and 7 massage oils/creams were screened to identify the content of organic substances in the products. None of the six phthalates of interest were identified in the samples.

4.2.9. Scenario 9: Other Products

Products not covered in the above scenarios are placed under the "Other" Products scenario. Examples of products in this category include modeling clay/ceramics, a variety of different air fresheners, and stain removers. Air fresheners and modeling clay represent the largest set of data in this category. Table 4.1-9 provides a summary of the maximum measured and estimated phthalate concentrations for each of these products.

The product with the highest phthalate concentration was polymer modeling clay with DnOP at 97,500 mg/kg (Stopford et al., 2003). Polymer modeling clay also contains BBP at a maximum concentration of 39,800 mg/kg. Schettler (2006) measured BBP, DEHP, and DnOP concentrations in indoor air after baking polymer modeling clay. The highest phthalate concentration detected these indoor air samples was DnOP at 6.67×10^6 mg/m^3. The EU (ECB DEHP, 2008) estimated a DEHP concentration of 0.55 mg/kg released to soil when formulating ceramics.

Table 4.1-9. Maximum Phthalate Concentrations Found in "Other" Products

Phthalate	Product Subcategory	Product Description	Maximum Concentration	Units	Location[a]	Reference
BBP	Modeling clay	Indoor air during baking process	$2.67x10^6$	mg/m^3	Unknown	Schettler, 2006
DEHP		Indoor air during baking process	$4.99x10^6$	mg/m^3	Unknown	Schettler, 2006
DnOP		Indoor air during baking process	$6.67x10^6$	mg/m^3	Unknown	Schettler, 2006
BBP		Polymer modeling clay	39,800	mg/kg	US	Stopford et al., 2003
DnOP		Polymer modeling clay	97,500	mg/kg	US	Stopford et al., 2003
DEHP[2]	Ceramics	Release to soil during formulation	0.55	mg/kg	N/A	ECB DEHP, 2008
DBP	Air freshener	General	4.50	mg/kg	Unknown	Federal Register, 2007
DEHP		Air sprays - indoor air	571,000	mg/m^3	EU	SCHER, 2006
DEHP		Electric diffusers (air fresheners)	7,000	mg/m^3	EU	SCHER, 2006
DEHP		Gel - indoor air	19,000	mg/m^3	EU	SCHER, 2006
DEHP		Incense - indoor air	$1.25x10^6$	mg/m^3	EU	SCHER, 2006
DEHP		Liquid - indoor air	67,000	mg/m^3	EU	SCHER, 2006
DEHP		Scented candles - indoor air	15,000	mg/m^3	EU	SCHER, 2006
DBP[b]	Stain remover	Stain remover - indoor air	22,500	mg/m^3	N/A	Jensen and Knudsen, 2006

a. Data locations include U.S., EU; countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.
b. Estimated value.

The indoor air surrounding a variety of air fresheners was analyzed to determine DEHP concentrations (SCHER, 2006). These different types of air fresheners include air sprays, electric diffusers, gels, incense, liquid fresheners, and scented candles. The air freshener with the highest DEHP air concentration was incense at $1.25x10^6$ mg/m^3. According to a TSCA Section 21 petition letter, a Natural Resources Defense Council (NRDC) study reported that air fresheners contain up to 0.55 mg/kg DEHP. Jensen and Knudsen (2006) from the Danish EPA estimated a DBP air concentration when using stain removers at 22,500 mg/m^3.

4.3. FOOD AND FOOD RELATED PRODUCTS

This section discusses the concentrations of phthalates found in food and food-related products which include beverages, food, food packaging, and utensils used for food consumption. All six phthalates were present in beverages that included milk and alcohol. The HSDB DEHP (2009) report contained the highest concentration among beverages: 80 mg/L in milk. Details of phthalate concentrations in food and food related products are shown in Table 4.1-10.

Table 4.1-10. Maximum Phthalate Concentrations Found in Food and Related Products

Phthalate	Food Subcategory	Detailed Description	Maximum Concentration	Units	Location[a]	Reference
BBP	Beverages	Beverages	0.04	mg/kg	Unknown	HSDB BBP, 2009
DBP		Vodka	0.25	mg/kg	Unknown	ECB DBP, 2003-04
DEHP		Milk	80.0	mg/L	Unknown	HSDB DEHP, 2009
DIDP		Raw milk	0.01	mg/kg	Unknown	Sorensen, 2006
DINP		Raw milk	0.01	mg/kg	Unknown	Sorensen, 2006
DnOP		Milk	2.30	mg/kg	Unknown	NTP-CERHR DnOP, 2003
BBP	Food	Butter	47.8	mg/kg	Unknown	ECB BBP, 2007
DBP		Gravy granules and parmesan cheese	62.0	mg/kg	EU	ATSDR, 2001
DEHP		Cheese	114	mg/kg	Unknown	ECB DINP, 2003
DIDP		Garlic in oil	173	mg/kg	EU	Pederson et al., 2008
DIDP		Pork	11.6	% w/w	Other	Freire et al., 2006
DINP		Peanut butter	99.0	mg/kg	EU	Pederson et al., 2008
DnOP		Infant formula	1.42	mg/kg	Unknown	NTP-CERHR DnOP, 2003
BBP	Food packaging	Heated (3 minute) lunch meal with contact with plastic wrap	0.28	mg/kg	Asia	Chen et al., 2008
DBP		Miscellaneous	5,860	mg/kg	EU	ATSDR, 2001
DEHP		Tempura (frying) powder packaging	3,680	mg/kg	Unknown	HSDB DEHP, 2009
DBP	Food utensils	Coffee filters	15.0	mg/kg	Unknown	HSDB DBP, 2009

a. Data locations include U.S., European countries (EU); countries other than Asia, Canada, U.S., and EU (Other), and Unknown for concentration values recorded without specifying a location.

The concentrations of all other phthalates are much lower than that of DEHP in milk. The concentrations of phthalates in food were considerably higher than those in beverages. Studies reviewed for this report had a variety of food items that included butter, cheese, oil, peanut butter, pork, and infant formula. Pederson et al. (2008) measured phthalate concentrations in various food products in glass jars with plastic gaskets in Denmark. They results indicated very high concentrations (DIDP at 173 mg/kg in garlic oil, and DINP at 99 mg/kg in peanut butter) and as a result, those food items were recalled from the market. In the ECB DINP, (2003) report, total phthalate concentration (expressed as DEHP) was estimated at 114 mg/kg for retail cheese. This estimate was based on a study conducted in three countries that included Norway, Spain, and the U.K.

Food packaging mainly includes plastic wraps and water containers. All phthalates except DIDP and DINP were detected in food packaging. ATSDR (2001) indicated a very high concentration

of DBP (5,860 mg/kg) in miscellaneous food packaging items. These included packaging for pudding, ice-lolly, waffles, eggs, and vegetable burger mix. The HSDB DEHP (2009) information showed concentration of 3,680 mg/kg for DEHP. Among food utensils, only DBP was detected at 15 mg/kg in coffee filters based on the HSDB DEHP report.

5. HUMAN EXPOSURE TO PHTHALATES

5.1. GENERAL OVERVIEW

The following subsections provide a summary of the literature review that was performed to characterize human exposure to phthalates. Section 5.2 summarizes information on biomonitoring of body fluids (e.g., urine, blood, breast milk) to measure the concentrations of phthalates, or phthalate metabolites, present in the human body due to exposure to phthalates. Section 5.3 summarizes information on occupational exposure to phthalates during production of phthalates, during manufacture of products that contain phthalates, and during industrial end use of products that contain phthalates.

Section 5.4 summarizes information on consumer exposure to products that contain phthalates for the following scenarios:

- Scenario 1: Toys and Baby Equipment
- Scenario 2: Medical Devices
- Scenario 3: Personal Care Products
- Scenario 4: Clothing, Gloves, and Footwear
- Scenario 5: Car and Public Transportation Interior
- Scenario 6: Building Materials and Furniture
- Scenario 7: Food and Food-Related Uses
- Scenario 8: Pharmaceuticals
- Scenario 9: Adult Toys and Pleasure Gels
- Scenario 10: Miscellaneous

Each scenario summarizes information on the concentration of phthalates contained in the various consumer products, descriptions of the situations that result in exposure to the consumer products, exposure estimates, and the approaches used by investigators to estimate exposure related to use of the products.

Section 5.5 summarizes information on exposure to the general population from phthalates present in the environment (e.g., air, water, soil). Section 5.6 summarizes reported cumulative exposures to phthalates calculated using two approaches (i.e., biomonitoring-based approach and the scenario-based approach). Section 5.7 summarizes information on exposure the available literature that addresses population groups with potential high exposures to phthalates (e.g., newborns, infants and children). Section 5.8 describes the uncertainty and data gaps found to exist in the exposure assessments for phthalates that were reviewed.

5.2. BIOMONITORING

Biomonitoring provides a direct measure of the amount of each phthalate or phthalate metabolite in the human body. The measured concentrations of the parent compounds or their metabolites in urine and other biomatrices, such as blood (including serum and plasma), human milk, saliva, and seminal fluids, are then used as biomarkers to assess human exposure based on the pharmacokinetics of individual phthalates (Calafat and McKee, 2006). (Data from other

biomatrices, e.g., feces, bile, and amniotic fluid, are more difficult to collect and do not lend themselves to a large sampling program, but may be useful in specific situations.) Biomarkers have the potential to integrate exposures to phthalates from all routes of exposure including oral, dermal, inhalation, and ingestion (Duty et al., 2003).

In the past 7 or 8 years, biomonitoring studies have focused on phthalate metabolites rather than the parent compounds (Kamrin, 2009). Generally, following exposure, phthalates are metabolized and excreted quickly (elimination half-life of 8-10 hrs in adults) and do not accumulate in the body (CDC, 2005; Hines et al., 2009). All phthalates are first metabolized to their hydrolytic monoesters (primary) and some phthalates can be further metabolized to their oxidative metabolites (secondary) (Hines et al., 2009). The tendency to form oxidative metabolites increases as the molecular weight of the phthalate increases. Depending on the respective phthalate, these metabolites are partially glucuronidated and excreted through urine and feces (Koch et al., 2003a). Table 5.2-1, below, presents the monoester metabolites and other oxidized metabolites of ten phthalates, including their commonly used abbreviations.

Traditionally, the hydrolytic monoesters have been measured because they are considered to be biologically active. However, the exclusive use of the hydrolytic monoester metabolites under represents exposure to high-molecular-weight phthalates (Hines et al., 2009). Recent studies have shown that the oxidative metabolites had a higher frequency of detection (e.g., 98% vs. 0%; Silva et al., 2006) and higher urinary concentrations, suggesting the oxidative metabolites are better biomarkers of exposure.

Since the choice of metabolite may have a significant influence on the exposure estimate, exposure values may vary significantly when they are based on different metabolites (Kamrin, 2009). Adding to the uncertainty is that conversion from body fluid concentrations to exposure levels is based on data collected from adults and it is not clear how applicable these data are to other age groups, especially infants and children. In addition, biomonitoring data indicate that there is significant variability in levels, and thus exposures, over time and among populations (Kamrin, 2009).

Other issues also exist with the use of biomonitoring data. Different researchers have used different factors to calculate the exposure levels that correspond to the measured phthalate concentrations (Kamrin, 2009). Researchers in the U.S. have selected factors that result in significantly lower exposure estimates for some phthalates, generally by a factor of about 5 for mean values, than those reported by researchers in Germany and Korea. However, there appears to be a closer agreement across countries of 95th percentile values than of the means. In addition to differences in exposure values due to different measurement approaches, exposures to some phthalates appear to be higher in Germany and Korea than in the U.S. (Kamrin, 2009).

Also influencing the biomonitoring data is the time of day at which measurements are made because certain activities (e.g., use of personal care products) tend to occur at a specific time during the day (Kamrin, 2009). In addition, collection of a single “spot” sample does not provide information on exposure over time in a particular individual or population.

Table 5.2-1. Phthalates and Their Metabolites

Phthalate Name (CAS number)	Abbreviation	Urinary Metabolite (CAS number)	Abbreviation
Dimethyl phthalate (131-11-3)	DMP	Mono-methyl phthalate (4376-18-5)	MMP*
Diethyl phthalate (84-66-2)	DEP	Mono-ethyl phthalate (2306-33-4)	MEP*
Dibutyl phthalate (84-74-2)	DBP	Mono-n-butyl phthalate (131-70-4)	MBP*
Diisobutyl phthalate (84-69-5)	DiBP	Mono-isobutyl phthalate	MiBP*
Benzylbutyl phthalate (85-68-7)	BBP	Mono-benzyl phthalate (2528-16-7)	MBzP*
		(some mono-n-butyl phthalate)	
Dicyclohexyl phthalate (84-61-7)	DCHP	Mono-cyclohexyl phthalate (7517-36-4)	MCHP*
Di-(2-ethylhexyl) phthalate (117-81-7)	DEHP	Mono-2-ethylhexyl phthalate (4376-20-9)	MEHP*
		Mono-(2-ethyl-5-oxohexyl) phthalate	MEOHP
		Mono-(2-ethyl-5-hydroxyhexyl) phthalate	MEHHP
		Mono-(2-carboxymethylhexyl) phthalate	MCMHP
		Mono-(2-ethyl-5-carboxypentyl) phthalate	MECPP
Di-n-octyl phthalate (117-84-0)	DnOP	Mono-n-octyl phthalate (5393-19-1)	MnOP*
		Mono-(3-carboxypropyl) phthalate	MCPP
Di-isononyl phthalate (28553-12-0)	DINP	Mono-isononyl phthalate	MiNP*
		MiNP with keto functional group Mono-(oxoisonyl) phthalate	MOiNP
		MiNP with hydroxy functional group Mono-(hydroxyisononyl) phthalate	MHiNP
		Mono-(carboxyisooctyl) phthalate	MCiOP
Di(isodecyl) phthalate (68515-49-1 and 26761-40-0)	DIDP	Mono-isodecyl phthalate	MiDP*
		Mono-(carboxyisononyl) phthalate	MCiNP
		Mono-(oxoisodecyl) phthalate	MOiDP
		Mono-(hydroxyisodecyl) phthalate	MHiDP

Sources: CDC, 2005; Fromme et al., 2007a; Silva et al., 2005; Silva et al., 2006; Silva et al., 2007.
*Primary (monoester) metabolite.

Use of a single matrix in a biomonitoring study (e.g., urine only) may also underestimate the phthalate exposure. Metabolism, excretion, and storage (for example, in bones or adipose tissue) of phthalates are determined by the pharmacokinetics of individual phthalates. For example, DEHP is seldom found in urine or blood except as a result of contamination, and is not recommended as a biomarker in studies involving these media but may be useful in studies involving other media (e.g., feces) (Calafat and McKee, 2006).

The following sections of the report describe some of the biomonitoring studies conducted in the U.S., Europe and Asia over the past ten years in five biomatrices: urine, blood, human milk, saliva, and seminal fluids. Two of the studies were conducted in multiple media. The majority of the biomonitoring studies were conducted for the general population using urine as the biomatrix. Studies conducted for specific populations such as children, women and men are also presented. The data presented are representative of "ambient" exposures. Biomonitoring data associated with specific scenarios are presented in Section 5.4 of this report.

5.2.1. Urine

The most common approach to assessing phthalate exposure in humans in biomonitoring studies is using urine as the matrix and phthalate metabolites as biomarkers. Urinary concentrations of phthalate metabolites are generally higher, as compared to other matrices, and collection is simple and non-invasive (Barr et al., 2005; Silva et al., 2005; Calafat and McKee, 2006). Data from studies conducted in the U.S. and other countries confirm that human exposure to phthalates is widespread (Calafat and McKee, 2006). Phthalates have been detected in all demographic groups at a frequency of detection as high as 100%, depending on the metabolite. More than 75% of the U.S. population has measurable levels of several phthalate metabolites in the urine (Stahlhut et al., 2007).

Brief summaries of various monitoring studies for the general population and specific populations are presented below. The studies were conducted in the U.S. as well as other countries. Several studies examined specific health effects with environmental phthalate exposures using urinary metabolite concentrations as exposure surrogates such as Duty et al. (2003); Hoppin et al. (2004); Jönsson et al. (2005); Swan (2006); and Swan et al. (2005). Most of the studies present concentrations adjusted to a constant creatinine concentration to correct for variable dilutions and for comparison purposes. Creatinine adjustment is the most widely used method for adjusting dilution and for determining whether a spot urine sample is valid for assessing chemical exposures. However, it should be noted that urinary concentrations differ dramatically among different demographic groups and will have an impact on the data (Barr et al., 2005). Urinary concentrations may also be adjusted based on specific gravity and osmolality, because creatinine may not adjust for all dilution-related variation.

General Population

The Centers for Disease Control and Prevention (CDC) collects urinary metabolite data for the general population, primarily through the National Health and Nutrition Examination Survey (NHANES), an ongoing national survey designed to evaluate the health and nutritional status of the U.S. population (CDC, 2005; Calafat and McKee, 2006). NHANES 1999–2000 and 2001–2002 provided nationally representative population-based urinary phthalate metabolite data from 2,541 and 2,782 individuals, respectively, based on one specimen per participant, for selected demographic subgroups (age, gender, and race/ethnicity) in the U.S. However, young (i.e., < 6 years of age) and older individuals (i.e., > 60 years of age) were not represented in the population sampled, and no data on prenatal exposures were collected (Calafat and McKee, 2006).

In NHANES 2001-2002, twelve monoester metabolites and other oxidized metabolites of eight phthalates (dimethyl phthalate (DMP), diethyl phthalate (DEP), DBP, BBP, DCHP, DEHP, DnOP, and DINP) were measured (CDC, 2005). Metabolites of 7 of the 8 of the phthalates were detected in all demographic subgroups. The one exception was DINP, which was detected in Mexican American and non-Hispanic blacks only at the 95th percentile. Concentrations of the metabolites of DEP and DEHP were present in the highest concentrations. The CDC (2005) indicates that the concentrations for the monoester phthalate metabolites in the NHANES 2001-2002 subsamples appear to be roughly similar to those seen in an earlier survey of U.S. residents (Blount et al., 2000), of pregnant women in New York City (Adibi et al., 2003), and in men from a Boston infertility clinic (Duty et al., 2003). The CDC (2005) further states that, with the

exception of one metabolite of DEP, the NHANES 1999-2000 and 2001-2002 subsamples show that children aged 6-11 years excrete higher concentrations of phthalate metabolites than older age groups, a finding that has been noted in other studies of German adults and children for DEHP metabolites (Koch et al., 2004a). The NHANES subsamples also show other differences in concentrations of specific phthalate metabolites by age, gender, and race/ethnicity. It is known that there is variation from person to person in the proportions or amounts of the metabolite excreted after people received similar doses, as well as variation in the same person during repetitive monitoring. The proportions of each metabolite for a given phthalate may vary also by differing routes of exposure. The CDC (2005) further notes that differences among the levels of various phthalate metabolites within an individual may be due to differences in either exposure or pharmacokinetics for each of those phthalates.

Tables 5.2-2 and 5.2-3, shown below, present the 95th and 50th (median) percentiles, respectively, of urine concentrations in the U.S. population from NHANES, 2001-2002. The data presented include creatinine-adjusted concentrations. As noted earlier, urinary biomonitoring data typically are adjusted to a constant creatinine concentration to correct for variable dilutions among spot samples.

Table 5.2-2. 95th Percentiles for Urine Levels of Phthalates Measured in NHANES 2001-2002

			Age (in years)			Gender		Race/Ethnicity		
Metabolite	Units	Total Population	6-11	12-19	20 and older	Male	Female	Mexican Americans	Non-Hispanic Blacks	Non-Hispanic Whites
MMP	µg/L µg/g of creatinine	9.80 7.97	11.6 12.5	12.7 7.27	9.10 7.72	9.10 6.42	10.3 10.0	8.30 7.53	10.8 8.02	9.70 8.29
MEP	µg/L µg/g of creatinine	2500 1860	808 837	2060 1330	2720 2080	3050 2080	1840 1430	2590 1900	3540 2070	2310 1590
MBP	µg/L µg/g of creatinine	108 81.3	157 146	147 88.6	95.4 71.6	95.2 60.0	120 91.5	112 86.7	138 85.6	107 81.4
MiBP	µg/L µg/g of creatinine	17.9 12.0	23.4 24.3	22.2 12.8	16.3 10.6	16.6 10.9	18.7 13.5	18.3 16.0	25.4 15.6	15.6 10.7
MBzP	µg/L µg/g of creatinine	122 90.4	226 195	169 99.7	99.7 64.9	122 80.3	122 95.8	91.6 72.0	139 101	121 89.2
MCHP	µg/L µg/g of creatinine	0.400 0.854	0.600 0.909	0.500 0.769	0.500 0.870	0.500 0.800	0.500 0.870	0.500 0.882	0.400 0.588	0.500 0.870
MEHP	µg/L µg/g of creatinine	38.9 32.8	29.9 31.2	42.5 25.2	39.5 33.3	37.9 31.2	42.5 35.1	28.4 24.5	52.1 39.8	37.9 32.8
MEOHP	µg/L	120	142	118	115	129	115	76.5	148	126

Table 5.2-2. 95th Percentiles for Urine Levels of Phthalates Measured in NHANES 2001-2002 (continued)

			Age (in years)			Gender		Race/Ethnicity		
Metabolite	Units	Total Population	6-11	12-19	20 and older	Male	Female	Mexican Americans	Non-Hispanic Blacks	Non-Hispanic Whites
	µg/g of creatinine	87.5	130	70.5	84.3	83.1	92.3	65.8	101	96.0
MEHHP	µg/L	192	210	202	175	212	170	123	276	212
	µg/g of creatinine	147	211	102	134	136	160	106	161	178
MCPP	µg/L	14.6	24.7	13.9	12.0	14.2	14.7	13.6	14.9	15.8
	µg/g of creatinine	11.4	26.4	9.44	7.71	11.6	11.1	11.2	10.0	11.8
MnOP	µg/L	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	µg/g of creatinine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
MiNP	µg/L	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.00	1.00	<LOD
	µg/g of creatinine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	2.31	1.62	<LOD

Source: CDC, 2005

Table 5.2-3. 50th Percentiles for Urine Levels of Phthalates Measured in NHANES 2001-2002

			Age (in years)			Gender		Race/Ethnicity		
Metabolite	Units	Total Population	6-11	12-19	20 and older	Male	Female	Mexican Americans	Non-Hispanic Blacks	Non-Hispanic Whites
MMP	µg/L	1.50	1.80	2.10	1.40	1.50	1.30	1.50	2.00	1.40
	µg/g of creatinine	1.33	2.32	1.51	1.21	1.17	1.45	1.47	1.39	1.30
MEP	µg/L	169	71.9	184	181	171	167	220	357	147
	µg/g of creatinine	147	81.2	140	159	126	171	199	227	136
MBP	µg/L	20.4	32.4	26.4	19.1	19.3	21.6	23.0	31.5	19.1
	µg/g of creatinine	17.4	35.1	20.3	15.4	13.7	21.5	19.2	20.2	16.5
MiBP	µg/L	2.60	4.40	3.80	2.40	2.70	2.50	3.40	5.30	2.20
	µg/g of creatinine	2.44	5.17	2.83	2.24	2.16	2.83	2.98	3.52	2.20
MBzP	µg/L	15.7	37.0	24.7	13.8	16.0	15.4	14.7	24.2	14.6
	µg/g of creatinine	13.5	37.2	18.1	11.8	11.9	15.1	11.9	15.7	13.0
MCHP	µg/L	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	µg/g of creatinine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

Table 5.2-3. 50th Percentiles for Urine Levels of Phthalates Measured in NHANES 2001-2002 (continued)

			Age (in years)			Gender		Race/Ethnicity		
Metabolite	Units	Total Population	6-11	12-19	20 and older	Male	Female	Mexican Americans	Non-Hispanic Blacks	Non-Hispanic Whites
MEHP	µg/L	4.10	4.40	4.50	4.10	4.30	4.10	4.70	6.70	3.60
	µg/g of creatinine	3.89	5.38	3.62	3.81	3.32	4.43	4.16	4.59	3.63
MEOHP	µg/L	14.0	22.6	18.5	12.2	14.6	13.0	13.2	20.0	13.1
	µg/g of creatinine	11.2	22.8	12.0	10.1	10.2	12.0	10.8	13.0	11.2
MEHHP	µg/L	20.1	32.9	25.2	17.7	21.2	18.2	19.0	30.9	19.2
	µg/g of creatinine	16.6	34.2	17.7	15.0	15.4	17.6	15.7	19.7	16.3
MCPP	µg/L	3.00	6.60	4.00	2.60	3.10	3.00	3.00	3.20	2.90
	µg/g of creatinine	2.45	7.07	2.93	2.19	2.20	2.75	2.36	2.07	2.56
MnOP	µg/L	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	µg/g of creatinine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
MiNP	µg/L	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	µg/g of creatinine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

Source: CDC, 2005

Silva et al. (2004) reported on the urinary phthalate metabolite data collected from NHANES 1999-2000. NHANES 1999-2000 measured the urinary monoester metabolites of seven phthalates (DEP, BBP, DBP, DCHP, DEHP, DINP, and DnOP) in approximately 2,540 samples. The metabolite of DEP was found in the highest concentration (median concentration: 141 µg/g of creatinine) and was detected in all of the samples. The metabolites of DBP, BBP, and DEHP were detected in 99%, 97% and 78% of the samples, respectively. The metabolites of DCHP, DnOP, and DINP were detected in less than 16% of the samples. Silva et al. (2004) found significant differences in metabolite concentrations across the various demographic groups. Children 6-12 years of age had higher concentrations of the DBP, BBP, and DEHP metabolites. Higher concentrations of the DEP metabolite were seen in adults. Non-Hispanic blacks had significant higher concentrations of the DEP metabolite than other race/ethnicity groups. Females of all ages had higher concentrations of the DBP metabolite than males of all ages. However, women of reproductive age (i.e., 20-39 years of age) had concentrations similar to adolescent girls and women ≥ 40 years of age.

Previously, Blount et al. (2000) reported on the monoester metabolite concentrations of seven commonly used phthalates (DEP, BBP, DBP, DCHP, DEHP, DINP, and DnOP) in urine samples from a reference population of 289 adult humans (males and females, 20-60 years). The urine samples for this study were originally collected from adults during 1988–1994 as part of NHANES III. This sampling of the NHANES III population was not designed to be

representative of the U.S. population but rather to serve as a reference range for a demographically described group. The metabolites of four phthalates (DEHP, DEP, BBP, and DBP) were detected in more than 75% of the samples. The metabolites of DEP, DBP, and BBP were found in the highest concentrations (median: 280, 19.5, and 33.4 μg/g of creatinine). Women of reproductive age (20-40 years) were found to have significantly higher levels of the DBP than other age/gender groups. Blount et al. (2000) state that the findings strongly suggest that although DEHP and DINP are produced in the largest quantities (at the time of this study), assessments of health risks should include exposures to DBP, DEP, and BBP.

One of the first, if not the first, study to determine secondary metabolites of phthalate diesters in urine of the general population was conducted in Germany. Koch et al. (2003a) determined the exposure to DEHP and other phthalates in the German general population based on urinary metabolite levels. Urine samples were collected in 2002 from 85 adults and children, age 7-64 years living in northern Bavaria who were not occupationally exposed to phthalates. The samples were analyzed for the monoester metabolites of DEHP, DEP, DBP, BBP and DOP, and two secondary (oxidative) metabolites of DEHP (MEHHP and MEOHP). The phthalate metabolites, primary and secondary, were detected in all samples. Concentrations varied strongly from phthalate to phthalate and individual to individual with differences spanning more than three orders of magnitude (highest concentration for DBP). The secondary metabolites of DEHP were excreted in much higher concentrations than the primary metabolite (approximately 4-fold). Koch et al. (2003a) state that this shows that the secondary metabolites indicate exposure to DEHP more accurately and more sensitively than the primary metabolite. In addition, the results indicate that not only is the exposure to DEHP considerable, but also exposure to DEP, DBP, and BBP. Detailed estimations of external exposure to phthalates based on the results of this biological study are available in Koch et al. (2003b).

Phthalate exposure in men and women in Germany has also been assessed by other researchers using urine as the matrix. Fromme et al. (2007a) measured urinary phthalate metabolite levels of five DEHP metabolites (one monoester and four secondary), two secondary metabolites of DINP, and the monoesters of DBP, DiBP, and BBP in 27 women and 23 men, 14-60 years of age. The samples were collected in 2005 over eight consecutive days to assess individual temporal variability. The analyses were performed as part of the ongoing Integrated Exposure Assessment Survey (INES). The primary metabolites (monoesters) of DBP and DiBP were detected in 100% of the samples, BBP in 99%, and DEHP in 95% of the samples. The secondary metabolites of DEHP and DINP were detected in 100% and 98% of the samples, respectively. The highest concentrations of the primary metabolites in this study were found for DiBP (median: 47.5 μg/g of creatinine), followed by DBP (43.6 μg/g), BBP (16.9 μg/g) and MEHP (4.3 μg/g). The median concentrations of the oxidized metabolites of DEHP were 2- to 5-fold higher than the median concentration of the primary metabolite of DEHP. The study found that phthalate metabolite levels did not consistently differ by sex or age, but there was substantial day-to-day variation of urinary levels with considerable within-subject variability. Fromme et al. (2007a) concluded that the secondary metabolites of DINP appear to be sensitive biomarkers of DINP exposure and that exposure assessment should not be based on a single urine measurement.

In a retrospective biomonitoring study, Wittassek et al. (2007a) determined the concentrations of primary and secondary metabolites of five phthalates (DBP, DiBP, BBP, DEHP, and DINP) in urine samples obtained from the German Environmental Specimen Bank for Human Tissues. The samples were collected from 634 subjects (326 females and 308 males, 20-29 years of age) over a period of 9 years between 1988 and 2003. The metabolites of the five phthalates were detected in over 98% of the urine samples, indicating, according to Wittassek et al. (2007a), the widespread exposure of the German population to all five phthalates over the last 20 years. The highest overall median concentration was for the DBP metabolite MBP (109 μg/g as creatinine). Wittassek et al. (2007a) state that high urinary MBP concentrations may occur after medication with drugs containing DBP as an adjuvant in enteric coatings. When compared to the data from NHANES 2001/2002 (CDC, 2005), the median levels of MBP and MiBP were consistently higher (4- to 13-fold, respectively). Wittassek et al. (2007a) further stated that these findings suggest higher exposure to dibutyl phthalates in Germany compared to the U.S. in the past, as well as today. Daily intakes of the parent phthalates were estimated from the urinary phthalate levels and can be used to assess trends. The median daily intakes of DBP and DEHP were constant between 1988 and 1993, but decreased continuously from 1996 to 2003. The daily intake values for DiBP increased slightly over the whole time period. Slightly decreasing values were observed for BBP. Intakes for DINP increased continuously, with the 2003 value being twice as high as the 1988 value. Wittassek et al. (2007a) attribute these trends to a change in production and usage pattern. Females had significantly higher daily intakes for the dibutyl phthalates (DBP and DiBP).

Wittassek and Angerer (2008) reported on a recent unpublished study that determined the concentrations of primary and secondary metabolites of DBP, DiBP, BBP, DEHP, and DINP in 102 people, 6-20 years of age, living in south Germany. Metabolites of all five phthalates were detected in virtually each urine sample. Median concentrations (μg/L) were 50.4 for MBP, 35.7 for MiBP, 5.4 for MBzP, 4.1 for MEHP, 6.3-21.6 for the secondary metabolites of DEHP, and 1.3-4.0 for the metabolites of DINP. When compared to the data from NHANES 2001/2002 (CDC, 2005), similar median concentrations were seen for the metabolites of DEHP. But the values in NHANES were lower for the butyl phthalate metabolites, whereas the values for monobenzyl phthalate were higher. Wittassek and Angerer (2008) state that the differences in concentrations may be due to different patterns of use in Germany and the U.S., resulting in different phthalate exposures.

Studies on the general population have also been conducted in Japan. Itoh et al. (2005) measured the levels of human exposure to phthalates in Japan using measurements of urinary metabolites of two phthalates and reconstruction of the daily intake of the corresponding parent compound. Urinary phthalate metabolite levels (monoester) of DBP and DEHP were measured in 36 male and female participants, 4-70 years of age, in May 2004. There were 35 adults and one child. The participants were from the Tokyo-Yokohama area, which has been the main DEHP production area in Japan. The metabolites were detected in over 95% of the samples, with the highest median concentration for DBP (31 μg/g of creatinine). However, the results provided for the study were for adults only. The estimated daily intakes of DBP and DEHP were lower than the corresponding TDI. When compared to the daily intake of DEHP estimated from data collected in 2000 in another study, Itoh et al. (2005) found the intake level to be lower. This they attributed to governmental regulations and a voluntary reduction in environmental emissions. In a later

study, Itoh et al. (2007) indicated that the primary metabolites of three other phthalates (DMP, DEP, and BBP) had also been detected in the urine samples from the 36 participants (includes the 1 child). The highest median concentrations were for DBP and DMP, followed by DEP, DEHP and BBP; however, the frequency of detection was not noted by Itoh et al. (2005).

Specific Populations

Children

Children may have greater exposures to environmental contaminants because of behavioral and physiologic characteristics. They are of special concern with respect to phthalate exposure because of their developmental state (Wittassek and Angerer, 2008). While earlier biomonitoring studies concentrated on phthalate exposures in adults, more recent studies have focused on phthalate exposures in children. Additional information on exposures in children is provided previously in the General Population section.

Brock et al. (2002) conducted a pilot study (originally designed to study pesticide exposure) in Imperial County, California, from January to March 2000, to examine the exposure of young children to phthalates. Urinary monoester metabolite levels of seven phthalates (DEP, DBP, BBP, DEHP, DINP, DnOP, and DCHP) were measured in the urine of 19 children, 12-18 months of age). All of the urine samples from the 19 children had detectable levels of metabolites for DEP, BBP, and DBP. Eight urine samples had detectable levels of the DEHP metabolite. These concentrations were the lowest observed. Metabolites of DINP, DnOP, and DCHP were not detected in any of the urine samples. Brock et al. (2002) stated that the mean urinary metabolite levels for the children in this study were above the 50^{th} percentile of the adult levels reported by Blount et al. (2000). Taking into account body weight, Brock et al. (2002) concluded that DBP, BBP, and DEHP exposures may be at least twice as high for these children as compared to the adults in NHANES III.

The temporal variability in urinary concentrations of ten primary and secondary metabolites of seven phthalates (DEP, DEHP, DBP, BBP, DiBP, DnOP, and DMP) was evaluated in 35 New York minority children, 6-10 years of age (Teitelbaum et al., 2008). The samples were collected over a period of 6 months during 2004-2005. The lowest frequency of detection was for the primary metabolite of DMP (58%). The frequency of detection for the remaining metabolites ranged from 94.3% to 100%. The median concentrations for all of the metabolites ranged from 1.9-149.5 µg/g of creatinine. The highest median concentration was for the primary metabolite of DEP. The median concentration for the sum of the primary and secondary metabolites of DEHP was 789.7 µg/g of creatinine. Teitelbaum et al. (2008) stated that, in general, the concentrations were of the same magnitude as the U.S. concentrations reported for over 300 6-11 year old children in CDC, 2005. However, relative to the U.S. general population, urinary concentrations of phthalate metabolites tended to be higher. Reproducibility was moderate for two phthalate metabolites (MBzP and MBP) and fair for the remaining metabolites. A relatively constant exposure to sources of phthalates was suggested for three metabolites (MBP, MBzP, and MCPP). The wide range of concentrations measured and the reasonable degree of temporal reliability observed provides further support for the use of these biomarkers of exposure in epidemiologic studies.

Children and Adults

Several studies have also examined phthalate exposures in children and compared them to exposures for adults.

The exposure of nursery school children (aged 2-6 years) in a rural area of Germany to DEHP was determined by Koch et al. (2004a) and compared to their parents' and teachers' exposure. Urine samples were collected from 36 children, 4 teachers and 15 parents in 2003. Samples were analyzed for three metabolites of DEHP (1 monoester and 2 secondary (oxidative)). The metabolites were detected in all of the urine samples. The median concentrations of both secondary metabolites were significantly higher in the children's urine than in the adults' urine. The median concentration of the monoester metabolite was lower in the children's urine and contributed only a minor share to the sum of the three metabolites. Enhanced oxidative metabolism may be taking place in children. Based on the sum of the three metabolites, Koch et al. (2004a) estimated the DEHP dose to children to be about twice as high as the dose to adults (98.8 vs. 50.9 μg/g of creatinine). Koch et al. (2004a) also stated the need for additional information on the biological activity and toxicity of oxidative metabolites, since these are the major metabolites.

Exposure to significant levels of phthalates has also been shown in Korea. Koo and Lee (2005) determined the levels of urinary phthalate diesters (DEHP, DEP, DBP, BBP) and the metabolite MEHP in Korean women and children. Urine samples were collected in 2003 from 300 participants (150 women, aged 20-73 years and 150 children, aged 11-12 years). Mean urinary concentrations varied by several orders of magnitude. In women, DBP and MEHP were present at the highest levels (mean: 49.5 and 39.6 μg/g of creatinine, respectively), where as in children the highest levels were for DBP (mean 46.4 μg/g of creatinine), followed by MEHP at 9.6 μg/g of creatinine. DEHP and DBP were detected in more than 95% of the urine samples collected from women and children. More than 74% of the samples had levels below the detection limit for BBP and DEP.

Women

Studies have been conducted to specifically determine phthalate exposure in women, including specific health effects associated with the exposures.

The temporal variability and reproducibility of phthalate levels in urine was explored by Hoppin et al. (2002). Seven phthalate monoester metabolites of BBP, DBP, DCHP, DEP, DEHP, DINP, and DnOP were measured in two consecutive first-morning urine samples collected from 46 African American women, 35-49 years of age, living in the Washington, DC area in 1996-1997. Four of the metabolites (MEP, MBP, MEHP, and MBzP) were detected in urine samples from all participants. More than 75% of the samples analyzed for MCHP, MiNP, and MnOP were below the detection limit. Individual phthalate concentrations ranged up to three orders of magnitude, with MEP detected at the highest levels (median: 134.8 μg/g of creatinine) of all phthalates analyzed. Hoppin et al. (2002) state that the results are similar to those reported in NHANES III

and NHANES IV. Phthalate levels did not differ from one day to the next suggesting that even with the short half-lives of phthalates, women's patterns of exposure may be relatively stable. Phthalate exposures in 25 pregnant women in New York City were characterized using personal air and urine samples collected between March and July 2000 (Adibi et al., 2003). Phthalate monoester metabolite levels of DEHP, BBP, DBP, DEP, DCHP, DnOP, DINP, and DMP were measured. Metabolites of four phthalates (DEP, DBP, BBP and DEHP) were detected in 100% of the samples. Metabolites of DEP and DBP were present in the highest concentrations in urine (median: 236 and 42.6 μg/g of creatinine, respectively) and in air (0.04 and 2.7 μg /m^3, respectively). The results indicate that pregnant women in New York are exposed to a range of phthalates in their personal environments and inhalation is an important route of exposure. Adibi et al., 2003 state that the data do not allow for conclusions on potential sources of the phthalates in the women's environment because the samples were analyzed *a posteriori* and data on individual lifestyle factors (i.e., geographic location, occupation, age difference, cosmetic uses, and dietary patterns) were not collected.

The association between phthalate exposure and thyroid hormones in 76 Taiwanese pregnant women was studied by Huang et al. (2007). Urine and serum (for hormone analysis) samples were collected during 2005-2006. Urinary monoester metabolites of five phthalates (DBP, DEP, DEHP, BBP and DMP) were measured and detected in 96, 100, 100, 17 and 63% of the samples, respectively. Median urinary levels were the highest for the metabolites of DBP, DEP, and DEHP (195.0, 68.0, and 60.8 μg/g of creatinine, respectively). The highest urinary level measured (metabolite of DEP) was found in a participant who was a cosmetologist for more than 10 years (5466 ppb).

Swan (2006) and Swan et al. (2005) reported results from the first study to examine the relationship between anogenital distance in boys and their mother's urinary concentration of phthalate metabolites. The study was conducted on 134 boys, 2-36 months of age. The mothers were originally participants in the first phase (1999-2002) of the Study for Future Families, a multicenter pregnancy cohort study conducted in at various prenatal clinics in the U.S. Urinary monoester metabolites of six phthalates (DBP, BBP, DCPP, DEP, DiBP, and DMP) and three secondary metabolites of DEHP were measured in 85 prenatal maternal samples. All of the metabolites were above the level of detection in more than 49% of women (lowest MMP), and most were above the level of detection in more than 90% of the samples.

Men

Phthalates are one of several commonly used industrial chemicals associated with reproductive toxicity in laboratory animals. Several studies have examined specific health effects associated with exposure.

The possible association of environmental levels of phthalates with altered sperm quality in men was studied by Duty et al. (2003). Eight monoester phthalate metabolites of DEP, DMP, DEHP, DBP, BBP, DnOP, DINP and DCHP were measured in the urine of 168 men from a Boston, Massachusetts infertility clinic between January 2000 and April 2001. The metabolite of DEP was detected all of the urine samples. The metabolites of DBP, BBP, and DMP were detected in over 95% of the samples, and 75% of the samples had detectable levels of the DEHP metabolite.

The highest metabolite levels were for DEP (median: 153 ng/mL), followed by DBP and then BBP.

In a more recent study, Jönsson et al. (2005) assessed the possible association of phthalate metabolite levels in urine with semen function and reproductive hormone parameters in 234 Swedish men, aged 18-21 years. The participants were from the general population and undergoing a medical examination before military service. Semen volume, sperm concentration, and motility were measured together with sperm chromatin integrity and biochemical markers of epididymal and prostate function. In addition, reproductive hormones were measured in serum and monoester metabolites of four phthalates (DEP, DEHP, BBP, and DBP), along with phthalic acid, were measured in urine. Metabolites of all four phthalates and phthalic acid were detected in the urine. The frequency of detection was not reported; however, the metabolites and phthalic acid were not found in all samples and Jönsson et al. (2005) reported a wide variation among individuals. The highest concentration was for the metabolite of DEP. The lowest levels were for BBP and DEHP.

Stahlhut et al. (2007) studied the possible association between phthalate exposure and antiandrogenic effects in adult human males, including decreased testosterone levels. Low testosterone levels, in turn, have been associated with increased prevalence of obesity, insulin resistance, and diabetes. In one of the first studies, if not the first, Stahlhut et al. (2007) investigated exposure to six urinary monoester and oxidative phthalate metabolites of DBP, DEP, DEHP, and BBP (MBP, MEP, MEHP, MEHHP, MEOHP and MBzP), and its associations with abdominal obesity and insulin resistance. The subjects were adult U.S. male participants in the NHANES 1999-2002. Exposure levels varied widely by metabolite, with MEHP having the lowest median concentration (11 µg/g creatinine) and MEP the highest (771 µg/g creatinine) level. Greater median levels were usually found in younger age groups. For all phthalate metabolites except MEHP, more the 95% of the subjects were at or above the level of detection; for MEHP, more than 80% of the subjects were at or greater than the level of detection. Concentrations also varied by race/ethnicity. Blacks had higher levels of exposure than whites and Mexican Americans for all metabolites. Mexican Americans had somewhat higher levels than whites for MBP, MEP and MEHP.

5.2.2. Blood

Blood (and its components, e.g., serum and plasma) is also a commonly used matrix for biomonitoring studies. Blood is generally a better matrix for compounds with a longer half-life than phthalates. The average blood volume of an individual remains relatively stable for a healthy individual who maintains a given body weight; therefore, changes in blood concentrations of a chemical can be readily evaluated (Barr et al., 2005). Serum concentrations of phthalates have been measured, but phthalates have been measured in much greater quantities in urine as compared with serum (Sathyanarayana, 2008). This may be due to the fact that serum contains enzymes that convert diesters into monoesters. However, the amounts of blood available are limited and its collection is invasive and more involved.

The study summarized below describes a specific health effect associated with exposure to phthalates. Additional studies conducted using blood, as a matrix, are summarized in section 5.2.6, Multiple Biological Media.

Reddy et al. (2006) evaluated the possible association between phthalate esters and the occurrence of endometriosis in Indian women. Blood samples were collected from 49 infertile women with endometriosis (the study group), 38 infertile women without endometriosis (control group), and 21 women with proven fertility (control group). Samples were analyzed for DBP, BBP, DnOP, DEP, DMP and DEHP. Women with endometriosis showed significantly higher concentrations of DBP, BBP, DnOP, and DEHP when compared to both control groups. DEP and DMP were not detected in the study group or in the control groups. The highest concentrations found were for DnOP (3.32 μg/mL) followed by DEHP (2.44 μg/mL). Reddy et al. (2006) state that the results support a 2003 study that reported higher concentrations of DEHP in women with endometriosis.

5.2.3. Human Milk

Interest in monitoring human milk for phthalates has increased because human milk is one possible route of exposure by the breast feeding infant (Calafat et al., 2004a). Because of the potential health impact of phthalates to nursing children, it is important to determine whether phthalates are present in human milk.

Phthalates were detected in pooled human milk samples from American women (Calafat et al., 2004a). In this study, a sensitive method to assess human exposure to phthalates was developed by measuring twelve phthalate metabolites (monoester and oxidized) of DMP, DEP, DBP, DiBP, DEHP, BBP, DCHP, DnOP, and DINP, along with phthalic acid. The applicability of the method was evaluated by analyzing three pooled human milk samples. The monoesters of DEHP, and DINP were detected in all of the samples, DBP in two of the pools, and phthalic acid, in one. The oxidative metabolites of DnOP and DEHP were also detected in all three pools. The highest mean concentration (total) in the three human milk pools was for DINP (15.9 ng/mL), followed by phthalic acid (13.0 ng/mL), DEHP (7.8 ng/mL), and DBP (1.5 ng/L). Calafat et al. (2004) state that the higher concentrations of DEHP and DINP may be due to sampling contamination (e.g., tubing for breast pumps). However, the detection of the three metabolites suggests environmental exposure because the oxidative phthalate metabolites cannot be formed from the enzymatic cleavage by the human milk enzymes of phthalate diesters. The concentrations of the oxidative metabolites were close to the level of detection and below the limit of quantification. The phthalate metabolites were mostly in their free form and the relatively higher lipophilicity of the free metabolites might have favored their transport into the human milk during the synthesis of the milk in the body. The results suggest that phthalates can be incorporated into human milk and transferred to the nursing child.

Main et al. (2006) evaluated adverse reproductive effects of exposure to phthalates in 130 newborn boys by correlating reproductive hormone levels at 3 months of age to the concentrations of six phthalate monoesters of DMP, DEP, DBP, BBP, DEHP, and DINP in human milk. Human milk samples were obtained from a joint prospective, longitudinal cohort study on cryptorchidism conducted in 1977-2001 at a hospital in Finland and Denmark. Except

for the metabolite of DMP, the phthalate metabolites were detectable in 100% of the human milk samples; the DMP metabolite 95%. The highest median concentration was for the metabolite of DINP in both the Finland and Denmark samples. A significant difference in absolute concentrations was observed between the two countries despite close geographic locations and lifestyles. No association was found between phthalate metabolite levels and cryptorchidism. However, subtle, but significant dose-dependent associations between neonatal exposure to phthalate monoesters (DEP, DBP DMP and DINP) in human milk and levels of reproductive hormones were observed.
Additional studies conducted using human milk, as a matrix, are summarized in Section 5.2.6, Multiple Biological Media.

5.2.4. Saliva

The use of an unconventional biomatrix has also been investigated. Silva et al. (2005) state that saliva is one of the most promising alternative matrices because its collection is easy, noninvasive, and inexpensive. While urine is an abundant matrix and its collection is easy and noninvasive, it only measures concentrations of compounds accumulated since the last void and is dependent on liquid intake. Blood can provide estimates of the level of non-persistent compounds and is not dependent on liquid intake. However, the amounts of blood available are limited and its collection is invasive and more involved. Saliva offers some advantages over blood as a biomatrix for determining exposure. Like serum and human milk, saliva contains enzymes capable of hydrolyzing phthalate diesters into their respective monoesters (Silva et al., 2005).

Silva et al. (2005) measured the salivary concentrations of 14 primary and secondary metabolites in 39 adults of both sexes. Six monoester metabolites of DMP, DEP, DBP, DiBP, BBP, and DEHP and phthalic acid were detected. The frequency of detection was the highest and lowest for the metabolites of DBP (85%) and DMP (8%), respectively. The oxidative metabolites of DnOP and DBP, and 2 of the three oxidative metabolites of DEHP were not detected. The highest concentrations observed were for the metabolites of BBP (353.6 ng/mL), followed by DEP (91.4 ng/mL) and DBP (65.8 ng/mL). The oxidative metabolites of DnOP and DEHP, and the metabolites of DCHP, DINP, and DIDP were not detected. Silva et al. (2005) compared the median salivary levels of MBP, MEHP, MBzP and MEP in this study with the urinary and serum levels of these metabolites in other population groups in the U.S. The median salivary concentrations were much lower than the median urinary levels from NHANES 1999-2000 (Silva et al., 2004), but were somewhat similar to the serum concentrations of these metabolites in a multiethnic population of 155 persons, 6 years and older. Silva et al. (2005) state that the similar levels in serum and saliva suggest that saliva could be used as a surrogate matrix in biomonitoring studies.

5.2.5. Seminal Fluids

A study published in 1992 reported that the quality of male sperm has declined 40%-50% in the past 50 years. But there are few studies on the association between phthalate levels in semen and semen quality.

Zhang et al. (2006) measured the levels of DEP, DBP, and DEHP in the semen of 52 men (23-48 years of age) living in Shanghai in 2002. The phthalates were detected in virtually all of the samples (specific detection not provided). The median concentration of all three phthalates in the semen was 0.30 mg/L (0.08-1.32 mg/L). There were no significant differences in concentrations for the three phthalates in the samples. Results of the study showed a significant positive association between liquefied time of semen and phthalate concentrations, and a negative correlation between semen volume and concentrations of DBP or DEHP. There was also a positive association between the rate of sperm malformation and DEHP concentrations. Zhang et al. (2006) concluded that people living in Shanghai are exposed to phthalates and an association of phthalate levels and reduced sperm quality exists.

5.2.6. Multiple Biological Media

Two recent studies examined and compared the concentrations of phthalate metabolites in a variety of biological media. The studies were conducted in the U.S. and Sweden.

Hines et al. (2009), as part of the U.S. Environmental Protection Agency's (U.S. EPA) Methods Advancement for Milk Analysis (MAMA) study, measured and compared the concentrations of oxidative monoester phthalate metabolites in milk and surrogate fluids (serum, saliva, and urine) in 33 lactating North Carolina women. Samples were analyzed for the oxidative phthalate metabolites of DEHP and DnOP. Because only urine lacks esterases, it was also analyzed for the hydrolytic phthalate monoesters of DBP, BBP, DEHP, DEP, DMP and DiBP. The phthalate metabolites of DEHP and DnOP were in less than 10% of the milk samples and less than 5% of the saliva samples. The metabolites of DEHP were detected in more than 80% of the serum samples. Urinary metabolites of DBP, BBP, DnOP, DEHP, DEP, and DiBP were detectable in more than 80% of the samples. DMP metabolites were in less than 15% of the samples. The highest concentration in urine was for the DEP metabolite. Metabolite concentrations differed by body fluid, with urine being the highest, followed by serum, milk, and saliva. Hines et al. (2009) state that questionnaire data suggest that frequent nail polish use, immunoglobulin A, and fasting serum glucose and triglyceride levels were increased among women with higher concentrations of urinary and/or serum phthalate metabolites; motor vehicle age was inversely correlated with certain urinary phthalate concentrations. Hines et al. (2009) concluded that the data suggest that phthalate metabolites are most frequently detected in urine of lactating women and are less often detected in serum, milk, or saliva. Urinary phthalate concentrations reflect maternal exposure and do not represent the concentrations of oxidative metabolites in other body fluids, especially milk.

A previous study on phthalate metabolites in multiple media (milk, urine, and blood or serum) from 42 lactating Swedish women abstaining from skin care product use collected milk and 1 week later collected urine and serum samples (Högberg et al., 2008). Samples were analyzed for DEP, DBP, BBP, DEHP and their metabolites. In this study, the rates of detection are in agreement with Hines et al. (2009). Most blood or serum and milk samples had phthalate and phthalate metabolite concentrations below the level of detection, but all urine samples had detectable concentrations of most metabolites. No blood or milk sample contained detectable concentrations of DIDP or DINP. Detectable concentrations in urine were comparable to those from the general population in the U.S. and in Germany. No correlations existed between urine

concentrations and those found in milk or blood/serum for single phthalate metabolites. The data are at odds with a previous study documenting frequent detection and comparatively high concentrations of phthalate metabolites in Finnish and Danish mothers' milk. Högberg et al. (2008) concluded that concentrations of phthalate metabolites in urine are more informative than those in milk or serum. Furthermore, collection of milk or blood may be associated with discomfort and potential technical problems such as contamination (unless oxidative metabolites are measured). Although urine is a suitable matrix for health-related phthalate monitoring, urinary concentrations in nursing mothers cannot be used to estimate exposure to phthalates through milk ingestion by breast-fed infants.

5.3. OCCUPATIONAL EXPOSURE

This section provides a summary of the literature review that was performed to obtain information on occupation exposure to DEHP, DBP, BBP, DINP, DIDP and DnOP. Section 5.3.1 summarizes available information on occupational inhalation and dermal exposure for specific phthalates. Detailed descriptions of the sources and/or studies containing information on occupational exposures to phthalates are presented in Section 5.3.2.

5.3.1. Summary of Occupational Inhalation and Dermal Exposures

In general, occupational exposure to these phthalates typically occurs by dermal contact and through inhalation of dust, vapors, or aerosols. Occupational exposure can occur during production of phthalates, during manufacture of products that contain phthalates, and during industrial end use of products that contain phthalates.

Occupational Exposure to DEHP

Occupational exposure to DEHP occurs in the production (manufacture) of DEHP, industrial use of DEHP as an additive, and during industrial end-use of semi-manufactured products and end-products containing DEHP. Workers are potentially exposed to high concentrations of DEHP during the compounding of DEHP with PVC. The ECB DEHP (2008) risk assessment reviewed sources of occupational inhalation and dermal exposure to DEHP. Inhalation exposure was assessed using both measured data and modeled data. Dermal exposure was estimated using the EASE model. Worker exposure to DEHP was found to occur mainly through the inhalation route. During production, the reasonable worst case inhalation exposure level was found to be 5 mg/m^3 (aerosol, 8-hr time weighted average (TWA)) (530 µg/kg-bw/d), during industrial use of DEHP as an additive the reasonable worst case inhalation exposure level was 10 mg/m^3 (8-hr TWA) (1,060 µg/kg-bw/d), and during industrial end-use of semi manufactured products and end-use products containing DEHP the reasonable worst case exposure level was 10 mg/m^3 (8-hr TWA) (1,060 µg/kg-bw/d). During production the reasonable worst case dermal exposure level was found to be 650 mg/day (460 µg/kg-bw/d), during industrial use of DEHP as an additive the reasonable worst case dermal exposure level was 420 mg/d (300 µg/kg-bw/d), and during industrial end-use of semi manufactured products and end-use products containing DEHP the reasonable worst case dermal exposure level was 1,300 mg/d (928 µg/kg-bw/d).

ATSDR (2002) found that workplace air levels of DEHP ranged from 0.02 to 4.1 mg/m^3 at facilities using or manufacturing the compound. These levels are below the current U.S. Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for DEHP for an 8-hr workday of 5 mg/m^3. Exposure for phthalate and PVC production workers to DEHP were estimated to be typically less than 143 and 286 µg/kg body weight/workday, respectively. According to NTP-CERHR DEHP (2000), the maximum occupational exposure is not likely to exceed 700 µg/kg-bw/d if the workplace air concentration meets the OSHA standard. Studies based upon workplace air measurements in Europe and the former USSR estimate that occupational exposures ranged from <2 to 6,600 µg/kg-bw/d. The American Chemistry Council (ACC) cites six studies that indicate that exposures to air concentration in the U.S. are generally below 1 mg/m^3 during production of phthalates and below 2 mg/m^3 during production of PVC. They estimated an exposure of less than 143 µg/kg-bw per workday for phthalate production workers. The corresponding exposure for PVC production workers was 286 µg/kg-bw per workday.

SCENIHR (2008) reviewed the safety of medical devices containing DEHP plasticized PVC or other plasticizers. The report stated that there is limited evidence linking DEHP exposures and some adverse effects in humans. The few follow-up studies performed after high DEHP exposures in neonates and in occupational settings, did not indicate that there is an effect of DEHP exposure on fertility and/or the human male reproductive system. Contradictory results were reported for the effect of DEHP on semen quality and female development. One study, Pan et al. (2006), looked at the effect of occupational exposure to high levels of DBP and DEHP at a manufacturing plant in China due to dermal contact and through inhalation of dust. The study concluded that there was a modest and significant reduction of serum free testosterone in workers with higher levels of urinary the metabolites mono-n-butyl phthalate and mono-2-ethylhexyl phthalate when compared to unexposed workers.

Occupational Exposure to DBP

Exposure to DBP in occupational settings can occur through skin contact and by inhalation of vapors and dust. ECB DBP (2003-2004) reviewed occupational exposure scenarios for DBP. Occupational exposure can occur during production of DBP (e.g., filling of tankers and drums, sampling, changing of filters, and other maintenance activities), during production of products that contain DBP (e.g., adding DBP to mixers, and during mixing and forming of the products by extruding and calendaring), and during industrial end use of products that contain DBP (e.g., in the polymer industry, painting industry, and printing industry). The highest occupational exposure levels were found to occur during industrial end use of products that contain DBP. The reasonable worst-case full-shift inhalation exposure level was estimated to be 10 mg/m^3 with typical values of 2 mg/m^3 and short-term exposure levels of up to 20 mg/m^3. Dermal exposure during prolonged spray application of products containing DBP was estimated to be up to 975 mg/day. Inhalation exposure to DBP using techniques that do not involve generation of aerosols (e.g., application of a product by means of a brush) was estimated to be negligible.

ATSDR (2001) and NTP-CERHR (NTP-CERHR DBP, 2003) found that workplace DBP levels in production facilities in the U.S. ranged from below the detection limit (0.01–0.02 mg/m^3) to 0.08 mg/m^3. The report stated that the ACC has estimated exposure to DBP in the workplace

based upon an assumed level of 1 mg/m^3 in the air during the production of phthalate. An exposure level was estimated using assumptions of a 10 m^3/d inhalation and a 70 kg body weight. The resulting exposure estimate was 143 µg/kg-bw/workday for workers employed in phthalate manufacturing.

One study, Kwapniewski et al. (2008), looked at the effect of using gloves on occupational exposure to DBP by manicurists. The study found that manicurists who did not wear gloves had a 50% increase in urinary concentration of mono-n-butyl phthalate (major metabolite of DBP) between the beginning and end of the work shift.

Pan et al. (2006) looked at the effect of occupational exposure to high levels of DBP and DEHP at a manufacturing plant in China resulting from dermal contact with the products and through inhalation of dust. The study concluded that there was a modest and significant reduction of serum free testosterone in workers with higher levels of urinary the metabolites mono-n-butyl phthalate and mono-2-ethylhexyl phthalate when compared to unexposed workers. Matsumoto et al. (2008) reviewed and summarized recent studies on phthalate acid esters (PAE) exposure and health effects in human populations. The article stated that in females, decreased rates of pregnancy and higher levels of miscarriage in factory workers were associated with occupational exposure of DBP.

Occupational Exposure to BBP

BBP may be released to the environment during production and also during incorporation of BBP into plastics or adhesives. ECB BBP (2007) reviewed occupational exposure scenarios for BBP. Worker inhalation and dermal exposure is possible during production of BBP (e.g., filling tanker trucks and rail tankers, drumming, process sampling, and cleaning and maintenance), industrial use of BBP-containing products (e.g., manufacture of flooring using the plastisol spread coating process, processing of PVC floats, processing of sealants, manufacture of flooring with calendering process, and processing of films with the extrusion process), and during professional end use of products containing BBP (e.g., use of polysulfide sealants for glass insulation, and use of polyurethane sealants/fillers/grouting agents).

The highest inhalation exposure was found to occur during manufacture of flooring using the calendering process (typical value 0.4 mg/m^3, reasonable worst case 3.0 mg/m^3). The highest dermal exposure was found to occur during processing of PVC floats (840 mg/d), and potentially during use of polyurethane sealants/fillers/grouting agents (84 to 840 mg/d). The NTP-CERHR (NTP-CERHR BBP, 2003) found that occupational exposure can occur through skin contact and by inhalation of vapors and dusts. The ACC has estimated exposure to BBP in the workplace based upon an assumed air concentration of 1 mg/m^3 during the production of phthalates and 2 mg/m^3 during the manufacture of flexible PVC. Exposure levels were estimated assuming a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimates were 143 µg/kg-bw/workday (for phthalate manufacturing) and 286 µg/kg-bw/workday (for flexible PVC production operations). The report stated that absorption of BBP through skin is expected to be minimal because of low absorption rate.

The NTP-CERHR BBP (2003) report stated that occupational exposure to phthalate mixtures containing BBP in PVC production has been associated with increased incidence of menstrual disorders and spontaneous abortions among female workers. Exposures to BBP-containing phthalate mixtures have been associated with elevated respiratory/neurological morbidity and increased risk of cancer in occupationally exposed population groups. A significant increase in the risk of multiple myeloma has been found among workers employed for 5 or more years in PVC production.

Occupational Exposure to DINP

The ECB DINP (2003) reviewed sources of occupational exposure to DINP. Occupational exposure to DINP can occur by skin contact with pure DINP, or by skin contact with mixtures (formulations) or by skin contact with end products that contain DIDP, or by inhalation of DINP containing vapors or aerosols. The report found that worker dermal exposure is possible during manufacture (e.g., drumming, cleaning, and maintenance), during handling at the first step of industrial use (e.g., pumping, emptying containers), and while working with formulations or end products containing DINP, especially in the liquid or paste form (e.g., application of coatings, adhesives, or inks). The maximum dermal exposure was estimated to be 5 mg/cm^2 for all scenarios. Worker inhalation exposure is possible during manufacture (when the lid on the reactor is opened at the end each batch, during cleaning and maintenance work, and during filling of tanks and drums), during manufacture of products containing DINP (PVC compounding, PVC processing), and professional end of products containing DINP (PVC and non-PVC products such as coatings, rubber, latex, mastics, sealants, inks, dyestuffs, lubricants, acrylic resins, paints and pressure-sensitive adhesives). During non-aerosol forming activities inhalation exposure will be negligible because of low vapor pressure. Significant exposure can occur during aerosol-forming activities. During production of DINP, the worst case and typical estimated inhalation exposures were 5 mg/m^3 and 2 mg/m^3 for an 8-hr TWA. During manufacture of products containing DINP, the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 3 mg/m^3 for an 8-hr TWA. During professional use of end products containing DINP, the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 1.5 mg/m^3 for an 8-hr TWA.

The NTP-CERHR DINP report (2003) stated that limited studies of occupational exposures suggest that inhalation exposure is below 1 mg/m^3 during production of DIDP and below 2 mg/m^3 during production of PVC. The report stated that absorption of BBP through skin is expected to be minimal because of low absorption rate. Exponent (2007) stated that occupational exposure limits such as a PEL or TLV due to the non-volatile nature of DINP have not been established by the OSHA, National Institute for Occupational Safety and Health at the CDC, or the American Conference of Governmental Industrial Hygienists (ACGIH). This is mostly due to the non-volatile nature of DINP. The report also states that few countries have defined occupational exposure limits for DINP. In the U.K., the Health and Safety Executive provides an occupational exposure standard (8-hr TWA) of 5 mg/m^3 for DINP. In Sweden, Swedish National Chemicals Inspectorate provides a "level limit value" of 3 mg/m^3 and a "short-term value" of 5 mg/m^3 that applies to phthalates such as DINP for which no specific limit values have been defined. SCENIHR (2008) stated that there are currently four producers of DINP in the EU. Approximately 95% of DINP are used in PVC as a plasticizer. DINP is used

as a plasticizer in toys, vinyl flooring, wire and cable, stationery, wood veneer, coated fabrics, gloves, tubing, artificial leather, shoes, sealants and carpet backing. The estimated maximum combined total daily intake for an occupationally exposed adult is 1.12 mg/kg-bw/d. These estimates were based on DINP measurements in several environmental media and consumer products.

Occupational Exposure to DIDP

ECB DIDP (2003) reviewed occupational exposure scenarios for DIDP. Worker dermal exposure is possible during manufacture (e.g., drumming, cleaning, and maintenance) and during handling at the first step of industrial use (pumping, emptying containers), and while handling formulations or end products containing DIDP (e.g., application of coatings, adhesives, or inks). The maximum dermal exposure was estimated to be 5 mg/cm^2 for all scenarios. The report found that worker inhalation exposure is possible during manufacture (when the lid on the reactor is opened at the end each batch, during cleaning and maintenance work, and during filling of tanks and drums), during manufacture of products containing DIDP (PVC compounding, PVC processing), and during profession use of end products containing DIDP (PVC and non-PVC products such as coatings, rubber, latex, mastics, sealants, inks, dyestuffs, lubricants, acrylic resins, paints and pressure-sensitive adhesives). During production of DIDP, the worst case and typical estimated inhalation exposures were 5 mg/m^3 (0.53 mg/kg-bw/d) and 2 mg/m^3 for an 8-hr TWA. During manufacture of products containing DIDP, the worst case and typical estimated inhalation exposures were 10 mg/m^3 (1.07 mg/kg-bw/d) and 3 mg/m^3 for an 8-hr TWA. During professional use of end products containing DIDP the worst case and typical estimated inhalation exposures were 10 mg/m^3 (1.07 mg/kg-bw/d) and 1.5 mg/m^3 for an 8-hr TWA. The report also listed the combined inhalation and dermal exposure for production of DIDP (0.56 mg/kg-bw/d), manufacture of products containing DIDP (1.10 mg/kg-bw/d), and use of end products containing DIDP (1.10 mg/kg-bw/d). NTP-CERHR DIDP (2003) report evaluated the potential reproductive and developmental toxicities of DIDP. The report found that occupational exposure occurs primarily through inhalation and dermal contact. Even though DIDP is manufactured within closed systems under negative pressure, exposure to workers can occur during loading/unloading of railroad cars and trucks. Higher exposures may occur during the production of PVC products because of elevated temperatures and more open processes. Limited studies of occupational exposures suggest that inhalation exposure is below 1 mg/m^3 during production of DIDP and below 2 mg/m^3 during production of PVC.

Occupational Exposure to DnOP

DnOP is approved by the FDA as an indirect food additive and is used in seam cements, bottle cap liners, and conveyor belts. NTP-CERHR DnOP (2003) evaluated the potential reproductive and developmental toxicities of DnOP. The report found that occupational exposure occurs primarily through inhalation and dermal contact. Even though phthalates are manufactured within closed systems, exposure to workers can occur during filtering or loading/unloading of tank cars. Higher levels of exposure to phthalates can occur during the production of flexible PVC because the processes are open and typically run at higher temperatures than are used in the manufacturing process. The ACC found that phthalate levels in air are generally lower than 1 mg/m^3 during the production of phthalates and 2 mg/m^3 during the production of flexible PVC.

Exposure levels were estimated by the ACC using assumptions of a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimates were 143 µg/kg-bw/workday for workers employed in phthalate manufacturing operations and 286 µg/kg-bw/workday for workers employed in flexible PVC manufacturing operations. The report stated that absorption of BBP through skin is expected to be minimal because of low absorption rate.

5.3.2. Occupational Inhalation and Dermal Exposure

Detailed summaries of pertinent sources of information on occupational exposures to phthalates are provided in this section.

Kwapniewski et al. (2008)

Kwapniewski et al. (2008) evaluated inhalation and dermal occupational exposure to DBP among manicurists in Boston and the surrounding area. The study showed that manicurists are occupationally exposed to DBP. Pre- and post-shift urine samples were collected from 27 manicurists. There was a statistically significant increase of 17.4 ng/mL in the urinary concentration of mono-n-butyl phthalate (the major metabolite of dibutyl phthalate) between the beginning of the work shift and the end of the work shift. In the study, gloves were worn by 7 of the manicurists and no gloves were worn by 27 of the manicurists. Data were missing for glove use for 3 of the manicurists. When gloves were worn by the seven manicurists, their mono-n-butyl phthalate urinary concentration decreased by 5% (15.1 ng/mL) between the beginning and end of the shift. Among manicurists who did not wear gloves (n=27) at work, their mono-n-phthalate urinary concentration increased by 50% (20.5 ng/mL) between the beginning and end of the work shift. The manicurists were found to be occupationally exposed to dibutyl phthalate and glove use was found to decrease dermal exposure. In the study, eight manicurists worked in salons that had local exhaust ventilation and 27 manicurists worked in salons that had no local exhaust ventilation. Data were missing for 2 manicurists with respect to the presence or absence of local exhaust ventilation. Manicurists in salons without local exhaust ventilation (n=27) had a 54% (21.5 ng/mL) increase in urinary mono-n-phthalate median concentration between the beginning and end of the work shift. Manicurists in salons with local exhaust ventilation (n=8) had a 7% (1.6 ng/mL) decrease in urinary mono-n-phthalate median concentration between the beginning and end of the shift. The decrease in concentration of mono-n-phthalate with use of local exhaust ventilation was found not to be statistically significant.

Pan et al. (2006)

Pan et al. (2006) assessed the effects of occupational exposure to high levels of phthalate esters (i.e., DBP and DEHP) used as plasticizers during production of unfoamed polyvinyl chloride at a manufacturing plant in China. The workers were exposed to DBP and DEHP by dermal contact and through inhalation of dust. Urine and blood samples were examined from 74 male workers (i.e., exposed workers) at the plant and compared to samples collected from 63 unexposed male workers (i.e., workers without occupational exposure who were matched for age and smoking status) from a construction company. Urinary levels of mono-n-butyl phthalate and mono-2-ethylhexyl phthalate and serum levels of free testosterone, luteinizing hormone, follicle-stimulating hormone and estradiol were measured to assess potential effects of worker exposure

to phthalates. Compared to unexposed workers, the exposed workers had significantly higher urinary concentrations of mono-n-butyl phthalate (i.e., 644.3 vs. 129.6 μg/g creatinine) and mono-2-ethylhexyl phthalate (i.e., 565.7 vs. 5.7 μg/g creatinine). Serum levels of free testosterone were found to be lower (i.e., 8.4 vs.9.7 μg/g creatinine) in exposed workers when compared with unexposed workers. Compared with unexposed workers, exposed workers had nonsignificant reductions of follicle-stimulating or luteinizing hormone. The study concluded that there was a modest and significant reduction of serum free testosterone in workers with higher levels of urinary mono-n-butyl phthalate and mono-2-ethylhexyl phthalate when compared to unexposed workers.

ECB DBP (2003-04)

The ECB DBP report (2003-04) reviewed occupational exposure scenarios for DBP. The report found that worker exposure was possible during production of DBP, during production of products that contain DBP, and during end use of products that contain DBP (e.g., in the polymer industry, painting industry, and printing industry). Occupational exposure to DBP was found primarily to be due to inhalation of vapors and skin contact. Exposure levels were estimated using measured data and by modeling using EASE. Occupational exposure during production of DBP was found to occur during activities such as filling of takers and drums, sampling, changing of filters, and other maintenance activities. Typical full-shift inhalation exposure levels during production of DBP were estimated to be below 2 mg/m^3 with a reasonable worst case of 5 mg/m^3. Short-term inhalation exposure levels of up to 10 mg/m^3 were found to be possible. Dermal exposure in production is expected to be highest during drumming of DBP and was estimated by EASE to be up to 420 mg/d. The production of products containing up to 15% DBP was found to result in inhalation and dermal occupational exposures while adding the substance to mixers, and during mixing and forming of the products by processes such as extruding and calendering. The estimated reasonable worst-case full-shift inhalation exposure level was 5 mg/m^3. Typically the exposure was < 2 mg/m^3 with a short-term exposure of 10 mg/m^3. Manual addition of DBP was estimated to result in a dermal exposure level of 420 mg/d. End use of products containing DBP occurs in the polymer industry, the painting industry, and the printing industry. The end use of products includes aerosol forming techniques (such as spray application) and techniques that do not generate aerosols. Inhalation exposure to DBP using techniques that do not involve aerosols (e.g., application of a product by means of a brush) was estimated to be negligible. The reasonable worst-case full-shift inhalation exposure level was estimated to be 10 mg/m^3 with typical values of 2 mg/m^3 and short-term exposure levels of up to 20 mg/m^3. Dermal exposure during prolonged spray application of products containing DBP was estimated to be up to 975 mg/d.

ECB DIDP (2003)

The ECB DIDP report (2003) reviewed occupational exposure scenarios for two di "isodecyl" phthalate products (i.e., 1,2-benzenedicarboxylic acid, di-C9-11-branched alky esters, C10-rich (CAS 68515-49-1), and di-"isodecyl" phthalate (CAS 26761-40-0)). These two products together are referred to as DIDP. The report found that occupational exposure to DIDP can occur by skin contact with pure DIDP, or by skin contact with mixtures (formulations) or by skin contact with end products that contain DIDP, or by inhalation of DIDP containing vapors or

aerosols. The report found that worker dermal exposure is possible during manufacture (drumming, cleaning, and maintenance) and during handling at the first step of industrial use (pumping, emptying containers). Dermal exposure is also possible handling formulations or end products containing DIDP, especially in the liquid or paste form (e.g., application of coatings, adhesives, or inks). No measured data were provided in the report for dermal exposure. The maximum daily external dermal exposure was estimated by modeling using the size of the permeant and its octanol/water partition coefficient. The maximum dermal exposure was assumed to be 5 mg/cm^2 for all scenarios. Actual dermal exposure is much lower in most occupational circumstances. The report found that worker inhalation exposure is possible during manufacture (when the lid on the closed vacuum system (reactor) is opened at the end each batch, during cleaning and maintenance work, and during filling of tanks and drums), during manufacture of products containing DIDP (PVC compounding, PVC processing), and while using end products containing DIDP (PVC and non-PVC products such as coatings, rubber, latex, mastics, sealants, inks, dyestuffs, lubricants, acrylic resins, paints and pressure-sensitive adhesives). During non-aerosol forming activities inhalation exposure will be negligible because of low vapor pressure. Significant exposure can occur during aerosol-forming activities. During production of DIDP the worst case and typical estimated inhalation exposures were 5 mg/m^3 and 2 mg/m^3 for an 8-hr TWA. During manufacture of products containing DIDP the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 3 mg/m^3 for an 8-hr TWA. During use of end products containing DIDP the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 1.5 mg/m^3 for an 8-hr TWA.

ECB DEHP (2008)

The ECB DEHP report (2008) reviewed sources of occupational inhalation and dermal exposure to DEHP. Inhalation exposure was assessed using both measured data and modeled data. Dermal exposure was estimated using the EASE model. Worker exposure to DEHP was found to occur mainly through the inhalation route. During production the inhalation exposure level was found to be 5 mg/m^3 (530 µg/kg-bw/d), during industrial use of DEHP as an additive the exposure level was 10 mg/m^3 (1,060 µg/kg-bw/d), and during industrial end-use of semi manufactured products and end-use products containing DEHP the exposure level was 10 mg/m^3 (1,060 µg/kg-bw/d). During production the dermal exposure level was found to be 650 mg/day (460 µg/kg-bw/d), during industrial use of DEHP as an additive the exposure level was 420 mg/day (300 µg/kg-bw/d), and during industrial end-use of semi manufactured products and end-use products containing DEHP the exposure level was 1,300 mg/day (928 µg/kg-bw/d).

ECB BBP (2007)

The ECB BBP report (2007) reviewed occupational exposure scenarios for BBP (CAS 85-68-7). The report found that worker inhalation and dermal exposure is possible during production of BBP, industrial use of BBP-containing products, and during professional end use of semi- and end products containing BBP. During production of BBP inhalation exposure can occur during filling tank trucks and rail tankers (reasonable worst case value 0.54 mg/m^3), drumming (reasonable worst case value 1.0 mg/m^3, short term value 2.6 mg/m^3), process sampling (1.0 mg/m^3), and cleaning and maintenance (1.0 mg/m^3). During industrial use of BBP-containing products inhalation exposure can occur during manufacture of flooring using the plastisol spread

coating process (typical value 0.035 mg/m^3, reasonable worst case value 1.2 mg/m^3), processing of PVC floats (typical value <0.005 mg/m^3), processing of sealants (<0.1 mg/m^3), manufacture of flooring with calendering process (typical value 0.4 mg/m^3, reasonable worst case 3.0 mg/m^3), and processing of films with the extrusion process (<0.03 mg/m^3). During professional end use of semi- and end products containing BBP inhalation exposure can occur due to use of polysulfide sealants for glass insulation (negligible), and use of polyurethane sealants/fillers/grouting agents (typical value <0.005 mg/m^3). In addition, the report states that exposure concentrations during professional end use of semi- and end products containing BBP would be similar to the exposures given for manufacture of flooring with calendering process (typical value 0.4 mg/m^3, reasonable worst case 3.0 mg/m^3). The majority of the concentration values were based on measured values except for the process sampling, cleaning and maintenance, and use of polysulfide sealants for glass insulation scenarios which were estimated using the EASE model. The report found that worker dermal exposure is possible during production of BBP, industrial use of BBP-containing products, and during professional end use of semi- and end products containing BBP. During production of BBP dermal exposure can occur during filling tank trucks and rail tankers (420 mg/d), drumming (420 mg/d), process sampling (420 mg/d), and cleaning and maintenance (84 mg/d). During industrial use of BBP-containing products dermal exposure can occur during processing of PVC floats (840 mg/d), processing of sealants (840 mg/d), and manufacture of flooring with calendering process (420 mg/d). During professional end use of semi- and end products containing BBP dermal exposure can occur due to use of polysulfide sealants for glass insulation (0 to 42 mg/d), and use of polyurethane sealants/fillers/grouting agents (84 to 840 mg/d). There were no measured values for dermal exposure. All exposure values were estimated using the EASE model.

ECB DINP (2003)

ECB DINP report (2003) reviewed sources of occupational inhalation and dermal exposure to 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, and C9-rich and Di-isononyl phthalate (CAS 68515-48-0 and CAS 28553-12-0). These products together are referred to as DINP. The report found that occupational exposure to DINP can occur by skin contact with pure DINP, or by skin contact with mixtures (formulations) or by skin contact with end products that contain DIDP, or by inhalation of DINP containing vapors or aerosols. The report found that worker dermal exposure is possible during manufacture (drumming, cleaning, and maintenance) and during handling at the first step of industrial use (pumping, emptying containers). Dermal exposure is also possible with formulations or end products containing DINP, especially in the liquid or paste form (e.g., application of coatings, adhesives, or inks). No measured data were provided in the report for dermal exposure. The maximum daily external dermal exposure was estimated by modeling using the size of the permeant and its octanol/water partition coefficient. The maximum dermal exposure was assumed to be 5 mg/cm^2 for all scenarios. Actual dermal exposure is much lower in most occupational circumstances. The report found that worker inhalation exposure is possible during manufacture (when the lid on the closed vacuum system (reactor) is opened at the end each batch, during cleaning and maintenance work, and during filling of tanks and drums), during manufacture of products containing DINP (PVC compounding, PVC processing), and while using end products containing DINP (PVC and non-PVC products such as coatings, rubber, latex, mastics, sealants, inks, dyestuffs, lubricants, acrylic resins, paints and pressure-sensitive adhesives). During non-aerosol forming activities

inhalation exposure will be negligible because of low vapor pressure. Significant exposure can occur during aerosol-forming activities. During production of DINP the worst case and typical estimated inhalation exposures were 5 mg/m^3 and 2 mg/m^3 for an 8-hr TWA. During manufacture of products containing DINP the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 3 mg/m^3 for an 8-hr TWA. During use of end products containing DINP the worst case and typical estimated inhalation exposures were 10 mg/m^3 and 1.5 mg/m^3 for an 8-hr TWA.

CPSC DINP (2001)

The CPSC DINP report (2001) stated that DINP is used as a general purpose plasticizer to render PVC flexible and has a broad range of applications in toy manufacturing, construction, and general consumer product markets. Human exposure to DINP may occur via inhalation or dermal routes. Potential inhalation exposure to DINP from occupational environments was considered negligible, because monitoring data have been at or below the limit of detection (typically 0.01 mg/kg).

David (2000) and Kohn et al. (2000)

David (2000) and Kohn et al. (2000) stated that phthalates are industrial chemicals used in a variety of applications and that these chemicals can be ingested, inhaled, or absorbed through the skin, resulting in human exposure and raising significant public health concerns. The article stated that the upper bound level for occupational exposure to DBP was estimated at 286 μg/kg/d by the Phthalates Expert Panel of the NTP-CERHR based on published data.

Exponent (2007)

Exponent (2007) stated that occupational exposure limits such as a PEL or TLV have not been established by OSHA of the U.S. Department of Labor, National Institute for Occupational Safety and Health at the CDC, or the ACGIH due to the non-volatile nature of DINP. This is mostly due to the non-volatile nature of DINP. The report also states that few countries have defined occupational exposure limits for DINP. In the U.K., the Health and Safety Executive provides an occupational exposure standard (8-hr TWA) of 5 mg/m^3 for DINP. In Sweden, Swedish National Chemicals Inspectorate provides a "level limit value" of 3 mg/m^3 and a "short-term value" of 5 mg/m^3 that applies to phthalates such as DINP for which no specific limit values have been defined.

HSDB BBP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for BBP. The database search results indicated that National Institute for Occupational Safety and Health (NIOSH) (National Occupational Exposure Survey (NOES) Survey 1981-1983) has statistically estimated that 331,841 workers (59,743 of these were female) were potentially exposed to BBP in the U.S. Occupational exposure to BBP may occur through inhalation of aerosols and dermal contact with this compound at workplaces where BBP is produced or used. No occupational exposure standards were provided. Exposure to

phthalate acid esters (mainly di-(2-ethylhexyl), diisodecyl and BBP) for workers in a polyvinyl chloride processing industry ranged from 0.02 to 2 mg/m^3 for various job categories. The workers excreted slightly but significantly higher levels of phthalate acid ester metabolites in urine than controls. In 54 workers studied clinically, there were no indications of peripheral nerve or respiratory system effects. Workers in a PVC processing plant, who were exposed to diisodecyl phthalate and/or BBP in the air, showed statistically higher levels of phthalate acid ester (not specified) in their urine than workers of the control group.

HSDB DBP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for DBP. The database search results indicated that NIOSH (NOES Survey 1981-1983) has statistically estimated that 512,631 workers (198,249 of these were female) were potentially exposed to dibutyl phthalate in the U.S. Occupational exposure to dibutyl phthalate may occur through inhalation of dusts or vapors and dermal contact with this compound at workplaces where dibutyl phthalate is produced or used. In 173 subjects with suspected occupational dermatoses to plastic or glue allergens, two subjects (1.2%) experienced irritation after applying a patch for testing with 5.0% n-dibutyl phthalate. None of the patients had allergic reactions. In a preliminary study of 150 to 250 workers exposed to vapors in air mixtures of DBP, diethyl phthalate, di-2-ethyl hexyl phthalate, 19 personal air samples (collected in the breathing zone of employees), 4 hr duration each, were collected over a period of 8 days at a number of locations in the vicinity of the operations. The results for the air samples ranged from 1 to 6 ppm, (8 to 15 mg/m^3). No phthalates in blood were found before and after the phthalate exposure.

HSDB DEHP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for DEHP. The database search results indicated that NIOSH (NOES Survey 1981-1983) has statistically estimated that 261,829 workers (84,056 of these are female) are potentially exposed to DEHP in the U.S. Occupational exposure to DEHP may occur through inhalation of aerosols and dermal contact with this compound at workplaces where DEHP is produced or used. Occupational exposure to atmospheric levels of 0.0006 to 0.01 ppm (0.001 to 0.016 mg/m^3) for 10 to 34 years did not increase frequency of chromosomal aberrations in blood leukocytes. A slight decrease in hemoglobin, slight increase in serum alpha-1-antitrypsin, and an increase in serum immunoglobulin A level were noted following occupational exposure. A study was described involving a Swedish PVC-processing factory. Peripheral nervous system symptoms and signs were investigated among 54 male workers exposed to DEHP, diisodecylphthalate, and some butylbenzylphthalate. Several biochemical parameters showed significant association with exposure. There was a slight decrease in the hemoglobin level with longevity of employment and with exposure in the last year. The serum alpha-1-antitrypsin level increased slightly with length of employment and the serum immunoglobulin A level rose with rising exposure during the last year. In a preliminary study of 150 to 250 workers exposed to vapors in air mixtures of dibutyl phthalate, diethyl phthalate, DEHP, 19 personal air samples (collected in the breathing zone of employees), 4-hr duration each, were collected over a period of 8 days at a number of locations in the vicinity of the operations. The results for the air

samples ranged from 1 to 6 ppm, (8 to 15 mg/m^3). No phthalates in blood were found before and after the phthalate exposure.

HSDB DIDP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for DIDP. The database search results indicated that NIOSH (NOES Survey 1981-1983) has statistically estimated that 80,441 workers (31,734 of these were female) were potentially exposed to DIDP in the U.S. Occupational exposure to DIDP may occur through inhalation and dermal contact with this compound at workplaces where DIDP is produced or used. No occupational exposure standards were provided. Workers were found to be exposed to phthalate acid esters mainly di(ethylhexyl), DIDP, and butylbenzyl phthalate in the air in a polyvinyl chloride processing industry with mean concentrations ranging from 0.02 to 2.0 mg/m^3.

HSDB DINP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for DINP. The database search results indicated that NIOSH (NOES Survey 1981-1983) has statistically estimated that 88,575 workers (20,954 of these were female) were potentially exposed to DINP in the U.S. Occupational exposure to DINP may occur through inhalation and dermal contact with this compound at workplaces where DINP is produced or used. No occupational exposure standards were provided.

HSDB DnOP (2008)

The following information was generated from the HSDB, a database of the National Library of Medicine's TOXNET system, for DnOP. The database search results indicated that NIOSH (NOES Survey 1981-1983) has statistically estimated that 7,678 workers (1,296 of these are female) are potentially exposed to DnOP in the U.S. Occupational exposure to DnOP may occur through inhalation of aerosols and dermal contact with this compound at workplaces where DnOP is produced or used as a plasticizer. No occupational exposure standards were provided.

Matsumoto et al. (2008)

Matsumoto et al. (2008) reviewed and summarized recent studies on phthalate acid esters (PAE) exposure and health effects in human populations. The article stated that in females, decreased rates of pregnancy and higher levels of miscarriage in factory workers were associated with occupational exposure of DBP.

NTP-CERHR BBP (2000)

The NTP-CERHR BBP report (2000) stated that the largest use of BBP is in vinyl tile. BBP is also a plasticizer in PVC that is subsequently used to manufacture food conveyor belts, carpet tile, artificial leather, tarps, automotive trim, weather stripping, traffic cones, and is used to a limited extent in vinyl gloves. BBP is also used in some adhesives. BBP may be released to the

environment during its production and also during incorporation into plastics or adhesives. Occupational exposure can occur through skin contact and by inhalation of vapors and dusts. The ACC has estimated exposure to BBP in the workplace based upon an assumed level of 1 mg/m^3 during the production of phthalates and 2 mg/m^3 during the manufacture of flexible PVC. An exposure level was estimated by using assumptions of a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimates were 143 µg/kg-bw/workday and 286 µg/kg-bw/workday for workers employed in phthalate manufacturing and flexible PVC production operations, respectively. Absorption of BBP through skin is expected to be minimal.

NTP-CERHR BBP (2003)

The NTP-CERHR BBP (2003) evaluated the potential reproductive and developmental toxicities of BBP. The report found that occupational exposure can occur through skin contact and by inhalation of vapors and dusts. Even though phthalates are manufactured within closed systems, exposure to workers can occur during filtering or loading/unloading of tank cars. Higher levels of exposure to phthalates can occur during incorporation of phthalate into the final product because the process is typically run at a higher temperature than is used in the manufacturing process. The ACC has estimated exposure to BBP in the workplace based upon an assumed air concentration of 1 mg/m^3 during the production of phthalates and 2 mg/m^3 during the manufacture of flexible PVC. Exposure levels were estimated assuming a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimates were 143 µg/kg-bw/workday (for phthalate manufacturing) and 286 µg/kg-bw/workday (for flexible PVC production operations). The report stated that absorption of BBP through skin is expected to be minimal because of low absorption rate. There were no human data available on the reproductive toxicity of BBP alone. Occupational exposure to phthalate mixtures containing BBP in PVC production has been associated with increased incidence of menstrual disorders and spontaneous abortions among female workers. Exposures to BBP-containing phthalate mixtures have been associated with elevated respiratory/neurological morbidity and increased risk of cancer in occupationally exposed population groups. A significant increase in the risk of multiple myeloma has been found among workers employed for 5 or more years in PVC production.

NTP-CERHR DBP (2000)

The NTP-CERHR DBP report (2000) stated that DBP is used mainly as a coalescing aid in latex adhesives. DBP is also used as a plasticizer in cellulose plastics and as a solvent for dyes. Exposure in occupational settings can occur through skin contact and by inhalation of vapors and dust. In a limited number of studies, DBP levels in U.S. plants were found to range from concentrations below the detection limit (0.01 to 0.02 mg/m^3) to 0.08 mg/m^3. OSHA established a permissible exposure limit of 5 mg/m^3 for DBP. Following a review of six studies, the ACC has estimated exposure to DBP in the workplace based upon an assumed level of 1 mg/m^3 during the production of phthalates. An exposure level was estimated by using assumptions of a 10 m^3/day inhalation rate and a 70 kg body weight. The resulting exposure estimate was 143 µg/kg-bw/workday for workers employed in phthalate manufacturing. Absorption of DBP through skin is expected to be minimal.

NTP-CERHR DBP (2003)

The NTP-CERHR DBP (2003) evaluated the potential reproductive and developmental toxicities of DBP. The report found that occupational exposure can occur through skin contact and by inhalation of vapors and dust. Even though phthalates are manufactured within closed systems, exposure to workers can occur during filtering or loading/unloading of tank cars. Higher levels of exposure to phthalates can occur during incorporation of phthalate into the final product because the process is typically run at a higher temperature than is used in the manufacturing process. DBP air concentration levels in U.S. plants (based on a limited number of surveys) range from below the detection limit (0.01 to 0.02 mg/m^3) to 0.08 mg/m^3. The OSHA established PEL is 5 mg/m^3 for DBP. The ACC estimated exposure to DBP in the workplace based upon an assumed level of 1 mg/m^3 during the production of phthalates. Exposure levels during the incorporation of DBP into plastics are not known. Exposure levels were estimated assuming a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimate was 143 µg/kg-bw/workday for workers employed in phthalate manufacturing. The maximum exposure, by regulation, would be five-fold greater. Information was not available on exposure to workers who use DBP to manufacture other products. The report stated that absorption of DBP through skin is expected to be minimal because of low absorption rate.

NTP-CERHR DEHP (2000)

The NTP-CERHR DEHP (2000) stated that DEHP is used as a plasticizer of PVC in the manufacture of a wide variety of consumer products. DEHP is used in building products (flooring and pavements, roof coverings, wallpaper, polymeric coatings, tubes and containers, wire and cable insulation), car products (vinyl upholstery, car seats, underbody coating, trim), clothing (footwear, raincoats), food packaging, children's products (toys, crib bumpers), and medical devices. Occupational exposure to DEHP occurs during the manufacture and processing of this compound. Workers may be exposed to high concentrations during the compounding of DEHP with PVC. The major route of exposure is inhalation. Maximum occupational exposures should not exceed 700 µg/kg-bw/d if the workplace air concentrations meet the OSHA standard. Studies based upon workplace air measurements in Europe and the former USSR estimate occupational exposures from <2 to 6,600 µg/kg-bw/d. The ACC cites six studies that indicate that exposures in the U.S. are generally below 1 mg/m^3 during production of phthalates and below 2 mg/m^3 during production of PVC. They estimated an exposure of less than 143 µg/kg-bw/workday for phthalate production workers. The corresponding exposure for PVC production workers was 286 µg/kg-bw/workday.

NTP-CERHR DIDP (2003)

The NTP-CERHR DIDP (2003) evaluated the potential reproductive and developmental toxicities of DIDP. DIDP is used as a plasticizer in a wide variety of PVC plastic products. These include coverings on wires and cables, artificial leather, toys, carpet backing, and pool liners. The report found that occupational exposure occurs primarily through inhalation and dermal contact. Even though DIDP is manufactured within closed systems under negative pressure, exposure to workers can occur during loading/unloading of railroad cars and trucks. Higher exposures may occur during the production of PVC products because of elevated

temperatures and more open processes. Limited studies of occupational exposures suggest that inhalation exposure is below 1 mg/m^3 during production of DIDP and below 2 mg/m^3 during production of PVC.

NTP-CERHR DINP (2003)

The NTP-CERHR DINP (2003) evaluated the potential reproductive and developmental toxicities of DINP. DINP is used to manufacture a broad range of consumer products such as garden hoses, pool liners, flooring tiles, tarps, and toys. The report found that occupational exposure occurs primarily through inhalation and dermal contact. Even though DIDP is manufactured within closed systems under negative pressure, exposure to workers can occur during loading/unloading of railroad cars and trucks. Higher exposures may occur during the production of PVC products because of elevated temperatures and more open processes. Limited studies of occupational exposures suggest that inhalation exposure is below 1 mg/m3 during production of DIDP and below 2 mg/m^3 during production of PVC.

NTP-CERHR DnOP (2003)

The NTP-CERHR DnOP (2003) evaluated the potential reproductive and developmental toxicities of DnOP. DnOP is used in the manufacture of a variety of commercial products including flooring and carpet tiles, tarps, pool liners, and garden hoses. DnOP is approved by the FDA as an indirect food additive and is used in seam cements, bottle cap liners, and conveyor belts. The report found that occupational exposure occurs primarily through inhalation and dermal contact. Even though phthalates are manufactured within closed systems, exposure to workers can occur during filtering or loading/unloading of tank cars. Higher levels of exposure to phthalates can occur during the production of flexible PVC because the processes are open and typically run at higher temperatures than are used in the manufacturing process. The ACC found that phthalate levels in air are generally lower than 1 mg/m^3 during the production of phthalates and 2 mg/m^3 during the production of flexible PVC. Exposure levels were estimated by the ACC using assumptions of a 10 m^3/d inhalation rate and a 70 kg body weight. The resulting exposure estimates were 143 µg/kg-bw/workday for workers employed in phthalate manufacturing operations and 286 µg/kg-bw/workday for workers employed in flexible PVC manufacturing operations. The report stated that absorption of BBP through skin is expected to be minimal because of low absorption rate.

CPSC BBP (2009)

The CPSC's Health Sciences staff performed an assessment of the potential toxicity associated with BBP. Occupational exposure to BBP is possible through skin contact and inhalation, but the study found that data on BBP concentrations in the occupational environment are limited. The data are insufficient to determine the extent of exposure through occupational exposure.

CPSC DBP (2009)

The CPSC's Health Sciences staff performed an assessment of the potential toxicity associated with DBP. Occupational exposures were described in the assessment. In one study, it was

reported that workers were exposed to DBP above the Maximum Allowable Concentration of 0.5 mg/m^3, however, quantitative data on exposure was not given. In another study, 189 women were given gynecological examination, 33% were normal, 33% showed deviations of the uterus, and 34% were undisclosed. A decrease in pregnancies and birth in the women exposed to DBP, as well as estrogen/progesterone cyclicity abnormalities were noted. However, inadequate documentation of exposure was provided, making it difficult to draw significant conclusions from this study.

CPSC DIDP (2009)

The CPSC's Health Sciences staff performed an assessment of the potential toxicity associated with DIDP. The study found that occupational exposure occurs from inhalation and dermal routes, while consumers are exposed mainly from dermal and oral routes. The manufacturer's exposure limits for DIDP is 5 mg/m^3 based on a value recommended by the ACGIH.

CPSC DnOP (2009)

The CPSC's Health Sciences staff performed an assessment of the potential toxicity associated with DnOP. No human studies have been found that determine absorption, distribution, metabolism, and excretion of DnOP from oral, dermal, or inhalation exposures. Evidence from one case report suggests that DnOP is a mild respiratory irritant (NICNAS, 2008d). In this case, respiratory irritation was reported in workers exposed to a mixture of phthalates (including DnOP).

SCENIHR (2008)

This report reviewed the safety of medical devices containing DEHP plasticized PVC or other plasticizers. There is limited evidence linking DEHP exposures and some adverse effects in humans. The few follow-up studies performed after high DEHP exposures in neonates and in occupational settings, did not indicate that there is an effect of DEHP exposure on fertility and/or the human male reproductive system. Contradictory results were reported for the effect of DEHP on semen quality and female development. The report stated that there are currently four producers of DINP in the EU. Approximately 95% of DINP are used in PVC as a plasticizer. DINP is used as a plasticizer in toys, vinyl flooring, wire and cable, stationery, wood veneer, coated fabrics, gloves, tubing, artificial leather, shoes, sealants and carpet backing. The estimated maximum combined total daily intake for an occupationally exposed adult is 1.12 mg/kg-bw/d. For non-occupational exposed adults and children a maximum exposure of 20 µg/kg-bw/d is estimated. These estimates were based on DINP measurements in several environmental media and consumer products.

SCHER (2006)

The European Consumers' Organisation, BEUC (Bureau Européen des Consommateurs), commissioned this study to analyze the chemical substances present in indoor air following the use of air fresheners. Most available toxicity data DBP are related to exposure via dermal and

oral route. The ACGIH proposed an inhalation exposure level of 5 mg/m^3 for occupational exposure to protect workers.

Jaakkola and Knight (2008)

Jaakkola and Knight (2008) reviewed studies on the effects of exposure to phthalates on the human respiratory system. The concentration of DEHP in different work sites in the polyvinyl processing industry ranged from 20 to 2,000 μg/m^3. The study states that in occupational settings the inhalation of phthalates constitutes a comparatively larger fraction of exposure for workers. The report found that there was evidence that occupation exposure to pyrolysis products of phthalates and other combustion products (e.g., from hot-wire cutting of PVC film) may increase the risk of asthma.

ATSDR DBP (2001)

ATSDR DBP (2001) found that occupational exposure to DBP can occur by inhalation of vapors and dust. The report stated that occupational exposure though inhalation has been estimated to be 143 μg/kg-bw/workday for workers employed in phthalate manufacturing. Studies of people occupationally exposed to DBP are needed to assess the effects of DBP on human health. The study reviewed the results of the NIOSH NOES from 1981 to 1983. Data from the survey show that an estimated 31,502 facilities use di-n-butyl phthalate in 199 industries involving 138 occupations. Exposed populations are estimated to be 512,631 employees (198,249 female and 314,382 male workers). Exposures in occupational settings can occur through skin contact and by inhalation of vapors and dust. Although phthalates are manufactured within closed systems, workers can be exposed during filtering operations or while loading/unloading tank cars. Higher exposures to phthalates can occur while incorporating the phthalate into the final product (e.g., plastics) if the process runs at a high temperature. In a limited number of surveys, DBP levels in production facilities in the U.S. ranged from below the detection limit (0.01 to 0.02 mg/m^3) to 0.08 mg/m^3. The report stated that following a review of six studies, the ACC has estimated exposure to DBP in the workplace based upon an assumed level of 1 mg/m^3 in the air during the production of phthalate. An exposure level was estimated using assumptions of a 10 m^3/day inhalation and a 70 kg body weight. The resulting exposure estimate was 143 μg/kg-bw/workday for workers employed in phthalate manufacturing.

ATSDR DEHP (2002)

ATSDR DEHP (2002) found that occupational exposure to DEHP might be important during the manufacture and processing of this compound. Workers can be exposed to relatively high concentrations of DEHP during the compounding of this plasticizer with resins and the manufacture of PVC plastic products. The study stated that NIOSH estimated that about 340,000 workers (approximately 106,900 were female) were potentially exposed to DEHP in the early 1980s. Workplace air levels of DEHP ranged from 0.02 to 4.1 mg/m^3 at facilities using or manufacturing the compound. These levels are below the current OSHA PEL for DEHP for an 8-hr workday of 5 mg/m^3. Exposure for phthalate and PVC production workers to DEHP were estimated to be typically less than 143 and 286 μg/kg-bw/workday, respectively.

5.4. CONSUMER EXPOSURE

5.4.1. INTRODUCTION

This section provides a summary of the literature review conducted to obtain information on exposure to phthalates from the use of consumer products. Ten different exposure scenarios for consumers are included in this section. Each exposure scenario summarizes information on the potential routes of exposure and exposure data related to the use of consumer products. Brief overviews of the ten exposure scenarios are provided in the paragraphs below. Detailed descriptions of the sources and/or studies containing information on consumer exposures to phthalates are presented for each scenario in Sections 5.4.1 through 5.4.10.

Scenario 1: Toys and Baby Equipment (Section 5.4.2)

Infants and children can be exposed to phthalates from contact with toys and children's articles containing phthalates. Types of products which have been shown to contain phthalates include teethers, squeeze toys, bath toys, mattresses, and bedding accessories. Oral exposure occurs through sucking, chewing and biting toys and dermal exposure occurs through skin contact with the toys and other child-care products. Inhalation exposure is not expected from these articles. Children's activity patterns, such as mouthing frequency and duration of contact, are an important part of estimating oral and dermal exposures. A number of studies have evaluated mouthing patterns, including Juberg et al. (2001), Tulve et al. (2002) and RIVM (1998). These studies show that mouthing behavior is dependent on age and types of items mouthed. Also important to estimating oral and dermal exposures is the amount of phthalate that migrates from objects during contact. Migration tests have been conducted using a variety of products, stimulants (i.e., saliva and sweat), and extraction methods (i.e., shaking, tumbling, scrubbing, etc.) to simulate both oral and dermal exposures to toys and child-care products. Migration testing results are available for DEHP, DINP and DIDP. One study also investigated the migration of DBP from a toy ball, however, according to NTP-CERHR (NTP-CERHR DBP, 2003), DBP is rarely used in toys. No migration testing data are available for BBP, however, according to ECB BBP (2007), BBP is not intentionally used in toys though may be present as a byproduct or impurity. Using the activity pattern data, migration testing or product concentration data, body weight, and/or other factors such as surface area contact and dermal absorption rates, oral and dermal exposures have been estimated in several studies for DEHP, DINP, and DIDP. For DEHP, calculated oral exposures ranged from <1 to 526 µg/kg/d, with the highest exposure calculated for heavy mouthing of a pacifier. Daily dermal exposures for DEHP ranged from 9 to 12.4 µg/kg/d, as calculated by ECB (ECB DEHP, 2008). Annual dermal exposures, as calculated by CPSC (1983a), ranged from 960 mg for playpens with vinyl covers to 1,200 mg for children wearing vinyl pants. For DIDP, the highest oral exposure calculated was 19 µg/kg/d (as reported in ECB DIDP, 2003), which was over than the 5000 times higher than the lowest value. Dermal exposure was estimated at 1 µg/kg/d by ECB (ECB DIDP, 2003). For DINP, the highest oral exposure calculated was 320 µg/kg/d, calculated based on mouthing times for teethers and other objects intended for mouthing (as reported in NTP-CERHR DINP, 2003). CPSC (1998a) report the 95th percentile oral exposure value of 94.3 µg/kg/d for DINP. Dermal exposure for DINP was estimated at 1 µg/kg/d by ECB (ECB DINP, 2003).

Scenario 2: Medical Devices (Section 5.4.3)

People undergoing certain medical procedures may be exposed to phthalates leaching from plasticized medical devices into blood or blood products (intravenous exposure), enteral nutrition solutions (oral exposure), or air in respiratory tubing (inhalation exposure). Phthalate exposure via medical devices has been addressed in comprehensive reviews of the available literature conducted by the FDA, the ECB, the NTP-CERHR, and Health Canada. The reported exposure values vary among the various reports as a result of the different assumptions used in deriving the estimates. However, a few medical procedures emerge as having the potential to cause exposure to high levels of DEHP, the most commonly used plasticizer in medical devices. These procedures include hemodialysis in adults (up to 3.1 mg/kg/d) and blood transfusions to trauma patients (8.5 mg/kg-bw/d) and infants (up to 23 mg/kg/d). Exposure values reported in the available literature should be considered in the context of the uncertainties associated with these estimates. For one thing, many of the exposure estimates rely on measurements of DEHP concentrations in various media (i.e., blood, intravenous (IV) solutions) and DEHP leaching rates from medical devices. However, estimates based only on measured DEHP levels in blood without considering metabolite concentrations may underestimate exposure since DEHP can be metabolized to MEHP by enzymes contained in blood products (NTP-CERHR DEHP, 2006). On the other hand, reported DEHP leaching rates often represent worst-case conditions which can lead to overestimates of DEHP exposures. It should also be noted that most of the available literature focuses on exposure from single medical procedures. Actual DEHP exposure levels may be higher than those reported for some patients such as critically ill neonates and adults undergoing extracorporeal membrane oxygenation (EMCO) and surgical procedures since these patients often require a combination of several medical procedures during the course of their treatment (FDA, 2001).

Scenario 3: Personal Care Products (Section 5.4.4)

Dermal exposure to phthalates in personal care products has been evaluated by various researchers based on measured or estimated levels of phthalates (mainly DEHP, DMP, DEP, DBP, and BBP) in the products and different assumptions regarding frequency, duration, and mode of product application and amount of product used. The exposure estimates vary among the studies and rely on limited data on dermal absorption of phthalates through animal skin. Most of the available studies address exposure from use of a specific product such as nail polish (ECB DBP, 2003-04); only one study (Koo and Lee, 2004) evaluated total daily exposure levels from the concurrent use of various personal care products including perfume, deodorant, nail polish and hair products, based on measured levels of DEHP, DEP, DBP, and BBP in cosmetic products. Total mean daily exposure levels to phthalates from use of multiple cosmetic products ranged from 0.0003 μg/kg/d for DEHP to 24.88 μg/kg/d for DEP (Koo and Lee, 2004). Dermal exposure to phthalates from use of baby care products was investigated by Sathyanarayana et al. (2008) who found increased urinary concentrations of MEP, MMP, and MiBP in infants younger than 8 months following use of infant lotion, powder and shampoo. Inhalation or incidental ingestion of phthalates from the use of personal care products may also be possible; however, very limited data are currently available regarding these exposure routes.

Scenario 4: Clothing, Gloves, and Footwear (Section 5.4.5)

Limited information is currently available regarding exposure to phthalates from clothing, gloves and footwear. Dermal exposure estimates are available for rainwear and sandals (CPSC, 2001), gloves (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008; Wormuth et al., 2006) and textile fabrics (Jensen and Knudsen, 2006). These estimates focus on DIDP, DINP and DEHP and are based on animal data and various assumptions on frequency and duration of product use. In the CPSC (2001) report, dermal exposures ranged from 0.45 µg/kg/d for adults wearing rainwear to 340 µg/kg/d for children wearing "jelly" sandals. Estimates of dermal exposure from gloves were reported by ECB (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008) as 0.7 µg/kg-bw/d for DIDP and DINP and 6.7 µg/kg-bw/d for DEHP. On the study by Wormuth et al (2006), gloves accounted for over 10% of the exposure to DINP and for 5 to 7% of the total exposure to DIDP in teenagers and adults. Oral (from sucking or chewing fabrics) and inhalation exposures have been addressed by only one current study (Jensen and Knudsen, 2006). In the study by Jensen and Knudsen (2006), oral intake for children sucking or chewing a textile piece was reported as 15.4 µg/kg-bw, while inhalation exposure to DEHP was reported to be very small (6.44×10^{-6} µg/kg-bw/d).

Scenario 5: Car and Public Transportation Interiors (Section 5.4.6)

Exposure to phthalates in car and public transportation interiors has not been extensively investigated. Currently, published estimates are only available for the inhalation route of exposure even though dermal exposure through contact with interior auto components and dust may also be an important source of exposure to phthalates inside cars. ECB (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008) estimated inhalation exposure to DIDP, DINP and DEHP for adults as 0.8 µg/kg-bw/day, 1.7 µg/kg-bw/d and 0.9 µg/kg-bw/day, respectively. Inhalation exposure levels of 1.9 µg/kg-bw/d, 3.9 µg/kg-bw/d, and 2 µg/kg-bw/d were estimated in children for DIDP, DINP and DEHP, respectively. It should be noted that the estimates provided in the ECB reports do not account for the high temperatures that may be found inside cars during summer, which can result in higher air concentrations of phthalates as described in Fujii et al (2003).

Scenario 6: Building Materials and Furniture (Section 5.4.7)

Exposure to phthalates in the home from building materials, furniture, and indoor dust has been evaluated by various researchers. Inhalation of airborne dust particles and/or ingestion of dust containing phthalates can be a significant route of exposure, especially among young children and infants (Jaakkola and Knight, 2008, Jensen and Knudsen, 2006, Wormuth et al., 2006). Jensen and Knudsen (2006) estimated the average daily intake of phthalates for a child exposed DEHP from all indoor sources to be 10-20 µg/kg-bw/d, but in worst cases as much as 50-250 µg/kg-bw/day for a child crawling on vinyl flooring. Dust ingestion, mouthing of textiles, and dermal contact with textiles contributed to total exposure. NTP-CERHR (NTP-CERHR DEHP, 2006) found that from sources other than food (which contributed to over 90% of exposure for those over 6 months) ingestion of dust was the most important route of exposure. For infants, dust ingestion was a significant route of exposure, with intakes of 39.3 to 54.1 µg/kg-bw/d. Indoor air exposure to DEHP was minimal in both of these studies and was deemed insignificant.

Studies for other phthalates (DEP, DBP, BBP, and dicyclohexyl phthalate) also reported low levels of exposure due to indoor air inhalation (Schettler 2006, Otake et al., 2004). EU studies found higher levels of exposure to phthalates due to indoor air inhalation; however, these estimates came from modeling that used conservative, worse scenario data, and thus may be artificially high. Wormuth et al. (2006) estimated the consumer exposure to eight phthalates (DMP, DEP, DiBP, DnBP, BBzP, DEHP, DINP, and DIDP) using a scenario-based exposure assessment approach that included various oral, dermal, and inhalation exposure pathways. They reported the percent contributions of dust ingestion and indoor air inhalation to total daily intake for various age groups for each of the eight phthalates. Dust ingestion was found to be a significant source of exposure for infants and toddlers for several of the phthalates (DiBP, BBzP, DEHP, and DIDP). Dust ingestion contributed more than 70% of the total daily intake for BBzP. Dust ingestion was found to have minimal contribution to total exposure for older children, teenagers, and adults. The contribution of indoor air inhalation to the total daily intake varied greatly depending upon physiochemical characteristics and uses of the specific phthalate. Indoor air inhalation of DMP contributed to nearly all the exposure for infants, toddlers, and children and 70-90% for adults and teenagers. Other phthalates (such as DiBP, BBzP, and DEHP) had little to no exposure due to indoor air inhalation.

Scenario 7: Food and Food-Related Uses (Section 5.4.8)

Food is likely to be the largest single exposure source of phthalates in the general population (Schettler, 2006; Chen et al., 2007; Shea, 2003; Wormuth, et al., 2006). However, the contribution of each phthalate to total phthalate exposure varies by compound (Wormuth, et al., 2006; Wenzl, 2009). Exposure estimates and dietary intakes for phthalates as related to food have been provided in a number of studies and primarily for DEHP, BBP, and DBP. Foods have been found to be contaminated with phthalates during growth, production, processing, or packaging (Shea, 2003; Kamrin, 2009). Possible sources of some phthalates found in food are cellulose-based food wraps and latex adhesives used in food processing in which the phthalate has migrated into the food (NTP-CERHR DnOP, 2003). The levels of selected phthalates in food, infant formula, and human milk have been shown in food surveys worldwide, with the majority of the data from European, with some Asian and American studies. However, according to Schettler (2006), the phthalate levels found in food are widely variable; the data are often old and may not reflect current dietary intake and exposure levels. IPCS (1997) also notes that dietary intake varies according to the types of food eaten and the types of material in which the food is packaged. The highest levels of phthalates in foods have been detected in the fatty foods such as oils, dairy, infant formula, meat, meat products, and fish (Fromme et al., 2007b; Wormuth et al., 2006; Shea, 2003). Fatty foods and oily foods are believed to be contaminated primarily because of their lipophilic characteristic (Wenzl, 2009). Wormuth et al. (2006) provided the percent contribution of food to total phthalate exposure in consumer groups as follows: DBP, 60% in infants and toddlers, >95% in teenagers and adults; DnBP, 40-90% for all consumer groups, DEHP, 50-98% for all consumer groups. For DIDP, food contributes to 55-70% of the exposure for teenagers and adults. Food is a major source (73%) of BBP exposure in children (73%), teenagers (> 20%) and adults (60%). Data on levels of DINP, DIDP, and DnOP in food are limited, therefore exposure estimates are few. For the most part, the phthalate food exposure estimates shown in the available literature are based on concentration data from the same food surveys. Wenzl (2009) noted that the data for the occurrence of phthalates in food

cannot be easily extrapolated from one country to another and potentially different contaminations levels can be expected in different geographical regions/countries.

Scenario 8: Pharmaceuticals (Section 5.4.9)

The polymer coating of some oral medications contains phthalate plasticizers such as DEP and DBP. These coatings are used on medications to allow the release of active ingredients into the small intestine or the colon (Hauser et al., 2004). Two studies have been conducted to evaluate medication as a potential source of exposure to phthalates, including a study comparing users and nonusers of certain medications using data from the NHANES for the years 1999–2004 (Hernández-Díaz et al., 2009) and a case study for one man who was taking Asacol (active ingredient mesalamine) (Hauser et al., 2004). Both studies assessed exposure by evaluating phthalate metabolite levels in urine. Based on the study results, Hernández-Díaz et al. (2009) concluded that select medications might be a source of high exposure to some phthalates. For mesalamine users, urinary concentrations of MBP (metabolite of DBP) were 50 times higher than the mean for nonusers. Users of didanosine, omeprazole, and theophylline products also had mean urinary concentrations of MEP (metabolite of DEP) significantly higher than the mean for nonusers. In the Hauser et al. (2004) study, the patient in the case study was determined to have urinary MBP level two orders of magnitude higher than the U.S. population 95th percentile. Hauser et al. (2004) linked this unusually high urinary MBP concentration with the use of the medication Asacol, which contains DBP. Hauser et al. (2004) states that further research is necessary to determine the proportional contribution of medications, as well as personal care and consumer products, to a person's total phthalate burden.

Scenario 9: Adult Toys and Pleasure Gels (Section 5.4.10)

The DEPA conducted two surveys to investigate the presence of chemicals, including phthalates, in adult toys, clothing and pleasure gels/creams/oils (Nilsson et al., 2005; Tønnig et al., 2005). The adult toy and clothing products tested were made of rubber, soft vinyl, natural latex, rubber, or thermoplastic rubber. Chemical screening analysis of 15 adults toys and clothing showed that some of the products contained DEP (n=1), DEHP (n=8), DnOP (n=2), and/or DINP (n=2). Migration testing was conducted on six select toys/clothing. The migration testing showed that migration increased significantly when an oil-based lubricant was used instead of a water-based lubricant. Based on the migration testing, exposures were only estimated for DEHP and DnOP. For DEHP, the maximum internal dose was for a soft vinyl toy. The internal dose for normal use was estimated as 0.0017 mg/kg body weight and the internal dose for worst-case use was calculated was 0.047 mg/kg body weight. For DnOP, Nilsson et al. (2005) assumed a worst case uptake of approximately 0.05 mg/kg body weight, based on results for DEHP. Phthalates (DEP) were only detected in one pleasure gel product, out of 22 different products total. Phthalate exposure was not determined for this product (Tønnig et al., 2005).

Scenario 10: Miscellaneous (Section 5.4.11)

Consumer products such as air fresheners, polymer clay, and stain removers can be sources of exposure to phthalates via the dermal and/or inhalation routes. Currently, there are limited data on consumer exposures resulting from the use of these products. A study by the European

Consumers' Organization (BEUC) on emissions from air fresheners, as described in SCHER (2006), measured indoor air concentrations of DEPH following the use of several types of air fresheners. However, a quantitative assessment of exposure was not performed. SCHER (2006) noted that data on use pattern of air fresheners is needed to assess actual exposure to consumers. Incidental ingestion of phthalates from polymer clay was estimated by Stopford et al. (2003) to range from 127 to 250 µg/d, depending on the type of polymer clay used. Schettler (2006), on the other hand, reported maximum inhalation exposures following baking of polymer clay for BBP, DnOP, and DEHP or similar compounds of 2,667, 6,670 and 4,993 µg, respectively. Inhalation exposure to DBP resulting from the use of stain remover was reported by Jensen and Knudsen (2006) as 3.19×10^{-6} mg/kg-bw/d, based on an estimated DBP air concentration of 22.5 $\mu g/m^3$.

5.4.1. Scenario 1: Toys and Children's Products

This section summarizes the available exposure estimates for DEHP, BBP, DINP, and DIDP when used in toys and children's articles. Exposure calculations, migration studies, and data supporting the presence of specific phthalates in toys and articles used by children have been extracted from the literature and presented in individual subsections. Exposure estimates and migration studies were not available for DBP and DnOP. DBP is rarely used in toys (NTP-CERHR DBP, 2003); however, a summary of one migration study has been included.

A major source of concern for dialkyl phthalate exposure is from plastic toys and other items for use by children (ECB DEHP, 2008; Stringer et al., 2000). Dialkyl phthalates have been used historically as plasticizers in PVC products, which are commonly used in many soft plastic toys, teethers, and other children's products (ECB DEHP, 2008; Stringer et al., 2000; CPSC, 1998b), including rattles, squeeze toys (CPSC, 1998b), pacifiers, crib bumpers, play pen covers, baby mattresses, and baby pants (CPSC, 1982). In a study conducted for Greenpeace, Stringer et al. (2000) report that dialkyl phthalates "comprised a sizeable proportion" (10-40% of total weight) in almost all 64 PVC toys or toys with PVC sections analyzed from 17 countries. ECB DEHP (2008) reports results from an investigation by the Laboratory of the Government Chemist U.K. indicating that 72% of 113 plastic teethers and toys tested contained phthalates. The date this study was performed is unknown. CPSC (1982) reported that based on data from the Juvenile Products Manufacturer's Association (JPMA) and U.S. Census Bureau on children's bedding accessories, such as crib mattresses, play-pen covers, and crib bumpers, approximately 90% of all vinyl products in this category contain DEHP as a plasticizer.

The principle plasticizer used in children's products is DINP (NTP-CERHR DINP, 2003; Sathyanarayana et al., 2008; CPSC, 1998b). The principal dialkyl phthalate used in children's products until 1985 was DEHP, at which time it was found to be carcinogenic and was voluntarily replaced by DINP in similar products. In 1999, manufacturers voluntarily removed DINP from children's toys, teethers and other products "intended to be mouthed" (CPSC, 2002a). ECB DEHP (2008) reports that DEHP is no longer used in pacifiers in Europe, however, they also present a study (date unknown) that states that almost 25% of 82 plastic teethers and toys tested contained DEHP as a major component. A nonprofit group, Environment California, identified DEHP as the primary phthalate in bath books (cited in Sathyanarayana et al., 2008) and also reported that DBP, DnOP, and DEP were found in teethers, bath toys, and other toys,

DnOP was found in a pacifier and baby bottle nipple and DINP was found in one pacifier. They also noted that most pacifiers and baby bottles did not contain phthalates (Sathyanarayana et al., 2008).

The primary route of exposure to phthalates from toys and other objects for small children is believed to be oral exposure because children mouth, suck, chew, and bite on toys or other objects containing phthalates (ECB DEHP, 2008; ECB DIDP, 2003). This combination of "chewing" coupled with the continuous flow of fresh saliva around these articles is reported to be an effective extraction process for phthalates such as DIDP (ECB DIDP, 2003). Since a direct method for calculating exposure from toys is not available (ECB DIDP, 2003), oral exposure from toys is calculated using (1) mouthing frequency; (2) the time objects are in a child's mouth; and (3) migration/release rates of phthalates (Exponent, 2007). Mouthing behavior is dependent on age and the types of items mouthed. Children in the 0- to 18-month age category have been found to have a significantly higher mouthing time of all non-pacifier objects (Juberg et al., 2001). Tulve et al. (2002) describe that mouthing in children progresses from sustenance to exploratory, during which time children put their hands and any object they come in contact with into their mouths, followed by teething which typically begins at 7 to 8 months. Nondietary ingestion of phthalates is a difficult source of exposure to quantify directly (Shea, 2003). Through the use of videotaping studies, use of parents as observers, and conducting surveys estimating, the frequency of mouthing behavior has been refined (Tulve et al., 2002). In a notable study, RIVM (1998) derived mean mouthing times using a 2-day parent observation study of 42 children, aged 3–36 months (cited in Babich et al., 2004).

Another factor in estimating oral exposure is the rate that phthalates are released from objects (Exponent, 2007). Only a fraction of the contaminant in a consumer product may be bioavailable during oral exposure (Brandon et al., 2006), therefore, the total amount of a contaminant that migrates from objects needs to be estimated. CPSC (1983a, b) reports that the accuracy of migration tests is impacted by: use of saliva or saliva simulants; effect of mucin and salt concentrations in simulated saliva; effect of squeezing or chewing; and the length of time saliva or saliva simulants are in contact with the objects.

In addition to oral exposure, there is a potential for dermal exposure from the handling of children's toys and articles. ECB DINP (2003) describes dermal exposure as the absorption of contaminants through the skin of the hands or through children's lips. Factors affecting the amount of contaminants absorbed include the area of skin in contact with the product, duration of that contact, availability/release of the phthalate, and penetration through the skin. CPSC (2008) discusses two different methods for estimating dermal exposure and percutaneous absorption. The CF method is an *in vivo* method which is similar to the method used in EU risk assessments and involves placement of PVC films on the backs of rats. The method measures migration and percutaneous absorption simultaneously, however, it may not account for exposure under all conditions. The second methodology, the AC method estimates percutaneous absorption using an empirically derived model in combination with the estimated 95th percentile migration rate from human subjects. ECB DEHP (2008) identifies two different models for calculating dermal exposure. One uses a dermal absorption rate for contact with articles, and the other calculates exposure based on the migration from products, and the percentage absorption through skin, corrected for interspecies differences.

Banned Phthalates - DEHP

DEHP is one of two primary phthalates historically used in plastic toys and pacifiers (Sathyanarayana et al., 2008). U.S. toy manufacturers began voluntary removal of DEHP from pacifiers and baby bottle nipples in 1986 (NTP-CERHR DINP, 2003). Many studies have been conducted since the mid 1980's that have confirmed the presence of DEHP in toys and children's products. A study conducted by Bouma and Schakel (2002) in the Netherlands found that 47 of 62 soft toys analyzed contained plasticized PVCs and that DEHP was present in 43% of these toys. Stringer et al. (2000) analyzed 64 PVC toys (or toys with PVC sections) from 17 countries in a study conducted by Greenpeace and report that DEHP was detected in 31 samples of which 23 were in trace amounts (less than 1%); however, in 7 toys it was present in concentrations ranging between 10-35% and used as a plasticizer. Brief summaries of four studies confirming DEHP content have been extracted from NTP-CERHR DEHP, (2000) and provided here as further evidence of DEHP presence in toys and children's articles: Health Canada (1998) found that 23 out of 41 children's products from the U.S., China, and Thailand contained DEHP; Lay (1987) reported that 4 commercially available pacifiers contained DEHP at concentrations ranging from 31.4 to 41.6% dry weight; a Spanish study (Marin, 1998) reported that DEHP was present in 40% of 15 toys tested at a range of <0.1 to 34% DEHP dry weight and 6 of those 15 samples contained >10% dry weight; and Rastogi (1998) reported that four commercially available teethers and 2 of 3 dolls analyzed contained DEHP.

Oral Exposure

ECB DEHP (2008) calculated individual oral DEHP exposures using migration rates reported from various studies. These values, as well as the exposure values calculated by ECB (ECB DEHP, 2008), have been provided in Table 5.4.1-1. Additional assumptions used by ECB (ECB DEHP, 2008) include a maximum exposure duration of 3 hrs/d, a mouthing area of 10 cm^2 for children, and a body weight of 8 kg. Since DEHP is no longer used in pacifiers in Europe, ECB DEHP (2008) excluded pacifiers when calculating exposure. They assumed 100% bioavailability of DEHP by the oral route for children. The maximum oral doses for DEHP as calculated by ECB DEHP (2008) have been presented in Table 5.4.1-1.

Table 5.4.2-1. Calculated Maximum Oral Dose of DEHP from Toys Using Migration Rates Derived Under Static and Dynamic Experimental Conditions

Leaching Rate of DEHP	Unit	Calculated Maximum Oral Dose[a] (µg/kg-bw/d)	Reference
ND[b] – 4,193	µg/dm^2/24 hr	13	Vikelsoe et al., 1997
ND	µg/dm^2/6 hr	-	Artsana in CSTEE, 1998a
1,790 – 2,130	µg/dm^2/6 hr	27	Pindar et al., in CSTEE, 1998a
30 – 720	µg/cm^2/hr	54	Spanish Ministry of Health and Consumer Affairs (cited in CSTEE 1998a)
10.5 – 652.9	µg/dm^2/6 hr	8.2	CSTEE, 1988a
200 – 1,000	µg/dm^2/hr	75	Greenpeace, 1998
< 4 – 10	µg/dm^2/24 hr	< 0.03	CEFIC-ECPI, 1998 (cited in CSTEE 1998a)
< 100	µg/dm^2/hr	< 8	CEFIC-ECPI, 1998 (cited in CSTEE 1998a)

Table 5.4.2-1. Calculated Maximum Oral Dose of DEHP from Toys Using Migration Rates Derived Under Static and Dynamic Experimental Conditions (continued)

Leaching Rate of DEHP	Unit	Calculated Maximum Oral Dose[a] (µg/kg-bw/d)	Reference
<50 – 180	µg/dm^2/24 hr	0.56	CEFIC-ECPI, 1998 (cited in CSTEE 1998a)
793	µg/dm^2/3 hr	19.8	Steiner, 1998a[c]
0.014 – 0.074	µg/cm^2/hr	--	Turnbull and Rodricks, 1989

Source: ECB DEHP, 2008.
a. Sucking by voluntary test persons
b. ND – Not Detected
c. 27 Pacifiers, 12 teethers and 18 toys

CPSC (1983a) estimated children's exposure to DEHP from the use of products such as pacifiers, teethers, squeeze toys, plastic baby pants, vinyl fabric covering of playpen pads, crib bumpers, and similar articles. Estimates are provided in Tables 5.4.1-2 through 5.4.1-4.

Table 5.4.2-2. Individual Exposure to DEHP through the Mouthing of Pacifiers

Estimated Pacifier Mouthing	Use/Child (hrs)	Total DEHP Exposure (mg) (Low Release)	Total DEHP Exposure (mg) (High Release)
Moderate (4 hrs/day/2 yr)	2920	44	175
Heavy (12 hrs/day/2 yr)	8760	131	526

Source: CPSC, 1983a
Note: Migration rates used in deriving exposure have not been provided.

Table 5.4.2-3. Individual Exposure to DEHP through the Mouthing of Teethers

Estimated Teether Mouthing	Use/Child (hrs)	Total DEHP exposure (mg) (Low Release) (Migration Rate: 28 µg/hr)	Total DEHP Exposure (mg) (High Release) (Migration Rate: 44 µg/hr)
Moderate (2 hrs/day/1 yr)	730	20	32
Heavy (6 hrs/day/1 yr)	2190	60	96

Source: CPSC, 1983a

Table 5.4.2-4. Individual Exposure to DEHP through the Mouthing of Vinyl Toys

Estimated Toy Mouthing	Total hrs. use/child	Total DEHP exposure (mg) (Low Release) (Migration Rate: 13 µg/hr)	Total DEHP Exposure (mg) (High Release) (Migration Rate: 6 µg/hr)
Moderate (1 hrs/day/1 yr)	365	2	5
Heavy (3 hrs/day/3 yrs)	3285	20	43

Source: CPSC, 1983a

Dermal Exposure

Direct physical contact of an infant's skin with a variety of products such as teethers, squeeze toys, crib bumpers, and playpen covers containing DEHP may be another form of exposure. ECB DEHP (2008) use two different models to calculate dermal exposure. One uses a dermal absorption rate recommended by Deisinger et al. (1998) for contact with articles containing DEHP, and the other calculates exposure based on the migration rate of DEHP from products (0.11 µg/cm^2/min) and the percentage absorption through skin, corrected for interspecies differences. Both approaches assumed a skin contact area of 100 cm^2 (estimated skin area around the mouth and hands in contact with the toy), a contact duration of 3 hrs/d, and a child body weight of 8 kg. The first approach yielded an exposure of 9 µg/kg-bw/d and the second yielded an exposure of 12.4 µg/kg-bw/d. ECB DEHP (2008) concluded that these two approaches are in close agreement.

CPSC (1983a) calculated dermal exposure for two scenarios. For children playing in playpens with vinyl covers, they assumed a skin contact area of 100 cm^2; a duration of 4 hr/d for one year; and a migration release value of 0.11 µg/cm^2/min. CPSC derived an annual exposure of 960 mg DEHP. In the second scenario, DEHP exposure to children wearing vinyl pants was calculated. Exposure was estimated assuming an exposure duration of 2 years and a skin contact area of 25 cm^2 for 20 hrs per day. This scenario yielded an estimate of 1,200 mg of skin surface exposed over a two year period and accounted for limited contact between skin and pants.

Migration Studies

Factors that impact the rate of DEHP migration include relative solubility in the PVC-polymer and in saliva; temperature; and thickness of the polymer and physical strength placed on the polymer (ECB DEHP, 2008).

Two studies that calculated migration to adult volunteers are presented by ECB DEHP (2008) and were conducted in Austria (Steiner et al., 1998b) and the Netherlands (Könemann, 1998). The mean DINP migration estimates after sucking on toys were found to be similar in the Dutch and Austrian studies, 146 and 132 mg/10 cm^2/hr, respectively. A worst-case scenario for infant daily internal exposure was calculated as 200 µg/kg/d. The calculations assumed a duration of 3 hrs, a body weight of 8 kg, and a product surface area of 10 cm^2. This release rate assumed that the toy was chewed.

The majority of the available extraction data represent dynamic leak tests and may underestimate real life situations. A study conducted by Steiner et al. (1998b) in Austria in 1998 used male and female adult volunteers who chewed or sucked on PVC sheets. Saliva was collected and tested for DEHP. Results from this method were then compared to static methods that used shaking or ultrasonic extraction and it was found that the sucking method results in the highest release of DEHP (ECB DEHP, 2008). The migration of DEHP was found to be similar for the two processes (64 ± 14 µg DEHP/dm^2 film and 41 ± 9 µg DEHP/g film, respectively) and a migration rate of 146 mg/10 cm^2/hr was calculated.

Niino et al. (2003) investigated the migration of DEHP from 11 commercially available toys in Japan. They found that DEHP was present in one soft doll (content 311 mg/g, migration rate of 52.8 μg/cm^2/hr), and in two balls (content 185 and 370 mg/g, migration rate of 69.6 and 85.2 μg/cm^2/hr). They report that the migration rate was not found to be closely related to DINP content.

Niino et al. (2001) studied the migration of phthalates in both volunteers who chewed toy products and by an *in vitro* method using simulated saliva and shaking of toy samples. They report a migration rate of 44.4 μg/10cm^2/hr *(in vivo)* and 315 μg/10cm^2/hr *(in vitro)* from a study that tested migration by chewing PVC toy products (ball one containing 185 mg/g of DEHP).

CPSC (1983a) outlined the summary results of DEHP migration from baby products for both oral and dermal routes from pacifiers, teethers, and soft plastic toys. A release rate of 6 μg/hr (low) and 13 μg/hr (high) was calculated from the results of the leaching study for six vinyl toys using estimated release from mouthed area. Results presented from scrubbing experiments suggest DEHP is available for skin contact.

CPSC (2002a) conducted a study on DINP and DEHP migration from 41 children's products (mainly soft plastic toys) using the "head-over-heels" laboratory method. They immersed and tumbled 10 cm^2 disks cut from PVC sections of the toys in a saliva simulant. Of the 41 products, 24 were made of PVC and, of these, 2 toys contained DEHP. The teethers tested did not contain any dialkyl phthalates. Segments were taken from the plastic areas of the products that contained multiple materials/parts made of different plastics, resulting in 85 samples. DEHP was measured in four of these samples (approximately 5%) and migration rates were estimated for three samples. Using the tumbling method, CPSC (2002a) found a migration range of 0.92 to 2.03 μg/10 cm^2/min for DEHP from soft plastic articles. The migration rate was not correlated with discs phthalate concentrations in the toys. The DEHP content of the articles ranged from 22.11 to 37.34 percent.

CPSC (1983a) conducted a migration study to determine surface availability of DEHP using cotton cloth and cotton cloth coated with lanolin to simulate oils in the skin. The pieces of cloth were scrubbed on flat vinyl products to test the release of DEHP to skin. Tests were run for two minutes with intervals at 2 minutes, 48 hrs and 30 days. Readings taken at later test times were comparable to the earliest readings at 2 minutes. The average migration per minute was found to be 0.147 μg/cm^2/min for a nursery pad; 0.117 μg/cm^2/min for vinyl fabric; and 0.124 μg/cm^2/min for a vinyl toy.

Banned Phthalates - BBP

Presence of BBP in Toys and Children's Products

ECB BBP (2007) reports that BBP is not intentionally used in toys and childcare but may be present in trace amounts as a byproduct/impurity. A few studies have detected BBP concentrations in toys. For example, Stringer et al. (2000) investigated the content of plasticizers in plastic teethers and toys from 17 countries. Of 72 toys tested, BBP was detected in 6 samples ranging from 0.001 to 0.020% of the weight of the toys. ECB BBP (2007) cites a Norwegian

study that analyzed for the presence of phthalates in 15 toys for use by small children. Although 12 were found to contain one or more phthalates, BBP was not detected in any of the toys tested (cited in ECB BBP, 2007). ECB BBP Summary (2008) used the highest release rates from RIVM (1998) to estimate a worst case maximum release of 0.95 μg/kg-bw/d. Assumptions included a body weight of 8 kg, a mouthing area of 10 cm^2, and an exposure duration hrs/d.

Banned Phthalates - DBP

Migration

Niino et al. (2001) analyzed the migration of phthalates from 11 toy products using both volunteers who chewed sections of the toys and by an *in vitro* method using simulated saliva and shaking of the toy samples. The authors found an *in vitro* migration rate of 11.7 μg/10 cm^2/hr and an *in vitro* migration rate of 339 μg/10 cm^2/hr. No other studies were found reporting migration, presence, or exposure to DBP.

Presence of DBP in Toys and Children's Products

NTP-CERHR DBP (2003) stated there is no evidence that DBP is used in toys. They reported a study that analyzed 17 plastic toys and DBP was detected in only one sample, a doll's head (0.01% by weight). The report concluded that the low concentration suggested DBP contamination rather than planned use.

Interim Banned Phthalates - DINP

DINP is the predominant plasticizer used in children's products (NTP-CERHR DINP, 2003; Stringer et al., 2000) since the mid-1980s (Babich et al., 2004). Bouma and Schakel (2002) studied 62 soft toys in the Netherlands and found that 47 contained plasticized PVCs. They report that DINP was present in 79% after mixing with a saliva stimulant. DINP was replaced by DEHP in the mid-1980s (NTP-CERHR DINP, 2003; Stringer et al., 2000; Babich et al., 2004). NTP-CERHR DINP (2003) summarized a Health Canada (1998) study that analyzed 41 children's products made in the U.S., China, and Thailand for the presence of DINP and DEHP. DINP was detected in 27 of the 41 products in concentrations that ranged from 3.9 to 44% dry weight. DINP content was also measured at 15.1 to 54.4% dry weight in 31 toys from a previous study (CPSC, 1998b, and CPSC, 2002a). HSDB DINP (2009) reported DINP concentrations ranging from 3.9 to 55% wet weight in 58 of 76 plastic toys tested, 19 to 40% in 4 of 4 teethers and 2 of 3 dolls tested, and from 10 to 40% in 72 toys analyzed.

Oral Exposure

CPSC (2002a) used the Monte Carlo bootstrap method to estimate distribution of the daily DINP exposures. A basic scenario addressing exposure to soft plastic toys and adjusting for the prevalence of DINP (42%) was reported as the best estimate of current oral exposure to DINP in children's products. This scenario resulted in a mean exposure among 12- to 24-month-olds of 0.08 μg/kg/d (95^{th} percentile value of 0.53 μg/kg/d). Using hypothetical scenarios, the bioavailability of DINP was assumed to be 100 percent. For the "all toys, teethers and rattles," scenario, the maximum estimated exposure was among the 3- to 12-month-olds with a mean

exposure of 2.9 (1.8 to 4.3) µg/kg/day and the 95th percentile exposure of 10.7 µg/kg/d. The maximum exposure was for pacifiers, which was greatest among 3- to 12-month-olds with a mean estimated exposure of 4.8 (2.2 to 8.0) µg/kg/d and the 95th percentile exposure of 24.6 µg/kg/d. Based on these results, CPSC (2002a) concluded that exposure to DINP from soft plastic toys due to mouthing does not present a health hazard to children. Teethers, rattles and pacifiers do not currently contain dialkyl phthalates, however, even if they contained DINP, they would still not pose a health hazard to children. These conclusions were based on the assumption that migration data from soft plastic toys would apply to teethers, rattles, and pacifiers.

Babich et al. (2004) report estimated exposure to DINP using migration rates from 24 toys and a new observational study of children's mouthing activities. Approximately 42% of soft plastic toys tested contained DINP. A Monte Carlo modeling (bootstrap) method was used to estimate exposure and develop confidence intervals for selected percentiles of the exposure distribution. Estimated DINP exposures for soft plastic toys were greatest among the children in the 12- to 23-months-old bracket. The mean exposure for this age group was 0.08 µg/kg-d, with a 95% confidence interval of 0.04-0.14 µg/kg/d and a 99th percentile of 2.4 µg/kg/d. The authors concluded that oral exposure to DINP from mouthing soft plastic toys is not likely to present a health hazard to children. Table 5.4.1-5 presents the estimated exposures to DINP from mouthing soft plastic toys for three age groups. Table 5.4.1-6 provides a summary of the estimated hypothetical oral exposures to DINP in children's products for each of the three age brackets.

Table 5.4.2-5. Estimated Oral Exposure (µg/kg/d) to DINP from Soft Plastic Toys

	Age		
	3-11 months	12-23 months	24-36 months
Mean	0.07 (0.03-0.13)	0.08 (0.04-0.14)	0.03 (0.01-0.06)
Median	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.00 (0.00-0.00)
95th Percentile	0.44 (0.15-0.82)	0.53 (0.24-0.89)	0.12 (0.04-0.23)
99th Percentile	1.4 (0.74-2.4)	1.5 (0.89-2.3)	0.56 (0.17-1.6)

Source: Babich et al., 2004

CPSC conducted a study on DINP and DEHP migration from 41 children's products (mainly soft plastic toys) using the "head-over-heels" laboratory method (CPSC, 2002a). They immersed and tumbled 10 cm^2 disks cut from PVC sections of the toys in a saliva simulant. Of the 41 products, 24 were made of PVC and of these, 16 contained DINP. The teethers tested did not contain any dialkyl phthalates. Because some of the products contained multiple pieces or parts made of different plastics, segments were taken from the plastic areas resulting in 85 pieces, of which, 36 (42%) samples contained DINP. Migration rates were obtained for 24 articles. Using the tumbling method, CPSC (2002b) reports a migration range of 1.0 to 11.09 µg/10 cm^2/min for DINP from soft plastic articles. The migration rate was not correlated with phthalate release. The DINP content in the articles ranged from 12.9 to 39.4 percent.

Table 5.4.1-7 provides summaries of estimated oral exposure to DINP in children's products (Babich et al., 2004).

Table 5.4.2-6. Hypothetical Oral Exposures (µg/kg/d) to DINP in Children's Products

Product	Age (months)	Mean
Hypothetical Case 1: Soft Plastic Toys	3-11	0.17 (0.08-0.29)
	12-23	0.22 (0.11-0.32)
	24-36	0.07 (0.02-0.14)
Hypothetical Case 2: Soft Plastic Toys, Teethers, and Rattles	3-11	0.45 (0.24-0.74)
	12-23	0.22 (0.12-0.34)
	24-36	0.08 (0.02-0.18)
Hypothetical Case 3: All Soft Plastic Items Except Pacifiers	3-11	0.63 (0.38-1.0)
	12-23	0.41 (0.26-0.60)
	24-36	0.37 (0.19-0.59)
Hypothetical Case 4: Pacifiers	3-11	4.8 (2.2-8.0)
	12-23	2.8 (1.2-5.0)
	24-36	1.7 (0.07-4.3)

Source: Babich et al., 2004

Table 5.4.2-7. Estimated Oral Exposure from DINP in Children's Products

Agency	Product(s)	Age (months)	Mean (µg/kg-d)	Median (µg/kg-d)	95% (µg/kg-d)	Range (µg/kg-d)	Reference
Dutch Consensus Group[a]	Teethers	3 - 6 6 - 12 12 - 18 18 - 36	9.66 7.79 2.33 1.13	7.17 4.8 1.06 0.521	26 25.5 10.5 4.32	− 70.7 -142 -51.5 -23	RIVM (1998)
Health Canada [a]	Teethers, Toys	3 - 12 13 - 26	44 39	– –	– –	4 – 320 5 – 228	Health Canada (1998)
	Pacifiers	3 - 12 13 - 26	120 62	– –	– –	18 – 640 5 – 458	
CPSC[b]	Teethers, Toys	3 - 12 13 - 26	5.7 0.7	– –	94.3 7.6	– –	CPSC (1998b)
Austrian Standards Institute	Teethers	–	31.25	–	–	–	Fiala et al. (2000)
Chronic Hazard Advisory Panel [c]	Toys	0 - 18 19 - 36	– –	– –	280 66	– –	CPSC (2001)
France [d]	Toys	3 - 12	–	–	200	31 − 226	ECN DINP (2003)

Source: Babich et al., 2004

a. Based on the migration rates measured with human subjects by the Dutch consensus group, 5th percentile body weights, and assuming mouthing times of 1 to 3 hrs for teethers and toys and 2 to 6 hrs for pacifiers.

b. The migration rate by the impaction method was multiplied by a scaling factor to adjust for the difference between impaction and human subjects.

c. Estimate for "relatively highly exposed children" based on the estimated 95th percentile migration with human subjects (CPSC 1998b) and assuming mouthing durations of 3 hrs/day for 0 – 18-month-olds and 1 hr/day for 19- to 36-month-olds.

d. Based on the maximum *in vivo* migration rate (8.9 µg/cm^2/min) in the Dutch Consensus Group study (RIVM, 1998), a 10 cm^2 surface area, a 3-hr exposure duration, and a 8-kg body weight (France, 2001). The low value in the range is based on the average migration rate in Steiner et al. (1998b). The high value is the 95 percent upper confidence interval of the 95th percentile exposure, as calculated by CPSC (1998b).

ECB DINP (2003) used DINP migration rates from toys from three studies (Steiner et al. (1998a), RIVM (1998a), and CPSC (1998b)) to calculate daily oral exposure. They assumed a surface area of 10 cm^2 for the product that would be in the mouth, a leaching time of 3 hrs, and a mean body weight of 8 kg. ECB DINP (2003) used the daily DINP intake of 200 µg/kg/d in their risk calculation because it is similar to the exposure estimates calculated by CPSC. The value was calculated based on migration rates in RIVM (1998). ECB DINP (2003) assumed 100% bioavailability by the oral route for young children. They noted that a validated analytical method that is capable of measuring consumer exposure from toys would be of interest since the major source of exposure to DINP is through toys (refer to Table 5.4.1-8).

Table 5.4.2-8. Estimated DINP Daily Oral Intake from Toys

Study	Release of DINP by Toys (µg/10 cm^2/min)	Bodyweight (kg)	Leaching Time (hrs)	Daily Intake (µg/kg-bw/d)
Steiner et al., 1998a	1.38[a]	8	3	31
RIVM, 1998	8.9[b]	8	3	200
CPSC, 1998b	--	--	--	225.6[c]

Source: ECB DINP (2003)
a. Average
b. Highest value
c. Calculated by CPSC (1998b)

The estimated exposure of children to DINP in teethers, rattles, and toys was 50.1 to 225.6 µg/kg/d in children 3 to 12 months old and 4.4 to 16.2 µg/kg/d in children 13 to 26 months old (CPSC, 1998b). For 3- to 12-month-old children, the average daily exposure was estimated to be 5.7 µg/kg/d, with a 95th percentile (reflecting variance in migration rates) value of 94.3 µg/kg-d. For 13- to 26-month-old children, the average daily exposure was estimated to be 0.7 µg/kg-d, with a 95th percentile value of 7.6 µg/kg-d (CPSC, 1998b). Mouthing activity was based on data from the RIVM (1998) study. Average body weights for the 3- to 12-month-old and 13- to 26-month-old age groups used in the exposure calculations were 7.3 kg and 10.7 kg, respectively. A mean migration rate of 8.2 µg/11 cm^2/hr was used. The average (geometric mean) mouthing durations for the 3- to 12-month-old and 13- to 26-month-old groups were estimated to be 12.0 and 2.1 min/d (Greene, 1998), respectively. Exposures were found to be highest for children aged 3 to 12 months and were considerably lower for children older than 3 years because children's weights increase and mouthing times decrease with increasing age.

CPSC (1998b) conducted a statistical analysis to estimate DINP exposure for children aged 3 to 12 months and 13 to 26 months. They calculated a migration rate of 1.66 µg/hr (surface area: 11 cm^2 area) based on data derived from 31 products containing DINP. Additional assumptions included a geometric mean mouthing time of 12.03 min for 3- to 12-month-olds. For the 13- to 26-month-olds, CPSC (1998b) assumed a geometric mean mouthing time of 2.1 min. They estimate a geometric mean exposure of 5.69 µg/7.3 kg and a maximum (95th percentile) exposure of 94.3 µg for children aged 3 to 12 months. CPSC estimate a geometric mean of 0.69 µg/10.7 kg/d and a maximum (95th percentile) exposure of 7.6 µg for children aged 13 to 26 months.

CPSC (2002a) calculated an exposure estimate of 94 µg/kg/d to DINP from teethers and soft toys (95th percentile). They identified sources of uncertainty which included the laboratory method

used to measure DINP migration, the lack of data on the amount of time that children mouth objects containing DINP, and the relevance of the rodent liver tumors to humans.

NTP-CERHR DINP (2003) cite a study by RIVM (1998) investigating the phthalate release from soft PVC toys which used Monte Carlo simulation to estimate mouthing time and migration rates from an *in vivo* study of 20 adults. In addition, mouthing times were derived using a 2-day parent observation study of 42 children, aged 3 to 36 months. Mean mouthing times were generated per age category, with ranges from 0 min/d in older children to 171.5 min/d in the 6- to 12-month age group. Calculations used the total mouthing time, but excluded the time spent mouthing pacifiers. The greatest exposure levels were calculated for children in the 3- to 12-month age group and are summarized in Table 5.4.1-9.

Table 5.4.2-9. DINP Exposure Estimates from Toys for Children Aged 3-12 Months

Agency	Estimated Intake Level (μg/kg-bw/d)			
	Mean	95th Percentile	99th Percentile	Maximum
RIVM[a]	6.53-14.4	20.7-39.7	39.8-77.3	70.7-204
CPSC	5.7	94.3	—	—
Health Canada[b]	44	73.9[3]	173.5[c]	320

Source: NTP-CERHR DINP, 2003

a. Exposure range for 3–6 month-old and 6–12 month-old children: range includes results from 2 specimens tested.
b. Calculated with mouthing times for teethers and other objects intended for mouthing.
c. Results using Monte Carlo simulations in children aged 3–6 months.

NTP-CERHR DINP (2003) states that exposure to DINP in the general adult population is lower than exposure to DEHP, which is estimated at 3 to 30 μg/kg-bw/d. They also state that children may incur significantly greater nondietary exposures from mouthing toys and other articles containing DINP.

Dermal Exposure

ECB DINP (2003) reports that DINP exposure may also occur through the skin of the hands and through the lips. DINP is partially dissolved in the saliva present on the hands and the mouth which can increase the amount of phthalate available for dermal absorption. The amount of DINP a child is exposed to can be calculated using assumptions regarding the area of skin in contact with the product, duration of the contact, surface availability of DINP from the product and the penetration of DINP through the skin (the dermal absorption rate).

ECB DINP (2003) selected a dermal absorption rate of 0.024 μg/cm^2/hr for DIDP based on a study performed by Deisinger et al. (1998). That study investigated the migration rate of DEHP from plastic film and its absorption through rat skin *in vivo* which found a dermal absorption rate of 0.24 μg/cm^2/hr for rats. ECB DINP (2003) adjusted the DEHP dermal absorption rate from Deisinger et al. (1998) based on another study conducted by Elsisi et al. (1989) where DIDP was shown to be 10 times less likely to be absorbed through skin than DEHP, and also based on the physico-chemical similarities between DIDP and DINP. A correction factor was not used to extrapolate from rats to humans. Other assumptions used by ECB DINP (2003) in calculating

dermal exposure included a skin contact area of 100 cm^2 (estimated skin area round the mouth and hands in contact with the product), a contact duration of 3 hr/day, and a body weight of 8 kg. The daily exposure of DINP was estimated to be 1 µg/kg-bw/d. ECB DINP (2003). This value was used as the maximum dermal exposure to DINP in toys for their risk assessment for newborn babies and infants.

Migration studies

Babich (1998) reports that DINP migration from children's products made from PVC have been evaluated using various laboratory methodologies. These have included extraction using saline or artificial saliva; mechanical action such as shaking (Fiala et al., 2000; Rastogi et al., 1997; Steiner et al., 1998b) ultrasound (Fiala et al., 2000; Steiner et al., 1998b), impaction (Chen 1998a,b; Health Canada, 1998), or tumbling (RIVM, 1998). Table 5.4.1-10 (CPSC, 2002a) summarizes the results of existing migration studies, highlighting the absence of a standard method, as well as a consistent methodology and form of comparison.

Table 5.4.2-10. Laboratory Measurements of DINP Migration from PVC Children's Products

Laboratory	Method	Product (s)	DINP %	N[a]	Units	Mean	µg/ 11cm^2/hr	SD	Range	Reference
Danish National Environmental Research Institute [b, c]	Shaking	Teethers	–	2	µg/g or ppm	–	–	–	89 - 24,691	Vikelsoe et al. (1997)
			–	1	µg/dm^2/hr	23,260	2,559	–	–	Rastogi et al. (1997)
TNO	Tumbling (TNO method)	Teether	–	1	µg/10 cm^2/min	3.1	205	0.5	2.5 - 4.2	RIVM (1998)
LGC [d]	Shaking (1) Shaking (4) Tumbling	Toys	–	2	µg/10 cm^2/min	0.3 1.8 1.6	20 119 106	0 0.4 1.1	0.3 - 0.3 1.6 - 2.1 0.8 - 2.3	Earls et al. (1998)
Health Canada [e]	Impaction	Teether, Toys, Pacifiers	3.9 – 44	27	µg/10 cm^2/hr	0.32	0.35	0.08	–	Health Canada (1998)
CPSC [f]	Impaction	Teether, Toys	15.1 - 54.4	31	µg/11 cm^2/hr	8.2	8.2	9.83	1.0 - 48.1	Chen (1998a)
CPSC [g]	Impaction	Teether	–	1	µg/dm^2/hr	119 7.2 - 102	13 0.8-11		105 – 133 7.2 – 102	Chen (1998b)
TNO [h]	Tumbling (TNO method)	Toys, Teethers	21.0 - 46.6	10	µg/10 cm^2/min	2.4	158	1.38	0.9 - 5.6	Rijk and Ehlert (1999); Rijk et al. (1999)
LGC [i]	Shaking 37°C Shaking 65oC	Teether, Toy	–	2 0	µg/10 cm^2/min	0.95 4.5	63 294	0.35 0.78	0.7 - 1.2 3.9 - 5.0	Axford et al. (1999)
Austrian Standards Institute [j]	Static Shaking Ultrasound	Teether	36	1	µg/dm^2/hr	12.7 36.3 387.3	1.4 4.0 42.6	– – –	– – –	Fiala et al. (2000); Steiner et al. (1998b)

Table 5.4.2-10. Laboratory Measurements of DINP Migration from PVC Children's Products (continued)

Laboratory	Method	Product (s)	DINP %	N[a]	Units	Mean	µg/ 11cm^2/hr	SD	Range	Reference
JRC [k]	Tumbling (JRC method) Shaking, Mild Shaking, Stringent	Toys, Teethers	26 – 41.7	5	µg/10 cm^2/min	4.0 0.89 4.6	264 59 304	1.45 0.51 2.5	1.9 - 5.4 0.49 - 1.75 2.6 - 8.8	Simoneau et al. (2001)
CPSC	Tumbling (JRC method)	Toys	12.9 – 39.4	24	µg/10 cm^2/min	4.1	269	2.7	1.0 - 11.1	Chen (2002)

Source: CPSC, 2002a

a. N, number of articles tested; SD, standard deviation.
b. Units were in micrograms per square decimeter per day.
c. CPSC staff were unable to replicate the high value using a disk cut from the same article by either the Danish test method or the CPSC method (Chen, 1998b).
d. Two toys were tested by shaking under various conditions (all at 37°C) or by tumbling (at 20°C). Shaking data for method 1 (no glass beads) and method 4 (glass beads at 200 strokes per minute) are shown. Units were micrograms per 10 square centimeters per minute.
e. Impaction was with a "bite form" used to test the resistance of toys to breaking. Units were micrograms per 10 square centimeters per hr.
f. Original units were micrograms per 11 square centimeters per hr.
g. Teether from Rastogi et al. (1997) tested using the CPSC impaction method and the NERI shaking method.
h. This is from an interlaboratory study coordinated by the TNO Nutrition and Food Research Institute. Original units were micrograms per minute.
i. This was from an interlaboratory study coordinated by the Laboratory of the Government Chemist. In this method, glass balls are added to the flask to aid extraction. Units were micrograms per 10 square centimeters per minute.
j. Original units were micrograms per square decimeter, for either 1 or 3 hrs. All values shown here were adjusted to 1 hr.
k. This is from an interlaboratory study coordinated by the Joint Research Centre. Five toys and a standard disk (not shown) were tested by three methods. Shaking methods were essentially those of Axford et al. (1999). Original units micrograms per square centimeter per minute

Niino et al. (2003) investigated the migration of DINP from 7 commercially available toys in Japan. DINP concentrations in these items ranged from160 to 583 mg/g, and migration rates ranged from 29.6 to 85.2 µg/cm^2/hr (111-320 µg/15 min) with RSD of 3-8%. They report that the migration rate was not found to be closely related to DINP content. Table 5.4.1-11 presents the migration rates from this study.

In a study conducted in 2002a, the laboratory method referred to as the "head over heels" method was tested by CPSC to measure the migration of DINP from children's products, particularly soft plastic toys (CPSC, 2002a). The method involved cutting disks from PVC products, immersing them in a saliva stimulant and tumbling for approximately 30 minutes. Using this method on 24 soft plastic children's products, it was determined that DINP migrated at rates from 1.0 to 11.1 µg/10 cm^2/min. The migration rate was not correlated with DINP content, which ranged from 12.9 to 39.4 percent. In another study, Niino et al. (2001) studied migration of phthalates in both volunteers who chewed toy products and by an *in vitro* method using simulated saliva and shaking of toy samples. They report a migration rate of 78 µg/10cm^2/hr *(in vivo)* and 535 µg/10cm^2/hr *(in vitro)* from a study that tested migration by chewing.

Table 5.4.2-11. DINP in PVC Toy Products and Migration Rates Evaluated by the Rotary Shaking Method

Toy product	Dialkyl phthalate	Content[a] (mg/g)	Amount[b] (µg/15 min)	Rate[b] (µg/cm^2/hr (C.V. [%]))
Rattle	DINP	380	320	85.2 (3)
Teether	DINP	389	194	51.6 (7)
Pacifier	DINP	583	275	73.2 (8)
Toy food	DINP	311	173	46.0 (6)
Soft doll A	DINP	160	111	29.6 (5)
Soft doll B	DINP	290	314	83.6 (7)
Ball C	DINP	256	126	33.6 (6)

Source: Niino et al., 2003

a. DINP contents in PVC products were measured by extraction using a rotary shaker at 300 rpm for 3 hrs.

b. These migration rates were obtained by *in vitro* migration tests of PVC products (surface area was 15 cm^2) for 15 min. Values are means (C.V.) *(n=5).*

Brandon et al. (2006) describe an *in vitro* method for determining the bioaccessiblity of a contaminant from a consumer product. Different models, representing sucking and or swallowing were developed. They derived a bioaccessibility of 0.029 to 0.033% for DINP for every time period tested, a migration rate of ±3.5 µg/min, and a mean leaching rate of 0.3 µg/min/cm^2.

Fiala et al. (2000) used an ultrasonic bath extraction and voluntary test personnel to test teethers from Italy, plastic animals and dolls from Vienna, Austria, using saliva stimulants. They reported a release of 10 cm^2/3 hrs and calculated a maximum DINP intake value of 54.5 and 84.5 µg/kg for sucking and chewing on the toys, respectively. They also calculated a maximum DEHP intake value of 54.39 and 84.36 µg/kg for sucking and chewing on the toys, respectively.

CPSC (1998b) conducted studies with human subjects and *in vitro* studies with simulants of saliva to compare the migration rate measured *in vivo* and those measured by impaction methods. Disks with a surface area of approximately 10.3 cm^2 taken from toys were found to contain15 to 54% DINP. DINP migration rates by the impaction method with saliva simulant ranged from 1.0 to 48.1 µg/hr for an area of 11 cm^2. Migration rates were not correlated with DINP content, manufacturing process, or sample thickness. The ratio between the *in vivo* and impaction methods measured migration rates averaged 39.5 with a range of 22.9 to 72.6.

NTP-CERHR DINP (2003) presented a study conducted by RIVM in the Netherlands where an *in vitro* study was conducted with 20 adult volunteers who were instructed to suck and bite on three teething rings of different shapes with a surface area of 10 cm^2. One specimen contained 38% DINP and the other two contained 43% DINP. Extraction of DINP was 1.38 (0.3–8.3) µg/min, 2.44 (0.9–8.9) µg/min, and 1.63 (0.9–5.7) µg/min for specimens 1, 2, and 3, respectively. Mean extraction was 1.8 µg/10 cm^2/min (or 120 µg/11cm^2/hr). The results did not indicate a correlation between extraction, pH, or protein content of the saliva and release rates appeared consistent.

CPSC (1998b) also conducted a study investigating migration from 5 toys using 10 adult volunteers. They found a mean migration rate of 241.3 μg/11cm^2/hr. This rate is reported to be almost 40 times higher than the average rate obtained using impaction of disks cut from the same 5 toys.

Steiner et al. (1998a) (cited in ECB DINP, 2003), investigated the DINP migration from PVC sheets and PVC toys using a saliva simulant. The average migration value during a one-hour sucking test was 830 μg/dm^2 (13.8 μg/dm^2/min). Where toys was shaken for 3 hrs in a simulant in an ultrasonic bath, the mean migration value was about 830 μg/dm^2 (607-1,162 μg/dm^2), corresponding to 4.6 μg/dm^2/min.

Table 5.4.1-12 provides DINP migration calculations from studies previously conducted summarized above (CPSC, 1998b).

Table 5.4.2-12. DINP Migration from PVC Children's Products Derived from Human Subjects Studies

Laboratory	Method	Product (s)	DINP %	N [a]	Units	Mean	μg/11cm^2/h	SD	Range	Reference
Dutch consensus group [b]	Mouthing	Standard disk, teether	–	20	μg/10 cm^2/min	1.8	119	–	1.38 – 2.4	RIVM (1998)
Austrian Standards Institute [c]	Sucking	Teether	36	9	μg/dm^2/hr	833	92	–	297 – 1,452	Fiala et al. (2000); Steiner et al. (1998b)
	Chewing		36	9		1,330	146	–	768 – 5,839	
CPSC [d]	Mouthing	Toy (disk)	43	10	μg/10 cm^2/hr	268.1	295	158.1	63 – 597	Chen (1998a)

Source: CPSC, 1998b

a. N, number of human subjects; SD, standard deviation.

b. Test articles included disks cut from a specially prepared PVC sheet, a teether, and disks cut from the same type of teether. Units were micrograms per 10 square centimeters per minute.

c. Original units were micrograms per square decimeter, for either 1 or 3 hrs. All values shown here were adjusted to 1 hr.

d. 20 disks were cut from 5 identical toys. Ten disks were tested by 10 subjects (the remaining 10 were tested by impaction). Units were micrograms per 10.3 square centimeters per hr. In the 1998 CPSC risk assessment, migration rates were treated as 5 pairs of volunteers, because the disks were taken from 5 toys (CPSC 1998b; Greene 1998).

Interim Banned Phthalates - DIDP

A number of references have documented the presence of DIDP in children's toys and teethers. ECB DIDP (2003) reported that many soft plastic toys and teethers are composed of PVC plastic and may therefore contain a high concentration of plasticizers such as DIDP. Stringer et al. (1997) conducted a study quantifying phthalates in children's toys. They found that DIDP was present in two teethers containing PVC. The first teether, produced in China, contained 20% DIDP and the second teether, produced in U.S., contained 15.7% DIDP.

NTP- CERHR DIDP (2003) reported results from a Danish survey of 17 children's toys. The toys without PVC parts did not contain phthalates; however, DIDP was detected in 4 of the 7 PVC toys (3 teethers and 1 doll) at concentrations ranging from 0.7 to 10.1% by weight (Rastogi, 1998). NTP-CERHR DIDP (2003) and ECB DIDP (2003) both reported results from a Dutch study (Janssen et al., 1997) that investigated phthalate content in teething rings and animal

figures. The total DIDP content in products tested was 1.4 to 15%. The U.K. Government has also monitored the content of plasticizers in toys. DIDP was found in 6 out of 18 toys in 1990 and in 4 out of 27 in 1991, but DIDP was not found in 16 toys in 1992 or in 29 toys in 1996.

ECB DIDP (2003) stated that the absence or rarity of DIDP in toys could be explained by the fact that DIDP was not analyzed in recent studies. Since DIDP has been previously used in toys, it is possible that it may be used as an alternative to other phthalates in the future.

Oral Exposure

NTP-CERHR DIDP (2003) stated that while *in vitro* or *in vivo* data on DIDP leaching from toys are not available; they feel that it is reasonable to assume that infants and toddlers who mouth DIDP-containing products will experience exposures that are several folds higher than the general population. They referenced DINP exposure estimates which are an order of magnitude higher for infants and young toddlers than older children and adults.

ECB DIDP (2003) used available migration data and calculated the daily dose. These are presented in Table 5.4.1-13. Dose was calculated on the assumption that the item mouthed would have a surface area of $10cm^2$; exposure duration of 3 hrs/d; and a child body weight of 8 kg. ECB DIDP (2003) also assumed that 100% of the DIDP leached is absorbed.

Table 5.4.2-13. Calculated Maximum Dose of DIDP

Calculated Maximum Dose of DIDP (µg/kg-bw/d)	Reference
17	CSTEE (1997a)
0.004	Artsana (in CSTEE 1997b)
< 4	CEFIC-ECPI (in CSTEE 1998b)
0.005	Artsana (in CSTEE 1997c)
19	Gesundheidsbescherming (in CSTEE 1997c)
7	RIVM (1998) (in CSTEE 1998a)

Source: ECB DIDP, 2003
Note: Assuming a baby body weight of 8 kg, surface area mouthed 10 cm^2, 3 hrs per day.

ECB DIDP (2003) noted that the highest exposure calculated is approximately 5,000 times higher than the lowest value. They stated that the differences result from laboratory test methods (i.e., static or dynamic); period of exposure; surface contacts; and type of stimulant. They indicated that the RIVM (1998) study demonstrated that the amounts of phthalates leached from PVC into saliva is lowest by the static method. Higher leaching is experienced using the agitation method and even greater concentrations are leached through the suction method (ECB DIDP, 2003)

ECB DIDP (2003) compared the calculated doses from Table 5.4.1-13 with exposures calculated by the RIVM (1998) *in vivo* study. The study investigated the DINP release from soft PVC baby toys and used Monte Carlo simulation to estimate mouthing time and migration rates from the *in vivo* study of 20 adults. ECB DIDP (2003) reported that the maximum level of release was 8.9

µg/min for a toy containing 43% of DINP, which corresponds to an internal exposure of 200 µg/kg-bw/d for newborn babies and infants when using the same assumptions (10 cm^2, 8 kg, 3 hrs, 100% bioavailability). ECB DIDP (2003) used 200 µg/kg-bw/d as their maximum internal oral exposure to DIDP in toys in their risk assessment.

Migration Studies

NTP-CERHR DIDP (2003) noted that *in vitro* and *in vivo* data on DIDP leaching from toys are unavailable, however, limited migration data was located in the ECB DIDP (2003) report. Table 5.4.1-14 presents reported migration of DIDP from toys to saliva under static and dynamic experimental conditions (ECB DIDP, 2003). They noted the absence of a standard method to simulate actual exposure during chewing. Another uncertainty noted is the different types of toys tested, and the actual concentration of the phthalates in the products is also unknown (ECB DIDP, 2003).

Table 5.4.2-14. Reported Leaching to Saliva of DIDP from Toys Under Static and Dynamic Experimental Conditions

Leaching of DIDP	Units	Reference
0.9 – 4.6	µg/cm^2/hr	CSTEE (1997a)
ND – 0.084	mg/kg/6 hr	Artsana (cited in CSTEE 1997b)
ND[a]	µg/dm^2/6 hr	CSTEE (1997d)
< 0.1	mg/dm^2/hr	CEFIC-ECPI in CSTEE 1998b
0.11	mg/kg/6 hr	Artsana (cited in CSTEE 1997c)
5	µg/cm^2/hr	Gesundheidsbescherming (cited in CSTEE 1997c)

Source: ECB DIDP (2003)
a. ND – Not detected

Dermal Exposure

ECB DIDP (2003) reports that direct dermal contact with items containing DIDP may result in DIDP exposure through dermal absorption. DIDP exposure is calculated using assumptions regarding the area of skin in contact with the product, duration of the contact, surface availability of DIDP from the product, and the penetration of DIDP through the skin (the dermal absorption rate).

ECB DIDP (2003) selected a dermal absorption rate of 0.024 µg/cm^2/hr for DIDP based on a study performed by Deisinger et al. (1998) that investigated the migration rate of DEHP from plastic film and its absorption through rat skin *in vivo* which found a dermal absorption rate of 0.24 µg/cm^2/hr for rats. ECB DIDP (2003) adjusted the dermal absorption rate from Deisinger et al. (1998) based on another study conducted by Elsisi et al. (1989) where DIDP was shown to be 10 times less likely to be absorbed through skin than DEHP. A correction factor was not used to extrapolate from rats to humans. Other assumptions used by ECB DIDP (2003) in calculating dermal exposure include a skin contact area of 100 cm^2 (estimated skin area round the mouth and hands in contact with the product), a contact duration of 3 hr/d and a body weight of 8 kg. The daily exposure of DIDP was estimated to be 1 µg/kg-bw/d. ECB DIDP (2003) used this value as

the maximum internal dermal exposure to DIDP in toys for their risk assessment for newborn babies and infants.

5.4.3. Scenario 2: Medical Devices

Medical devices made of plasticized PVC or containing PVC components are a source of exposure to phthalates for people undergoing medical procedures. Phthalates are used as plasticizers in PVC medical devices to impart desirable properties such as stability, strength, flexibility, optical clarity, and resistance to temperature variations (NTP-CERHR DEHP, 2006; Green et al., 2005). Currently, DEHP is the most commonly used phthalate in a variety of PVC medical devices including blood storage bags, IV solution storage bags, umbilical catheters, examination gloves and tubing sets for hemodialysis, mechanical ventilation, nasogastric feeding, and ECMO (NTP-CERHR DEHP, 2006; Green et al., 2005). The DEHP content of PVC medical devices can range from 20 to 40 % by weight (Health Canada, 2002). Since DEHP is not covalently bound to the PVC matrix, it can leach into blood, blood products (i.e., platelets, plasma), and lipid-containing solutions in contact with the PVC material or into air passing through PVC ventilation tubing (Green et al., 2005; Schettler, 2006). Several studies have measured DEHP leaching rates into whole blood, plasma and other blood products, and dialysis fluids under experimental conditions (ECB DEHP, 2008; Green et al., 2005). The reported leaching rates varied considerably since the rate at which DEHP migrates out of the PVC matrix depends on the type of solution, storage time and temperature, and DEHP content in the product among other factors (ECB DEHP, 2008; Green et al., 2005). Lipid-containing solutions, for example, can readily extract DEHP from the PVC matrix. High temperatures can also increase the leaching of DEHP from the medical device (Health Canada, 2002).

Given the potential for DEHP to migrate out of PVC materials, patients undergoing medical procedures involving the use of DEHP-containing devices may be exposed to DEHP via the intravenous, inhalation, or ingestion routes (Schettler, 2006; Matsumoto et al., 2008; Health Canada, 2002). DEHP exposure is of special concern in infants undergoing intense medical treatments, given the extensive use of DEHP-containing medical devices in neonatal intensive care units (NICUs) (Calafat et al., 2004b; Green et al., 2005). It has been suggested that exposure to infants in NICUs may be 2 to 3 orders of magnitude higher than exposure to the general population (NTP-CERHR DEHP, 2006). In general, DEHP exposure levels in all age groups subjected to certain medical procedures are believed to be higher than those of the general population (NTP-CERHR DEHP, 2006).

Intravenous Exposure

The intravenous route is the major source of exposure to DEHP from medical procedures employing plasticized medical devices (Health Canada, 2002). Hemodialysis, blood or plasma transfusions, ECMO, cardiopulmonary bypass and intravenous administration of saline solutions, pharmaceuticals, enteral nutrition, and total parenteral nutrition (TPN) solutions are examples of medical procedures that can lead to intravenous exposure to DEHP (NTP-CERHR DEHP, 2006; Health Canada, 2002). Various studies that have investigated DEHP exposure in adults and infants resulting from these procedures are briefly described below.

FDA (2001)

An assessment of the safety of DEHP-containing medical devices was completed by the FDA Center for Devices and Radiological Health (CDRH) in 2001. As part of the safety assessment, FDA CDRH conducted a comprehensive review of the available literature at the time and estimated time-averaged daily doses of DEHP received by patients undergoing certain medical procedures. Daily exposure estimates for the parenteral, oral and inhalation routes were generated and compared to Tolerable Intake (TI) values for DEHP to assess risks associated with patient exposure to DEHP. Table 5.4.2-1 shows the DEHP exposure estimates via the intravenous route for select medical procedures calculated by FDA (2001). As shown in the table, DEHP doses in adults ranged from 0.005 mg/kg/d for infusion of crystalloid IV solutions to 8.5 mg/kg/d for blood transfusions in trauma patients. The highest DEHP dose in neonates (22.6 mg/kg/d) was associated with replacement transfusions. Brief details regarding the data and assumptions used by FDA (2001) in developing these estimates are provided in the table footnotes. For more information, the reader is referred to FDA (2001).

Table 5.4.3-1. DEHP Exposure Estimates for Select Medical Procedures Reported in FDA (2001)

Medical Procedure	DEHP Dose (mg/kg/d)	
	Adults (70 kg)	Neonate (4 kg)
Crystalloid IV solution infusion	0.005[a]	0.03[b]
Infusion of pharmaceuticals with solubilization vehicles		
Based on manufacturer instructions	0.04[c]	0.03[d]
Mixed and stored at room temperature for 24 hrs	0.15[e]	
TPN administration		
Without added lipid	0.03[f]	0.03[f]
With added lipid	0.13[g]	2.5[h]
Blood transfusion		
Trauma patient	8.5[i]	
Transfusion/(ECMO)in adult patients	3.0[j]	
Exchange transfusion in neonates		22.6[k]
Replacement transfusions in neonates in NICU		0.3[l]
Cardiopulmonary bypass		
Coronary artery bypass grafting	1[m]	
Orthotopic heart transplant	0.3[m]	
Artificial heart transplant	2.4[m]	
ECMO		14[n]
Hemodialysis	0.36[o]	
Apheresis	0.03[p]	

a. Based on the upper-bound DEHP concentration (0.344 mg/day) in crystalloid IV solutions reported by Corley et al. (1977) and assuming a patient receives 2 L of solution/day.
b. Based on a DEHP dose of 116 µg resulting from infusion of iv solution through PVC tubing for 24 hrs, as reported in Loff et al. (2000).
c. Based on a dose of 3 mg/day from agitation of a pre-mixed solution in PL-146 bags for 24 hrs at room temperature.
d. Based on DEHP dose (132 µg) received by neonates during infusion of fentanyl, as reported by Loff et al. (2000).

e. Based on DEHP content (21 µg/mL) of quinine/multivitamin solution stored for 48 hrs at 45ºC (from Faouzi et al., 1999) and the assumption that a patient receives 500 mL of the solution.
f. Based on data by Mazur et al. (1989).
g. Based on data by Mazur et al. (1989) and assuming that the TPN solution has a lipid concentration of 10%.
h. Based on a dose of 10 mg of DEHP from administration of TPN solution over a 24-hr period, as reported in Loff et al. (2000).
i. DEHP dose received by a gunshot victim as reported by Jaeger and Rubin (1972).
j. Value estimated from DEHP concentration in blood and blood products and based on the assumption that patients with anemia and clotting disorders receive over 600 units of blood during treatment and hospitalization.
k. From Plonait et al. (1993).
l. Based on a volume of 33.6 mL of packed red blood cells received by neonates (from Ringer et al., 1998) and DEHP concentration in packed cells as reported by Plonait et al. (1993).
m. Based on data on DEHP dose received during cardiac surgery reported by Barry et al. (1989). These values represent total dose from all sources including CPB device, tubing and transfusions.
n. Based on data from Karle et al. (1997) and Shneider et al. (1989) and assuming treatment lasted 10 days.
o. Derived from data on amount of DEHP retained in a single dialysis session (up to 59.6 mg, as reported by Faouzi et al., 1999) and assuming 3 dialysis sessions per week.
p. Based on information reported in Doull et al. (1999).

The estimates of daily doses were derived from measured data on DEHP concentrations in various media (i.e., blood, IV solutions, and TPN formulations) and estimates of the leaching rate of DEHP from medical devices obtained from the scientific literature. In general, the exposure values derived by FDA (2001) represent worst-case estimates of the DEHP doses patients may receive from specific procedures. The actual DEHP doses received by patients, therefore, may be lower than the reported values. For example, FDA (2001) notes that the estimate of the DEHP dose received during IV infusion of drugs is based on the concentration of DEHP in quinine/multivitamin solutions stored for 48 hrs at 45ºC; however, storage of IV drugs solutions at this temperature is unlikely. FDA (2001) also acknowledged that there was considerable uncertainty associated with the dose estimate for donors undergoing apheresis. At the time of preparation of the report, no data were available on DEHP exposure resulting from platelet/plasma donations. The dose of 0.03 mg/kg/d was derived using estimates from Doull et al. (1999), which were based on DEHP releases during dialysis, and various assumptions regarding duration and frequency of the apheresis procedure.

Health Canada (2002)

Health Canada (2002) conducted an extensive review of available scientific information on DEHP exposures from PVC medical devices to generate exposure estimates for adults and infants. The Health Canada report included many of the studies reviewed by FDA (2001). Based on the information reviewed by Health Canada (2002), blood transfusion to trauma patients and blood transfusions during ECMO are the short-term medical procedures that expose adult patients to the highest DEHP daily doses: 8.5 mg/kg-bw/d and 3 mg/kg-bw/d, respectively. The daily DEHP dose to trauma patients is based on data reported for whole blood in Jaeger and Rubin (1972), as was done in FDA (2001). However, the report notes that this estimate may not be clinically relevant since whole blood is rarely given to patients requiring transfusions. Hemodialysis treatment resulted in the highest exposure estimate for adults undergoing long-term procedures. The highest daily DEHP dose delivered by hemodialysis (2.2 mg/kg/d) was estimated from the amount of DEHP per session (ranging from 23.8 to 360 mg DEHP) calculated by Pollack (1985) from AUC measurements and assuming 3 dialysis sessions per week. This dose estimate is considerably higher than the worst-case dose derived by FDA (2001) based on the amount of DEHP retained per dialysis session reported by Faouzi et al., 1999. Health

Canada (2002) notes that there is a wide range of estimates of the amount of DEHP a patient is exposed to per dialysis session; this may be due to patient characteristics and the type of dialysis protocol employed.

For adult patients, daily exposure estimates associated with short- and long-term medical procedures were generated based on measured DEHP levels in blood, delivered doses estimated by area under the curve (AUC) calculations, or DEHP leaching rates from medical devices. Health Canada (2002) notes that exposure estimates based on measured DEHP levels in blood or published DEHP leaching rates are not as accurate as those derived from AUC dose calculations. Short-term medical procedures for which estimates were derived include blood transfusions, ECMO procedures, cardiopulmonary bypass and intravenous administration of drugs. Medical procedures leading to long-term exposures to DEHP included in Health Canada's analysis were hemodialysis, continuous ambulatory peritoneal dialysis (CAPD), transfusions of blood and blood products to patients with leukemia, and TPN therapy in critically ill patients, among others.

Health Canada (2002) also evaluated DEHP exposure in infants from medical procedures. According to Health Canada (2002), no direct measurements of DEHP exposures were available for routine procedures in NICUs such as replacement blood transfusions and TPN administration. Therefore, estimates were generated from theoretical calculations based on available data on DEHP levels in blood and leaching of DEHP from PVC infusion lines. The short-term procedure with the highest exposure level (up to 23 mg/kg/d based on Plonait et al., 1993) was double volume exchange transfusion. ECMO was the sub-acute medical procedure with the highest exposure level in newborns (up to 14 mg/kg/d after 10 days of treatment based on Shneider et al., 1989).

NTP-CERHR DEHP (2006)

As part of its evaluation of the potential human reproductive and developmental effects of DEHP, the NTP-CERHR Expert Panel summarized the available scientific literature on medical exposures to DEHP (NTP-CERHR DEHP, 2006). Studies reviewed in the Expert Panel report provide measured and estimated levels of DEHP in blood, plasma, and lipid-containing solutions resulting from use of medical devices under a wide range of exposure conditions. Exposure estimates were also provided for some of the studies summarized in the report. The Expert Panel's report included many of the studies reviewed in FDA (2001) and Health Canada (2002) but also provided new information on DEHP exposure from plasma/platelet donations obtained from measurements of serum DEHP concentrations (Buchta et al., 2003) and measurements of urinary concentrations of DEHP metabolites (Koch et al., 2005a).

Select data from the CERHR Expert Panel reports that may be relevant to patient exposure via the intravenous route are presented below in Table 5.4.2-2. The reader is referred to NTP-CERHR (2006) or the individual studies for additional information.

As noted above, NTP-CERHR (NTP-CERHR DEHP, 2006) reviewed the studies conducted by Koch et al. (2005a) and Buchta et al. (2003) regarding DEHP exposure levels in voluntary plasma/platelet donors. In the study by Buchta et al. (2003), serum DEPH levels, measured in 36 platelet pheresis donors before and after pheresis sessions, increased from a median at baseline

of 92.2 ng/mL to 214 ng/mL after the pheresis session. The estimated DEHP doses ranged from 1.8 to 20.3 µg/kg-bw. Koch et al. (2005a) measured concentrations of DEHP metabolites (MEHP, MEHHP, and MEOHP) in urine samples from 6 plasma donors, 6 donors who underwent dual-needle-continuous-flow platelet pheresis and 6 donors who had single-needle discontinuous-flow platelet pheresis. Donors undergoing continuous-flow platelet pheresis had the highest mean daily DEHP exposure (32.1 µg/kg/d; range: 28.2 to 38.1 µg/kg/d). The discontinuous-flow technique resulted in a mean dose of 18.1 µg/kg/d (range: 14.3 – 23.8 µg/kg/d). Plasma donation, on the other hand, resulted in exposure levels comparable to levels in the control group. Koch et al. (2005a) suggested that the low exposure levels in plasma donors are due to removal of most of the DEHP in the lipid-rich plasma.

The CERHR Expert Panel noted that DEHP can be metabolized to MEHP by enzymes contained in blood products. Therefore, studies such as Loff et al. (2000) that rely solely on measurements of DEHP in blood, and not its metabolites, may underestimate exposures to DEHP (NTP-CERHR DEHP, 2006).

Table 5.4.3-2 DEHP Levels in Various Media and Exposure Estimates from Literature Reviewed by NTP-CERHR Expert Panel

Medical Device	Medium	DEHP Levels in Medium	DEHP Exposure Estimate	Primary Reference Cited
IV tubing	Parenteral nutrition solutions	424.4 µg/mL over 24 hrs	5 mg/kg-bw for a 2 kg infant receiving 25 mL of soln.	Loff et al. (2000)
	Aminoacid/glucose solution	0.83 µg/mL, 24 hrs		Loff et al. (2000)
	1% propofol, continuous		6,561 µg for a 2 kg infant	Loff et al. (2000)
	Fentanyl solution (28.8 mL)		132.5 µg for a 2 kg infant	Loff et al. (2000)
	Midazolam (24 mL)		26.4 µg for a 2 kg infant	Loff et al. (2000)
	Lipid-containing solution at 27 ˚C	422 µg/mL	10 mg for a 2 kg infant receiving 24 mL of soln.	Loff et al. (2002)
	Lipid-containing solution at 33 ˚C	540 µg/mL	13 mg for a 2 kg infant receiving 24 mL of soln.	Loff et al. (2002)
	Hydrogenated castor oil in saline or water	775 µg after 4 hrs		Hanawa et al. (2003)
	Hydrogenated castor oil in sugar solutions	150 µg over 4 hrs		Hanawa et al. (2003)
Blood bag and tubing	Packed red blood cells, 20 mL		608 µg for a 2 kg infant	Loff et al. (2000)
	Platelet-rich plasma		928 µg for a 2 kg infant	Loff et al. (2000)
	Fresh frozen plasma		552 to 8,108 µg for a 2 kg infant	Loff et al. (2000)
Ethyl vinyl acetate bags with PVC connectors and tubing	Parenteral nutrition solutions stored at 4 ˚C for 24 hrs or 1 week		0.8 to 2 mg/day	Kambia et al. (2003)

Table 5.4.3-2 DEHP Levels in Various Media and Exposure Estimates from Literature Reviewed by NTP-CERHR Expert Panel (continued)

Medical Device	Medium	DEHP Levels in Medium	DEHP Exposure Estimate	Primary Reference Cited
Hemodialysis simulated in a PVC blood circuit system	Bovine blood	1718 µg/L after 4 hrs from a baseline of 249 µg/L. MEHP 80 µg/L after 4 hrs	0.067 mg/kg-bw/day for adults	Haishima et al. (2004)
Hemodialysis	Blood (11 patients)		16.4 mg (range 3.6–59.6 mg) after a 4- hr dialysis session	Dine et al. (2000)
Platelet pheresis	Blood (36 donors)		Median dose : 6.46 µg/kg-bw (range 1.8–20.3 µg/kg-bw)	Buchta et al. (2003)
	Blood (12 donors)		Continuous-flow Mean dose: 32.1 µg/kg-bw (range 28.2–38.1µg/kg-bw) Discontinuous-flow Mean dose: 18.1 µg/kg-bw (range 14.3–23.8µg/kg-bw)	Koch et al. (2005a)

Source: NTP-CERHR DEHP, 2006

ECB DEHP (2008)

ECB DEHP (2008) compiled estimates of exposure via medical treatments from various studies conducted prior to the year 2000. Treatments evaluated in the cited studies included blood transfusion in adults and infants, hemodialysis, artificial ventilation in preterm infants, ECMO, and cardiopulmonary bypass, among others. Estimates of exposure to DEHP from medical treatments reported in ECB DEHP (2008) are provided below in Table 5.4.2-3.

Based on the information reviewed, ECB DEHP (2008) concluded that the medical procedures with the highest exposures are long-term hemodialysis in adults (3.1 mg/kg/d), long-term blood transfusion in children (0.075 mg/kg/d), and transfusions in neonates (1.7 mg/kg/d). ECMO in children was also considered a high-exposure procedure but a quantitative estimate of average daily exposure was not provided. ECB DEHP (2008) notes that impaired kidney function in hemodialysis patients may affect excretion of DEHP and metabolites leading in longer retention times of these compounds in the body and increased internal exposure.

SCENIHR (2008)

In its evaluation of the safety of DEHP-containing medical devices, SCENIHR (2008) summarized information on DEHP exposure from medical devices obtained from various sources including Health Canada (2002), FDA (2001), Koch et al. (2005a) and Buchta et al., (2003). Regarding exposure estimates reported in FDA (2001), SCENIHR (2008) notes that the exposure estimates for newborns were based on a body weight of 4 kg, and therefore, actual

exposure to DEPH may be higher since most newborns that require intensive medical treatments are born prematurely and weight significantly less than 4 kg.

Table 5.4.3-3 DEHP Exposure from Medical Devices

Medical Procedure	DEHP Exposure	Reference
Short-term		
Blood transfusion in adults	200 – 8,500 µg/kg/treatment period	Jaeger and Rubin (1972) Sjöberg et al. (1985a) Huber et al. (1996)
Blood transfusion in newborns	500 – 4,200 µg/kg/treatment period	Sjöberg et al. (1985a) Shneider et al. (1989) Sjöberg et al. (1985b)
	500 – 700 MEHP µg/kg/treatment period	Sjöberg et al. (1985a) Sjöberg et al. (1985b)
	1,200 – 22,600 µg/kg/treatment period	Plonait et al. (1993)
Platelet concentrates in adults	400 – 2,500 µg/kg/treatment period	Rubin and Schiffer (1976) Peck et al. (1978)
Platelet concentrates in newborns	1,900 µg/kg/treatment period	Shneider et al. (1989)
ECMO in infants	42,000 – 140,000 µg/kg/treatment period	Shneider et al. (1989)
Cardiopulmonary bypass	30 – 2,400 µg/kg/treatment day	Jaeger and Rubin (1972) Barry et al. (1989)
	4 – 300 MEHP µg/kg/treatment day	Jaeger and Rubin (1972) Barry et al. (1989)
Autopheresis	8.1 µg/kg/day	Doull et al. (1999)
Long-term		
Platelet and whole blood transfusion in infants	2,100 – 27,500 µg/kg/year 6 – 75 µg/kg/day	Jacobson et al. (1977)
Hemodialysis	10 – 7,200 µg/kg/session 4 – 3,100 µg/kg/day	Nässberger et al. (1987) Lewis et al. (1978) Ono et al. (1975) Shneider et al. (1989) Gibson et al. (1976) Bommer et al. (1985) Pollack et al. (1985) Flaminio et al. (1988) Ganning et al. (1984)
Peritoneal dialysis	800 µg/kg/year 2 µg/kg/day	Nässberger et al. (1987)
Clotting factors in hemophiliacs	30 µg/kg/day	Huber et al. (1996)
Autopheresis	8.1 µg/kg/day	Doull et al. (1999)
Transfusion of platelets	36 µg/kg/day	Doull et al. (1999)
Neonatal transfusion	1,700 µg/kg/day	Hileman (2000)

Source: Adapted from ECB DEHP, 2008

Oral Exposure

DEHP exposure via the oral route can occur in patients that receive enteral feedings delivered from PVC bags and tubing or that undergo nasogastric intubation. Currently, there is limited information on DEHP exposures from enteral infusions or nasogastric tubes. Based on data from Mazur et al. (1989), FDA (2001) estimated the upper-bound dose received by patients from enteral feeding to be 9.5 mg/d or 0.14 mg/kg/d. This estimate is based on the assumption that leaching of DEHP from enteral nutrition storage bags occurs at the same rate as that from TPN solution storage bags and that the lipid content of the enteral nutrition admixture is similar to the lipid content of parenteral admixture. However, FDA (2001) notes that a more typical daily dose from enteral feeding would be approximately 0.04 mg/kg/d.

FDA (2001) also points out that nursing infants of mothers medically exposed to DEHP may be exposed to DEHP through ingestion of breast milk. However, due to lack of data on DEHP levels in milk from mothers undergoing medical procedures, quantitative estimates of DEHP exposures in these infants are highly uncertain (FDA, 2001).

Inhalation Exposure

The use of PVC tubing in respiratory therapy can expose patients to DEHP via the inhalation route. However, this type of exposure has not been studied in detail. The DEHP leaching rate from PVC tubing and components of breathing circuits is dependent on a variety of factors such as flow velocity, respiratory rate, tubing diameter, and temperature. Thus, accurate measurement of this rate under clinical conditions is difficult (Health Canada, 2002).

Health Canada (2002) reported that ventilation using heated respiratory tubing would expose an adult to 1.1 mg DEHP/day and an infant to 0.35 mg DEHP/d or 0.2 mg/kg-bw/d. This is a worst-case estimate based on the assumption that the patient is exposed to air saturated with DEHP throughout the procedure (Health Canada, 2002). According to Health Canada (2002), oxygen therapy may result in exposure levels of 1.6 mg/d for adults and 0.5 mg/d for infants (or 0.25 mg/kg-bw/d for a 2-kg infant), assuming exposure to saturated air at 37ºC and a flow rate of 15 L/min as a worst-case scenario. In adult, intubation with endotracheal tubing may result in exposure levels of 1.1 mg/d, based on the same assumptions for the worst-case scenario for artificial ventilation with heated respiratory tubing. For neonates, Health Canada (2002) estimated exposure from endotracheal tubes to be 2.8 mg/d (1.4 mg/kg-bw/d for a 2-kg neonate). This worst-case estimate takes into account the amount of DEHP delivered by respiratory air stream and DEHP extracted by respiratory tract mucus (Health Canada, 2002).

Hill (1997), as cited in FDA (2001) and Schettler (2006), estimated inhalation exposure to DEHP based on direct measurements of DEHP concentration in air passing through PVC respiratory tubing. The doses estimated by Hill (1997) ranged from 28.4 to 94.6 µg/d, which corresponds to 0.0004 to 0.001 mg/kg-bw/d.

Exposure from Multiple PVC Devices

Many of the available studies described above focus on exposure from single medical procedures. However, some patients such as critically ill neonates and adults undergoing ECMO and surgical procedures may require a combination of several medical procedures during the course of their treatment (FDA, 2001).

FDA (2001) estimated aggregate exposures to DEHP for neonates and adults resulting from the use of multiple medical devices. The upper-bound daily dose for NICU infants receiving IV administration of sedatives, TPN administration and replacement transfusion was estimated to be 3 mg/kg/d, based on a body weight of 4 kg. Adults undergoing ECMO may be exposed to over 4 mg DEHP/kg/d from PVC tubing in the ECMO device, multiple blood transfusions, and IV administration of drugs. FDA (2001) notes that the major contributor to total dose in ECMO patients is transfused blood products. For adults undergoing coronary artery bypass graft (CABG) surgery, sources of DEHP exposure include endotracheal tubes, IV bags, chest tubes, nasogastric tubes, and blood bags, among others. Based on data on levels of DEHP and MEHP from Barry et al. (1989), as cited in FDA (2001), total dose received during CABG surgery is 1 mg/kg/d.

DEHP Exposure Based on Urinary Metabolite Concentrations

Most of the current literature on DEHP exposure from medical devices provide estimates of exposure generated from data on DEHP content and leaching rates from medical devices. A few studies, however, have used measured levels of DEHP or metabolites in urine or blood to evaluate DEHP exposure in people undergoing medical treatments. Some researchers have noted that the use of urinary concentrations of metabolites as biomarkers of exposure provide the most accurate exposure assessments since they represent exposure from multiple sources and routes (Calafat and McKee, 2006). Recent studies that have evaluated exposure in NICU infants using urinary metabolite concentrations are briefly described below.

Calafat et al. (2004b)

Calafat et al. (2004b) evaluated exposure to DEHP in premature infants undergoing medical procedures in a neonatal intensive care unit setting. Urinary levels of the DEHP metabolites MEHP, MEHHP, and MEOHP were measured in 41 samples obtained from 6 premature newborns (4 girls and two boys). Of the samples analyzed, 33 had detectable levels of all three metabolites. The study authors reported median concentrations of 2,221 ng/mL for MEHHP, 1,697 ng/mL for MEOHP, and 129 ng/mL for MEHP in the 33 samples. According to Calafat et al. (2004b), these results are in agreement with previous studies that show higher concentrations of the oxidative metabolites MEOHP and MEHHP compared to MEHP. Calafat et al. (2004b) also compared MEHP levels found in the study infants to levels reported for children and adults in previous studies. According to Calafat et al. (2004b), the geometric mean MEHP concentration in the premature infants was significantly higher than the mean urinary concentration of MEHP in 19 toddlers aged 12 to 18 months. In addition, Calafat et al. (2004b) reported that the median MEHP concentration in the premature infants was significantly higher than the U.S. median in children 6 to 11 years of age from the 1999-2000 National Health and

Nutrition Examination Survey. Median concentrations of MEHHP and MEOHP were also higher in the premature infants compared to those in a nonrepresentative population of 62 children and adults. Based on the results of this study, the authors concluded that infants that undergo intensive medical procedures such as blood transfusions, intravenous therapy, enteral and parenteral nutrition support, and dialysis are exposed to higher concentrations of DEHP than the general population.

Green et al. (2005) and Weuve et al. (2006)

Green et al. (2005) measured urinary concentrations of DEPH metabolites in samples obtained from 54 newborns admitted to NICUs at two hospitals. Prior to collection of samples, infants were assigned to one of three exposure groups (low, medium and high), based on the medical procedures used in their treatment. The low exposure infants were those receiving mainly bottle and/or gavage feedings. Newborns in the medium-exposure group received enteral feedings, IV hyperalimentation, and/or nasal continuous positive airway pressure. The high exposure infants were those receiving more intensive care which included umbilical vessel catherization, endotracheal intubation, IV hyperalimentation, and indwelling gavage tube. Urine samples were analyzed for 10 phthalate monoesters including MEHP, MEHHP, and MEOHP; but only MEHP levels were reported in Green et al. (2005). Median urinary MEHP levels were 4, 28, and 86 ng/mL in the low-, medium-, and high-exposure groups, respectively. After adjusting for gender and institution of hospitalization, the study authors found increasing urinary MEHP levels with increasing intensity of care and use of DEHP-containing medical devices: urinary MEHP levels in infants in the medium and high exposure groups were 2 times and 5 times higher, respectively, than those of infants in the low exposure group.

In a follow-up report, Weuve et al. (2006) reported the urinary concentrations of MEHHP and MEOHP in the 54 newborns studied in Green et al. (2005). Similar to the results reported for MEHP, urinary levels of MEHHP and MEOHP were higher in the group of infants receiving more intensive care compared to infants in the low exposure group. Urinary concentrations of MEHHP and MEOHP, adjusted for gender and institution, were at least 13 times higher in the high exposure group than in the low exposure group. Infants in the medium exposure groups had adjusted urinary MEHHP and MEOHP concentrations that were approximately 4 times higher than concentrations found in the low exposure group. Weuve et al. (2006) also estimated the daily intake of DEHP from medical procedures for infants in the high exposure group using the urinary metabolite concentrations of MEHHP and MEOHP and assuming a uniform creatinine clearance rate of 9.8 mg/kg. The median daily intake of DEHP for the high exposure infants was estimated to range from 233 to 352 µg/kg-bw/d based on MEHHP and MEOHP urinary levels, respectively. The study authors noted that this intake level is one to two orders of magnitude higher than exposures in adults and above the U.S. EPA's reference dose of 20 µg/kg-bw/d.

5.4.4. Scenario 3: Personal Care Products

The use of lotions, shampoos, cosmetics, and other personal care products can expose consumers to phthalates through the dermal and inhalation routes. Incidental ingestion of phthalate-containing personal care products is also a potential source of exposure (Wormuth et al., 2006); however, this exposure route has not been studied in detail. Most of the available scientific literature regarding exposure from use of personal care products has focused on dermal exposure. Only a few studies have addressed inhalation or incidental ingestion. While the dermal exposure route has received more attention than other routes of exposure to personal care products, there are important uncertainties associated with published dermal exposure estimates. For example, there are limited data available on dermal absorption of phthalates through human skin. Most studies rely on data from animal studies and assumptions based on the limited human data to model dermal absorption through human skin. Assumptions regarding frequency, duration and mode of product application and amount used vary among studies, which also contribute variability and uncertainties to the estimates. In addition, there are currently limited data on the phthalate content of personal care products, particularly for those products intended for use on infants and children (Sathyanarayana et al., 2008).

Summary information on exposure to personal care products from the available literature is provided below.

ECB DBP (2003)

In its risk assessment for DBP (ECB DBP, 2003), the ECB estimated dermal exposures to DBP from the use of nail polish using a mathematical model for calculating consumer exposure (ConsExpo-version 1.03, van Veen, 1995). Based on the assumptions that nail polish is used twice per week for 10 min (0.25 g DBP per event) and that dermal contact occurs via air, the ECB estimated that the concentration of DBP in air from the use of nail polish is 4.34×10^{-12} mg/cm^3. Uptake of DBP following application of nail polish was estimated to be negligible.

The ECB risk assessment report for DBP (ECB DBP, 2003) also estimated inhalation exposure resulting from the use of nail polish. Using the same assumptions regarding frequency and duration of use as employed in calculating dermal exposure, the average air concentration per event was estimated by the ConsExpo model to be 4.34×10^{-6} mg/m^3. The total dose via the inhalation route is 2×10^{-9} mg/kg-bw/d.

Koo and Lee (2004)

Koo and Lee (2004) measured levels of DEHP, DEP, DBP, and BBP in 102 cosmetic products and collected information on frequency and volume of cosmetic use to estimate human exposure to phthalates. The mean, median, and 90th percentile values for frequency of use were used to estimate daily exposure levels using three models based on different assumptions with regards to dermal or inhalation absorption. Total daily exposure levels were calculated by combining exposure estimates for the use of perfume, deodorant, nail polish and hair products. The mean estimated exposure levels for the concurrent use of these cosmetic products based on the three models used in the study are presented in Table 5.4.3-1 below.

Table 5.4.4-1 Total Mean Daily Exposure Levels[1] (µg/kg/day) to Phthalates from Cosmetics

Phthalate	Model 1	Model 2	Model 3
DEHP	0.0003	0.00013	0.005
DEP	5.971	0.183	24.879
DBP	2.361	0.018	3.935
BBP	0.002	Not reported	Not reported

1. Combined exposure from concurrent use of perfume, deodorant, nail polish and hair products.

For Model 1, Koo and Lee (2004) assumed that absorption through human skin is similar to absorption through rat skin and estimated exposure levels based on rat in vivo dermal absorption data. Total mean exposure levels ranged from 0.0003 µg/kg/d for DEHP to 5.971 µg/kg/d for DEP. For the highly exposed users (90th percentile of frequency of use), total estimated exposure levels were 65.696 µg/kg/d for DEP, 30.463 µg/kg/d for DBP, 0.036 µg/kg/d for BBP, and 0.004 µg/kg/d for DEHP. Koo and Lee (2004) also calculated in vivo dermal absorption rates in humans using rat in vivo and rat and human skin in vitro data (Model 2). Based on the estimated in vivo dermal absorption rates, total mean levels were ranged from 0.00013 µg/kg/d for DEHP to 0.183 µg/kg/d for DEP. For the highly exposed subgroup of users, total estimated exposure levels were 2.017 µg/kg/d for DEP, 0.228 µg/kg/d for DBP, and 0.0013 µg/kg/d for DEHP. Rat in vivo and rat and human skin in vitro data were not available for BBP, thus, exposure levels to BBP could not be determined by this approach. Assuming that phthalates in cosmetics are absorbed exclusively via inhalation (Model 3), Koo and Lee (2004) estimated total mean exposure levels ranging from 0.005 µg/kg/d for DEHP to 24.879 µg/kg/d for DEP. For the highly exposed subgroup of users, total exposure levels were estimated to be 273.739 µg/kg/d for DEP, 50.772 µg/kg/d for DBP, and 0.069 µg/kg/d for DEHP.

Based on the estimated inhalation exposure levels for the highly exposed subgroup, hazard indices (daily exposure level/TDI, MRL or ADI) were estimated to be 0.0007 for DEHP, 0.012 for DEP, and 0.347 for DBP. Koo and Lee (2004) noted that the estimates generated in this study suggest that exposure to phthalates in cosmetics is small; however, total exposure to phthalates from several sources should be further investigated.

Hubinger and Havery (2006)

Hubinger and Havery (2006) analyzed 48 cosmetic products, including hair care products, deodorants, lotions, creams, nail products, fragrances and body washes, and found the highest levels of phthalate esters in nail enamel (59,815 ppm DBP) and fragrance (38,663 ppm DEP) samples. Phthalates found in nail enamel included DMP, DEP, BBP, and DBP. The only phthalate detected in fragrance samples was DEP. Hubinger and Havery (2006) noted that phthalate exposure due to application of nail polish, soaps, shampoos, and conditioners is limited. Nail polish hardens rapidly after application, which inhibits absorption of phthalates through the nail. Soaps, shampoos, and conditioners, on the other hand, are washed off the skin shortly after application limiting phthalate contact with the skin.

Wormuth et al (2006)

Wormuth et al. (2006) investigated consumer exposure to eight phthalates (DMP, DEP, DiBP, DnBP, BBzP, DEHP, DINP, and DIDP) using a scenario-based risk assessment approach that included various oral, dermal, and inhalation exposure pathways. Included in this analysis was consumer exposure to personal care products resulting from dermal contact and incidental ingestion of the products. Wormuth et al. (2006) calculated total consumer exposure for seven different age and gender groups by adding the single exposure estimates for all the exposure pathways. In addition, the study authors reported on the relative contribution of various sources to the total daily exposure. In all consumer groups investigated, dermal application and incidental ingestion of personal care products were the main sources of exposure to DEP, accounting for at least 65% of the total DEP exposure. Application and incidental ingestion of personal care products accounted for 15% to 50% of the total exposure to DnBP in teenagers and female adults. Personal care products were not a significant source of exposure to the other five phthalates investigated. In this study, there was considerable variability in the daily exposure estimates. According to the study authors, this was due to uncertainty and natural variability in the input parameters used in the calculations.

Sathyanarayana et al. (2008)

Sathyanarayana et al. (2008) examined the use of infant care products applied to the skin as a potential source of exposure to phthalates in infants and toddlers. Data on urinary phthalate metabolite concentrations and use of infant care products were obtained by Sathyanarayana et al. (2008) for a group of 163 infants born between 2000 and 2005. Through a questionnaire, the infants' mothers provided information on the use of infant powder, talc, cornstarch, diaper creams, shampoo, wipes and lotion during the 24 hrs prior to sample collection. Urine samples were collected from wet diapers provided by the mothers and analyzed for 9 phthalate metabolites.

Use of infant wipes was reported by 94% of the mothers while 54% of the mothers reported use of infant shampoo. Only 14% of mothers reported using baby powder prior to sample collection. The most frequently detected metabolites were MEP and MBP found in 98% and 99% of the samples, respectively. MEP also had the highest mean (178.2 µg/L) and median (60.9 µg/L) values of all the metabolites detected. The study authors noted that all urine samples had a least 1 phthalate compound above the limit of detection. In this study, multiple linear regression analyses, using data adjusted for infant age and creatinine levels, were conducted to investigate the association between metabolite concentrations and product use. The results of these analyses showed that the reported use of infant lotion, powder and shampoo was significantly associated with increased urinary concentrations of the metabolites MEP, MMP, and MiBP, especially in infants younger than 8 months. The use of diaper creams or infant wipes, on the other hand, was not strongly associated with urinary concentrations of any of the metabolites detected. Based on the study findings, Sathyanarayana et al. (2008) suggested that dermal exposure may be an important route of exposure to some phthalates for young infants.

5.4.5. Scenario 4: Clothing, Gloves and Footwear

Clothing and footwear made of plasticized PVC, fabric coated with plasticized PVC, or synthetic leather can be a source of consumer exposure to phthalates. However, knowledge of the amount and type of phthalates used in these products is limited (ECB DEHP, 2008). Exposure from these products is expected to occur primarily by direct contact with the skin; mouthing of clothing is a potential source of exposure to phthalates in infants but has not been addressed in many of the available studies. The magnitude of dermal exposure depends on the skin area in contact with the product, the contact duration, the surface availability of the phthalate and the percutaneous absorption through the skin (ECB DEHP, 2008). As is the case with other types of dermal exposures, limited information is available on dermal uptake of phthalates through human skin; therefore, available estimates of dermal exposure from clothing, gloves, and footwear are based on animal data and various assumptions regarding uptake through human skin, and frequency and duration of product use leading to uncertainty and variability in the estimates. Few studies have examined dermal exposure to phthalates from clothing, gloves and footwear made with plasticized materials. The available studies are summarized below.

CPSC DINP (2001)

In its 2001 report to CPSC, the Chronic Hazard Advisory Panel (CHAP) on DINP evaluated potential dermal exposures to DINP from PVC-containing rainwear and sandals. Dermal exposure doses of DINP were calculated using two approaches, the contact-flux (CF) and the aqueous-clearance (AC) methods. These methods employed different assumptions and data on dermal uptake of DINP from plasticized clothing and footwear. Table 5.4.4-1 shows time-weighted average daily DINP exposures calculated by the CHAP. Daily exposures generated by the AC method ranged from 11 µg/kg/d for adults wearing rainwear to 340 µg/kg/d for children wearing "jelly" sandals. The CF method resulted in daily exposure estimates ranging from 0.45 µg/kg/d for adults wearing rainwear to 14 µg/kg/d for children wearing "jelly" sandals. In the CF method, dermal uptake of DINP was estimated based on the effective dermal flux estimate (0.24 µg/cm^2/hr) from Deisinger et al. (1998), which evaluated DEHP migration and percutaneous absorption into rat skin under static exposure conditions. In the AC approach, an effective dermal flux of 60 µg/cm^2/hr was used as the upper bound estimate of DINP migration from PVC in a moist and dynamic contact environment, as would occur during sustained contact of the skin with PVC clothing or footwear. The dermal flux estimate was based on a CPSC study of DINP extraction from toys by mouthing (Chen, 1998a). These estimates were based on body weights of 10 kg for children (19-36 months old) and 70 kg for adults, and a total of 400 cm^2 of skin in contact with a DINP-containing rainpants and/or raincoat for 4 hrs/d and 30 d/yr.

As shown in Table 5.4.4-1, exposure estimates based on the AC method were consistently higher than those generated by the CF approach. CPSC DINP (2001) noted that estimates of dermal exposure based on the CF methods are negligible, while the AC method generates dermal exposure estimates that are higher than a proposed ADI of 0.12 mg/kg/d. It further noted that information on DINP content of consumer products such as sandals and rainwear was not available and there was considerable uncertainty in the estimated dermal uptakes of DINP. As a result, CPSC DINP (2001) concluded that the estimates of potential dermal exposure from PVC rainwear and footwear are speculative.

Table 5.4.5-1 Estimated Dermal Exposures (µg/kg/d) from PVC-containing Clothing and Footwear

Age Group	Product	Exposure (µg/kg/d)	Methodology[a]
Children (19-36 months old)	Rainwear	3.2	CF
		79	AC
	Sandals	14	CF
		340	AC
Adults	Rainwear	0.45	CF
		11	AC
	Sandals	3.9	CF
		98	AC

Source: CPSC, 2001

a CF = Contact-flux method; based on migration and dermal absorption from Deisinger et al. (1998) AC = Aqueous-clearance method; based on DINP migration study of Chen (1998a) and dermal absorption modeled by Bogen, 1994.

ECB (ECB DIDP (2003); ECB DINP (2003); ECB DEHP (2008))

Dermal exposure from gloves was estimated by the European Chemical Bureau for DIDP, DINP and DEHP (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008) based on data on DEHP dermal uptake in rat skin (0.24 µg/ cm^2/hr) from Deisinger et al. (1998). For DIDP, ECB (ECB DIDP, 2003) assumed a dermal absorption rate of 0.024 µg/cm^2/hr since the dermal absorption of DIDP has been shown to be 10 times less than DEHP based on Elsisi et al. (1989). The same factor of 10 was used to extrapolate from DEHP to DINP given the similarities in physical and chemical properties between DINP and DIDP (ECB DINP, 2003). There were no corrections for interspecies differences. For each of these phthalates, the maximum internal exposure (Umax) by dermal contact to gloves was calculated based on assumptions regarding skin area contact of both hands (840 cm^2), duration of contact (2 hrs/d), and adult body weight (60 kg). The daily dermal exposures were estimated to be 0.7 µg/kg-bw/d for DIDP and DINP and 6.7 µg/kg-bw/d for DEHP. Dermal exposures for children were not estimated.

ECB (ECB DEHP, 2008) also estimated daily dermal exposure to DEHP using data on migration of DEHP from products and percent absorption through the skin (5%), already corrected for interspecies differences. The resulting dose estimate was 9.3 µg/kg-bw/d; however, the dose estimated selected for the risk characterization was the value (6.7 µg/kg-bw/d) derived based on the percutaneous adsorption rate derived from Deisinger et al. (1998).

Wormuth et al (2006)

Wormuth et al. (2006) noted that exposure to phthalates from gloves, other than plastic gloves, is infrequent and short in duration, so dermal exposure is insignificant. However, use of plastic gloves (i.e., for doing dishes) can be an important source of dermal exposure to various phthalates. To assess exposure through this scenario, Wormuth et al. (2006) used information on frequency of dishwashing per day, duration per event, and phthalate concentrations in gloves from various studies. The dermal uptake of phthalates from gloves was based on studies of dermal uptake through rat skin, assuming that dermal uptake of phthalates through human skin is less than that through rat skin by a factor of 7, based on information for DEP from Mint et al. (1994). Based on their analysis of the contribution of the various scenarios to total exposure,

gloves accounted for over 10% of the exposure to DINP and for 5 to 7% of the total exposure to DIDP in teenagers and adults.

Jensen and Knudsen (2006)

Jensen and Knudsen (2006) reported estimated values for dermal, oral and inhalation exposure to DEHP from textile fabrics. Dermal exposure to DEHP was reported to be 0.00275 mg/kg-bw and 0.0096 mg/kg-bw for adults and children, respectively. A dermal uptake of 5% was assumed for both children and adults. Oral intake for children sucking or chewing a textile piece (400 cm^2) was reported as 15.4 µg/kg-bw, based on a body weight of 10 kg and 100% absorption. Inhalation exposure to DEHP was reported to be very small (6.44 $x10^{-6}$ µg/kg-bw/d) based on DEHP saturated air concentration, 10 kg of clothes, a exposure duration of 24 hrs and a room volume of 20 m^3.

5.4.6. Scenario 5: Car and Public Transportation Interiors

Plasticized PVC materials found in car and public transportation interiors can be a source of phthalate exposure to drivers and passengers. The release of phthalates from seat fabrics, dashboard, and interior trim, for example, can lead to high concentrations of phthalates in the air inside vehicles especially at high temperatures (ECB DEHP, 2008; Fujii et al., 2003). However, very few measured data are available on phthalate concentrations in the air inside cars. Data are also lacking on the phthalate content of interior auto components.

While the main route of exposure to phthalates in car interiors is assumed to be inhalation, dermal exposure may also occur through contact with seats, dashboards and other materials made of plasticized PVC (ECB DEHP, 2008). Skin contact with dust containing phthalates may also be a source of exposure to these chemicals inside cars. However, published estimates are only available for inhalation exposure from interior auto components and are presented below.

ECB (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008)

The ECB estimated inhalation exposures to DIDP, DINP, and DEHP for adults and children in car and public transportation interiors (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008). The estimated daily inhalation exposures to DIDP, DINP, and DEHP are presented in Table 5.4.5-1, below. As shown in the table, children had the highest exposure levels for all phthalates analyzed.

Table 5.4.6-1 Daily Exposure to DIDP, DINP, and DEHP from Car Interiors

Age Group	DIDP		DINP		DEHP	
	Conc. in Air (µg/m^3)	Daily Exposure (µg/kg-bw/day)	Conc. in air (µg/m^3)	Daily Exposure (µg/kg-bw/day)	Conc. in Air (µg/m^3)	Daily Exposure (µg/kg-bw/day)
Adults	20	0.8	40	1.7	21	0.9
Children		1.9		3.9		2

Given the limited measured data available on phthalate concentrations in the air inside cars and other exposure parameters, various assumptions were used to quantify exposure to these chemicals via the inhalation route. As a worst-case scenario, the saturated vapor pressure of these chemicals at 20˚C was used as a starting point to calculate phthalate concentrations in the air inside cars. To account for particle-bound phthalates, the saturated vapor concentration was multiplied by a factor of 4, derived from a study of DEHP adsorption onto particles in residential environments. In addition, assumptions regarding bioavailability (75% for adults; 100% for children), inhalation rate (20 m^3/d for adults; 9.3 m^3/d for children), and exposure duration (4 hrs/day for adults; 2 hrs/d for children) were used to generate inhalation exposure estimates.

ECB (ECB DIDP, 2003) noted that the release of phthalates from PVC materials inside cars depends on the temperature inside the car; therefore, high concentrations of phthalates can be expected during the summer months when cars are parked in sunlight. However, the estimates provided in the ECB reports do not account for the high temperatures that may be found inside cars during summer. It should be noted that one recent study by Fujii et al (2003) estimated air concentrations of DEPH that were approximately 100 times higher than the DEHP air concentration used to generate inhalation exposures by the ECB. In the Fujii et al. (2003) study, the temperature dependence of phthalate emissions from various plastic materials was investigated using a passive flux sampler. Phthalate emissions from synthetic leather, vinyl flooring, and wallpaper were measured at 20˚C, 50˚C, and 80˚C. The measured maximum phthalate emissions from all three types of plastic materials were significantly higher at 80˚C compared to those at 20˚C. Using the results of the flux study, Fujii et al. (2003) estimated the DBP and DEHP concentrations at 70˚C and 80˚C in air inside an average-sized car containing 3.0 m^2 of synthetic leather. Estimated concentrations were generated for four types of synthetic leather; only the highest concentrations were reported. At 80˚C, the DEPH concentration inside a car with an interior volume of 2.0 m^3 was estimated to be 2,000 $\mu g/m^3$. The DBP concentration (7.7 $\mu g/m^3$) was considerably lower than that of DEHP.

5.4.7. Scenario 6: Building Materials and Furniture (House Dust)

This section summarizes exposure data for banned and interim banned phthalate from building materials, furniture, and indoor dust. Although the emission of phthalates from interior surface materials in normal indoor environmental conditions is not well understood, they are known to off-gas and are present in residential indoor air (Jaakkola and Knight; 2008, Wormuth et al., 2006; Fujii et al., 2003). Phthalates migrate from PVC tile, vinyl flooring, wallpaper, paint, adhesives, glues, sealing compounds, and synthetic leather to house dust, and, as a result, inhalation of particles and/or ingestion of dust containing phthalates is a plausible route of exposure, especially among children (Jaakkola and Knight, 2008; Jensen and Knudsen , 2006; Wormuth et al., 2006).

Jensen and Knudsen (2006)

Jensen and Knudsen (2006) assessed the importance of consumer products as a source of indoor pollution. They assessed the exposure of the residents and described the total chemical impacts of consumer products in various places inside the home. Phthalates data from the Danish EPA's consumer product reports were complemented with other Danish and foreign studies to estimate the exposure for children crawling on the floor. Phthalate concentrations ranged from 2 to 63%

in consumer goods made of PVC, such as shower curtains, bags, gloves, vinyl floor, carpet tiles, and vinyl wallpaper. The most abundant phthalate measured indoors was DEHP, found in 10 out of 12 goods, followed by DINP/DIDP in half of the goods, DBP in a third of the items, and BBP in two products.

An average daily intake of phthalates for a child exposed to house dust via ingestion was estimated to be 100 µg/day or 10 µg/kg-bw/day, assuming a body weight of 10 kg. Exposure was based on a concentration of 1,000 mg/kg phthalates in house dust, of which DEHP amounts to 60-70%, and an assumed absorption rate of 100%. In rooms with vinyl flooring or wallpaper and poor cleaning, the content may be ten times higher. DEHP exposure to children by direct dermal migration from contact with textiles was calculated to be 9.6 to 195 µg/kg-bw/d. Exposure to adults by direct migration from contact with textiles was calculated to be 2.75 to 55 µg/kg-bw/day. Calculations assumed 5% and 100% absorption through the skin and a DEHP textile concentration of 8 mg/kg. Exposure to children from suckling of textiles was calculated to be 15.4 µg/kg-bw per event for a child who sucks/chews an phthalate-impregnated textile of 400 cm^2 or 20 g. Exposure by inhalation was small at 6.4 x 10^{-6} µg DEHP/kg-bw/d and deemed insignificant. Typical daily child absorption of DEHP from all indoor sources was calculated to be 10-20 µg/kg-bw/d or 100-200 µg/d, but in the worst case, for a much exposed crawling child on a PVC floor, the exposure may be as much as 50-250 µg/kg-bw or 0.5-2.5 mg/d.

Table 5.4.7-1 Exposure to Phthalates in Indoor Air and Home Dust (µg/kg-bw/d)

	Total phthalates	DEHP				
	Dust (Ingestion)	Dust (Ingestion)	Textiles (Mouthing)	Textiles (Dermal)	Inhalation	All Indoor Sources
Children	10	6 - 7	15.4 (µg/kg-bw/event)	9.6 -195	6.4 x10^{-6}	10 - 250
Adults	-	-	-	2.75 - 55	-	-

Wormuth et al. (2006)

Wormuth et al. (2006) investigated consumer exposure to eight phthalates (DMP, DEP, DiBP, DnBP, BBzP, DEHP, DINP, and DIDP) using a scenario-based risk assessment approach that included various oral, dermal, and inhalation exposure pathways. Included in this analysis was consumer exposure to dust resulting from dermal contact and air inhalation. Wormuth et al. (2006) calculated total consumer exposure for seven different age and gender groups by adding together the single exposure estimates for all the exposure pathways. In addition, the study authors reported on the relative contribution from various sources to the total daily exposure. Exposure from ingestion of dust was calculated for minimal, mean, and maximum amounts of ingested dust. It was assumed that children ingest 16.7% and teenagers and adults 1.1% of the amounts of dust ingested by infants and toddlers. Detailed analysis of dermal pathways, including contact with dust, textiles, and cushions, resulted in insignificant daily exposure in relation to other pathways. Inhalation exposure to phthalates was calculated taking into account the time that consumers spend in various microenvironments, the concentrations of phthalates in air (including particles available for inhalation), and activity-dependent inhalation volumes. Table 5.4.6-1 provides the percent contributions from dust ingestion and air of the mean total daily exposure for eight phthalates.

Table 5.4.7-2 Dust Ingestion and Air Contributions to the Mean Total Daily Exposure to Phthalates

	DMP		DEP		DiBP		DnBP		BBzP		DEHP		DINP		DIDP	
	Dust	Air	Dust	Air	Dust	Air	Dust	Air	Dust	Air	Dust	Air	Dust	Air	Dust	Air
Infant	*	~100%	*	≤30%	30%	>8%	10%	20 - 40%	>70%	5%	>35%	*	*	*	40%	*
Toddler	*	~100%	*	≤30%	30%	>8%	10%	20 - 40%	>70%	5%	>35%	*	*	*	40%	*
Children	*	~100%	*	≤30%	*	*	10%	20 - 40%	*	*	*	*	*	*	40%	16%
Teenagers	*	70 - 90%	*	≤30%	*	*	*	14 - 22%	*	*	*	*	>30%	~30%	>10%	9 - 13%
Adults	*	70 - 90%	*	≤30%	*	*	*	*	*	*	*	*	>30%	~30%	>10%	9 - 13%

* indicates insignificant contribution

NTP-CERHR DEHP (NTP-CERHR DEHP (2006 and 2000))

NTP-CERHR DEHP (2006) reported the estimated exposure to DEHP using probabilistic analysis based on concentrations from an unpublished report prepared for industry (Table 5.4.6-3). They reported the primary exposure for the general population to be from food, with over 90% of exposure for those over 6 months occurring from food. From sources other than food, ingestion of dust was the most important route of exposure. Estimated exposure for infants was 54.1 µg/kg-bw/d from dust ingestion for formula-fed infants and 39.3 µg/kg-bw/day for breast-fed infants. NTP-CERHR DEHP (2000) found few studies on indoor air concentrations of DEHP. Exposure estimates were based on the available information, which had concentrations from 8 ng/m^3 to 3 µg/m^3, with most measurements in the 10-100 ng/m^3 range.

Table 5.4.7-3 DEHP Intake from Environmental Sources by Age Group (µg/kg-bw/day)

	20–70 yrs	12–19 yrs	5–11 yrs	7 months – 4 yrs	0- 6 months	
					Formula-fed	Breast-fed
Indoor Air[a]	1.0	0.9	1.0	0.9	1.5	1.1
Indoor Air[b]	0.85	0.95	1.2	0.99	0.86	
Ingested Dust[a]	4.3	4.2	5.0	6.6	54.1	39.3

a NTP-CERHR DEHP, 2006, estimated from research published from 2000 to 2005.
b NTP-CERHR DEHP, 2000, estimated from research published prior to 2000

Otake et al. (2004)

Otake et al. (2004) calculated the exposure to DBP from indoor air to be 136 µg/d, based on a maximum indoor air concentration of 6.18 µg/m^3 and an inhalation rate of 22 m^3/d. A mean concentration of 0.75 µg/m^3 resulted in an exposure of 15 µg/d.

Schettler (2006)

Schettler calculated estimated mean adult inhalation exposure from a mean indoor dust concentration of 960 μg total phthalates/g (measured in 38 homes in Norway). DEHP was the largest contributor (mean 640 μg/g dust; range 100–1610 μg/g) resulting in a mean adult inhalation exposure of 0.76 μg/d from this source. Ingestion of dust contaminated at 640 μg DEHP/g dust yielded a dose of 64 μg/d (assuming 100 mg of dust was ingested per day).

Schettler also calculated inhalation exposures from phthalate levels in indoor air of 27 houses in Tokyo reported by Otake et al. (2004). Reported median concentrations of DEP, DBP, BBP, dicyclohexyl phthalate, and DEHP were 0.10, 0.39, 0.01, 0.07, and 0.11 $\mu g/m^3$, respectively (Otake et al., 2004). These concentrations resulted in inhalation exposures of 2, 78, 0.2, 1.4, and 22 μg/d, respectively, for an adult breathing 20 m^3/d (Schettle, 2006).

ECB (ECB DIDP (2003); ECB DINP (2003); ECB BBP (2007); ECB DEHP (2008))

The European Chemical Bureau estimated inhalation exposures to BBP, DIDP, DINP and DEHP for adults and young children from indoor air (ECB DIDP, 2003; ECB DINP, 2003; ECB BBP, 2007; ECB DEHP, 2008). The estimated daily inhalation exposures to BBP, DIDP, DINP and DEHP are presented in Table 5.4.6-4, below. As shown in the table, children had the highest exposure levels for all phthalates analyzed.

The ECB DEHP (2008) study estimated exposure based on indoor air concentrations of DEHP to be 21.2 $\mu g/m^3$, with 5.3 $\mu g/m^3$ from DEHP as vapor in the air and 15.9 $\mu g/m^3$ from DEHP adhered to particles in the air. The ECB BBP (2007) study estimated utilized indoor air concentrations of BBP, taken from a California EPA monitoring study, of 140 ng/m^3 (90^{th} percentile of day-time sampling) as a worst-case scenario. The ECB DINP (2003) study estimated exposure based on indoor air concentrations of DINP to be 40 $\mu g/m^3$, with 10 $\mu g/m^3$ from DINP as vapor in the air and 30 $\mu g/m^3$ from DINP adhered to particles in the air. The ECB DIDP (2003) study estimated exposure based on indoor air concentrations of DIDP to be 20.0 $\mu g/m^3$, with 5 $\mu g/m^3$ from DIDP as vapor in the air and 15 $\mu g/m^3$ from DIDP adhered to particles in the air.

Given the limited measured data available on phthalate concentrations and other exposure parameters, various assumptions were used to quantify exposure to these chemicals via the inhalation route. As a worst-case scenario, the saturated vapor pressure of these chemicals at 20°C was used as a starting point to calculate phthalate concentrations in indoor air. To account for particle-bound phthalates, the saturated vapor concentration was multiplied by a factor of 3, derived from a study of DEHP adsorption on to particles in residence environments. In addition, assumptions regarding bioavailability (75% for adults; 100% for children), inhalation rate (20 m^3/day for adults; 9.3 m^3/day for children), body weight (60 kg for adults; 8 for children), and exposure duration (20 hrs/day for adults and 22 hrs/day for children were used to generate inhalation exposure estimates.

The authors indicated that dermal exposure to phthalates caused by contact with building materials, such as flooring, can be a significant route for children, however exposure from this route was not estimated.

Table 5.4.7-4 Summary of Indoor Air Inhalation Exposure (µg/kg-bw/day)

Exposure scenario	Adults and Older Children	Young Children (0-3 yrs)
DEHP	4.4	22.4
BBP	0.032	0.083
DIDP	4.2	21.3
DINP	8.3	42.6

Becker et al. (2004)

In this study urine samples of 254 children (3 to 14 years old), participating in the pilot study for the German Environmental Survey for Children, were analyzed for the concentrations of DEHP metabolites. The levels of DEHP in house dust samples, collected with vacuum cleaners in the homes of the children, were also analyzed. Concentrations of DEHP in house dust covered a wide range encompassing about two orders of magnitude, with a geometric mean of 508 mg/kg and a 95th percentile of 1840 mg/kg (Becker et al., 2004). The study authors calculated the correlations between the concentrations of each of the three metabolites in urine and DEHP in house dust. These calculations resulted in coefficients close to zero in all cases. Additional calculations were performed with different subgroups: children from households with wall coverings of PVC, with vacuum cleaning of PVC floorings and children less than 8 years of age. None of the calculations revealed significant results. Restricting the calculation to the highest values of urine and dust concentrations did not result in significant correlation coefficients either. However, the authors not that the findings do not fully allow the exclusion of house dust as a potential pathway of children's exposure to DEHP as the link between DEHP house dust levels and urinary DEHP metabolite concentrations may not become visible if the pooled results of children of all age groups are analyzed, rather than those of the very young children who are likely to come into closer contact with house dust because they are crawling on the floor. Unfortunately, the relatively small number of such children in this sample did not permit a separate statistical evaluation for this age group. Additionally, the youngest child in this study was three years old, while information from other studies indicate that the dust ingestion exposure pathway is more significant among infants and toddlers.

5.4.8. Scenario 7: Food and Food-Related Uses

This section provides summary data on human exposure to food and food-related sources from the available literature. Food is likely to be the largest single exposure source of phthalates in the general population (Schettler, 2006; Chen et al., 2007; Shea, 2003; Wormuth, et al., 2006). However, the contribution of each phthalate to total phthalate exposure varies by compound (Wormuth, et al., 2006; Wenzl, 2009). Foods have been found to be contaminated with phthalates during growth, production, processing, or packaging (Shea, 2003; Kamrin, 2009).

Possible sources of some phthalates found in food are cellulose-based food wraps and latex adhesives used in food processing in which the phthalate has migrated into the food (NTP-CERHR DnOP, 2003). The levels of selected phthalates in food have been shown in food surveys worldwide, with the majority of the data from European, with some Asian and American studies. However, according to Schettler (2006), the levels found in food are widely variable, the data are often old, and may not reflect current dietary intakes and exposure levels. IPCS (1997) also notes that dietary intake vary according to the types of food eaten and the types of material in which the food is packaged. The highest levels of phthalates in foods have been detected in the fatty foods such as oils, dairy, infant formula, meat, meat products, and fish; they have also been detected in human milk (Fromme et al., 2007b; Wormuth et al., 2006; Shea, 2003). Fatty foods and oily foods are believed to be contaminated primarily because of their lipophilic characteristic (Wenzl, 2009). Wenzl (2009) has reported that published data for food matrices studied are scattered in terms of the number of samples analyzed and varies between studies, countries, and then geographical areas within the countries. Some surveys cover individual items or total diet samples. The largest survey in this respect was conducted in Germany, covering more than a total of 3400 samples analyzed between the years 2000-2009 with percent of occurrence varying among the phthalates tested (Wenzl, 2009). Of the 2745 samples that were tested for DBP contamination, only 2.3 percent had positive results. Of the 264 food samples tested for DEHP, 31 percent had positive results and of the 174 samples tested for DINP, 23.4 percent had positive results. More than 59 percent of the samples tested were positive for DIBP, however the samples size (32) and the food categories tested (2) were limited (Wenzl, 2009). Wenzl (2009) further notes that the data for the occurrence of phthalates in food cannot be easily extrapolated from one country to another because the contamination greatly depends on the predominant pathway of the phthalate input into the food. In addition, a recent study that investigated phthalate contents in fatty and oily food concluded that the differences in phthalate content for the same foods was due to extent of contact between the fatty food and food packaging and handling during the shelf life (Wenzl, 2009). Wenzl (2009) noted that based on this information in order for a reliable assessment of exposure to phthalates from food, analysis methods to achieve comparability of data, and monitoring to decrease the potential influence of geography on contamination levels are needed. In addition, analysis of a representative number of samples to diminish the influence of the history of a particular food sample on the average phthalate content of the particular type is needed.

The most recent comprehensive reports evaluating phthalates in food have been published by ECB and the NTP-CERHR. The documents have addressed overall human exposures to phthalates as well as exposure to phthalate-contaminated food. The ECB and NTP-CERHR reports are individual documents for each phthalates via food. Food exposures that were addressed in the ECB and NTP-CERHR reports are summarized below in this section. In some instances, a summary of primary studies cited in the ECB and NTP-CERHR documents has been included below to provide supporting or additional information not provided in the studies. In addition, data are provided for studies that have been conducted since the ECB and NTP-CERHR reports were last published, as appropriate.

There are several articles that provide a review/compilation of the available information on the human exposures of phthalates via food. They include, but are not limited to Wormuth et al. (2006), Schettler (2006), Kamrin (2009), and Shea (2003). Wormuth et al. (2006) addressed

sources of exposure to phthalic acid esters in Europeans and concluded that food is a main source of DiBP, DnBP, and DEHP exposures in consumers. In addition, it appears from the available data, that levels of DEHP are usually higher in food than for the other phthalates (Schettler, 2006). Schettler (2006) reported maximal daily intake for several phthalates in food as follows: for DBP as 0.48 µg/kg/day, for DEHP as 4.9 to 18 µg/kg/day and the range for BBP as 0.11 to 0.29 µg/kg/day. Kamrin (2009) provides a summary review on the exposures and risks to phthalates from selected exposure pathways, including food. Shea (2003) gears the review towards pediatric phthalates exposure. All of the review articles mentioned here are briefly summarized in this section.

ECB DEHP (2008)

In the ECB risk assessment for DEHP, human exposures estimates to human milk, consumer milk, infant formula, and food were provided (ECB DEHP, 2008). The estimated exposures and intakes are based on the specific data from some of the studies reviewed in the risk assessment. This method was used by ECB providing estimates of exposures from ingesting phthalate-contaminated foods for all of the ECB phthalate risk assessments. For DEHP, a reasonable worst case daily exposure for human milk was estimated for infants aged 0-3 months at 21µg/kg/day, and 8 µg/kg/day for infants 3-12 months of age. The DEHP concentration (160 µg /kg) used in the estimate was the highest value reported within 2 studies. The body weights used in the estimates were 6 kg for infants 0-3 months of age and 10 kg for infants 3-12 months of age. The human milk ingestion rates used were 0.8 kg/day and 0.5 kg/day for infants 0-3 months old and 3-12 month old, respectively.

For milk, the estimated daily exposure to DEHP and MEHP was 6.2 µg/kg/d and 2.4 µg/kg/d for infants 0-3 months and 3-12 months, respectively (ECB DEHP, 2008). ECB (ECB DEHP, 2008) assumed a 47 µg/L (95^{th} percentile value) for milk concentration for DEHP and MEHP. The ECB estimated an exposure of 4.6 µg/kg/d to MEHP for a newborn (0-3 months of age) using a 95^{th} percentile concentration of 35 µg MEHP/L for Danish mothers. This estimate does not consider the unknown contribution of DEHP that is expected to be in the milk.

The exposure estimate as a result of DEHP in food was 1.1 mg/day or equivalent to16 µg/kg-bw/day for a 70 kg person. In a Danish study, the highest concentration of DEHP in a total diet sample was 0.49 mg/kg and based on a total daily intake of 10 mega joules (MJ) (energy content in food) gave an exposure estimate of 1.1 mg/d.

Mean daily food exposures of 9 and 3 µg/kg/d were estimated based on a 60 kg-bw. The estimates were based on mean food intakes in a Japanese duplicate diet study of 519 µg/d/person and 160 µg/k/d/person of DEHP. These intake values were presented as estimates before and after regulation on the use of PVC gloves for food, respectively. The mean daily exposure to infants was estimated at 59.9 µg/kg/d. The estimate is based on an 8 kg baby consuming 1 package per day (80g/d) of baby food with a mean concentration of 5,990 ng/g of DEHP.

ECB BBP (2007)

The ECB reported an estimated average intake of BBP based on a total diet study as 0.008 mg/person/day and the highest intake estimate at 0.02 mg/person/d (ECB BBP, 2007). For a worst case approach, ECB (ECB BBP, 2007) used 0.02 mg/person/d and 70 kg bodyweight, resulting in 0.0003 mg/kg-bw/d intake value. These data were from U.K. Ministry of Agriculture, Fisheries and Food (MAFF) (1996a) study where BBP was detected in stored fatty foods.

ECB (ECB BBP, 2007) reported the average intake of BBP from infant formula as 0.2 µg/kg-bw/day, at birth and 0.1 µg/kg-bw/day at 6 months of age; these estimates are based on the MAFF (1998) study concentration data. The estimate incorporates an 8 kg body weight. The estimated average intake of BBP from infant formula for children is 0.000187 mg/kg-bw/d (based on an 8 kg body weight) and the intake via food is 0.00083 mg/kg-bw/d. The total estimated intake of BBP from infant formula and via food for infants is 0.00102 mg/kg-bw/day (ECB BBP, 2007).

ECB (ECB BBP, 2007) reported that a small, but significant use of BBP in food wrap or food packaging. However, this use has diminished over the years because of technological developments. BBP has been detected in foods including poultry, yogurt, cheese, butter, milk, eggs, and baked goods due to the use of food-packaging materials containing BBP. The MAFF (1996a) study reported lower levels of BBP in food as compared to levels reported in earlier studies (ECB BBP, 2007).

ECB DBP (2003-04)

ECB (ECB DBP, 2003-04) presented the estimates of the MAFF (1987) study as the maximum daily intake of DBP from food to be 1.9 mg/person/day with a calculated average intake of 0.23 mg/person/day. The 1.9 mg/person/day is considered a worst case estimate approach. These estimates are based on an English diet. DBP has been identified in many food sources such as margarine, vodka, confectionary, chips, milk, butter, vegetable soup, as described in several older studies such as Hatanaka et al.(1994); Page and Lacroix (1992); Castle et al.(1989); Morita et al.(1973). ECB (ECB DBP, 2003-04) noted that it was difficult to calculate the daily intake of DBP from food sources, but did not provide detail on the difficulty.

ECB (ECB DBP, 2003-04) reported that the estimated exposure to infants from human milk varied between 1.2 and 6 µg/kg-bw/day. The exposure of babies to DBP was calculated using data from a World Health Organization (WHO) (1998) study. In the study, the concentrations of DBP in human milk ranged from 10 to 51 µg/kg. ECB (ECB DBP, 2003-04) assumed that an infant for the first three months consumes an average of 120 g/day of human milk per kilogram of body weight and the intake decreases after 3 months. It was noted that whether the DBP in human milk originates from direct or indirect sources is not clear, but that indirect exposure is more likely.

ECB DINP (2003)

The estimated daily dietary intake of DINP from food was reported by ECB (ECB DINP, 2003) to be 0.2 µg/kg-bw/d for adults. The estimate is based on the MAFF (1996a) study where DINP was not detected in the analysis of composite fatty foods and the detection limit used was 0.01 mg/kg of food. For the estimate, ECB (ECB DINP, 2003) considered the detection limit and assumed a daily food intake of 1 kg for a 60 kg adult to give a daily intake of DINP from food as <0.17 µg/kg-bw/d. Therefore, the 0.2µg/kg-bw/d daily intake was derived based upon this analysis.

ECB (ECB DINP, 2003) reported an estimated daily intake of DINP in infant formula at 2.4 µg/kg/d for newborns 0-6 months old, and 1.8 µg/kg/d for infants >6 months old. The daily intake of infant formula was based on the feeding guide information provided on the formula packaging, and an assumed DINP concentration of 0.1 mg/kg dry weight of powder. The authors also assumed a daily intake of 0.131 kg of powdered formula (newborns) and the newborn weight at 5.5 kg. For infants, an assumed daily intake of 0.41 kg infant formula powder and a weight of 8 kg were used.

ECB DIDP (2003)

The ECB (ECB DIDP, 2003) estimated the daily dietary intake of DINP from food to be 0.2µg/kg-bw/d for adults. The estimated daily intake of DINP in infant formula was 2.4 µg/kg/d for newborns 0-6 months old, and 1.8 µg/kg/day for infants >6 months old. ECB (ECB DIDP, 2003) used the same method for estimating daily intakes for DIDP as described in the section above for DINP. In addition, the estimated daily intakes are the same. ECB (ECB DIDP, 2003) noted that limited data are available to characterize DIDP concentrations in food. Most studies have been conducted to determine the level of total phthalates in food versus levels by specific phthalate. The study conducted by MAFF (1996a) investigated the level of individual phthalates in 74 samples of composite fatty foods and DIDP was not detected in any of the samples for this study (ECB DIDP, 2003).

NTP-CERHR DEHP (2006)

Exposure estimates based on DEHP levels in food were summarized by NTP-CERHR DEHP (2006). NTP-CERHR provided DEHP intake estimates from environmental samples and food from a probabilistic analysis of Clark et al. (2003). For the analysis, Clark et al. (2003) used DEHP concentrations from an unpublished report prepared for industry. The analysis showed that more than 90% of the estimated DEHP intake was from food. The estimated intakes from Clark et al. (2003) for foods only are shown in Table 5.4.7-1. The highest DEHP intakes shown in Table 5.4.7-1 are for fats and oils for all age categories and then followed by grains.

The estimated DEHP intakes for formula-fed and human milk-fed infants (not shown in the table) were 43.7 µg/kg-bw/d and 59.6 µg/kg-bw/d, respectively. Other studies mentioned in NTP-CERHR are also summarized later in this section (Main et al. (2006); Fromme et al. (2007b); Yano et al. (2005); Mortensen et al. (2005); Tsumura et al. (2003)).

Table 5.4.8-1 Intake of DEHP from Food Sources (µg/kg-bw/d)

Source	Adult (20-70 yrs)	Teen (12-19 yrs)	Child (5-11 yrs)	Toddler (7 months – 4 yrs)
Beverages (excludes water)	11.2	5.2	3.3	2.2
Cereals	2.4	2.0	3.5	5.5
Dairy products (excludes milk)	13.2	11.7	12.2	12.9
Eggs	1.1	0.7	0.8	1.3
Fats and oils	16.9	19.1	16.5	11.1
Fish	1.6	0.8	0.7	0.4
Fruit products	0.9	0.8	1.1	1.4
Grains	13.4	16.1	18.1	11.1
Meats	5.5	5.2	3.7	3.3
Milk	3.1	6.7	8.6	12.6
Nuts and beans	1.0	1.0	0.9	0.8
Other foods	10.3	11.2	11.3	18.9
Poultry	3.9	3.5	3.5	3.6
Processed meats	3.4	3.4	3.4	2.5
Vegetable products	6.6	6.1	6.1	4.9

Source: NTP-CEHR DEHP, 2006
Note: Dairy products exclude milk and beverages exclude water. The "other foods" category was not described.

NTP-CERHR BBP (2003)

BBP exposure to the general population is based almost entirely on the intake of foods (NTP-CERHR BBP, 2003). NTP-CERHR BBP (2003) reported that the best estimate of BBP exposure from food to the general population is 2 µg/kg-bw/d. The estimate was made by the International Programme on Chemical Safety (IPCS) (1997) assuming a 70 kg body weight and a daily consumption rate of 13.61 g butter, 1.54 g yogurt, 22.73 g pork, 3.45 g crackers, and 3.81 g cheddar cheese. IPCS (1999) used concentration levels found in foods that were purchased in a Canadian supermarket between 1985 and 1988. IPCS also noted that exposure to infants and children could be up to three fold higher and concluded that consuming food that contains trace levels of BBP is a significant source of exposure to the general population (NTP-CERHR BBP, 2003).

MAFF (1996a) used the concentrations detected in fatty foods from a U.K. survey and estimated a mean intake of BBP from foods to be 8/µg/person/day and a high intake at 20 µg/person/day (NTP-CERHR BBP, 2003). Using an assumed body weight of 70 kg, the exposure values were converted to 0.11-0.29 µg/kg-bw/day.

In the MAFF (1996b) study, the reported estimated exposure levels to newborns and infants from the consumption of infant formula were 0.2 µg/kg-bw/day at birth and 0.1 µg/kg-bw/day at 6

months old (NTP-CERHR BBP, 2003). The estimate was based on body weights of 2.5 to 3.5 kg at birth and 7.5 kg at 6 months old, BBP concentration data from a 1998 survey, and formula intakes from the manufacturer label instructions.

NTP-CERHR DBP (2003)

The largest source of DBP exposure to the general population is food (NTP-CERHR DBP, 2003). Food exposures for adults based on a 1986 Canadian market basket survey of 98 food types were estimated at 7 μg/kg/bw/day and 1.9 μg/kg/bw/day (NTP-CERHR DBP, 2003). These estimates were calculated by IPCS (1997) and Chan and Meek (1994), respectively. The exposures in children from food were also estimated by Chan and Meek (1994). The estimates ranged from 2.3 μg/kg/bw/day for children aged 12−19 years to 5.0 μg/kg-bw/day for children aged 6 months to 4 years.

Mean and high level DBP dietary intakes in the U.K. were estimated by MAFF (1996a) at 13 μg/person/day and 31 μg/person/day, respectively (NTP-CERHR DBP, 2003). The estimated DBP intakes were calculated based on a 1993 U.K. survey of fatty foods. The exposure values were then converted to 0.20 to 0.48 μg/kg/bw/day using an assumed body weight of 64 kg (NTP-CERHR DBP, 2003).

NTP-CERHR DBP (2003) reported a dietary estimate of 0.007-0.02 μg/kg/bw/day that was provided in ATSDR (1990). However, this estimate is based entirely on 70-200 μg/kg DBP levels found in fish from studies published between 1973 and 1987 (NTP-CERHR DBP, 2003).

In the MAFF (1996b) study, exposures to infants from consuming infant formula based on 1998 survey data were reported at 2.4 μg/kg-bw/day at birth and 1.4 μg/kg-bw/day at 6 months of age. The assumed body weights used in the estimate were 2.5-3.5 kg at birth and 7.5 kg at 6 months old. The formula intake rates were based on manufacturer label instructions. NTP-CERHR DBP (2003) stated that "infants in the U.S. are likely exposed to lower levels of DBP through formula than are infants in the U.K.". NTP-CERHR DBP (2003) also stated that the dietary exposure of DBP in children may be lower than the exposures from non-dietary intake through mouthing of DBP-containing objects.

NTP-CERHR DnOP (2003)

NTP-CERHR DnOP (2003) reported exposure estimates of <0.1-43 μg/kg-bw/day and <0.1-24 μg/kg-bw/day at birth and 6 months of age, respectively. Note that the estimates are based on levels of DOP isomers (excluding DEHP) detected in 8 of 12 infant formulas at concentration range of 0.21-1.42 mg/kg, in a U.K. survey. In a follow-up survey conducted by MAFF, the presence of DOPs was not found in 39 samples of examined infant formulas (NTP-CERHR DnOP, 2003). DnOP was detected in nutmeg in a 1999 German study, but was less than the detection limit of 0.01 mg/kg in milk (human and commercial), cream, nuts, and baby food (NTP-CERHR DnOP, 2003). NTP-CERHR DnOP (2003) stated that the most likely source of DnOP exposure to humans is dietary intake. DnOP is approved by the FDA for use as an indirect food additive in sealants used for food packaging. DnOP has been detected in Vodka and packaged fatty foods in the U.K.

NTP-CERHR DINP (2003)

NTP-CERHR DINP (2003) reported that DINP was identified but not quantified in 4 of 12 infant formulas from the U.K. In a follow-up survey conducted by MAFF, DINP was not detected in 39 samples of infant formula from the U.K. Additionally, DINP was not detected in a U.K. survey of fatty foods (e.g., dairy products, meats, fish, eggs, and oils). In the available food and infant formula studies, the levels of DINP have not been quantitated or have been at or below the detection limit (0.01 mg/kg) (NTP-CERHR DINP, 2003). NTP-CERHR DINP (2003) stated that DINP has limited use in food packaging. It was concluded that the ingestion of DINP through food does not appear to be common and that children's exposure to DINP via food would not exceed the levels estimated for DEHP (NTP-CERHR DINP, 2003).

NTP-CERHR DIDP (2003)

NTP-CERHR DIDP (2003) reported that in a U.K. study, retail samples consisting of carcass meat, meat products, offal, poultry, eggs, fish, fats and oils, milk, and milk products were used to test for the presence of DIDP in foods. In the 74 composite samples tested, DIDP was not detected at a detection limit of 0.01 mg/kg (NTP-CERHR DIDP, 2003). In addition, in the study, DIDP was not detected in 39 samples of infant formula at an analytical detection limit of 0.1 mg/kg nor was it found in 59 samples of 15 different brands in an earlier U.K. study. NTP-CERHR DIDP (2003) noted that because DIDP concentrations in foods and infant formulas were below detection limits in the three surveys that have been conducted by MAFF, the American Chemical Council (1999) considered dietary exposure to humans negligible (NTP-CERHR DIDP, 2003). The sampling results for infant formula tested by the FDA "suggests that phthalates are present in lower frequency and concentrations in the U.S. than in Europe" (NTP-CERHR DIDP, 2003).

Kamrin (2009)

Kamrin (2009) provides a summary of recent evaluations of phthalate risks, and the public health implications of enacted regulation. The author addressed exposure and risks for selected phthalates (DIDP, DEHP, DBP, DINP, BBP, DnOP). The brief summary statements provided to follow are those which Kamrin (2009) provided for each phthalate that was characterized as it relates to food exposure. Food is the largest non-medical exposure to DEHP for adults, children, and infants. Daily exposure to DEHP for infants and children from ingestion of human milk, cow's milk and infant formula ranges from 1-10 µg/kg/day. It appears that from monitoring data, food is the main source of human exposure to DBP. Biomonitoring data for DBP in human milk, cow's milk and infant formula indicates daily exposures are less than 1 µg/kg/day. However, ECB (ECB DBP, 2003-04) noted that it was difficult to calculate the daily intake of DBP from food sources. For DnOP, the data are limited for concentrations in food as well as for other products. DIDP has not been detected in studies assessing its presence in food, suggesting that levels in food are negligible. The presence of DINP at low levels in food probably does not represent a significant exposure source. Recent studies indicate the presence of DINP in human milk, but not infant formula. Levels in human milk are inconsistent from study to study and it would be difficult to quantitate, with confidence, the exposure contribution of DINP from human milk. Studies on BBP levels show that foods are the main source of BBP exposure in most age

groups. Recent studies show that BBP in human milk and infant formula were not detected or levels were found just above the detection limit. Modeling has shown that BBP exposures in all age groups from human milk and infant formula are less than 1 μg/kg/day.

Wormuth et al. (2006)

The sources of exposure to the eight most frequently used phthalic acid esters in Europeans were investigated by Wormuth et al. (2006). The percent contribution of food to phthalate exposure in consumer groups is as follows: DBP, 60% in infants and toddlers, >95% in teenagers and adults; DnBP, 40-90% for all consumer groups; DEHP, 50-98% for all consumer groups. For DIDP, food contributes to 55-70% of the exposure for teenagers and adults. Food is a major source (73%) of BBP exposure in children (73%), teenagers (> 20%) and adults (60%). Overall exposure estimates were presented in the study, but estimates of exposure attributed exclusively to food were not provided. Data were compiled from 14 studies (mostly European, some Asian, and American) that provided concentrations of phthalates in various foods. The mean daily amounts consumed of selected foods including, but not limited to vegetables, meats, alcoholic beverages, deserts, human milk, and infant formula were calculated. The daily amounts consumed were calculated for infants, toddlers, children, adolescents and adults using data from European food surveys. Wormuth et al. (2006) concluded that food is a main source of DBP and DEHP exposures in consumers. The authors also noted that the food industry can contribute to reduced exposure by avoiding the use of phthalates in food packages and food processing equipment.

Shea (2003)

Shea (2003) evaluated existing data on exposure to phthalates, because of the recent concerns for pediatric exposures to phthalate plasticizers. Shea (2003) addressed sensitive endpoints of reproductive and developmental toxicity and the unique aspects of pediatric exposures to phthalates. Shea (2003) provided estimated daily intake of DEHP in food by age ranges from Meek and Chan (1994). The daily intakes are as follows: 0 to 6 months, 7.9 μg/kg-bw/day; 6 months to 4 years, 18 μg/kg-bw/day; 5 to 11 years, 13 μg/kg-bw/day; 12 to 19 years, 7.2 μg/kg-bw/day; 20 to 70 years, 4.9 μg/kg-bw/day. The data shows that the highest intake of DEHP is for children 5 months to 4 years old (18 μg/kg-bw/day). Overall, the highest levels of DEHP are shown for children less than 19 years old. The author also noted that infants and young children consume relatively more dairy and other fatty foods than adults and consume more calories per kilogram of body weight, therefore dietary exposures are expected to be higher than for adults. DEHP and DINP were used as specific examples because of pediatric concerns and that these phthalates are ubiquitous contaminants in food and toys. Food surveys have documented the highest levels of DEHP in fatty foods such as meat, oils, dairy, infant formula, and fish (Shea, 2003).

Chen et al. (2008)

Chen et al. (2008) investigated the exposure of Taiwanese to phthalates by measuring the migration of phthalates from PVC films by simulating food handling. Selected foods were covered with PVC films and then microwaved to estimate a worst-case scenario (Chen et al,

2008). Congeners measured were DMP, DEP, DBP, DEHP, and BBP. Results showed that under heating conditions, the calculated intake of phthalate from eating one 400 g packaged meal was 46.4 µg, 707.6 µg, 1705.6 µg, and 68.8 µg for DEP, DBP, DEHP, and BBP, respectively (Chen et al., 2008). These estimates were based on heating the meal where the plastic was in contact with the food. The estimated intakes for a 400g meal where the plastic did not come in contact with the food were 72 µg, 740 µg, 1168.4 µg, and 68.8 µg for DEP, DBP, DEHP, and BBP, respectively. The authors noted that even though the food was not in contact with the plastic covering, an air current will occur between the cold air above the food and the food. "As the heat convection comes in contact with the cold air, the water and lipids will condense on the surface of the plastic wrap and the wash down the mobilized monomeric plasticizer" (Chen et al., 2008).

Matsumoto et al. (2008)

Matsumoto et al. (2008) reviewed some of the more recent literature on phthalate acid esters (PAEs) and their potential adverse effect on human health. Matsumoto et al. (2008) reported the estimated daily maximum intake of PAEs in infants for human milk as 301, 1.21, and 0.87 µg/kg/day for DEHP, DBP, and DEP, respectively. These values are from Zhu et al. (2006). The reported estimated maximum daily intake for infant formula was 6.9 µg/kg/day and 1.07 µg/kg/day for DEHP and DBP, respectively, from Yano et al. (2005). The 95th percentile intake levels in human milk were 41.1 µg/kg/day and 0.12 µg/kg/day for DEHP and DBP, respectively. The estimates were calculated assuming an average daily milk consumption of 700 mL and average infant body weight of 7 kg.

Fromme et al., (2007b)

Fromme et al. (2007b) conducted a study in non-occupationally exposed subjects in Germany to quantify dietary intake of phthalates using duplicate diet samples. The median (95th percentile) daily intake via food was the following: DEHP, 2.4 (4.0) µg/kg/bw; DnBP 0.3 (1.4) µg/kg/bw; and DiBP, 0.6 (2.1) µg/kg/bw. The age of the female participants ranged from14-60 years and males from 15-56 years of age. The median body weights used in the analysis were 66 kg and 76 kg for females and males, respectively. The dietary intake of phthalates in µg/day and µg/kg-bw/day over seven sampling days is shown in Table 5.4.7-2. The highest median value was for DEHP. The data indicated that food was the predominant source of DEHP in the adult population (Fromme et al., 2007b).

Fromme et al. (2007b) also reported the estimated daily intakes of DEHP and DnBP for adults from other select studies for comparison with the results found in this study. These intake values are provided in Table 5.4.7-3.

Table 5.4.8-2 Dietary Intake[a] of Phthalates of 50 Study Subjects

Substance	N>LOD[b]	Min	Median	95th percentile	Max	Min	Median	95th Percentile	Max
		µg/day				µg/kg body weight			
DnBP	37	9.2	16.3	90.6	109.1	0.12	0.26	1.35	1.63
DiBP	48	13.6	42.0	157.4	229.3	0.23	0.57	2.14	3.47
BBP	19	9.2	15.3	25.2	28.3	0.11	0.23	0.38	0.50
DEHP	50	58.6	161.7	309.1	387.6	1.00	2.43	3.95	4.80

a. Intake derived from the median value of seven sampling days.
b. LOD: Limit of quantification; values below the LOD were assigned half of the LOD.

Source: Fromme et al., 2007b.

Table 5.4.8-3 Estimated Daily Intake of DEHP and DnBP of an Adult Population

Source	DEHP (µg/kg/bw)		DnBP (µg/kg/bw)	
	Mean (median)	Max	Mean (median)	Max
Intake based on a total diet study				
Kuchen et al. (1999)[a]	2.8	no data	4.2	no data
MAFF (1996a)[a]	2.1	4.3[b]	0.2	0.4[b]
Intake based on food duplicates				
Pfannhauser et al. (1995)	4.9	8.3	2.9	5.7
Petersen and Briendahl (2000)[a]	2.7-4.3	15.7	1.8-4.1	10.3
DEHRM (2003)[a]	5.0 (2.8)	12.0	0.39 (0.33)	0.85
Fromme et al. (2007b)	2.5 (2.4)	4.8	0.58 (0.26)	1.63
Intake from external exposure data				
Chan and Meek (1994)	4.9	no data	1.1	no data
Bosgra et al.(2005)	4.1[c]	7.2[d]	no data	no data
Wormuth et al. (2006)				
Adult males	(2.9)	16.3	(3.6)	18.6
Adult females	(2.5)	14.7	(3.5)	38.6

a. Derived using body weight of 70 kg; b. 97.5th percentile; c. Geometric mean; d. 95th percentile.
Source: Fromme et al. (2007b).

The results for DEHP in this study were comparable to the previously reported intakes from other studies using the duplicate diet portion or market basket approaches (Fromme et al., 2007b). It was stated in the study that although the data of Wormuth et al. (2006) are based on overall intake, it was concluded that food contributed to 98% of the total DEHP intake in the adult population.

Main et al. (2006)

Phthalate monoesters were measured in breast milk of a Danish-Finnish cohort study group by Main et al. (2006). One human milk sample was taken from each mother 1-3 months postnatal (64 samples in Denmark and 65 samples from Finland). The median, minimum and maximum body weights for infant males were 3.68, 2.78, and 4.81 kg for birth weight, respectively, and 6.58, 5.31, and 8.51 kg for body weights at 3 months, respectively. The estimated individual monoester intakes from human milk in µg/kg/day for Denmark and Finland are shown in Table 5.4.7-4.

Yano et al. (2005)

Phthalate levels in powdered baby milk were measured by Yano et al. (2005). Yano et al. calculated daily intakes of 16.1 µg/kg-bw/day for DEHP and 2.5 µg/kg-bw/day for DBP. The estimates were based on a 3 kg infant, 700 mL of aqueous milk, and the respective concentrations found in milk samples from Turkey and Japan. Yano et al. (2005) collected 27 samples of baby milk powders from retail markets in Europe, America, Canada and Asia during 2001-2002. All of the samples analyzed contained both DBP and DEHP. The amount of DEHP ranged from 34-281 ng/g and the amount of DBP ranged from 15-77 ng/g. The concentration of DEHP was consistently higher than DBP in samples from all countries, with the highest level in milk powders sold in Turkey (281 ng/g) and Japan (218 ng/g) (Yano et al., 2005).

Table 5.4.8-4 Estimated Monoester Dietary Intakes from Human Milk

	Denmark (µg/kg/bw)			Finland (µg/kg/bw)		
Monoester	**Median**	**Minimum**	**Maximum**	**Median**	**Minimum**	**Maximum**
MMP	0.012	<0.01	0.66	0.011	<0.01	0.04
MEP	0.111	0.01	4.03	0.115	0.03	4.97
MBP	0.517	0.07	1,310	1.450	0.28	14.8
MBzP	0.104	0.02	1.71	0.169	0.06	3.17
MEHP	1.14	0.18	23	1.56	0.47	169
MiNP	12.17	3.20	56.3	10.97	3.40	27.6

Source: Main et al., 2006.

Tsumura et al. (2001 and 2003)

Tsumura et al. (2001) analyzed for the concentration of eleven phthalate esters in one-week diet samples from three hospitals in Japan. The estimated daily intake based on all samples was 519 µg/day for DEHP, 65 µg/day for DINP and 4.7 µg/day of BBP. The goal of the study was to estimate daily intake of phthalates from daily meals. Tsumura et al., collected 63 samples in 1999 and found that DEHP had the highest levels compared to other phthalates, ranging from 10-4,400 ng/g. Average DEHP levels in the 1-week diet samples were 384 ng/g, 46 ng/g, and 478 ng/g for the three hospitals, respectively. The authors noted that the high DEHP content in the

meals were suspected of being due to the use of PVC gloves during meal preparation. Tsumura et al. (2003) conducted a similar study and found the average daily intake of DEHP at 160 µg or 3.2 µg/kg-bw/day using a 50 kg body weight.

Fiala et al. (2000)

Fiala et al. (2000) investigated the migration of DEHP and DINP from PVC articles. The authors noted that the major source of exposure to the general population for DEHP is through food. In a Canadian study, the estimated daily intake from food was 8 µg/kg-bw/day and18 µg/kg-bw/day for children aged 0 to 6 months and 6 months to 4 years, respectively (Fiala et al., 2000). In the U.K., the estimated average DEHP intake for infants up to 6 months of age ranged from 6.1 to 35 µg/kg-bw/day (Fiala et al., 2000). The EU conducted a study on the intake of DEHP in human milk and infant formula where the maximum level was reported at 25 µg/kg-bw/day (Fiala et al., 2000).

5.4.9. Scenario 8: Pharmaceuticals

The polymer coating of some oral medications contain phthalate plasticizers such as DEP and DBP. These coatings are used on medications to allow the release of active ingredients into the small intestine or the colon (Hauser et al., 2004). Two studies have been conducted to evaluate medication as a potential source of exposure to phthalates, including a study comparing users and nonusers of certain medications using data from the NHANES for the years 1999–2004 (Hernández-Díaz et al., 2009) and a case study for one man who was taking Asacol (active ingredient mesalamine) (Hauser et al., 2004).

Hernández-Díaz et al. (2009)

Hernández-Díaz et al. (2009) evaluated whether users of medications potentially containing phthalates as inactive ingredients have higher urinary concentrations of phthalate metabolites than nonusers using data from NHANES for the years 1999–2004. The medications selected for evaluation included mesalamine, didanosine, omeprazole, and theophylline products.

For mesalamine users (n=6) the mean urinary concentration of MBP, the main DBP metabolite, was 50 times higher than the mean for nonusers (2,257 µg/L vs. 46 µg/L; $p < 0.0001$). The individual MBP concentrations ranged from 59 to 4,691 µg/L (creatinine-adjusted concentrations of 29.4 to 6,426 µg/L). The mean concentrations of MCPP, a minor metabolite of DBP and also a metabolite of some other high-molecular-weight phthalates, was about 10 times higher in users than non-users ($p < 0.0001$). The mean MCPP concentration was 52.6 µg/L. A high mean MEP concentration was also observed among mesalamine users, however, this was completely attributable to one patient taking theophylline and mesalamine simultaneously.

Users of didanosine (n=3), omeprazole (n=91), and theophylline (n=27) had significantly higher urinary concentrations of MEP than did nonusers ($p < 0.0001$ or $p < 0.05$). The mean MEP concentration was 4,660 µg/L among didanosine users, 1,210 µg/L among omeprazole users, and 2,924 µg/L among theophylline users. Mean concentrations of MCPP were also higher among users of omeprazole and theophylline compared with nonusers ($p < 0.0001$). The mean MCPP

concentration was 41.7 μg/L among omeprazole users and 44.6 μg/L among theophylline users. Statistically significant differences ($p < 0.0001$ or $p < 0.05$) were not observed between the didanosine, omeprazole, and theophylline users and nonusers for the other metabolites detected.

Hernández-Díaz et al. (2009) found high urinary concentrations only for the metabolites of the phthalate diesters that might be present as inactive ingredients in the medications.

Hernández-Díaz et al. (2009) stated that the study is limited by the inexact measures of medication use and subsequent likely misclassification of phthalate exposure. Pertinent medication use information that was lacking included dose, subject adherence (i.e., missed dose before urine collection), and brand names. Since brand names were not part of the NHANES survey, this assessment may have included subjects that were taking a medication that did not contain a phthalate. The finding of a few exposed subjects with very high phthalate concentrations rather than a generalized elevation for all users supports the likelihood that the study incorrectly classified some nonexposed subjects as exposed.

Hauser et al. (2004)

Hauser et al. (2004) reports on medication use as a likely source of DBP exposure in one male subject. The subject, who was part of an ongoing study on environmental agents and male reproductive health, took Asacol (active ingredient mesalamine) for the treatment of ulcerative colitis. Asacol tablets are coated with methacrylic acid copolymer B. Many site-specific dosage medication, such as Asacol, have enteric coatings which generally consist of various polymers that contain plasticizers, including triethyl citrate, dibutyl sebacate, and phthalates such as DEP and DBP. In a spot urine sample from the subject collected 3 months after he started taking Asacol, the concentration of MBP, a DBP metabolite, was 16,868 ng/mL (6,180 μg/g creatinine). The MEP, MEHP, and MBzP concentrations were 443.7 ng/mL (162.6 μg/g creatinine), 3.0 ng/mL (1.1 μg/g creatinine), and 9.3 ng/mL (3.4 μg/g creatinine), respectively. Compared with the 1999–2000 NHANES data set, the subject's urinary MEP, MEHP, and MBzP levels were unremarkable. However, the patient's concentration of MBP in urine was two orders of magnitude higher than the U.S. population 95th percentile for males reported in the NHANES 1999–2000. The subject was in his early thirties and had no known workplace exposures. Because this case report is based on single patient, it can not be definitively concluded that the medication was the main contributor to the very high urinary concentration of MBP.

5.4.10. Scenario 9: Adult Toys and Gels

The DEPA conducted two surveys to investigate the presence of chemicals, including phthalates, in adult toys, clothing and pleasure gels (Nilsson et al., 2006; Tønnig et al., 2006). Based on the results, migration testing was conducted and exposures were calculated for phthalates in adult toys.

Nilsson et al. (2006)

Nilsson et al. (2006) measured levels of DEP, DEHP, DnOP, and DINP in 15 different plastic adult plastic toys and clothing, conducted migration testing on six of the toys based on realistic

worst-case scenarios, and collected information on frequency of use to estimate adult oral exposure of phthalates. The toys tested were made of soft vinyl, natural latex, rubber, and thermoplastic rubber. Special clothing tested was made of natural latex and soft vinyl.

Ten of the fifteen samples tested contained phthalates. Specifically, DEP was detected in one sample at 0.12 g/kg (natural latex clothing), DEHP was detected in eight samples at 0.73 to 702 g/kg (soft vinyl toys, soft vinyl clothing and rubber toy), DnOP was detected in two samples at 161 and 239 g/kg (soft vinyl toy), and DINP was detected in two samples at >500 and 600 g/kg (soft vinyl toys).

Migration testing was carried out by immersing the product in a liquid stimulant for one hr at 40ºC in either artificial sweat or artificial saliva (gag only). Under these conditions, DEHP migration was at <0.5 to 6 $\mu g/dm^2$, DnOP migration was at 8 $\mu g/dm^2$, and DINP migration was at <0.5 $\mu g/dm^2$. Migration testing was also conducted with one toy using a water based lubricant and an oil based lubricant. The migration of DEHP increased significantly to 40 $\mu g/dm^2$ when water based lubricant was used and to 5,480 $\mu g/dm^2$ when oil based lubricant was used.

Based on the content analysis and migration testing results, exposures were only estimated for DEHP and DnOP. It was assumed that substances can be absorbed in the body by oral intake and by penetration through skin and mucous membranes. Internal doses were calculated under the assumption that contact with the skin and mouth would be comparable to oral use.

For DEHP, the maximum internal dose was for a soft vinyl vibrator. The internal dose for normal use was calculated as 0.0017 mg/kg body weight/day and the internal dose for worst-case use was calculated was 0.047 mg/kg-bw/d. These estimates are based on a migration value of 5,480 $\mu g/dm^2$ (test conducted using oil based lubricant), the surface area of the toy to represent the exposed area of the skin (120 cm^2), an exposure duration of 0.0357 hrs/d for normal use and 1 hr/day for worst-case use, an absorption factor of 50%, and a body weight of 70 kg. It should be noted that the migration value for the same product when the migration test was conducted using artificial sweat as the liquid stimulant was only 6 $\mu g/dm^2$. When using water based lubricant, the migration value was 40 $\mu g/dm^2$. For the other products, it was assumed that the internal doses would be in the same range or lower, especially for the gag (which is only used in the mouth and not with oil based lubricants) and for clothing (which only has direct skin contact and no additional lubricants are added when used).

For DnOP, Nilsson et al. (2006) also assumed a worst case uptake of approximately 0.05 mg/kg body weight/day. This estimate was calculated using the same inputs as for DEHP.

Tønnig et al. (2006)

Tønnig et al., 2006 conducted a survey and health assessment of chemicals substances in adult pleasure gels for the Danish Ministry of the Environment. As part of the study 15 gels and 7 massage oils/creams were screened to identify the content of organic substances in the products. DEHP was detected in one sample, a pleasure gel. The diethyl phthalate concentration was not provided.

5.4.11. Scenario 10: Miscellaneous Exposure Scenarios

This section provides information on human exposure to consumer products not covered in the preceding sections. These consumer products include air fresheners, polymer clay, and stain removers.

Air Fresheners

A study by the European Consumers' Organization (BEUC) on emissions from air fresheners, as described in SCHER (2006), found indoor air concentrations of DEPH ranging from non-detect to 1,251 $\mu g/m^3$ following the use of several types of air fresheners. In the BEUC study, air concentrations of DEPH, benzene, formaldehyde, and other compounds were measured in enclosed rooms following the use of products such as incense, natural products, scented candles, aerosols, liquid and electric diffusers, and gels. The highest air concentrations of DEPH were observed with the use of incense (1,251 $\mu g/m^3$) and sprays (571 $\mu g/m^3$). SCHER (2006) noted that DEPH emissions from incense have not been reported in other studies of air fresheners. SCHER (2006) also pointed out that while the BEUC study was the first to directly measure emissions from air fresheners, the representativeness of the measured data is unknown. Moreover, there was a wide variability in measured concentrations among samples of the same product category. Regarding consumer exposure, SCHER (2006) noted that long-term exposure to emissions from air freshener products is unknown and more data are required on the use pattern of air fresheners to assess actual exposure to consumers.

Polymer Clay

Stopford et al. (2003) investigated hand-to-mouth and hand-to-food transfer of phthalates associated with the use of polymer clay. Three types of polymer clay, containing BBP, DnOP, di-n-hexyl phthalate (DnHP), di-n-decyl phthalate (DnDP), and di(2-ethyl hexyl) terephthalate(DOTP), were used in the study. The rate of total phthalate transfer to hands, measured under laboratory conditions and standardized for hand surface area, ranged from 0.09 to 0.23 mg/cm^2 per 45 minutes of clay handling. It was noted that the transfer rates measured in the laboratory were considerably higher than rates determined for professional polymer clay artists under actual use conditions. Hand-to-mouth transfer of phthalates ranged from <0.2 to <4.4% of the amount deposited on the hands. Hand-to-food transfer of phthalates ranged from <0.11 to 1.30% of the amount deposited on the hands. In general, measured amounts of transferred phthalates were below the analytical detection limits. Stopford et al. (2003) estimated that ingestion of total phthalates range from 127 to 250 µg/d, depending on the type of polymer clay used.

Based on measured air concentrations following baking of polymer clay from Maas et al. (2004), Schettler (2006) estimated maximum inhalation exposures for BBP, DnOP, and DEHP or similar compounds of 2,667, 6,670 and 4,993 µg, respectively. These estimates were based on a 1-hr exposure period and a respiratory volume of 1.0 m^3/hr for children <18 years of age.

Stain Removers

In a report by the DEPA, the inhalation exposure to DBP resulting from the use of stain remover was reported as 3.19×10^{-6} mg/kg-bw/d, based on an estimated DBP air concentration of 22.5 $\mu g/m^3$ (Jensen and Knudsen, 2006). The estimated exposure value was obtained from a previous DEPA report on DBP in stain removers. Jensen and Knudsen (2006) do not provide information regarding the assumptions (i.e., frequency of use or duration of exposure) used to estimate the exposure value.

5.5. HUMANS EXPOSED VIA THE ENVIRONMENT

The general population may be exposed to phthalates from the air, water, soil, and some foods. The main source of phthalate exposure for the general population differs, based on the phthalate, but is most often from food. Exposure to indoor air and dust can also be important exposure pathways for some phthalate and some age groups.

Release of phthalates to the environment can occur during the production and during the incorporation of the phthalates into plastics. Because phthalates are not bound to plastics, they can be released during the use or disposal of the product. Phthalates released to the environment can be deposited on or taken up by crops intended for human or livestock consumption, and thus, may enter the human food supply.

NTP-CERHR DEHP (NTP-CERHR DEHP, 2006 and 2000)

NTP-CERHR (NTP-CERHR DEHP, 2006 and 2000) reported estimated exposure from environmental media to DEHP. DEHP was reported to enter the environment in several different ways. These include: during production, distribution, and incorporation into PVC resin; disposal in industrial and municipal landfills; waste incineration; and leaching from consumer products during use or after disposal. The release of DEHP directly into the atmosphere is believed to be the most important mode of entry into the environment. Because of low vapor pressure and poor water solubility, concentrations of DEHP in outdoor air and water were reported to be low, often at or below detection limits. DEHP adsorbs strongly to sediments and aerosol particulates; it also bioaccumulates in invertebrates, fish, and plants. Biomagnification is not observed, but biodispersal occurs at higher trophic levels in the food chain because of metabolism (NTP-CERHR DEHP, 2000).

NTP-CERHR DEHP (2006) reported exposure estimates using probabilistic analysis based on concentrations from an unpublished report prepared for industry (Tables 5.5-1 and 5.5-2). They reported the primary exposure for the general population to be from food, with over 90% of exposure for those over 6 months occurring from food. Estimated exposure for infants was 43.7% from food for formula-fed and 59.6% for breast-fed. Ingestion of dust made up nearly all the remaining exposure for infants.

Table 5.5-1. DEHP Intake from Environmental Sources by Age Group (µg/kg-bw/d)

Environmental Source	Age Group					
	20–70 yrs	12–19 yrs	5–11 yrs	7 months – 4 yrs	0- 6 months	
					Formula-fed	Breast-fed
Ambient Air	0.0	0.0	0.0	0.0	0.1	0.0
Indoor Air	1.0	0.9	1.0	0.9	1.5	1.1
Drinking Water	0.1	0.1	0.1	0.1	0.7	0.0
Ingested Soil	0.0	0.0	0.0	0.0	0.0	0.0
Ingested Dust	4.3	4.2	5.0	6.6	54.1	39.3

Estimated from research published from 2000 to 2005.

Table 5.5-2. DEHP Intake from Environmental Sources by Age Group (µg/kg-bw/d)

Environmental Source	Age Group				
	20–70 yrs	5–19 yrs	5–11 yrs	0.5–4 yrs	0–0.5 yrs
Ambient Air: Great Lakes	0.00003–0.0003	0.00003–0.0003	0.00004-0.0004	0.00003–0.0003	0.00003- 0.0003
Indoor Air	0.85	0.95	1.2	0.99	0.86
Drinking Water	0.02–0.06	0.02–0.07	0.03–0.10	0.06–0.18	0.13–0.38
Soil	0.00003	0.000004	0.00014	0.000042	0.000064

Estimated from research published prior to 2000.

NTP-CERHR BBP (NTP-CERHR BBP, 2000)

NTP-CERHR BBP (2000) reported estimated exposure from environmental media to butyl BBP. BBP was only detected in one sample (2.8 µg/L) collected in 1991 in a survey of 300 drinking water sites in two Canadian provinces from 1985 to 1994. Exposure to BBP through drinking water was considered to be negligible; exposure through soil intake was also considered negligible. BBP exposure through inhalation was reported to be minimal because of BBP's low vapor pressure. The available data, though minimal, support this view.

NTP-CERHR DnOP (NTP-CERHR DnOP, 2003 and 2000)

NTP-CERHR (NTP-CERHR DnOP, 2003 and 2000) reported estimated exposure from environmental media to DnOP. Exposure to DnOP through air was reported to be possible but expected to be minimal. Reported concentrations of DnOP in ambient air range from 0.06 to 0.94 ng/m^3. The highest reported concentration resulted in a calculated inhaled dose of 0.29 ng/kg-bw/d for an adult. Reported concentrations in river water have ranged from 0.024 to 1 ppb. U.S. EPA estimates that DnOP levels in drinking water influents are less than 0.5 ppb. These levels are several orders of magnitude lower than levels found in food.

The available data did not allow for estimation of DnOP exposures to the general population. However, a comparison of production volumes for DnOP-containing compounds versus those that contain DEHP suggests that human exposure to DnOP is well below the exposure estimate for DEHP of 3 to 30 μg/kg-bw/d (NTP-CERHR DnOP, 2003). Exposures may be higher in children due to dietary preferences or mouthing of DnOP-containing articles.

ATSDR (2002)

ATSDR (2002) provided information regarding DEHP exposure. ATSDR (2002) reported DEHP to be a widely used chemical that enters the environment both through disposal of industrial and municipal wastes in landfills and by leaching into consumer products stored in plastics. DEHP tends to sorb strongly to soils and sediments and to bioconcentrate in aquatic organisms. Biodegradation is expected to occur under aerobic conditions.

The general population is exposed to DEHP via oral, dermal, and inhalation routes of exposure. ATSDR (2002) reported estimates of the average total daily individual ambient exposure to DEHP in the U.S. to range from 0.210 to 2.1 mg/d. These estimates do not include workplace air exposures or exposures to DEHP off gassing from building materials. ATSDR (2002) reported estimated DEHP exposures in the Canadian population of 8.9–9.1, 19, 14, 8.2, and 5.8 μg/kg-bw/d for age groups 0–0.5, 0.5–4, 5–11, 12–19, and 20–70 yrs, respectively (NTP-CERHR DEHP, 2000). Populations residing near hazardous waste disposal sites or municipal landfills might be subject to higher than average levels of DEHP in ambient air and drinking water. Even so, the concentrations of DEHP in these media may be greatly limited by the low volatility and low water solubility of DEHP.

ATSDR (2002) reported the principal route of human exposure to DEHP as oral, but noted that current exposures are changing due to changes in DEHP use in certain applications. ATSDR (2002) reported that oral exposure from drinking water is not expected to be a significant route of exposure, based on estimates of <30 ppb for DEHP in water. It was reported that exposures from breathing ambient air are low, and thus inhalation exposure from ambient air and indoor air is not considered to be a significant route of exposure to DEHP. Industrial areas were reported to have higher concentrations in some cases, such as near DEHP production or PVC manufacturing facilities. Thus, it is anticipated that people living near these facilities might be exposed to elevated levels of DEHP.

ATSDR (2002) noted that DEHP will be absorbed following ingestion of contaminated drinking water and foodstuffs and inhalation of contaminated ambient air. Absorption following dermal exposure to soils is expected to be limited because of the strong sorption of DEHP to soils and because, in the absence of solvents, DEHP does not penetrate skin well. However, additional information would be useful to determine whether DEHP would be absorbed following dermal exposure to contaminated water and soils and ingestion of contaminated soils. This information will be helpful in assessing the relative importance of these pathways for exposed humans.

ATSDR (2002) reported that bioconcentration of DEHP in aquatic organisms has been documented and based on the relatively high K_{ow}, it appears that accumulation can occur.

However, it was reported that rapid metabolism of DEHP in higher organisms seems to prevent biomagnification in the food chain.

ATSDR (2001)

ATSDR (2001) provided information regarding di-n-butyl phthalate exposure. They reported that di-n-butyl phthalate is present in both urban and rural air (1 to 6 ng/m^3), some drinking waters (0.1 to 0.5 µg/L; the data are >20 years old), and some foods (3 to 1,500 µg/kg). Based on these data, the highest exposure to di-n-butyl phthalate is most likely to come from some dairy products, fish, and seafood, if these foods comprise a large part of the diet. ATSDR (2001) concluded that, for the general population, air is the main source of DBP (di-n-butyl phthalate) exposure if dairy products and seafood are not important in the diet. The level of di-n-butyl phthalate exposure for the general population is expected to be in the low ppb range; in Canada, the estimated daily intake was reported to be 1.9 to 5.0 µg/kg body weight.

ATSDR (2001) reported results from Chan and Meek (1994) estimation of the daily intake of DBP by the population of Canada (see Table 5.5-3). Based on the medium-specific intakes, it was estimated that the average daily intake of DBP for the various age groups ranged from 1.9 to 5.0 µg/kg-bw/d. It should be noted that these estimates do not include intake from consumer products.

Table 5.5-3. Estimated Intake by Age Groups of DBP (µg/kg-bw/d)

Environmental Source	Age Group				
	0–0.5 yrs	0.5–4 yrs	5–11 yrs	5–19 yrs	20–70 yrs
Ambient Air	0.00021–0.0003	0.00033–0.0004	0.00033–0.00041	0.00028–0.00038	0.00025–0.00034
Indoor Air	0.68	0.91	1.1	0.87	0.78
Drinking Water	0.11	0.062	0.033	0.022	0.021
Soil	<0.0005– 0.007	<0.00038–0.0054	<0.00013–0.00049	<0.000035–0.00049	<0.000028–0.0004

Source: Chan and Meek 1994, as reported in ATSDR 2001.

ATSDR (2001) reported that young children sometimes ingest soil either intentionally through pica (the desire to eat substances, such as soil or chalk, not normally eaten) or unintentionally through hand-to-mouth activity. ATSDR (2001) noted that while no childhood exposures to DBP from soil ingestion or dermal soil exposure were documented, this phthalate has been detected in soil. In addition, they reported that DBP has also been detected in atmospheric fallout in both urban and rural areas, and is not expected to migrate rapidly to groundwater or to volatilize rapidly from soil surfaces. DBP is anticipated to degrade rapidly, and exposures to this chemical from other sources are anticipated to be much greater. Therefore, they suggested that exposures of children to DBP from soil would likely be slight.

ATSDR (2001) reported that DBP tends to be taken up and metabolized by invertebrates and fish. ATSDR (2001) stated that numerous studies have shown that the accumulation of DBP in

the aquatic and terrestrial food chain is limited by biotransformation, which progressively increases with trophic level. Therefore, DBP will not biomagnify through the food chain.

ATSDR (1997)

ATSDR (1997) provided information regarding DnOP exposure. They reported that exposure to DnOP is expected to occur mainly in the workplace. Exposure of the general population to DnOP was reported to occur through ingestion of foods contaminated by leaching of the compound from plastic containers, transfusions of blood or other fluids through medical tubing, ingestion of aquatic organisms that have bioconcentrated the compound, and consumption of contaminated drinking water. An additional potential source of human exposure was reported to be contact with contaminated media at hazardous waste sites, as DnOP has been detected in on-site sediment and groundwater samples and off-site sediment samples collected at NPL hazardous waste sites. It is not known whether dermal contact with DnOP at hazardous waste sites would represent an exposure pathway of concern, as data were not available on the dermal absorption of DnOP.

ATSDR (1997) reported that members of the general population living in the vicinity of industrial facilities that manufacture or process the compound or plastic materials containing the compound, as well as individuals living near hazardous waste sites known to be contaminated with DnOP, are also expected to have potentially high exposures through contact with contaminated environmental media.

DnOP bioconcentrates in aquatic organisms (ATSDR, 1997). However, ATSDR reported that, as a result of metabolism of the compound, biomagnification in aquatic food chains does not occur. It was reported that the compound is not bioconcentrated by terrestrial plants or animals or biomagnified in terrestrial food chains. However, only limited data was available regarding the bioaccumulation and biomagnification of DnOP, and the potential for human exposure resulting from the bioaccumulation of the compound is not well understood.

ATSDR (1997) reported that no information was found regarding the absorption of DnOP by humans or laboratory animals following inhalation or dermal exposures. No information is available about absorption following oral exposure in humans. However, indirect evidence from animal studies suggests that the compound is readily absorbed by this route. They suggested additional information is needed on the absorption of DnOP as a result of inhalation of contaminated air, ingestion of contaminated food and water, and dermal contact with contaminated soils and sediments.

ATSDR (1995)

ATSDR (1995) provided information regarding diethyl phthalate exposure. Mean diethyl phthalate (DEP) exposure from drinking water in Toronto, Canada, was reported to be 0.0058 mg/yr per person based on exposure for years 1978-1984.

ATSDR (1995) reported DEP to have been detected in ambient air, drinking water, surface waters, sediments, and food; however, limited current monitoring data was found. DEP had been detected in the surface waters, groundwater, and soil samples taken at a limited number of NPL

sites. Additional information on the concentrations of DEP in hazardous waste-site media is needed to help identify the most important exposure pathways for populations living near these sites.

DEP was reported to have been detected in aquatic organisms and was been found to bioconcentrate modestly in these organisms (ATSDR, 1995). The database is, however, too limited to determine a representative range of bioaccumulation potential throughout the food chain. Further data on the accumulation potential for DEP, including biomagnification in terrestrial and aquatic food chains, is needed.

ECB (ECB DEHP, 2008)

ECB (ECB DEHP, 2008) indicated that DEHP may be released to the environment through wastewater and air effluents at the sites where it is produced, transported, formulated, processed, used and after end-use of articles containing it. Indirect exposure of humans to DEHP via the environment may occur by intake of food, drinking water, and inhalation of air. Those indirect exposure routes via the environment as well as concentration utilized estimate exposure are provided in Table 5.5-4

Table 5.5-4. Estimated Daily Intake of DEHP

Environmental Source	Adult	Child
Air (m^3/d)	20	9.3
Root Drops (kg/d)	0.384	0.192
Leafy Plant Crops, Including Grains (kg/d)	1.20	0.6
Drinking Water (m^3/d)	0.002	0.001
Meat (kg/d)	0.301	0.229
Fish (kg/d)	0.115	0.084
Milk (kg_{wwt}/d)	1.333	1.68
Total		1.3×10^4

ECB (ECB BBP, 2007)

ECB (ECB BBP, 2007) indicated that BBP is widely distributed in the environment as a consequence of its manufacture, use, and disposal. The estimated concentrations of BBP in leaf crops and root crops are results of exposure via air and via soil, as calculated by EUSES using default values. Translocation of BBP within the plant is probably of minor importance. There are indications that the uptake of BBP from soil is limited. Therefore exposure via roots may be overestimated using EUSES default values for uptake from soil. In the EUSES estimations the partition coefficient between plant tissue and water is set to 1. The calculated daily human intake of BBP (mg/kg-bw/d) is presented in Table 5.5-5.

Table 5.5-5. Estimated Daily Intake of BBP

Environmental Source	BBP Concentration (µg/kg)	Total human intake (mg/kg-bw/d)
Air	NR	1.8×10^{7}
Root crops	0.023	1.3×10^{7}
Leafy plant crops	0.011	2.0×10^{7}
Drinking water	0.086	2.4×10^{6}
Meat	0.012	5.2×10^{8}
Fish	76.8	3.1×10^{4}
Milk	0.0038	1.3×10^{8}
Total		1.3×10^{4}

ECB (ECB DBP (2003-04); ECB DINP (2003); ECB DIDP (2003))

ECB (ECB DBP, 2003-04, ECB DINP 2003, ECB DIDP, 2003) provided estimated exposure via the environment for various local environments near production and processing plants for DBP, DINP, and DIDP. The authors used the EUSES model (OPS module) to estimate local atmospheric concentrations from the daily amounts of DBP released to ambient air, which were then utilized to estimate total daily intake from all environmental sources. Regional exposure was estimated with the SIMPLEBOX model, integrated in EUSES. Estimated exposure concentrations are provided in Tables 5.5-6, 5.5-7, and 5.5-8.

Table 5.5-6. Estimated Total Daily Intake of DBP for Adults (mg/kg-bw/d)

Scenario	Total Daily Intake
Production A	0.0187
Production B	0.00091
Production C	0.000786
Processing polymers	0.0925
Formulation adhesives	0.0364
Processing adhesives	0.00622
Formulation printing inks	0.00539
Processing printing inks	0.00909
Production glass fibers	0.0395
Regional	0.000359

Table 5.5-7. Estimated Daily Intake of DIDP (mg/kg-bw/d)

Scenario	Adult and Child (3 - 15 yrs)	Child (0.5 - 3 yrs)
Production	0.002	0.013
Use in PVC	0.028	0.156
Use in non-PVC polymers	0.018	0.087
Formulation of sealing compounds	0.026	0.141
Use of sealing compounds	0.001	0.006
Formulation of paper inks	0.026	0.141
Processing of paper inks	0.004	0.020
Paper recycling	0.004	0.021
Formulation of paints	0.026	0.141
Processing of paints	0.005	0.024
Regional	0.001	0.0065

Table 5.5-8. Estimated Total Daily Intake of DIDP (mg/kg-bw/d)

Scenario	Adult and Child (3 - 15 yrs)	Child (0.5 - 3 yrs)
Production	0.010	0.063
Use in PVC	0.027	0.166
Use in non-PVC polymers	0.017	0.102
Formulation of anti-corrosion paints	0.014	0.076
Application of anti-corrosion paints	negligible	negligible
Formulation of anti-fouling paints	negligible	negligible
Application of anti-fouling paints	0.012	0.066
Formulation of sealing compounds	0.014	0.076
Formulation of textile inks	0.014	0.077
Application of textile inks	0.003	0.013
Regional	0.002	0.013

5.6. CUMULATIVE EXPOSURE

5.6.1. Introduction

This section summarizes reported cumulative exposure estimates to phthalates calculated using two different methods. The first method calculates exposures based on phthalate or phthalate metabolite levels in urine (i.e., biomonitoring-based approach). Cumulative exposures have not been calculated based on biomonitoring data from other human fluids such as blood (including serum and plasma), human milk, saliva, and seminal fluids. The second method calculates exposures based on environmental concentrations in media and human behaviors (i.e., scenario-based approach). Each approach has its own uncertainties and limitations, which are discussed below. In general, the biomonitoring approach is often preferred since it provides a direct and accurate magnitude of exposures; however, this approach does not provide information on the sources or routes of exposure, as can be determined in the scenario-based approach. One researcher (Wormuth et al., 2006) compared exposures calculated using both methods and determined exposures were similar, however, caution should be taken, as this was only one study (Kamrin, 2009).

The articles summarized in this section are shown below in Table 5.6-1 for the biomonitoring exposure calculation approach and Table 5.6-2 for the indirect scenario exposure calculation approach. These tables indicate for which populations cumulative exposure data are available. The population categories used in this report are neonates, children, adults, women only, men only, and general population (children and adults combined).

A detailed description of the two approaches is discussed below in Sections 5.6.2 and 5.6.3. These sections also highlight important differences in exposure calculation assumptions and provide a brief overview of the articles reviewed. Summaries of the exposures reported in the articles reviewed are shown in Section 5.6.4 for banned phthalates (DEHP, DBP, and BBP), Section 5.6.5 for interim banned phthalates (DINP, DIDP, and DnOP), and in Section 5.6.6 for other phthalates (DEP, DMP, DIBP, and DCHP).

Table 5.6-1. Summary of Available Exposure Calculated Using Biomonitoring Data

Exposure Study	Biomonitoring Study	Sampling Date	Population Assessed[a]									
			Banned Phthalates			Interim Banned Phthalates			Other Phthalates			
			DEHP	DBP	BBP	DINP	DIDP	DnOP	DMP	DEP	DiBP	DCHP
Exposures Based on U.S. Biomonitoring Data												
Kohn et al., 2000	Blount et al., 2000 (NHANES)	1988–1994	A,W	A,W	A,W	A,W	--	A,W	--	A,W	--	A,W
David, 2000			A,W	A,W	A,W	A,W	--	A,W	--	A,W	--	A,W
Fromme et al., 2007b			A	A	A	--	--	--	--	A	--	--
Calafat and McKee, 2006			A	--	--	--	--	--	--	A	--	--
SCENIHR, 2008			A	--	--	--	--	--	--	--	--	--

Table 5.6-1. Summary of Available Exposures Calculated Using Biomonitoring Data (continued)

Exposure Study	Biomonitoring Study	Sampling Date	Population Assessed[a]									
			Banned Phthalates			Interim Banned Phthalates			Other Phthalates			
			DEHP	DBP	BBP	DINP	DIDP	DnOP	DMP	DEP	DiBP	DCHP
Calafat and McKee, 2006	Hoppin et al., 2002	1996-1997	W	--	--	--	--	--	--	W	--	--
Fromme et al., 2007b			W	W	W	--	--	--	--	W	W	--
Calafat and McKee, 2006	Silva et al., 2004 (NHANES)	1999-2000	C	--	--	--	--	--	--	C	--	--
Fromme et al., 2007b			W,M	W,M	W,M	--	--	--	--	W,M	--	--
SCENIHR, 2008			GP	--	--	--	--	--	--	--	--	--
Fromme et al., 2007b	Swan et al., 2005	1999-2002	W	W	W	--	--	--	--	W	W	--
Marsee et al., 2006			W	W	W	--	--	--	--	W	W	--
SCENIHR, 2008			W	--	--	--	--	--	--	--	--	--
Calafat and McKee, 2006	Brock et al., 2002	2000	C	--	--	--	--	--	--	C	--	--
Calafat and McKee, 2006	Adibi et al., 2003	2000	W	--	--	--	--	--	--	W	--	--
Calafat and McKee, 2006	CDC, 2005 (NHANES)	2001-2002	A,C,W, M	--	--	--	--	--	--	A,C, W, M	--	--
Fromme et al., 2007b			W,M	W,M	W,M	--	--	--	--	W,M	W,M	--
SCENIHR, 2008			A,C	--	--	--	--	--	--	--	--	--
Calafat and McKee, 2006	Calafat et al., 2004b	2002	N	--	--	--	--	--	--	N	--	--
SCENIHR, 2008	Silva et al., 2006	2003-2004	A	--	--	--	--	--	--	--	--	--
Calafat and McKee, 2006	Duty et al., 2004	NR	M	--	--	--	--	--	--	M	--	--
SCENIHR, 2008	Barr et al., 2003	NR	X	--	--	--	--	--	--	--	--	--
Exposures Based on Japanese Biomonitoring Data												
Itoh et al., 2007	Itoh et al., 2005	2004	A	A	A	--	--	--	A	A	--	--
Itoh et al., 2005			A	A	--	--	--	--	--	--	--	--
Fujimaki et al., 2006 (from Matsumoto et al., 2008)	NR	NR	W	--	--	--	--	--	--	--	--	--
Exposures Based on German Biomonitoring Data												
Wittassek,	Wittassek,	1998-2003	A,W,M	A,W,M	A,W,	A,W,	--	--	--	--	A,W,	--

Table 5.6-1. Summary of Available Exposures Calculated Using Biomonitoring Data (continued)

Exposure Study	Biomonitoring Study	Sampling Date	Population Assessed[a]									
			Banned Phthalates			Interim Banned Phthalates			Other Phthalates			
			DEHP	DBP	BBP	DINP	DIDP	DnOP	DMP	DEP	DiBP	DCHP
2007a	2007a				M	M					M	
		2001/ 2003	A	--	--	--	--	--	--	--	--	--
Koch, 2007	Becker et al., 2004	2001/ 2002	--	C	C	--	--	--	--	--	--	--
Wittassek, 2007b			C	--	--	--	--	--	--	--	--	--
Calafat and McKee, 2006			C	--	--	--	--	--	--	--	--	--
SCENIHR, 2008			C	--	--	--	--	--	--	--	--	--
Koch et al., 2003b	Koch et al., 2003b	2002	GP,W, M	GP,W, M	A,W, M	--	--	GP,W, M	--	GP, W,M	--	--
Calafat and McKee, 2006			GP	--	--	--	--	--	--	GP	--	--
Fromme et al., 2007b			W,M	W,M	W,M	W,M	--	--	--	W,M	W,M	--
SCENIHR, 2008			GP	--	--	--	--	--	--	--	--	--
ECB DEHP, 2008			GP	--	--	--	--	--	--	--	--	--
Calafat and McKee, 2006	Koch et al., 2004a	2003	A,C	--	--	--	--	--	--	--	--	--
SCENIHR, 2008			A,C	--	--	--	--	--	--	--	--	--
Fromme et al., 2007b	Fromme et al., 2007a	2005	A,W,M	A,W,M	A,W, M	A,W, M	--	--	--	--	A,W, M	--
Wittassek and Angerer, 2008	Unpublished by Koch et al.	NR	GP	GP	GP	GP	--	--	--	--	GP	--
Exposures Based on South Korean Biomonitoring Data												
Koo and Lee, 2005	Koo and Lee, 2005	2003	W, C	--	--	--	--	--	--	--	--	--
Fromme et al., 2007b			W	--	--	--	--	--	--	--	--	--
Exposures Based on Taiwanese Biomonitoring Data												
Chen et al., 2008	Chen et al., 2008	NR	A	A	A	--	--	--	--	A	--	--

a. Population Key
A = adult (men and women combined, over 18-20 years)
C = children (under 18-20 years)
GP = general population (children and adults combined)
M = men (over 18-20 years)
N = neonates
W = women (over 18-20 years)
X = population not reported

* Original study was not reviewed. Results are from the secondary source reported in parentheses.

-- = Exposures not calculated

NR = Not Reported

Table 5.6-2. Summary of Studies with Exposures Calculated Using Scenario-Based Data from Environmental Analysis and Behaviors[a]

Study	Country	Type of Exposure	Routes of Exposure	Sources of Exposure	Banned			Interim Banned			Other			
					DEHP	DBP	BBP	DINP	DIDP	DnOP	DMP	DEP	DiBP	DCHP
With Consumer Products														
Wormuth et al., 2006	Europe	Internal	Oral, dermal, inhalation	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, and spray paints	C,W,M	C,W,M	C,W,M	C,W,M	C,W,M	--	C,W,M	C,W,M	C,W,M	--
Müller et al., 2003	Denmark	External	Oral, dermal, inhalation	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, and nail polish	C,A	C,A	C,A	C,A	C,A	--	--	--	--	--
ECB DEHP, 2008	Europe	Internal	Oral, dermal, inhalation	Indoor air (building materials), gloves, and car interior	C,A	--	--	--	--	--	--	--	--	--
ECB DINP, 2003; ECB DIDP, 2003	Europe	Internal	Oral, dermal, inhalation	Building materials and furniture, car and public transport interiors, clothing, gloves and footwear, and food and food-related uses, toys, air, drinking water, and food	--	--	--	C,A	C,A	--	--	--	--	--
Without Consumer Products, But Including Indoor Air														
Wilson et al., 2003	U.S.	External	Oral, inhalation (dermal assumed to be negligible)	Indoor air, outdoor air, play area soil and floor dust (incidental ingestion), and food	--	C	C	--	--	--	--	--	--	--
ECB BBP, 2007	Europe	Internal	Oral, inhalation	Food and food packaging, indoor air, and drinking water	--	--	C,A		--	--	--	--	--	--
*Chan et al., 1994 (NTP-CERHR DBP, 2000)	Canada	Internal	Oral, inhalation	Ambient air, indoor air, drinking water, food, and soil. Does not include consumer products.	--	C,A	--	--	--	--	--	--	--	--

Table 5.6-2. Summary of Studies with Exposures Calculated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study	Country	Type of Exposure	Routes of Exposure	Sources of Exposure	Banned			Interim Banned			Other			
					DEHP	DBP	BBP	DINP	DIDP	DnOP	DMP	DEP	DiBP	DCHP
Clark et al., 2003	Canada	External	Oral, inhalation	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. Does not include children's and consumer products.	C,A	C,A	C,A	--	--	--	C,A	C,A	--	--
*Meek and Chan, 1994 (SCENIHR, 2008)	Canada	Internal	Oral, inhalation	Air, drinking water, and food. Does not include consumer products.	C,A	--	--	--	--	--	--	--	--	--
Without Consumer Products, Excluding Indoor Air														
ECB DBP, 2003-04	Europe	Internal	Oral, inhalation	Air, drinking water, and food	--	C,A	--	--	--	--	--	--	--	--
ECB DEHP, 2008	Europe	Internal	Oral, inhalation	Air, drinking water, and food	C,A	--	--	--	--	--	--	--	--	--
Doull et al., 1999 (from Huber et al., 1996)	U.S.	Internal	Oral	Food only	GP	--	--	--	--	--	--	--	--	--

a. Population Key
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M = men (over 18-20 years)
N = neonates
W = women (over 18-20 years)
X = population not reported

* Original study was not reviewed. Results are from the secondary source reported in parentheses.

-- = Exposures not calculated
NR = Not Reported

5.6.2. Description of the Biomonitoring Approach to Calculating Cumulative Exposure

Biomonitoring studies may include the measurement of metabolites in urine and other biomatrices, such as blood (including serum and plasma), human milk, saliva, seminal fluids, and human amniotic fluid (see Section 5.2). The most common approach for evaluating phthalate exposures is the measurement of phthalate metabolite concentrations (biomarkers) in urine. Phthalate concentrations in blood have been reported, although these samples have been mostly assessed for diester concentrations. While other media may provide useful information, challenges associated with sampling may limit their use. For purposes of large screening efforts, media other than urine may not be practical, but they may be useful in specific situations (Calafat and McKee, 2006). In this report, only biomonitoring exposures back-calculated from phthalate metabolite concentrations in urine are summarized.

The exposure values reported in the studies evaluated were not all calculated using the same methods. Factors which can influence the calculations include which metabolite was measured in the urine samples, if exposures were calculated from spot urine samples or 24-hr urine samples, the method used to extrapolate the phthalate metabolite concentrations in the spot samples into daily values (creatinine-based or urine volume-based), the metabolite conversion method, and other model specific factors (i.e., creatinine excretion values). A discussion of these factors and the different extrapolation and exposure back-calculation models is provided below.

Sampling and Analysis Factors

Sample Collection

Twenty-four-hr urine samples provide the best estimate of daily metabolite excretion, as discussed in Section 5.2. For example, the use of personal care products prior to a spot sample could cause overestimation of exposures (Kamrin, 2009). However, collecting 24-hr samples is both difficult and not practical, particularly when children are being studied. Only one study evaluated for this report (Wittassek et al., 2007a) estimated daily intake from 24-hr samples. For the other studies, the urinary metabolite concentrations in the spot samples required extrapolation to daily (i.e., 24-hr) values. This was accomplished using either a creatinine excretion-based model or a volume-based model (discussed below).

Metabolites Measured

As discussed in Section 5.2, the metabolite selected for measurement may have a significant influence on the exposure results. Traditionally, the hydrolytic monoesters have been measured, however, more recent studies measure the oxidative metabolites, which have been shown to have greater analytical sensitivity and also cannot be formed as a result of sampling contamination (Calafat and McKee, 2006). For example, early daily intake calculations for the phthalate DEHP were based on the excretion of the simple monoester MEHP only (such as David, 2000 and Kohn et al., 2000). More recent estimations of DEHP daily intake include the secondary DEHP metabolites in addition to MEHP (such as Koch et al., 2003a, Wittassek et al., 2007a, and Wittassek et al., 2007b). Exposure evaluations based on three or five DEHP metabolites may provide more accurate estimations of the daily DEHP intake (SCENIHR, 2008). The secondary

DEHP metabolites mono-(2-ethyl-5-hydroxyhexyl) phthalate (5OH-MEHP) and mono-(2-ethyl-5oxohexyl) phthalate (5oxo-MEHP) reflect short-term exposure levels of DEHP in urine. Other secondary oxidized metabolites of DEHP such as mono-(2-ethyl-5-carboxypentyl) phthalate (5cx-MEPP) and mono-[2-(carboxymethyl) hexyl] phthalate (2cx-MMHP) have long half-times of elimination and therefore are considered excellent parameters for measurement of the time-weighted body burden of DEHP. Oxidized metabolites of DINP have also been recently introduced (Matsumoto et al., 2008).

Extrapolation Models

As previously mentioned, only one study evaluated for this report (Wittassek et al., 2007a) estimated daily intake using 24-hr samples. The remaining studies used spot samples, which require extrapolation of the urinary metabolite concentrations to daily (i.e., 24-hr) values. Extrapolation methods can generally be categorized as creatinine excretion-based or urine volume-based. The majority of the studies evaluated used a creatinine excretion-based extrapolation method.

Creatinine Excretion-Based Model

Creatinine excretion-based extrapolation models use a creatinine excretion value (g/kg-bw/day) to adjust the concentrations. Earlier studies such as David (2000), Kohn et al. (2000) and Koch et al. (2003b) used constant values for creatinine excretion (CE) for adult males and females. According to Kohn et al. (2000), creatinine excretion is known with 10% accuracy. Several recent studies, such as Itoh et al. (2005 and 2007) and Koch et al. (2007), have used individual estimates of CE. According to Itoh et al. (2005), urinary creatinine levels are dependent on personal musculature, which varies from individual to individual, as well as between adult males and females. For that reason, the creatinine-adjusted concentration should be corrected based on an individual's characteristics, such as amount of muscle tissue, age, and sex. Therefore, Itoh et al. (2005) used personal daily CE values (normalized by individual body weight) predicted on individual gender, age, body weight, and height measurements, as well as a regression equation from Kawasaki et al. (1991). Koch et al. (2007) also emphasized the importance of using personal rather than constant CE values, especially in children where creatinine had been shown to vary greatly among children of different ages, body weight, gender, and race. Koch et al. (2007) used body height- and gender-based reference values for urinary creatinine excretion for healthy Caucasian children aged 3 to 18 years in grams creatinine per day taken from the study of Remer et al. (2002). These values were normalized to the body weight of each individual participant. Table 5.6-3 presents the creatinine excretion values used in the different studies, when available.

Table 5.6-3. Assumed Creatinine Excretion Rates (CEs) and Body Weights (BWs)

Exposure Study	Biomonitoring Study	Creatinine Excretion Rate (CE) (mg/kg/d)	Body Weight (BW) (kg)
David, 2000	Blount et al., 2000	W: 20	Not reported
Calafat and McKee, 2006	Adibi et al., 2003; Becker et al., 2004; Blount et al., 2000; Brock et al., 2002; Calafat et al., 2004b; CDC, 2005; Duty et al., 2004; Hoppin et al. , 2002; Koch et al., 2003a; Koch et al., 2004b; Silva et al., 2004	Not reported	Not reported
Calafat and McKee, 2006	Brock et al., 2002	Individual values from Brock et al., 2004	Not reported
Chen et al., 2008	Chen et al., 2008	W: 18; M: 23	W: 50; M: 70
ECB BBP, 2007	Blount et al., 2000; Brock et al., 2002; CDC, 2003; Hoppin et al. , 2002; Koch et al., 2003a	W: 18; M: 23	Not reported
Fromme et al., 2007b	Fromme et al., 2007a	W: 18; M: 23	Not reported
Fujimaki et al., 2006 (reported in Matsumoto et al, 2008)	Fujimaki et al., 2006	Not reported	Not reported
Itoh et al., 2005	Itoh et al., 2005	Predicted for each individual	Individual values
Itoh et al., 2007	Itoh et al., 2005	Predicted for each individual	Individual values
Koch et al., 2003b	Koch et al., 2003a	W: 18; M: 23	W: 50; M: 70
Koch et al., 2007	Koch et al., 2007	Height & gender specific (Remer et al., 2002)	Individual values
Kohn et al., 2000	Blount et al., 2000	W: 18; M: 23	Not reported
Koo and Lee, 2005	Koo and Lee, 2005	W: 18; C: 22	Not reported
Marsee et al., 2006	Swan et al., 2005	W: 18	Not reported

Key:
C = children
M = men (over 18-20 years)
W = women (over 18-20 years)

Volume-Based Model

Wittassek et al., 2007b, and Koch et al., 2007, calculated exposures in children using the volume-based approach, as well as the creatinine excretion-based approach. As with the creatinine excretion approach, the total volume of urine excreted per day varies by age. Both of the studies took this into account and used reference values regarding age for the daily excreted urinary volume normalized to body weight. Reference values were from CIBA-GEIGY, 1977. Koo and Lee (2005) also calculated exposures using the volume-based approach. Koo and Lee (2005) used a total daily volume of 1200 mL in their calculations for both women and children.

Extrapolation Method Comparison

All three studies which calculated phthalate exposure values using the volume-based extrapolation method also calculated phthalate exposures using the creatinine-based extrapolation method. Wittassek et al. (2007b) and Koch et al. (2007) both reported that exposure in children was on average twice as high using the volume-based method than the creatinine-based method. Results from the Koo and Lee (2005) study show that exposures calculated using the volume-based method were 10 times lower than the exposures calculated using the creatinine-based method. However, it should be noted that Koo and Lee (2005) did use different metabolite conversion methods between the two extrapolation methods (discussed below).

Exposure Calculation Models

Models for the spot samples, as well models for the 24-hr samples, use metabolite conversion factors to back-calculate phthalate exposures from the daily metabolite concentrations. In general, two different models have been used. The first model, as reported in Kohn et al. (2000), is a complex linear two-compartment model which implements rate constants, ratio of urinary fecal excretion and doses eliminated in time (Koch et al., 2003b). The second model is a simplified version, as described in David (2000) and reported in Koch et al., 2003b. A majority of the studies examining phthalate exposure utilize the David (2000) method.

The equations for the two models are presented below. Both models are presented using the creatinine excretion-based concentration extrapolation method. The variables used in the two models are the same, except that the David (2000) formula uses an F_{UE} value (the molar fraction of the urinary excreted monoester related to the parent diester), whereas the Kohn et al. (2000) model uses an *f* value (ratio of urinary excretion of the monoester to total elimination).

Equation 5.6-1. Kohn et al. (2000) Daily Intake Calculation

$$\text{Daily intake (DI)} = \frac{\text{ME}\,(\mu\text{g/g creatinine}) \times \text{CE}\,(\text{g/kg body weight/day}) \times \left[\text{MW diester}\,(\text{g/mol})/\text{MW monoester}\,(\text{g/mol})\right]}{\left[\text{f} \times 1000\,(\text{mg/g})\right]}$$

Where:

ME = urine concentration,

CE	=	creatinine excretion,
MW	=	molecular weight, and
f	=	ratio of urinary excretion of the monoester to total elimination (k_u/k_{total}).

The f value (k_u/k_{total}) is calculated using published values for the excreted fractions of each parent diester. The normalized integrated rate equations for fractional excretion are as follows:

$$FE = 1 - \exp(-k_{total} \times t)$$

and

$$FU = \frac{k_u}{k_{total}}\left[1 - \exp(-k_{total} \times t)\right]$$

Where:

FE	=	total urine eliminated in time, t,
FU	=	urinary fraction of the dose eliminated in time, t,
t	=	time,
k_{total}	=	apparent first-order rate constant for total elimination, and
k_u	=	apparent first-order rate constant for elimination of urinary monoester.

Equation 5.6-2. David (2000) Daily Intake Calculation (as expressed by Koch et al., 2003b):

$$\text{Daily intake (DI) (}\mu\text{g/kg/day)} = \frac{\text{UE (}\mu\text{g/g creatinine)} \times \text{CE (mg/kg body weight/day)} \times \left[\text{MWd/MWm)}\right]}{\left[F_{UE} \times 1000\text{ (mg/g)}\right]}$$

Where:

UE	=	urine concentration/excretion of metabolite(s) per gram creatinine,
CE	=	creatinine excretion/clearance rate normalized by body weight,
MWd	=	molecular weight of the diester,
MWm	=	molecular weight of the monoester, and
F_{UE}	=	fractional urinary excretion, ratio of monoester in urine to diester ingested.

Note: For the volume-based extrapolation method, UVnorm (daily excreted volume normalized to body weight, L/kg-bw/day) is substituted for CE and the urine concentration (UE) is in terms of µmol/L).

A couple of studies compared results using both exposure models. Koch et al. (2003b) produced nearly the same results when starting from the same excretion values, with the Kohn et al. (2000) model producing slightly higher exposures. Marsee et al. (2006) concluded similarly that there is reasonable agreement between the models and parameters used. Marsee et al. (2006) stated that the David method produces exposure estimates that are typically about 20% lower than the Kohn et al. (2000), with the exception for DEHP, which was about 30–80% higher based on the David method, depending on which metabolites are used for the calculation.

Koo and Lee (2005) used a slightly different approach to calculating daily intake when using the volume-based extrapolation method. They assumed that the daily urine excretion rate of MEHP is 20 percent of the body loading for DEHP. The equation they used is as follows:

Equation 5.6-3. Koo and Lee (2005) Daily Intake Calculation

$$\text{Daily Intake } (\mu\text{g/kg body weight/day}) = \frac{T_M \times 5}{\text{BW (kg)/day}}$$

Where:

TM = total MEHP excretion level = M x V,
M = MEHP level (μg/mL urine),
V = total daily excretion volume (1200 mL), and
BW = body weight.

Fractional Urinary Excretion Values

Using different fractional urinary excretion values can yield several fold differences in estimated values even if the levels of the urinary metabolites are the same.

Table 5.6-4 shows the FE and FU values used by Kohn et al. (2000). Animal and human excretion data were used. According to Kohn et al. (2000), the FE values are generally accurate to approximately 50% and FU can vary 15-fold among species, with humans in the middle of the range. Table 5.6-5 shows the f values assumed by Kohn et al. (2000) and other studies utilizing the same model.

The F_{UE} values assumed in studies using the David (2000) equation are shown in Table 5.6-6. For DEHP especially, there are multiple studies with conversion factors that can be used, each with their own limitations, as discussed in ECB DEHP (2008) and Calafat and McKee (2006). For the metabolite MEHP, for example, the F_{UE} values used ranged from 2.4% to 13%. When a lower F_{UE} value is used, a higher daily intake results.

Table 5.6-4. Total Fractional Excretion (FE) and Fractional Urinary Excretion of Monoester (FU) During 24 hr after a Single Oral Dose of Diester

Monoester	Diester	FE	FU
Ethyl (MEP)	Diethyl (DEP)	0.94	0.52
n-Butyl (MBP)	Di-*n*-butyl (DBP)	0.94	0.52
Benzyl (MBzP)	*n*-Butyl benzyl (BBP)	0.70	0.36
Cyclohexyl (MCHP)	Dicyclohexyl (DCHP)	0.65	0.069
2-Ethylhexyl (MEHP)	Di(2-ethylhexyl) (DEHP)	0.65	0.069
n-Octyl (MnOP)	Di-*n*-octyl (DnOP)	0.65	0.043
i-Nonyl (MiNP)	Di-*i*-nonyl (DINP)	0.65	0.069

Details on sources for values of FE and FU can be found in Table 1 of Kohn et al., 2000.

Table 5.6-5. Values for Ratio of Urinary Excretion to Total Elimination (f) Used in Calculating Daily Intake Using the Kohn et al. (2000) Approach

Phthalate Diester	Metabolite Measured	Exposure Study	f	Source
BBP	MBzP	Kohn et al., 2000; Marsee et al., 2006	0.51	Nativelle et al., 1999; Eigenberg et al., 1986
DBP	MBP	Kohn et al., 2000; Marsee et al., 2006	0.55	Tanaka et al, 1978; Foster et al.1983
	MBP+MiBP	Marsee et al., 2006	0.55	Tanaka et al, 1978; Foster et al.1983
DCHP	MCHP	Kohn et al., 2000	0.11	Assumed to be same as DEHP
DEHP	MEHP	Kohn et al., 2000; Marsee et al., 2006	0.11	Peck and Albro, 1982; Kluew, 1982
DEP	MEP	Kohn et al., 2000; Marsee et al., 2006	0.55	Assumed same as DBP
DIBP	MiBP	Marsee et al., 2006	0.55	Assume same as MBP and DBP
DINP	MINP	Kohn et al., 2000	0.11	Assumed to be same as DEHP
DnOP	MnOP	Kohn et al., 2000	0.066	Assumed to be same as DEHP; Albro and Moore, 1974.

The specific values used by David for F_{UE} were not provided in his published correspondence, but the F_{UE} values assumed by other studies are presented in Table 5.6-6. As with f values used in the daily intake calculations by Kohn et al. (2000) and Marsee et al. (2006), a F_{UE} value for DEP or DIBP has not been determined experimentally. Most studies have assumed that DEP and DIBP are similar to the value determined for DBP, 0.69, by Anderson et al. (2001).

Table 5.6-6. Urinary Excretion Factor (F_{UE}) Values Used in Calculating Daily Intake Using the David (2000) Approach

Phthalate Diester	Metabolite Measured	Exposure Study	F_{UE}	Source
BBP	MBzP	Chen et al., 2008; Fromme et al., 2007b; Itoh et al., 2007; Koch et al., 2003b; Koch et al., 2007; Marsee et al., 2006; Wittassek et al., 2007a	0.73	Anderson et al., 2001
		David, 2000	Not reported	Schmid and Schlatter, 1985?
		SCHER, 2008		Koch et al., 2004b
	MBeP	ECB BBP, 2007	0.73	Anderson et al., 2000
DBP	MBP	Chen et al., 2008; Itoh et al., 2005 and 2007; Koch et al., 2003b; Koch et al., 2007; Fromme et al., 2007b; Marsee et al., 2006; Wittassek et al., 2007a	0.69	Anderson et al., 2001

Table 5.6-6. Urinary Excretion Factor (F_{UE}) Values Used in Calculating Daily Intake Using the David (2000) Approach (continued)

Phthalate Diester	Metabolite Measured	Exposure Study	F_{UE}	Source
		SCHER, 2008	Not reported	Koch et al., 2004b
		David, 2000		Schmid and Schlatter, 1985?
	MBP+MiBP	Marsee et al., 2006	0.69	Anderson et al., 2001
DEHP	MEHP	Koch et al., 2003b; Koo and Lee, 2005; Chen et al., 2008	0.024	Schmid and Schlatter, 1985
		Marsee et al., 2006; Fromme et al., 2007b; Wittassek et al., 2007a	0.059	Koch et al., 2004a and 2005b; Koch and Angerer, 2007
		Itoh et al., 2005	0.073	Koch et al., 2004b
		Itoh et al., 2007	0.062	Koch et al., 2005b
		Calafat and McKee, 2006	0.13	Anderson et al., 2001
		David, 2000	Not reported	Schmid and Schlatter, 1985?
	MEHHP	Koch et al., 2003b	0.074	Schmid and Schlatter, 1985
		Calafat and McKee, 2006; Fromme et al., 2007b; Marsee et al., 2006; Wittassek et al., 2007a	0.23	Koch et al., 2005b
		ECB DEHP, 2008	0.247	Koch et al., 2003b
		SCHER, 2008	Not Reported	Koch et al., 2004b
	MEOHP	Koch et al., 2003b	0.055	Schmid and Schlatter, 1985
		Calafat and McKee, 2006; Marsee et al., 2006; Fromme et al., 2007b; ECB DEHP, 2008; Wittassek et al., 2007a	0.15	Koch et al., 2003b, 2004a, and 2005b; Koch and Angerer, 2009
	5cx-MEPP	Wittassek et al., 2007a	0.185	Koch et al., 2005b
	2cx-MMHP	Wittassek et al., 2007a	0.042	Koch et al., 2005b
	Sum of 5cx-MEPP, MEHHP, MEOHP, 2cx-MMHP, MEHP	Wittassek et al., 2007a	0.669	Koch et al., 2005b
		SCENIHR, 2008	Not Reported	Anderson et al., 2001; Koch et al., 2004b; Koch et al., 2005b; Schmid and Slatter, 1985.
	Sum of MEHP, MEHHP and MEOHP	Wittassek et al., 2007b	0.442	Koch et al., 2005b
		SCENIHR, 2008	Not Reported	Koch et al., 2003b; Wittassek et al., 2007a and b
DEP	MEP	Koch et al., 2003b; Calafat and McKee, 2006; Marsee et al., 2006; Chen et al., 2008	0.69	Assume same as DBP (Anderson et al., 2001)

Table 5.6-6. Urinary Excretion Factor (F_{UE}) Values Used in Calculating Daily Intake Using the David (2000) Approach (continued)

Phthalate Diester	Metabolite Measured	Exposure Study	F_{UE}	Source
		Itoh et al., 2007	1 and 0.69	No human data available. Range of 0.69 to 1 based on hydrophilic properties.
		David, 2000	Not reported	Schmid and Schlatter, 1985?
DIBP	MiBP	Marsee et al., 2006; Fromme et al., 2007b; Wittassek et al., 2007a	0.69	Assume same as MBP and DBP (Anderson et al., 2001)
		SCHER, 2008	Not reported	Koch et al., 2004b
DINP	MINP	David, 2000	Not reported	Schmid and Schlatter, 1985?
	OH-MiNP	Fromme et al., 2007b	0.202	Koch et al., 2004b and 2005b; Koch and Angerer, 2007
		Wittassek et al., 2007a	0.19	Koch and Angerer, 2007
	oxo-MiNP	Wittassek et al., 2007a	0.10	Koch and Angerer, 2007
	Sum of OH-MiNP and oxo-MiNP	Wittassek et al., 2007a	0.29	Koch and Angerer, 2007
DMP	MMP	Itoh et al., 2007	0.69 and 1	No human data available. Range of 0.69 to 1 based on hydrophilic properties.
DnOP	MnOP	Koch et al., 2003b	0.043	Albro and Moore, 1974

5.6.3. Description of the Indirect Scenario Approach to Calculating Cumulative Exposure

The indirect scenario approach to estimating cumulative exposure involves summing together exposures calculated from all exposure routes (oral, dermal, and inhalation) and sources. Example exposure sources include food, water, outdoor air, soil, indoor air, toys, personal care products, and other consumer products. Section 5.4 summarizes exposures calculated for the individual pathways of exposure.

The accuracy of the resulting cumulative exposures depends on the knowledge of a variety of factors, as discussed in Kamrin (2009). These factors include identification of significant sources of phthalates, concentrations of phthalates in the media and how the concentrations vary over time and location, and human behavior characteristics that impact exposure frequency and duration (e.g., such as amount and type of food ingested). As these types of data are difficult to assess, uncertainties in the indirect-scenario approach can be significant. Underestimation could occur if not all sources of exposure are known. Overestimation could occur if samples are contaminated from environmental sources or in the analytical process. As noted in ECB DEHP (2008), another issue with the indirect scenario approach is that the addition of several reasonable worst-case values (e.g., 95th percentile exposure values) could lead to unreasonable over estimation of exposures, as it is unlikely that an individual is part of the 5% highest exposed

individuals for all different exposure routes and sources. Also, modeling results may be misleading when they are influenced by infrequent, but high magnitude exposures, such as spray paint (Kamrin, 2009).

Cumulative exposures were calculated using the indirect scenario approach for populations in Europe, Canada, and the U.S. in studies conducted between 1994 and 2008. In addition to the use of different concentration data and country-specific use patterns, numerous other differences exist in how the exposures were calculated among the studies. One major difference is the sources/pathways of exposure included in the estimates. For example, some studies only provided cumulative exposure for the environmental routes (i.e., food, water, and air) or only consumer products. Another major difference is if internal or external exposures were reported and what factors were used to calculate internal exposures. Additionally, factors such as breathing rates and body weights varied among studies. As such, comparisons between the different studies should be made with caution.

The exposures calculated in the studies evaluated are presented in tables in Section 5.6.4 for banned phthalates, Section 5.6.5 for interim banned phthalates, and Section 5.6.6 for other phthalates. The tables are organized by population group. Brief descriptions of the studies are presented below.

Study Descriptions

Wormuth et al. (2006)

Wormuth et al. (2006) used a scenario-based approach to calculate cumulative daily internal exposures to eight phthalates (DEHP, DBP, BBP, DINP, DIDP, DnOP, DMP, and DIBP) in Europeans for seven age and gender groups (infants, toddlers, children, teenagers, and adults). For teenagers and adults, exposures were calculated separately for male and females. Daily internal exposures were converted from external exposures by applying uptake rates of different organs (*r*uptake, fraction of amount of phthalates that is transferred into the human body). Fifteen different exposure pathways were investigated. The oral scenarios included consumption of food, ingestion of dust and soil, mouthing plastic objects, and incidental ingestion of personal care products. Dermal scenarios included use of personal care products and plastic gloves. Dermal exposure from the use of other products such as textiles, cushions, toys, soil, dust, adhesives, and paints were considered insignificant. Inhalation scenarios included indoor air (buildings and cars), outdoor air, and spray paints. The personal care products included for the adult and adolescent exposures were deodorant, perfume, aftershave, hairstyling, shampoo, skin care, nail care, and makeup. Personal care products for babies included shampoo, oils, creams, lotions, and other preparations. The exposures were calculated using measured concentrations from a variety sources and other information such as frequency data. The study used realistic assumptions, even for maximum parameter values. Wormuth et al. (2006) state that the results may underestimate exposure to children slightly due to data that inappropriately reflect children's behavior. Also, additional sources can contribute to the consumer exposure to phthalates that are not included, such as certain pharmaceuticals which have been shown to contain high amounts of DnBP and DEHP. The results showed that infants and toddlers experience highest daily exposures in relation to their body weight to all eight investigated

phthalates. The use of consumer products and different indoor sources dominate the exposure to DMP, DEP, BBP, DINP, and DIDP, whereas food has a major influence on the exposure to DIBP, DBP, and DEHP.

Müller et al. (2003)

Müller et al. (2003) estimated cumulative daily exposures to five phthalates (DEHP, DBP, BBP, DINP, and DIDP) for adults and children in Denmark using a variety of exposure pathways similar to those assessed in Wormuth et al. (2006). However, estimates calculated by Müller et al. (2003) are considered external because the bioavailability of the substances were not been taken into account, except for the dermal exposure scenarios (toys and clothes, etc.) where a measured dermal absorption rate was used. The cumulative exposures in Müller et al. (2003) accounted for oral, inhalation, and dermal exposures from consumer products (consumer exposure) and the intake of food, air, and water contaminated with phthalates (indirect exposure via the environment). The estimated exposures via the environment includes both oral and inhalation exposure, but the inhalation exposure only constituted a minor part of the total daily intake; therefore, the exposure via the environment was considered oral. Consumer exposures were included for several scenarios including toys, building materials etc., infant formula and baby food, artificial leather and gloves, paints etc., and nail polish. They were in general estimated based on total amounts in the consumer products, emission data from products, as well as measured concentrations. Exposure to the environment was calculated multiple ways, including using measured concentrations in the environment and using local scale and regional scale estimations from the European Union System for Evaluation of Substances (EUSES) computer model calculations. The local scale provides estimates for exposures near point sources. At the regional scale, concentrations are averaged over a larger area. The local scale exposure estimations from EUSES were the highest, thus these estimations were used when available to calculate the cumulative exposures. An exception is for BBP in which no EUSES calculations were made. When combining all the exposure pathways, Müller et al. (2003) state that the most important route of exposure to the phthalates assessed is the oral route. Food is the dominant source, no matter how the EUSES estimations were made, except for DEHP, DINP and DIDP in the young children, where oral exposure through mouthing on toys also potentially could play a significant role. Müller et al. (2003) state that it is uncertain whether all exposure pathways have been identified and that not all of the identified pathways can be quantified properly.

European Union Risk Assessment Reports

Other studies which included consumer products in the cumulative exposure calculations are the ECB Risk Assessment Reports for DIDP and DINP (ECB DIDP, 2003 and ECB DINP, 2003). These studies included adult and children exposures from building materials and furniture, car and public transport interiors, clothing, gloves and footwear, food and food-related uses, toys, air, drinking water, and food. The indirect environmental portion of exposure (air, drinking water and food) was calculated using EUSES, as was also done by Müller et al. (2003). The maximum local scale estimates of exposure from EUSES were used in the calculation of cumulative exposure. The cumulative exposure estimates used worst-case estimates from typical exposure situations.

The ECB Risk Assessment Reports for DEHP, BBP, and DBP calculated consumer exposures for each pathway separately and for environmental exposures separately (food, air, water). They did not provide a single cumulative estimate. The EU report for DEHP states that adding worst-case exposures (i.e., 95th percentile) from different pathways would results in unrealistic exposure estimates because it is unlikely that a person would be in the top 5 percent category for each pathway. The individual consumer pathway scenarios assessed included food and food packing/infant formula, indoor air, and baby equipment and toys for BBP, indoor air, gloves, car interior, toys and child-care articles for DEHP, and nail polish, adhesives, cellophane wrapped food, and children's toys for DBP. The DEHP report did provide a combined estimate for multiple consumer pathways for adults (indoor air, gloves, and car interior) and children (indoor air, toys and child-care articles, and car interior). The environmental estimates in these reports were calculated using EUSES.

Chan and Meek (1994), Meek and Chan (1994), and Clark et al. (2003)

Three Canadian studies reported cumulative exposures for adults and children that included indoor air, outdoor air, drinking water food (including formula and breast milk), soil, and/or indoor dust. The studies are Chan et al. (1994), Meek et al. (1994), and Clark et al. (2003). Chan and Meek (1994) and Meek and Chan (1994) reported internal exposures for DBP and DEHP, respectively. Clark et al. (2003) is a probabilistic exposure assessment that reported external exposures for DEHP, DBP, BBP, DMP, and DEP. The Clark et al. (2003) study is based on concentrations in the environment from an unpublished industry report. None of the studies included exposure to consumer products in the estimates. According to Clark et al (2003), the possible underestimation of exposure from not including personal care products may be partially cancelled out by the over estimation of food exposure, particularly DEHP, BBP, and DBP, due to changes in food processing over time, loss of phthalates from cooking, and background contamination. Clark et al. (2003) determined that for all phthalates evaluated, the median estimated daily intake was highest for toddlers and lowest for infants. Additionally, Clark et al. (2003) determined that food represents the most important source of exposure (except BBP exposure for formula-fed infants). Ingestion of dust and inhalation of indoor air represented the most important non-food sources of exposure to the phthalates evaluated.

Wilson et al. (2003)

Wilson et al. (2003) calculated aggregate daily doses (sum of inhalation, dietary and non-dietary daily doses) to DBP and BBP for nine preschool children in the U.S. The doses represented exposure from home and day care centers. The day care centers were located in North Carolina and served low- and middle-income clients. Exposures were calculated using data collected in the study, including samples of indoor and outdoor air (inhalation dose), play area soil and floor dust (non-dietary dose), as well as duplicate diets (dietary dose). Other factors specific to each child were also used to calculate the doses, including time spent indoors and outdoors, time spent at home and daycare, ventilation rate (8.3 m^3/day), bodyweight, and weight of food intake. Calculated doses assumed 100% absorption, thus are considered external.

5.6.4. Cumulative Exposure Estimates for Banned Phthalates

This section summarizes cumulative exposures calculated for the banned phthalates DEHP, DBP, and BBP, as reported in various exposure studies. Cumulative exposures have been estimated using both the biomonitoring approach and the scenario approach.

5.6.4.1. DEHP

Table 5.6-7 summarizes the DEHP exposures calculated using the biomonitoring-based approach and Table 5.6-8 summarizes the DEHP exposures calculated using the scenario-based approach.

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
Adults								
United States								
David, 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot	MEHP	--	0.60	--	3.05	38.48
SCENIHR, 2008	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot	MEHP	--	--	1.3	--	--
Calafat and McKee, 2006	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot	MEHP	--	0.5	--	3.3	--
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot	MEHP	<LOD	--	0.71	3.6	46
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs ; n=192 (excluding women 20-40); spot	MEHP	<LOD	--	0.71	3.5	46
SCENIHR, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; >20 yrs; n=1,647; spot	MEHHP, MEOHP, MEHP	--	--	2.1	--	--
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; >20 yrs; 1,638; spot	MEHHP	--	--	1.7	15	--
SCENIHR, 2008	Silva et al., 2006	2003-2004; Age not reported; n=129; spot	5cx-MEPP, MEHHP, MEOHP, 2cx-MMHP, MEHP	--	--	1.9	--	--
Germany								
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=60; 24-hr	Sum of MEHP, MEHHP, MEOHP, 5cx-MEPP, 2cx-MMHP	0.78	--	3.9	9.9	39.8
		1989; 21-29 yrs; n=60; 24-hr		0.84	--	4.2	10.0	33.6
		1991; 22-29 yrs; n=60; 24-hr		1.2	--	4.0	18.8	23.6
		1993; 20-29 yrs; n=60; 24-hr		1.4	--	4.2	12.9	14.1
		1996; 20-29 yrs; n=145; 24-hr		0.76	--	3.7	13.4	30.4
		1998; 20-29 yrs; n=68; 24-hr		0.19	--	3.1	8.1	10.9

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
		1999; 21-28 yrs; n=60; 24-hr		1.0	--	2.7	9.6	13.9
		2001; 20-29 yrs; n=60; 24-hr		1.1	--	3.1	7.4	20.1
		2003; 20-28 yrs; n=59; 24-hr		0.82	--	2.4	5.7	7.1
		1988-2003; 20-29 yrs; n=632; 24-hr		0.19	--	3.5	10.1	39.8
		2001/2003; 20-29 yrs; n=119; 24-hr		0.82	--	2.7	6.4	20.1
SCENIHR, 2008	Wittassek et al., 2007c	2001/2003; 20-29; n=120; 24-hr	5cx-MEPP, MEHHP, MEOHP, 2cx-MMHP, MEHP	--	--	2.3	--	--
Calafat and McKee, 2006	Koch et al., 2004a	2003; 20-59 yrs; n=19 (M: 5; W: 14); first morning voids	MEHP	--	--	1.9	5.4	--
			MEHHP	--	--	3.2	5.5	--
			MEOHP	--	--	3.1	6.2	--
SCENIHR, 2008	Koch et al., 2004a	2003; Age not reported; n=36; spot	MEHHP, MEOHP, MEHP	--	--	3.8	--	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=50; spot	MEHP	--	--	2.2	7.2	--
			MEOHP	--	--	2.3	7.2	--
			MEHHP	--	--	2	6.5	--
Japan								
Itoh et al., 2005	Itoh et al., 2005	2004; 20-70 yrs (~71% M, ~ 74% between 20 and 29 yrs); n=35; spot	MEHP	0.37	--	1.8 (GM SD of 2.17)	--	7.3
Itoh et al., 2007	Itoh et al., 2005	2004; 20-70 yrs (~71% M, ~ 74% between 20 and 29 yrs); n=35; spot	MEHP	2.0 (min 95% CI)	2.7 (avg)	--	--	3.3 (max 95% CI)
Taiwan								
Chen et al., 2008	Chen et al., 2008	Year not reported; 20-60 yrs; n=60 (68% women); spot	MEHP	0.1	--	33.9	--	309.6
Children								
United States								
Calafat and McKee, 2006	Brock et al., 2002	2000;12-18 mo; n=19 (14 boys, 5 girls); spot	MEHP	--	2.8 (avg)	--	ND	--
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
Calafat and McKee, 2006	Silva et al., 2004 (NHANES 1999-2000)	1999-2000; 6-11 yrs; n=328; spot	MEHP	--	0.6	--	5.0	--
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-11 yrs; n=392; spot	MEHP	--	0.6	--	3.7	--
			MEHHP	--	2.4	--	13.2	--
			MEOHP	--	2.6	--	12.8	--
SCHER, 2008	CDC, 2005 (NHANES 2001-	2001-2002; 6-11 yrs; n=392; spot	MEHHP	--	--	3.8	24	--

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
	2002)							
SCENIHR, 2008	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-11 yrs; n=392; spot	MEHHP, MEOHP, MEHP	--	--	3.7	--	--
SCENIHR, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; 12-19 yrs; n=742; spot	MEHHP, MEOHP, MEHP	--	--	3	--	--
SCHER, 2008	Teitelbaum et al., 2008	2004; 6-10 yrs; n=35 (Hispanic and Black); spot (6 samples each over 6 mo.)	MEHHP	--	--	8.7	67	125
SCHER, 2008	Wolff et al., 2007	2004/2005; 6-9 yrs; n= 90 (all girls, 4 racial/ethnic groups); spot samples and early morning voids	MEHHP	--	--	5.0	--	--
Germany								
Calafat and McKee, 2006	Becker et al., 2004	2001-2002; 3-14 yrs; n=254; spot	MEHP	--	0.7	--	2.8	--
			MEHHP	--	2.6	--	10.7	--
			MEOHP	--	3.1	--	11.7	--
SCENIHR, 2008	Becker et al., 2004	2001-2002; 3-14 yrs; n=254; spot	MEHP	--	--	6.3	--	--
Wittassek et al., 2007b	Becker et al., 2004	2001-2002; 2-14 yrs; n=239; first morning voids	Sum of MEHP, MEHHP and MEOHP	0.6[a]	--	4.3[a]	15.2[a]	140[a]
				0.4[b]	--	7.8[b]	25.2[b]	409[b]
		2001-2002; 2-4 yrs; n=31; first morning voids		1.8[a]	--	5.7[a]	23.4[a]	140[a]
				0.4[b]	--	10.7[b]	45.0[b]	409[b]
		2001-2002; 5-6 yrs; n=46; first morning voids		1.3[a]	--	6.1[a]	14.7[a]	28.8[a]
				2.9[b]	--	10.0[b]	19.4[b]	43.7[b]
		2001-2002; 7-8 yrs; n=53; first morning voids		2.0[a]	--	4.9[a]	12.1[a]	19.7[a]
				2[b]	--	7.7[b]	18.3[b]	22.3[b]
		2001-2002; 9-11 yrs; n=56; first morning voids		0.6[a]	--	3.3[a]	13.9[a]	73.5[a]
				1.5[b]	--	8.1[b]	25.4[b]	139[b]
		2001-2002; 12-14 yrs; n=53; first morning voids		0.8[a]	--	2.7[a]	8.2[a]	33.1[a]
				1.2[b]	--	4.8[b]	16.8[b]	34[b]
Calafat and McKee, 2006	Koch et al., 2004a	2003; <7 yrs; n=36; spot	MEHP	--	1 (avg)	--	3.3	--
			MEHHP	--	3.5 (avg)	--	7.1	--
			MEOHP	--	3.8 (avg)	--	7.4	--
SCENIHR, 2008	Koch et al., 2004a	2003; 2-6 yrs; n=19; spot	MEHHP, MEOHP, MEHP	--	--	5.6	--	--
Koo and Lee, 2005	Koo and Lee, 2005	2003; 11-12 yrs; n=150; spot	MEHP	--	Males: 9.9; Females: 17.8[a] (avg)	6[a]	37.2[a]	--
			MEHP	--	--	2.072[b]	--	--

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
General Population								
United States								
Calafat and McKee, 2006	Silva et al., 2004 (NHANES 1999-2000)	1999-2000; 6≥20 yrs; n=2,536; spot	MEHP	--	0.7	--	4.0	--
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
SCENIHR, 2008	Silva et al., 2004 (NHANES 1999-2000)	1999/2000; >6 yrs; n=2,541; spot	MEHHP, MEOHP, MEHP	--	--	1.6	--	--
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6->20 yrs; =2,772; spot	MEHP	--	0.9	--	7.1	--
			MEHHP	--	2.1	--	16.8	--
			MEOHP	--	2.2	--	15.6	--
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; age not reported; n=702 (non-Hispanic blacks); spot	MEHP	--	1.0	--	8.6	--
			MEHHP	--	2.4	--	18.4	--
			MEOHP	--	2.5	--	18.0	--
SCENIHR, 2008	Barr et al., 2003	Year and age not reported; n= 62; spot	MEHHP, MEOHP, MEHP	--	--	4.3	--	--
Germany								
Koch et al., 2003b	Koch et al., 2003b	2002; 7-63 yrs; n=85 (women: 53; men: 32); first-morning voids	MEHP	<LOQ	--	10.3	38.3	165
			MEOHP	2.9	--	14.2	52.8	147
			MEHHP	2.3	--	13.5	51.4	185
			Øsec. DEHP metabolites MEOHP and MEOHP)	2.6	--	13.7	52.1	166
Calafat and McKee, 2006	Koch et al., 2003a	2002; 7-63 yrs; n=85 (women: 53; men: 32); first-morning voids	MEHP	--	2.7	--	7.5	--
			MEHHP	--	6.5	--	16.3	--
			MEOHP	--	7.4	--	18.9	--
SCENIHR, 2008	Koch et al., 2003a	2002; 7-63 yrs; n=85 (women: 53; men: 32); first-morning voids	MEHHP, MEOHP, MEHP	--	--	5.8	--	--
ECB DEHP, 2008	Koch et al., 2003a	2002; 7-63 yrs; n=85 (women: 53; men: 32); first-morning voids	Average of MEHHP and MEOHP	--	--	--	17[e]	--
Wittassek and Angerer, 2008	Unpublished (Koch et al.)	Year not reported; 6-80 yrs; n=102; sample type not reported	Sum of MEHP, MEHHP, MEOHP, cx-MEHP	--	--	2.7	--	42.2
Calafat and McKee, 2006	Calafat et al., 2004b	2002; 4-83 days; n=6; spot (41)	MEHP	--	85.0	--	641	--
			MEHHP	--	931	--	3523	--
			MEOHP	--	1256	--	4566	--
SCENIHR, 2008	Kato et al., 2004	2001; age not reported; n=127; spot	MEHHP, MEOHP	--	--	2.4	--	--
Men Only								
United States								
Calafat and McKee,	CDC, 2005 (NHANES 2001-	2001-2002; 6-60 yrs; n=1,367; spot	MEHP	--	0.8	--	6.8	--
			MEHHP	--	2.0	--	15.5	--

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
2006	2002)		MEOHP	--	2.1	--	14.8	--
Calafat and McKee, 2006	Duty et al., 2004	Year and age not reported; n=220; spot	MEHP	--	1.5	--	28.4	--
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30;24-hr	Sum of MEHP, MEHHP, MEOHP, 5cx-MEPP, 2cx-MMHP	--	--	3.8	13.5	--
		1989; 21-29 yrs; n=30; 24-hr		--	--	4.5	22.2	--
		1991; 22-29 yrs; n=30; 24-hr		--	--	3.5	10.2	--
		1993; 20-29 yrs; n=30; 24-hr		--	--	4.7	12.7	--
		1996; 20-29 yrs; n=77; 24-hr		--	--	3.7	14.0	--
		1998; 20-29 yrs; n=38; 24-hr		--	--	2.9	8.4	--
		1999; 21-28 yrs; n=30; 24-hr		--	--	2.1	10.0	--
		2001; 20-29 yrs; n=30; 24-hr		--	--	3.3	6.8	--
		2003; 20-28 yrs; n=30; 24-hr		--	--	2.2	6.4	--
		1988-2003; 20-29 yrs; n=352; 24-hr		--	--	3.4	10.2	--
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=25; first-morning voids	Øsec. DEHP metabolites (MEOHP and MEHHP)	--	--	16.9	65.0	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 15-56 yrs; n=23; spot	MEHP	--	--	2.4	7.6	--
			MEOHP	--	--	2.5	6.5	--
			MEHHP	--	--	2.3	6	--
Women Only								
United States								
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MEHP	<LOD	--	0.71	3.8	10
Calafat and McKee, 2006	Hoppin et al., 2002	1996-97; 35-49 yrs; n=35 (African-American); first morning voids	MEHP	--	2.7 (avg)	--	--	16.7
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
Calafat and McKee, 2006	Adibi et al., 2003	2000; 18-35 yrs; n=25; spots	MEHP	--	8.8 (avg)	--	--	97.4
			MEHHP	--	ND	--	ND	--
			MEOHP	--	ND	--	ND	--
SCENIHR, 2008	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MEHHP, MEOHP, MEHP	--	--	1.4	--	--
Marsee et al., 2006	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MEHHP	<LOD [c]	--	1.33 [c]	9.11 [c]	128.5 [c]
			MEOHP	<LOD [c]	--	2.00 [c]	12.8 [c]	158.9 [c]
			avg. MEHHP + MEOHP	<LOD [c]	--	1.7 [c]	10.72 [c]	143.7 [c]
			MEHP	<LOD [c]	--	2.37 [c]	16.8 [c]	73.9 [c]
			MEHP	<LOD [d]	--	1.32 [d]	9.32 [d]	41.1 [d]

Table 5.6-7. DEHP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-60 yrs; n= 1,405; spot	MEHP		1.0	--	7.6	--
			MEHHP		2.2	--	18.3	--
			MEOHP		2.4	--	16.5	--
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	Sum of MEHP, MEHHP, MEOHP,5cx-MEPP, 2cx-MMHP	--	--	3.9	22	--
		1989; 21-29 yrs; n=30; 24-hr		--	--	3.5	9.4	--
		1991; 22-29 yrs; n=30; 24-hr		--	--	5.0	23.0	--
		1993; 20-29 yrs; n=30; 24-hr		--	--	4.2	13.8	--
		1996; 20-29 yrs; n=68; 24-hr		--	--	3.5	12.7	--
		1998; 20-29 yrs; n=30; 24-hr		--	--	3.2	8.3	--
		1999; 21-28 yrs; n=30; 24-hr		--	--	3.1	11.6	--
		2001; 20-29 yrs; n=30; 24-hr		--	--	2.7	13.6	--
		2003; 20-28 yrs; n=29;24-hr		--	--	2.5	5.7	--
		1988-2003; 20-29 yrs; n=307; 24-hr		--	--	3.5	10.5	--
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=34; first-morning voids	Øsec. DEHP metabolites (MEOHP and MEHHP)	--	--	12.5	27.4	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=27; spot	MEHP	--	--	1.9	7.1	--
			MEOHP	--	--	2.3	8.2	--
			MEHHP	--	--	1.7	7	--
Fujimaki et al., 2006 (reported in Matsumoto et al, 2008)	Fujimaki et al., 2006	2003; age not reported; n=40 (pregnant); spot	MEHHP	0.66	--	4.55	--	17.9
			MEOHP	1.47	--	3.51	--	8.57
			MEHP	3.45	--	10.4	--	41.6
Koo and Lee, 2005	Koo and Lee, 2005	2003; 20-73 yrs; n=150; spot	MEHP	--	41.7 (avg)	21.4	158.4	--
				--	--	4.434	--	--

a. Daily intake calculated using the creatinine method (David, 2000).
b. Daily intake calculated using the volume-based method.
c. Daily intake calculated using the David (2000) method.
d. Daily intake calculated using the Kohn et al. (2000) method.

-- = Statistic not reported/calculated
CI = Confidence interval
GM SD = Geometric standard deviation
LOD = Limit of detection
LOQ = Limit of quantitation
M = Men
max = Maximum
min = Minimum
ND = Not detected
W = Women

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample type (spot/first-morning void/24 hr)
- Metabolites reported as 5oxo-MEHP and 5OH-MEHP are reported in this report as MEOHP and MEHHP, respectively.
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-8. DEHP Daily Intake Values (µg/kg/d) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal (by applying uptake rates of different organs)	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format for infants and toddlers. Highest average daily intake was highest for infants. For toddlers, intake was between infants and children.	Ingestion of food (~50%), ingestion of dust (>35%), mouthing toys (8 to 9%)
			1-3	13		Ingestion of food (~50%), ingestion of dust (>35%), mouthing toys (8 to 9%)
			4-10	27	5th Percentile: 0.1 Median: 1.78 95th Percentile: 15.8	Ingestion of food (~90%)
			11-18	57.5	Results only reported in graph format for adolescents (male and female separately). Average daily intake was similar to children.	Ingestion of food (>90%).
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	0.5-1	8	Worst case: 285[a] (273.8 via oral, 1.9 via inhalation, 9.0 via dermal)	Mouthing toys and ingestion of food
			1-6	8	Worst case: 151 [a] (133.4 via oral, 1.9 via inhalation, 15.9 via dermal)	Ingestion of food
			7-14	26	Worst case: 49 [a] (40 via oral, 0.9 via inhalation, 7.8 via dermal)	Ingestion of food
ECB DEHP, 2008 (Europe)	Internal	Example multiple consumer pathway: Indoor air (building materials), toys, childcare products, and car interior[b]	NR	8	233.4	NR
		Environmental only[b] (outdoor air, drinking water, and food)	NR	8	19.4 (regional scale) 83.1 (local scale, near sewage treatment plant)	NR
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products***	0-0.5	NR	Median: 5-7.3	Formula or breast milk (~50%), ingestion of dust (~50%), indoor air (1%)
			0.5-4	NR	Median: 25.8	Ingestion of food (92% to 95%), ingestion of dust (4.2% to 6.6%), indoor air (1%)
			5-11	NR	Median: 18.9	Ingestion of food (92% to 95%), ingestion of dust (4.2% to 6.6%), indoor air (1%)

Table 5.6-8. DEHP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
			12-19	NR	Median: 10	Ingestion of food (92% to 95%), ingestion of dust (4.2% to 6.6%), indoor air (1%)
*Meek and Chan, 1994 (as reported in Shea, 2003; SCENIHR, 2008; and NTP-CERHR DEHP, 2006) (Canada)	Internal	Ambient air, indoor air, drinking water, food, and soil. ***Does not include consumer products.***	0-0.5	NR	Median: 9	Food, followed by indoor air and drinking water, ambient air and soil.
			0.5-4	NR	Median: 19	
			5-11	NR	Median: 14	
			12-19	NR	Median: 8.2	
Adults						
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	20-70	70	Worst case: 26 [a] (20 via oral, 0.5 via inhalation, 5.8 via dermal)	Oral pathway
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food, soil, and indoor dust. ***Does not include consumer products.***	20-70	NR	Median: 8.2	Ingestion of food (92% to 95%), ingestion of dust (4.2% to 6.6%), indoor air (1%)
*Meek and Chan, 1994 (as reported in Shea, 2003; SCENIHR, 2008; and NTP-CERHR DEHP, 2006) (Canada)	Internal (?)	Ambient air, indoor air, drinking water, food, and soil. ***Does not include consumer products.***	20-70	NR	Median: 5.8	Food, followed by indoor air and drinking water, ambient air and soil.
*Meek and Chan, 1994 (as reported in Shea, 2003; SCENIHR, 2008; and NTP-CERHR DEHP, 2006) (Canada)	Internal (?)	Ambient air, indoor air, drinking water, food, and soil. ***Does not include consumer products.***	20-70	NR	Median: 5.8	Food, followed by indoor air and drinking water, ambient air and soil.
ECB DEHP, 2008 (Europe)	Internal	Example multiple pathway: Indoor air (building materials), gloves, and car interior	NR	60	12*	NA
		Environmental only (air, drinking water, and food)	NR	70	1.93 (regional scale) 14.8 (local scale near sewage treatment plant)	NA
Doull, 1999 (from Huber et	Internal	Food only	NR	NR	3-30 [c]	Food

Table 5.6-8. DEHP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
al., 1996) (United States)						
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints Oral, dermal, inhalation	18-80	60	5th Percentile: 0.2 Median: 2.54 95th Percentile: 14.7	Ingestion of food (98%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints Oral, dermal, inhalation	18-80	70	5th Percentile: 0.24 Median: 2.85 95th Percentile: 16.3	Ingestion of food (98%)

a. Exposure estimates using measured concentrations in the environment instead of the maximum local exposure from EUSES are 30 to 40 times lower.
b. ECB DEHP (2008) did not derive total combined exposures because of unrealistic results when summing worst-case values. EU suggests using biomonitoring data to assess combined exposure.
c. Estimate reported in NTP-CERHR DEHP (2006).

NA = Not Applicable
NR = Not Reported

5.6.4.2. DBP

Table 5.6-9 summarizes the DBP exposures calculated using the biomonitoring-based approach and Table 5.6-10 summarizes the DBP exposures calculated using the scenario-based approach.

Table 5.6-9. DBP Daily Intakes Estimated From Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
Adults							
United States							
David, 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%W); spot	MBP	--	1.56 (GM)	6.87	116.96
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%W); spot	MBP	0.084	1.5	7.2	110
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; >20 yrs; 1,638; spot	MBP	--	0.6	2.6	--
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=60; 24-hr	MBP	0.72	7	24.2	27.8
		1989; 21-29 yrs; n=60; 24-hr	MBP	1.5	7.5	21.7	70.1
		1991; 22-29 yrs; n=60; 24-hr	MBP	2.1	6.4	14.3	28.7
		1993; 20-29 yrs; n=60; 24-hr	MBP	1.5	6.6	44.4	56.3

Table 5.6-9. DBP Daily Intakes Estimated From Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
		1996; 20-29 yrs; n=145; 24-hr	MBP	1.1	3.7	15.5	90.2
		1998; 20-29 yrs; n=68; 24-hr	MBP	0.22	3.1	11.9	20.3
		1999; 21-28 yrs; n=60; 24-hr	MBP	0.83	2.8	16.2	32.8
		2001; 20-29 yrs; n=60; 24-hr	MBP	0.81	2.5	19.4	116
		2003; 20-28 yrs; n=59; 24-hr	MBP	0.49	1.9	5.3	71.8
		1988-2003; n=20-29; n=632; 24-hr	MBP	0.22	4.1	19.1	116
		2001/2003; 20-29 yrs; n=119; 24-hr	MBP	0.49	2.2	7.3	116
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=50; spot	MBP	--	1.7	4.2	--
Japan							
Itoh et al., 2005	Itoh et al., 2005	2004; 20-70 yrs (~ 74% between 20 and 29 yrs); n=35(~71% men); spot	MBP	0.22	1.3 (2.1 GM SD)	--	4.5
Itoh et al., 2007	Itoh et al., 2005	2004; 20-70 yrs (~ 74% between 20 and 29 yrs); n=35(~71% men); spot	MBP	1.2 (min 95% CI)	1.7 (avg)	--	2.2 (max 95% CI)
Taiwan							
Chen et al., 2008	Chen et al., 2008	Year not reported; 21-67 yrs; n=60 (68% women); spot	MBP	ND	2.2	--	23.5
Children							
United States							
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; 6-11 yrs; n=392; spot	MBP	--	1.3	5.3	--
SCHER, 2008	Teitelbaum et al., 2008	2004; 6-10 yrs; n=35 (Hispanic and Black); spot (6 samples each over 6 mo.)	MBP	--	1.9	6.0	24.0
Germany							
Koch et al., 2007	Koch et al., 2007	2001-2002; 2-14 yrs; n=239; first morning voids	MBP	0.66[a]	4.07[a]	14.9[a]	76.4[a]
				0.91[b]	7.61[b]	30.5[b]	110[b]
		2001-2002; 2-4 yrs; n=31; first morning voids	MBP	1.36[a]	6.46[a]	18.1[a]	25.9[a]
				0.09[b]	10.5[b]	37.2[b]	54.8[b]
		2001-2002; 5-6 yrs; n=46; first morning voids	MBP	1.9[a]	5.05[a]	12.3[a]	25.3[a]
				3.16[b]	7.47[b]	19.5[b]	31.5[b]
		2001-2002; 7-8 yrs; n=53; first morning voids	MBP	1.69[a]	4.85[a]	23.3[a]	76.4[a]
				1.6[b]	7.17[b]	33[b]	88.9[b]
		2001-2002; 9-11 yrs; n=56; first morning voids	MBP	0.81[a]	4.02[a]	9.1[a]	11.8[a]
				1.55[b]	8.47[b]	27.2[b]	40.5[b]
		2001-2002; 12-14 yrs; n=53; first morning voids	MBP	0.66[a]	3.09[a]	11.2[a]	73.3[a]
				0.91[b]	5.29[b]	24.5[b]	110[b]
		2001-2002; 2-14 yrs; n=133 (boys only); first morning voids	MBP	0.66[a]	4.46[a]	12.3[a]	73.2[a]
				0.98[b]	7.04[b]	28.2[b]	110[b]
		2001-2002; 2-14 yrs n=106 (girls only); first morning voids	MBP	0.81[a]	4.74[a]	17.1[a]	76.4[a]
				0.91[b]	7.76[b]	30.1	88.9[b]

Table 5.6-9. DBP Daily Intakes Estimated From Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
General Population							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs (excluding women 20-40); n=192; spot	MBP	0.084	1.4	6.5	50
Germany							
Koch et al., 2003b	Koch et al., 2003b	2002; 7-63 yrs; n=85 (W: 53; M: 32); first-morning voids	MBP	1.84	5.22	16.2	22.6
Wittassek and Angerer, 2008	Unpublished (Koch et al.)	Year not reported; 6-80 yrs; n=102; sample type not reported	MBP and 3cx-MPP (sum)	--	2.1	--	230
Men Only							
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	MBP	--	5.9	17.6	--
		1989; 21-29 yrs; n=30; 24-hr	MBP	--	6.3	23.4	--
		1991; 22-29 yrs; n=30; 24-hr	MBP	--	6.0	11.3	--
		1993; 20-29 yrs; n=30; 24-hr	MBP	--	6.8	51.5	--
		1996; 20-29 yrs; n=77; 24-hr	MBP	--	3.4	17.2	--
		1998; 20-29 yrs; n=38; 24-hr	MBP	--	3.2	13.5	--
		1999; 21-28 yrs; n=30; 24-hr	MBP	--	2.3	23.7	--
		2001; 20-29 yrs; n=30; 24-hr	MBP	--	2.8	34.0	--
		2003; 20-28 yrs; n=30; 24-hr	MBP	--	1.5	4.3	--
		1988-2003; 20-29 yrs; n=352; 24-hr	MBP	--	3.7	16.2	--
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=25; first-morning voids	MBP	--	6.0	19.9	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 15-56 yrs; n=23; spot	MBP	--	1.8	3.9	--
Women Only							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MBP	0.24	1.7	32	113
Marsee et al., 2006	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MBP	<LOD [c]	0.84 [c]	2.34 [c]	5.86 [c]
				<LOD [d]	0.67 [d]	1.87 [d]	4.70 [d]
			MBP + MiBP	<LOD [c]	0.99 [c]	2.68 [c]	5.98 [c]
				<LOD [d]	0.79 [d]	2.15 [d]	2.15 [d]
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	MBP	--	7.9	26.8	--
		1989; 21-29 yrs; n=30; 24-hr	MBP	--	7.7	42.8	--
		1991; 22-29 yrs; n=30; 24-hr	MBP	--	7.3	22.4	--
		1993; 20-29 yrs; n=30; 24-hr	MBP	--	6.6	27.6	--
		1996; 20-29 yrs; n=68; 24-hr	MBP	--	4.1	27	--
		1998; 20-29 yrs; n=30; 24-hr	MBP	--	3.1	9.3	--
		1999; 21-28 yrs; n=30; 24-hr	MBP	--	2.8	20	--
		2001; 20-29 yrs; n=30; 24-hr	MBP	--	2.5	55.7	--
		2003; 20-28 yrs; n=29;24-hr	MBP	--	2.2	39.3	--
		1988-2003; 20-29 yrs; n=307; 24-hr	MBP	--	4.6	20.3	--

Table 5.6-9. DBP Daily Intakes Estimated From Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=34; first-morning voids	MBP	--	8.1	24.1	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=27; spot	MBP	--	1.7	4.4	--

a. Daily intake calculated using the creatinine method (David, 2000).
b. Daily intake calculated using the volume-based method.
c. Daily intake calculated using the David (2000) method.
d. Daily intake calculated using the Kohn et al. (2000) method.

-- = Statistic not reported/calculated
CI = Confidence interval
GM = Geometric Mean
GM SD = Geometric Standard Deviation
LOD = Limit of Detection
M = Men
Max = Maximum
Min = Minimum
W = Women

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample type (spot/first-morning void/24 hr)
- Metabolites reported as MnBP and MnBuP are reported in this report as MBP.
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-10. DBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of Exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal (by applying uptake rates of different organs)	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format for infants and toddlers. Highest average daily intake was highest for infants. For toddlers, intake was between infants and children.	Ingestion of food (~65%), indoor air (~20%), and dust (10%)
			1-3	13		Ingestion of food (~60%), indoor air (~30%), and dust (10%)
			4-10	27	5th Percentile: 0.15 Median: 1.21 95th Percentile: 16.9	Ingestion of food (~60%), indoor air (20%-40%), and dust (10%)
			11-18	57.5	Results only reported in graph format for adolescents (male and female separately). Average daily intake was similar to	Ingestion of food (~30%-60%), inhalation of indoor air (14%-22%), personal care products (15%-50%)

Table 5.6-10. DBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of Exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
					children.	
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	0.5-1	8	Worst case: 208.4[a] (208 via oral, 0.4 via inhalation)	Ingestion of food
			1-6	8	Worst case: 400.4 [a] (400 via oral, 0.4 via inhalation)	Ingestion of food
			7-14	26	Worst case (without floor wax): 200.18 [a] (200 via oral, 0.18 via inhalation) Worst case with floor wax: 210.3 [a] (200 via oral, 10.3 via inhalation)	Ingestion of food
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products.***	0-0.5	NR	Median: 1.5-2.9	Ingestion of food (62.7% - 82.6%), ingestion of dust (9.7% – 19.1%), indoor air (7.7%-15.2%), drinking water (0%-2.9%)
			0.5-4	NR	Median: 14	Ingestion of food (94.7%), indoor air (4.0%), ingestion of dust (1.1%)
			5-11	NR	Median: 11	Ingestion of food (94.7%), indoor air (4.4%)
			12-19	NR	Median: 6.4	Ingestion of food (95.6%), indoor air (3.6%)
Chan and Meek, 1994 (as reported in NTP-CERHR DBP, 2000) (Canada)	Internal (?)	Ambient air, indoor air, drinking water, food, and soil. ***Does not include consumer products.***	0-0.5	NR	Median: 2.4	Food, followed by indoor air and drinking water, soil and ambient air.
			0.5-4	NR	Median: 5.0	
			5-11	NR	Median: 5.3	
			12-19	NR	Median: 2.3	
Wilson et al., 2003 (United States)	External	Indoor air, outdoor air, play area soil and floor dust, food	Preschool children	NR	Average: 1.44 Median: 1.14 Range: 0.745 – 2.85	NR
ECB DBP, 2003-04	Internal	Environmental only (air, drinking water, and food)	NR	??	0.786 – 92.5 (local scale)	NR

Table 5.6-10. DBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of Exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
(Europe)		***Does not include consumer products.***			0.359 (regional scale)	
General Population						
NTP-CERHR DBP, 2000 and 2003 (United States)	NR	NR	NR	NR	2-10 [c]	NR
Adults						
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	20-70	70	Worst case (without floor wax): 60.23 [a] (60 via oral, 0.2 via inhalation, 0.03 via dermal) Worst case (with floor wax): 66.03 [a] (60 via oral, 6 via inhalation, 0.03 via dermal)	Oral pathway
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food, soil, and indoor dust. ***Does not include consumer products.***	20-70	NR	Median: 5.6	Ingestion of food (95.8%), indoor air (3.6%)
Chan and Meek, 1994 (as reported in NTP-CERHR DBP, 2000) (Canada)	Internal (?)	Ambient air, indoor air, drinking water, food, and soil. ***Does not include consumer products.***	20-70	NR	Median: 1.9	Food, followed by indoor air and drinking water, soil and ambient air.
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	5th Percentile: 1.48 Median: 3.53 95th Percentile: 38.6	Ingestion of food (~80%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	5th Percentile: 1.6 Median: 3.61 95th Percentile: 18.6	Ingestion of food (~90%)

a. Exposure estimates using measured concentrations in the environment instead of the maximum local exposure from EUSES are 30 to 40 times lower. Quantitative data on the use pattern of DBP were scarce and several assumptions had to be made to generate the quantitative data.
b. Exposures via the consumer route were calculated for individual pathways (nail polish, adhesives, cellophane wrapped food, and children's toys), but not added together to provide a total cumulative exposure.
c. NTP Conclusion of the Expert Panel.

NR = Not Reported

5.6.4.3. BBP

Table 5.6-11 summarizes the BBP exposures calculated using the biomonitoring-based approach and Table 5.6-12 summarizes the BBP exposures calculated using the scenario-based approach.

Table 5.6-11. BBP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		
						50th	95th	Max
Adults								
United States								
David, 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%women); spot	MBzP	--	0.73	--	3.34	19.79
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%women); spot	MBzP	0.094	--	0.88	4.0	29
ECB BBP, 2007	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%women); spot	MBzP	--	0.78	--	3.5[a]	--
ECB BBP, 2007	CDC, 2003	1999-2000; >20 yrs; n=1,461; spot	MBzP	--	0.45	--	2.2	--
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; >20 yrs; 1,638; spot	MBzP	--	--	0.4	2.2	--
Germany								
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=60; 24-hr	MBzP	0.02	--	0.25	0.77	6.6
		1989; 21-29 yrs; n=60; 24-hr	MBzP	0.07	--	0.3	2.2	2.8
		1991; 22-29 yrs; 60 yrs; 24-hr	MBzP	0.11	--	0.43	1.6	2.8
		1993; 20-29 yrs; n=60; 24-hr	MBzP	0.07	--	0.27	1.9	2.2
		1996; 20-29 yrs; n=145; 24-hr	MBzP	0.04	--	0.29	5.5	27.3
		1998; 20-29 yrs; n=68; 24-hr	MBzP	0.01	--	0.22	1.4	4.0
		1999; 21-28 yrs; n=60; 24-hr	MBzP	0.03	--	0.21	3.7	10.9
		2001; 20-29 yrs; n=60; 24-hr	MBzP	0.02	--	0.22	0.75	0.99
		2003; 20-28 yrs; n=59; 24-hr	MBzP	0.05	--	0.22	0.91	1.74
		1988-2003; 20-29 yrs; n=632; 24-hr	MBzP	0.01	--	0.26	1.6	27.3
		2001/2003; 20-29 yrs; n=119; 24-hr	MBzP	0.02	--	0.22	0.75	1.74
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=50; Spot	MBzP	--	--	0.2	1.2	--
Japan								
Itoh et al., 2007	Itoh et al., 2005	2004; 20-70 yrs (~71% M, ~ 74% between 20 and 29 yrs); n=35; spot	MBzP	0.074 (min 95% CI)	0.093 (average)	--	--	0.11 (max 95% CI)
Taiwan								
Chen et al., 2008	Chen et al., 2008	Year not reported; 20-60 yrs; n=60 (68% W); spot	MBzP	ND	--	0.2	--	1.6
Children								
United States								
ECB BBP, 2007	Brock et al., 2002	2000;12-18 mo; n=19 (14 boys, 5 girls); spot	MBzP	--	4.9	--	--	18.2[b]
ECB BBP, 2007	CDC, 2003	1999-2000; 6-11 yrs; n=328; spot	MBzP	--	1.54	--	5.46[c]	--
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; 6-11 yrs; n=392; spot	MBzP	--	--	1.2	6.5	
SCHER, 2008	Teitelbaum et al., 2008	2004; 6-10 yrs; n=35 (Hispanic and Black); spot samples (6 samples each over 6 mo.)	MBzP	--	--	1.2	9.6	27.5

Table 5.6-11. BBP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		
						50th	95th	Max
SCHER, 2008	Wolff et al., 2007	2004/2005; 6-9 yrs; n= 90 (all girls, 4 racial/ethnic groups); spot samples and early morning voids	MBzP	--	--	1.0	--	--
Germany								
Koch et al., 2007	Koch et al., 2007	2001-2002; 2-14 yrs; n=239; first morning voids	MBzP	0.06[a] 0.05[b]	-- --	0.42[d] 0.77[e]	2.57[d] 4.48[e]	13.9[d] 31.3[e]
		2001-2002; 2-4 yrs; n=31; first morning voids	MBzP	0.18[a] 0.05[b]	-- --	0.61[d] 1.25[e]	2.38[d] 3.92[e]	3.88[d] 13.2[e]
		2001-2002; 5-6 yrs; n=46; first morning voids	MBzP	0.15[a] 0.2[b]	-- --	0.49[d] 0.8[e]	1.56[d] 3.57[e]	3.35[d] 5.77[e]
		2001-2002; 7-8 yrs; n=53; first morning voids	MBzP	0.16[a] 0.18[b]	-- --	0.54[d] 0.94[e]	2.46[d] 3.69[e]	13.9[d] 25.1[e]
		2001-2002; 9-11 yrs; n=56; first morning voids	MBzP	0.06[a] 0.14[b]	-- --	0.29[d] 0.74[e]	2.97[d] 7.79[e]	11.7[d] 31.3[e]
		2001-2002; 12-14 yrs; n=53; first morning voids	MBzP	0.09[a] 0.11[b]	-- --	0.3[d] 0.45[e]	1.98[d] 4.12[e]	3.28[d] 5.59[e]
		2001-2002; 2-14 yrs; n=133 (boys only); first morning voids	MBzP	0.09[a] 0.12[b]	-- --	0.48[d] 0.91[e]	3.03[d] 5.56[e]	13.9[d] 25.1[e]
		2001-2002; 2-14 yrs n=106 (girls only); first morning voids	MBzP	0.06 0.05	-- --	0.31[d] 0.72[e]	1.81[d] 3.78[e]	11.7[d] 31.3[e]
General Population								
United States								
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs (excluding women 20-40); n=192; spot	MBzP	0.11	--	0.78	3.4	29
Germany								
Koch et al., 2003b	Koch et al., 2003b	2002; 7-63 yrs; n=85 (W: 53; M: 32); first-morning voids	MBzP	0.16	--	0.60	2.52	4.51
ECB BBP, 2007	Koch et al., 2003b	2002; 7-63 yrs; n=85 (W: 53; M: 32); first-morning voids	MBzP	--	0.60	--	2.52	--
Wittassek and Angerer, 2008	Unpublished (Koch et al.)	Year not reported; 6-80 yrs; n=102	MBzP	--	--	0.3	--	2.2
Men Only								
Germany								
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	MBzP	--	--	0.25	0.72	--
		1989; 21-29 yrs; n=30; 24-hr	MBzP	--	--	0.31	2.4	--
		1991; 22-29 yrs; n=30; 24-hr	MBzP	--	--	0.39	1.4	--
		1993; 20-29 yrs; n=30; 24-hr	MBzP	--	--	0.28	1.3	--
		1996; 20-29 yrs; n=77; 24-hr	MBzP	--	--	0.29	9.1	--
		1998; 20-29 yrs; n=38; 24-hr	MBzP	--	--	0.23	1.9	--
		1999; 21-28 yrs; n=30; 24-hr	MBzP	--	--	0.19	6.5	--
		2001; 20-29 yrs; n=30; 24-hr	MBzP	--	--	0.2	0.87	--
		2003; 20-28 yrs; n=30; 24-hr	MBzP	--	--	0.19	0.68	--
		1988-2003; 20-29 yrs; n=352; 24-hr	MBzP	--	--	0.25	1.9	--
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=25; first-morning voids	MBzP	--	--	1.1	4.1	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 15-56 yrs; n=23; spot	MBzP	--	--	0.2	1	--

Table 5.6-11. BBP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		
						50th	95th	Max
Women Only								
United States								
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MBzP	0.094	--	1.2	4.5	7.8
ECB BBP, 2007	Hoppin et al., 2002	1996-1997; 35-49 yrs; n=46 (African American); first morning void (2 consecutive days each)	MBzP	--	0.8	--	--	3.6
Marsee et al., 2006	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MBzP	<LOD[c] <LOD[d]	-- --	0.50[f] 0.35[g]	2.47[f] 1.74[g]	15.5[f] 10.9[g]
Germany								
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	MBzP	--	--	0.26	3.4	--
		1989; 21-29 yrs; n=30; 24-hr	MBzP	--	--	0.27	1.7	--
		1991; 22-29 yrs; n=30; 24-hr	MBzP	--	--	0.47	2.1	--
		1993; 20-29 yrs; n=30; 24-hr	MBzP	--	--	0.26	2.1	--
		1996; 20-29 yrs; n=68; 24-hr	MBzP	--	--	0.29	3.4	--
		1998; 20-29 yrs; n=30; 24-hr	MBzP	--	--	0.2	1.3	--
		1999; 21-28 yrs; n=30; 24-hr	MBzP	--	--	0.26	6.6	--
		2001; 20-29 yrs; n=30; 24-hr	MBzP	--	--	0.24	0.75	--
		2003; 20-28 yrs; n=29; 24-hr	MBzP	--	--	0.26	1.4	--
		1988-2003; 20-29 yrs; n=307; 24-hr	MBzP	--	--	0.28	1.5	--
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=34; first-morning voids	MBzP	--	--	1.4	5.0	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=27; spot	MBzP	--	--	0.2	1.5	--

a. 95th percentile value used for adults in the EU Risk Assessment Report (ECB BBP, 2007)
b. 95th percentile value used for young children (1-2 yrs) in the EU Risk Assessment Report (ECB BBP, 2007)
c. 95th percentile value used for children 6-11 yrs in the EU Risk Assessment Report (ECB BBP, 2007)
d. Daily intake calculated using the creatinine method (David, 2000).
e. Daily intake calculated using the volume-based method.
f. Daily intake calculated using the David (2000) method.
g. Daily intake calculated using the Kohn et al. (2000) method.

-- = Statistic not reported
CI = Confidence Interval
LOD = Limit of Detection

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample Type (spot/first-morning void/24 hr)
- Phthalates reported as BBzP are reported in this report as BBP.
- Metabolites reported as MBeP are reported in this report as MBzP.
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-12. BBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format for infants and toddlers. Highest average daily intake was highest for infants. For toddlers, intake was between infants and children.	Ingestion of dust (>70%), food (20%), and air (5%)
			1-3	13		
			4-10	27	5th Percentile: 0.005 Median: 0.04 95th Percentile: 1.08	Ingestion of food (73%), indoor air (26%), and dust (10%)
			11-18	57.5	Results only reported in graph format for adolescents. Average daily intake was similar to adults.	Inhalation of spray paint (>70%), ingestion of food (>30%)
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	0.5-1	8	Worst case: 4.2 (4.1 via oral, 0.12 via inhalation)	Ingestion of food
			1-6	8	Worst case: 6.0 (5.9 via oral, 0.12 via inhalation)	Ingestion of food
			7-14	26	Worst case: 2.5 (2.4 via oral, 0.05 via inhalation)	Ingestion of food
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breast milk), and indoor dust. ***Does not include consumer products.***	0-0.5	NR	Median: 1.5	Ingestion of dust (70.2%), ingestion of food (27.4%), drinking water (2.0%)
			0.5-4	NR	Median: 9.3	Ingestion of food (91.1%), ingestion of dust (8.5%)
			5-11	NR	Median: 7.9	Ingestion of food (94.3%), ingestion of dust (5.3%)
			12-19	NR	Median: 5.7	Ingestion of food (95.5%), ingestion of dust (4.2%)
Wilson et al., 2003 (United States)	External	Indoor air, outdoor air, play area soil and floor dust, food	Pre-school childr en	NR	Average: 1.90 Median: 1.96 Range: 0.744 – 2.88	Not Reported
ECB BBP, 2007 (Europe)	Internal	Food and food packaging, toys, infant formula, indoor air and the environment (outdoor air, drinking water, and food)	0-2	NR	31.55 (29.5 from environment using local scale estimate) 2.18 (0.13 from environment using regional scale estimate)	Not Reported
NTP-CERHR BBP, 2003 And NTP-CERHR BBP, 2000	NR	Food	NR	NR	Up to three-fold higher than adults, which is estimated at 2	Primary pathway is food. Negligible exposures from infant formula, dermal absorption, drinking water, or soil intake.
Adults						
Müller et al., 2003	External (except for	Food, air, drinking water, toys, building materials,	20-70	70	Worst case: 1.0	Oral pathway

Table 5.6-12. BBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
(Denmark)	dermal exposures)	artificial leather and gloves, paints, nail polish.			(0.97 via oral, 0.03 via inhalation, 0.03 via dermal)	
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food, soil, and indoor dust. ***Does not include consumer products.***	20-70	NR	Median: 3.7	Ingestion of food (95.5%), indoor air (4.2%)
ECB BBP, 2007 (Europe)	Internal	Food and food packaging, indoor air and the environment (outdoor air, drinking water, and food)	NR	NR	29.83 (29.5 from environment using local scale estimate) 0.46 (0.13 from environment using regional scale estimate)	Not Reported
NTP-CERHR BBP, 2003 and NTP-CERHR BBP, 2000 (United States)	Internal	Food	NR	NR	2 (Estimate from IPCS, 1999, based on Canadian food survey)	Primary pathway is food. Negligible exposures from infant formula, dermal absorption, drinking water, or soil intake.
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	5th Percentile: 0.03 Median: 0.27 95th Percentile: 1.65	Ingestion of food (60%), inhalation of spray paint (40%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	5th Percentile: 10.03 Median: 0.31 95th Percentile: 1.9	Ingestion of food (60%), inhalation of spray paint (40%)

NR = Not Reported

5.6.5. Cumulative Exposure for Interim Banned Phthalates

This section summarizes cumulative exposures calculated for the interim banned phthalates DINP, DIDP, and DnOP. Cumulative exposures have been calculated using both the biomonitoring approach and the scenario approach for DINP. For DIDP, cumulative exposures have only been calculated using the scenario approach. For DnOP, cumulative exposures have only been calculated using the biomonitoring approach.

5.6.5.1. DINP

Table 5.6-13 summarizes the DINP exposures calculated using the biomonitoring-based approach and Table 5.6-14 summarizes the DINP exposures calculated using the scenario-based approach.

Table 5.6-13. DINP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
Adults							
United States							
David, 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot samples	MINP	--	0.21 (GM)	1.08	14.35
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot samples	MINP	<LOD	<LOD	1.7	22
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs ; n=192 (excluding women 20-40); spot	MINP	<LOD	<LOD	1.4	22
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=60; 24-hr	Sum of OH-MiNP and oxo-MiNP	0.04	0.20	1.4	2.2
		1989; 21-29 yrs; n=60; 24-hr		0.03	0.24	2.2	12.9
		1991; 22-29 yrs; n=60; 24-hr		0.05	0.22	4.5	20.2
		1993; 20-29 yrs; n=60; 24-hr		0.04	0.27	1.7	2.6
		1996; 20-29 yrs; n=145; 24-hr		0.02	0.33	1.6	3.4
		1998; 20-29 yrs; n=68; 24-hr		0.06	0.30	7.8	11.7
		1999; 21-28 yrs; n=60; 24-hr		0.05	0.32	1.9	3.1
		2001; 20-29 yrs; n=60; 24-hr		0.10	0.34	2.3	4.4
		2003; 20-28 yrs; n=59; 24-hr		0.12	0.40	1.5	3.2
		1988-2003; 20-29 yrs; n=632; 24-hr		0.03	0.29	1.7	20.2
		2001/2003; 20-29 yrs; n=119; 24-hr		0.1	0.37	1.5	4.4
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=50; spot	OH-MiNP	--	0.7	3.5	--
General Population							
Germany							
Wittassek and Angerer, 2008	Unpublished (Koch et al.)	Year not reported; 6-80 yrs; n=102; sample type not reported	Sum of MINP, oxo-MiNP, OH-MiNP, and cx-MiNP	--	0.6	--	36.8
Men Only							
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30;24-hr	Sum of OH-MiNP and oxo-MiNP	--	0.2	1.8	--
		1989; 21-29 yrs; n=30; 24-hr		--	0.24	0.99	--
		1991; 22-29 yrs; n=30; 24-hr		--	0.19	3	--
		1993; 20-29 yrs; n=30; 24-hr		--	0.26	1.6	--
		1996; 20-29 yrs; n=77; 24-hr		--	0.31	1.8	--
		1998; 20-29 yrs; n=38; 24-hr		--	0.29	9.6	--
		1999; 21-28 yrs; n=30; 24-hr		--	0.22	3.0	--

Table 5.6-13. DINP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
		2001; 20-29 yrs; n=30; 24-hr		--	0.35	1.7	--
		2003; 20-28 yrs; n=30; 24-hr		--	0.37	2.7	--
		1988-2003; 20-29 yrs; n=352; 24-hr		--	0.27	1.7	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 15-56 yrs; n=23; spot	OH-MiNP	--	0.8	3.5	--
Women Only							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MINP	<LOD	<LOD	3.7	7.8
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	Sum of OH-MiNP and oxo-MiNP	--	0.19	1.2	--
		1989; 21-29 yrs; n=30; 24-hr		--	0.24	8.7	--
		1991; 22-29 yrs; n=30; 24-hr		--	0.32	11.8	--
		1993; 20-29 yrs; n=30; 24-hr		--	0.27	2.1	--
		1996; 20-29 yrs; n=68; 24-hr		--	0.34	1.5	--
		1998; 20-29 yrs; n=30; 24-hr		--	0.3	7.7	--
		1999; 21-28 yrs; n=30; 24-hr		--	0.37	1.3	--
		2001; 20-29 yrs; n=30; 24-hr		--	0.33	3.7	--
		2003; 20-28 yrs; n=29;24-hr		--	0.45	1.3	--
		1988-2003; 20-29 yrs; n=307; 24-hr		--	0.32	1.7	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=27; spot	OH-MiNP	--	0.6	3.5	--

-- = Statistic not reported
LOD = Limit of detection

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample Type (spot/first-morning void/24 hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-14. DINP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal (by applying uptake rates of different organs)	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints (Oral, dermal, inhalation)	0-1	5.5	Results only reported in graph format. Infants had the highest average daily intake, followed by toddlers, children, and adolescents.	Mouthing soft plastic objects (>90%)
			1-3	13		
			4-10	27		
			11-18	57.5		Dust (>30%), air (~30%), spray paints (20%), and gloves (>10%)

Table 5.6-14. DINP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	0.5-1	8	Worst case: 218 (217 via oral, 0.05 via inhalation, 1 via dermal)	Ingestion of food
			1-6	8	Worst case: 65.1 (63.4 via oral, 0.05 via inhalation, 1.6 via dermal)	Ingestion of food
			7-14	26	Worst case: 10.8 (10 via oral, 0.02 via inhalation, 0.8 via dermal)	Ingestion of food
ECB DINP, 2003 (Europe)	Internal	Toys, building materials, furniture, car and public transport interiors, food and food related uses, air, drinking water.	0.5 - 3	??	410 with toys[a] (250 via consumer exposure and 160 via local scale environmental exposure) (Consumer exposure is 50 without toys)	Not Reported
		Building materials, furniture, car and public transport interiors, clothing, gloves and footwear, food and food related uses, air, drinking water. ***No toys***	3-15	??	20[a] (10 via consumer exposures and 10 via local scale environmental exposure)	Not Reported
NTP-CERHER DINP, 2003 (United States)	Internal	Food	NR	NR	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998). Children are expected to be in the upper portion of the range, and may exceed the estimate due to mouthing toys and other objects that contain DINP.	
Adults						
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	20-70	70	Worst case: 5.7 (5.1 via oral, 0.01 via inhalation, 0.6 via dermal)	Oral Pathway
ECB DINP, 2003 (Europe)	Internal	Building materials, furniture, car and public transport interiors, clothing, gloves and	NR	NR	20[a] (10 via consumer exposures and 10 via local scale	NR

Table 5.6-14. DINP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
		footwear, food and food related uses, air, drinking water.			environmental exposure)	
NTP-CERHER DINP, 2003 (United States)	Internal	Food	NR	NR	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998).	
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	Results only reported in graph format.	Dust (>30%), air (~30%), spray paints (20%), and gloves (>10%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	Results only reported in graph format.	Dust (>30%), air (~30%), spray paints (20%), and gloves (>10%)
General Population						
NTP-CERHER, 2003 (United States)	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998).					

a. Total combined exposure may be higher because all sources of human exposure may not have been quantified.

NR = Not reported

5.6.5.2. DIDP

Table 5.6-15 summarizes the DIDP exposures calculated using the scenario-based approach. Cumulative exposures have not been calculated using the biomonitoring-based approach for DIDP.

Table 5.6-15. DIDP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of exposure)	Age	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format. Infants had the highest average daily intake, followed by toddlers, children, and adolescents.	Mouthing soft plastic objects (~55-60%), dust (40%)
			1-3	13		
			4-10	27		Mouthing soft plastic objects (82%), indoor air(16%)
			11-18	57.5		Food (>55%, dust (>10%), gloves (5%-7%), spray paint (5%-7%)
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	0.5-1	8	Worst case: 211 (210 via oral, 0.009 via inhalation, 1 via dermal)	Ingestion of food
			1-6	8	Worst case: 55 (53.4. via oral, 0.01 via inhalation, 1.6 via dermal)	Ingestion of food
			7-14	26	Worst case: 7.6 (6.8 via oral, 0.004 via inhalation, 0.8 via dermal)	Ingestion of food
ECB DIDP, 2003 (Europe)	Internal	Toys, building materials, furniture, car and public transport interiors, food and food related uses, air, drinking water.	0.5-3	NR	200 without toys [a] 400 with toys [a] (230 via consumer exposure with toys and 30 via consumer exposure without toys; 170 via local scale environmental exposure)	Not Reported
		Building materials, furniture, car and public transport interiors, clothing, gloves and footwear, food and food related uses, air, drinking water. ***No toys***	3-15	NR	20[a] (10 via consumer exposures and 10 via local scale environmental exposure)	Not Reported
NTP-CERHER DIDP, 2003 (United States)	Internal	Food	NR	NR	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998). However, NTP-CERHR DIDP (2003) states that exposure in children could represent an important exception to the propriety of extrapolating DIDP exposures from DEHP data. Potential unique exposures from mouthing toys and other objects that may contain DIDP do not allow adequate confidence of using DEHP estimates for estimating DIDP exposure in infants and toddlers.	

Table 5.6-15. DIDP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of exposure)	Age	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Adult						
Müller et al., 2003 (Denmark)	External (except for dermal exposures)	Food, air, drinking water, toys, building materials, artificial leather and gloves, paints, nail polish.	20-70	70	Worst case: 3.5 (2.9 via oral, 0.002 via inhalation, 0.6 via dermal)	Oral pathway
ECB DIDP, 2003 (Europe)	Internal	Building materials, furniture, car and public transport interiors, clothing, gloves and footwear, food and food related uses, air, drinking water.	NR	NR	20 [a] (10 via consumer exposures and 10 via local scale environmental exposure)	NR
NTP-CERHER DIDP, 2003 (United States)	Internal	Food	NR	NR	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998).	
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	Results only reported in graph format.	Food (70%), dust (>10%), air (13%), gloves (5%-7%), and spray paints (5%-7%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	Results only reported in graph format.	Food (70%), dust (>10%), air (13%), gloves (5%-7%), and spray paints (5%-7%)

NR = Not Reported

5.6.5.3. DnOP

Table 5.6-16 summarizes the DnOP exposures calculated using the biomonitoring-based approach and Table 5.6-17 summarizes the DnOP exposures calculated using the scenario-based approach.

Table 5.6-16. DnOP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	50th Percentile	95th Percentile	Max
Adults							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; 56%W; n=289; spot	MnOP	<LOD	0.0096	0.96	13
General Population							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs (excluding women 20-40 yrs); n=192; spot	MnOP	<LOD	0.015	1.0	13
Germany							
Koch et al., 2003b	Koch et al., 2003b	2002; 7-63 yrs; 62% women; n= 85; first-morning voids	MnOP	--	<LOQ	0.6	--
Men Only							
Germany							
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=25; first-morning voids	MnOP	--	<LOQ	0.6	--
Women Only							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MnOP	<LOD	<LOD	0.65	1.5
Germany							
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=34; first-morning voids	MnOP	--	<LOQ	0.4	--

<LOD = Less than the detection limit
<LOQ = Less than the limit of quantitation
-- = Statistic not reported

- Metabolites reported as MOP are reported in this report as MnOP.
- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample Type (spot/first-morning void/24 hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-17. DnOP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
NTP-CERHER DnOP, 2003 (United States)	Based on the physiochemical characteristics, exposure to DINP is expected to be lower than DEHP, which is estimated to range from 3 to 30 (Doull, 1998).					

5.6.6. Cumulative Exposure for Other Phthalates (Not Banned or Interim Banned)

This section summarizes cumulative exposures calculated for phthalates other than banned or interim banned. Cumulative exposures have been calculated using the biomonitoring-based

approach for DMP, DEP, DiBP, and DCHP. Using the scenario-based approach, cumulative exposures have been calculated using for DMP, DEP, and DiBP.

5.6.6.1. DMP

Table 5.6-18 summarizes the DMP exposures calculated using the biomonitoring-based approach and Table 5.6-19 summarizes the DMP exposures calculated using the scenario-based approach.

Table 5.6-18. DMP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)	
				Average	95% CI
Adults					
Japan					
Itoh et al., 2007	Itoh et al., 2005	2004; 20-70 yrs (~71% M, ~ 74% between 20 and 29 yrs); n=35; spot	MMP	1.4	0.64 - 2.1
			MMP	2.0	0.93 - 3.1

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample Type (spot/first-morning void/24 hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-19. DMP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal (by applying uptake rates of different organs)	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints (Oral, dermal, inhalation)	0-1	5.5	Results only reported in graph format. Infants had the highest average daily intake and adolescents had the lowest.	Indoor/outdoor air (almost 100%)
			1-3	13		
			4-10	27		
			11-18	57.5		Indoor/outdoor air (almost 80%-90%)
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products***	0-0.5	NR	Median: 0.01-0.05 (non-food sources)	Indoor air (8.2 36%), ingestion of dust (14.4%-63.5%), drinking water (0%-77.3%)
			0.5-4	NR	Median: 1.6[a]	Ingestion of food (97.8%), drinking water (1.3%)
			5-11	NR	Median: 1.4 [a]	Ingestion of food (97.9%), drinking water (1.2%)

Table 5.6-19. DMP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
			12-19	NR	Median: 0.7 [a]	Ingestion of food (98.3%), drinking water (1.0%)

Table 5.6-19. DMP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors (continued)

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed (Routes of exposure)	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Adults						
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products.***	20-70	NR	Median: 0.7 [a]	Ingestion of food (98.7%)
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	Results only reported in graph format.	Indoor air (~70%), personal care products (~20%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	Results only reported in graph format.	Indoor air (~80%), personal care products (~10%)

a. Exposures from food calculated using ½ detection limit for DEP.

NR = Not reported

5.6.6.2. DEP

Table 5.6-20 summarizes the DEP exposures calculated using the biomonitoring-based approach and Table 5.6-21 summarizes the DEP exposures calculated using the scenario-based approach.

Table 5.6-20. DEP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
Adults								
United States								
David, 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%W); spot samples	MEP	--	12.34	--	93.33	242.81
Calafat and McKee, 2006	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%W); spot samples	MEP	--	11.4	--	86.6	--
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56%W); spot samples	MEP	<LOD	--	12	110	320
Germany								
Calafat and McKee, 2006	Koch et al., 2004a	2003; 20-59 yrs; n=19; (M= 5, W=14; first morning voids	MEP	--	ND	--	ND	
Japan								
Itoh et al., 2007	Itoh et al., 2005	2004; 20-70 yrs (~ 74% between 20 and 29 yrs); n=35(~71% M); spot	MEP	0.39[a] (min 95% CI)	0.77[a] (avg)	--	--	--
				0.56[b] (min 95% CI)	1.2[b] (avg)	--	--	--
Taiwan								
Chen et al., 2008	Chen et al., 2008	Year not reported; 21-67 yrs; n=60 (68% women); spot	MEP	n.d.	--	n.d.	--	27.9
Children								
United States								
Calafat and McKee, 2006	Brock et al., 2002	2000;12-18 mo; n=19 (14 boys, 5 girls); spot	MEP	--	6.3 (avg)	--	ND	--
Calafat and McKee, 2006	Silva et al., 2004 (NHANES 1999-2000)	1999-2000; 6-11 yrs; n=328; spot	MEP	--	1.7	--	11.4	--
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-11 yrs; n=392; spot	MEP	--	1.8	--	15.3	--
Germany								
Calafat and McKee, 2006	Becker et al., 2004	2001-2002; 3-14 yrs; n=254; spot	MEP	--	ND	--	ND	--
Calafat and McKee, 2006	Koch et al., 2004a	2003; <7 yrs; n=36; spot	MEP	--	ND	--	ND	--
General Population								
United States								
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs (excluding women 20-40); n=192; spot	MEP	<LOD	--	11	130	320
Calafat and McKee, 2006	Silva et al., 2004 (NHANES 1999-2000)	1999-2000; 6->20 yrs; n=2,536; spot	MEP	--	5.4	--	64.7	--
Calafat and	CDC, 2005 (NHANES	2001-2002; 6->20 yrs; n=2,772;	MEP	--	5.5	--	61.7	--

Table 5.6-20. DEP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)				
				Min	Geo. Mean	Percentile		Max
						50th	95th	
McKee, 2006	2001-2002)	spot						
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; age not reported; n=702 (non-Hispanic blacks); spot	MEP	--	8.2	--	68.7	--
Germany								
Koch et al., 2003b	Koch et al., 2003b	2002; 7-63 yrs; n=85 (W: 53; M: 32); first-morning voids	MEP	0.33	--	2.32	22.1	69.3
Calafat and McKee, 2006	Koch et al., 2003b	same	MEP	--	5.5	--	22.2	--
Neonates								
United States								
Calafat and McKee, 2006	Calafat et al., 2004b	2002; 4-83 days; n= 6; spot samples (41)	MEP	--	ND	--	ND	--
Men Only								
United States								
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-60 yrs; n=1,367; spot	MEP	--	4.9	--	69.0	--
Calafat and McKee, 2006	Duty et al., 2004	Year and age not reported; n=220;	MEP	--	6.1	--	66.4	--
Germany								
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=25; first-morning voids	MEP	--	--	2.4	20.0	--
Women Only								
United States								
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MEP	0.90	--	13	90	170
Calafat and McKee, 2006	Hoppin et al., 2002	1996-97; 35-49 yrs; n=35 (African-American); first morning voids	MEP	--	6 (avg)	--	--	20.2
Marsee et al., 2006	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MEP	<LOD[c]	--	6.64[c]	112.3[c]	1263[c]
				<LOD[d]	--	5.32[d]	90.0[d]	1013[d]
Calafat and McKee, 2006	Adibi et al., 2003	2000; 18-35 yrs; n=25;spot	MEP		22.9 (avg)	--	--	183.1
Calafat and McKee, 2006	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-60 yrs; n=1,405; spot	MEP		6.2	--	47.4	--
Germany								
Koch et al., 2003b	Koch et al., 2003b	2002; 18-40 yrs; n=34; first-morning voids	MEP	--	--	4.4	33.6	--

a. Daily intake calculated using an F_{UE} value of 0.69.
b. Daily intake calculated using an F_{UE} value of 1.0.
c. Daily intake calculated using the David (2000) method.
d. Daily intake calculated using the Kohn et al. (2000) method.

LOD = Limit of detection
ND = Not Detected
-- = Statistic not reported

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample type (spot/first-morning void/24-hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-21. DEP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age (yrs)	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format. Infants had the highest average daily intake and children had the lowest.	Dermal and incidental ingestion of personal care products (up to 80%), indoor air (up to 30%),
			1-3	13		
			4-10	27		
			11-18	57.5		
			7-14	26		Dermal and incidental ingestion of personal care products (>80%), indoor air (~10%)
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products.***	0-0.5	NR	Median: 0.2 (does not include food because food data not available)	Indoor air (70.6%-89.9%), ingestion of dust (6.2%-7.8%), drinking water (0%-21.4%)
			0.5-4	NR	Median: 10.6	Ingestion of food (97.1%), indoor air (2.6%)
			5-11	NR	Median: 5.7	Ingestion of food (95.2%), indoor air (4.5%)
			12-19	NR	Median: 3.0	Ingestion of food (95.5%), indoor air (4.2%)
Adults						
Clark et al., 2003 (Canada)	External	Indoor air, outdoor air, drinking water, food (including infant formula and breads milk), soil, and indoor dust. ***Does not include consumer products.***	20-70	NR	Median: 2.5	Ingestion of food (95.3%), indoor air (4.4%)
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	5th Percentile: 0.005 Median: 1.43 95th Percentile: 64.9	Dermal and incidental ingestion of personal care products (>80%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	70	5th Percentile: 0.02 Median: 1.15 95th Percentile: 50.09	Dermal and incidental ingestion of personal care products (>80%)

NR = Not Reported

5.6.6.3. DiBP

Table 5.6-22 summarizes the DiBP exposures calculated using the biomonitoring-based approach and Table 5.6-23 summarizes the DiBP exposures calculated using the scenario-based approach.

Table 5.6-22. DiBP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	50th Percentile	95th Percentile	Max
Adults							
United States							
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001/2002; >20 yrs; 1,638; spot samples	MIBP	--	0.1	0.4	--
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=60; 24-hr	MiBP	0.27	1.1	3.6	6.2
		1989; 21-29 yrs; n=60; 24-hr	MiBP	0.30	1.0	4.2	12.9
		1991; 22-29 yrs; n=60; 24-hr	MiBP	0.36	1.2	8.7	20.2
		1993; 20-29 yrs; n=60; 24-hr	MiBP	0.39	1.2	2.8	4.8
		1996; 20-29 yrs; n=145; 24-hr	MiBP	0.45	1.6	8.4	29
		1998; 20-29 yrs; n=68; 24-hr	MiBP	0.10	1.4	5.8	12.2
		1999; 21-28 yrs; n=60; 24-hr	MiBP	0.41	1.5	4.4	15.1
		2001; 20-29 yrs; n=60; 24-hr	MiBP	0.29	1.6	4.6	12.6
		2003; 20-28 yrs; n=59; 24-hr	MiBP	0.46	1.4	3.9	5.2
		1988-2003; 20-29 yrs; n=632; 24-hr	MiBP	0.10	1.4	5.7	29
		2001/2003; 20-29 yrs; n=119; 24-hr	MiBP	0.29	1.5	4.2	12.6
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=50; spot	MiBP	--	1.7	5.2	--
Children							
United States							
SCHER, 2008	CDC, 2005 (NHANES 2001-2002)	2001-2002; 6-11 yrs; n=392; spot	MIBP	--	0.2	0.9	
SCHER, 2008	Teitelbaum et al., 2008	2004; 6-10 yrs; n=35 (Hispanic and Black); spot samples (6 samples each over 6 mo.)	MIBP	--	0.7	1.8	5.7
SCHER, 2008	Wolff et al., 2007	2004/2005; 6-9 yrs; n= 90 (all girls, 4 racial/ethnic groups); spot samples and early morning voids	MIBP	--	0.4	--	--
General Population							
Germany							
Wittassek and Angerer, 2008	Unpublished (Koch et al.)	Year not reported; 6-80 yrs; n=102; sample type not reported	MiBP	--	1.5	--	27.3

Table 5.6-22. DiBP Daily Intakes Estimated from Biomonitoring Studies (continued)

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	50th Percentile	95th Percentile	Max
Men Only							
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30;24-hr	MiBP	--	1.0	4.5	--
		1989; 21-29 yrs; n=30; 24-hr	MiBP	--	0.89	3.1	--
		1991; 22-29 yrs; n=30; 24-hr	MiBP	--	1.1	7.6	--
		1993; 20-29 yrs; n=30; 24-hr	MiBP	--	1.2	4.0	--
		1996; 20-29 yrs; n=77; 24-hr	MiBP	--	1.6	7.4	--
		1998; 20-29 yrs; n=38; 24-hr	MiBP	--	1.3	5.7	--
		1999; 21-28 yrs; n=30; 24-hr	MiBP	--	1.5	5.8	--
		2001; 20-29 yrs; n=30; 24-hr	MiBP	--	1.3	7.7	--
		2003; 20-28 yrs; n=30; 24-hr	MiBP	--	1.3	2.8	--
		1988-2003; 20-29 yrs; n=352; 24-hr	MiBP	--	1.3	4.8	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 15-56 yrs; n=23; spot	MiBP	--	1.8	5.3	--
Women Only							
United States							
Marsee et al., 2006	Swan et al., 2005	1999-2002; >18 yrs; n= 214 (pregnant); spot	MiBP	<LOD[a]	0.12[a]	0.41[a]	2.9[a]
			MiBP	<LOD[b]	0.09[b]	0.33[b]	2.3[b]
Germany							
Wittassek et al., 2007a	Wittassek et al., 2007a	1988; 21-29 yrs; n=30; 24-hr	MiBP	--	1.2	4.5	--
		1989; 21-29 yrs; n=30; 24-hr	MiBP	--	1.1	8.2	--
		1991; 22-29 yrs; n=30; 24-hr	MiBP	--	1.3	14.8	--
		1993; 20-29 yrs; n=30; 24-hr	MiBP	--	1.2	2.7	--
		1996; 20-29 yrs; n=68; 24-hr	MiBP	--	1.5	10.1	--
		1998; 20-29 yrs; n=30; 24-hr	MiBP	--	1.6	9.2	--
		1999; 21-28 yrs; n=30; 24-hr	MiBP	--	1.5	9.2	--
		2001; 20-29 yrs; n=30; 24-hr	MiBP	--	1.9	7.4	--
		2003; 20-28 yrs; n=29;24-hr	MiBP	--	1.5	4.7	--
		1988-2003; 20-29 yrs; n=307; 24-hr	MiBP	--	1.4	6.6	--
Fromme et al., 2007b	Fromme et al., 2007a	2005; 14-60 yrs; n=27 Spot	MiBP	--	1.6	4.7	--

a. Daily intake calculated using the David (2000) method.
b. Daily intake calculated using the Kohn et al. (2000) method.

-- Statistic not reported
LOD = Limit of detection

- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample Type (spot/first-morning void/24 hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

Table 5.6-23. DiBP Daily Intake Values (µg/kg/day) Estimated Using Scenario-Based Data from Environmental Analysis and Behaviors

Study (Country)	Type of Exposure Calculated	Sources of Exposure Assessed	Age	Body-weight (kg)	Daily Intake (µg/kg/day)	Primary Pathways of Exposure
Children						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, mouthing plastic objects, personal care products, plastic gloves, indoor air, outdoor air, spray paints	0-1	5.5	Results only reported in graph format. Infants had the highest average daily intake, followed by toddlers, adolescents, and children	Food (60%), dust (30%), indoor air (>8%)
			1-3	13		
			4-10	27		Food (~85%)
			11-18	57.5		Food (>95%)
Women Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	Results only reported in graph format.	Food (>95%)
Men Only						
Wormuth et al., 2006 (Europe)	Internal	Food, dust, personal care products, plastic gloves, indoor air, outdoor air, spray paints	18-80	60	Results only reported in graph format.	Food (>95%)

5.6.6.4. DCHP

Table 5.6-24 summarizes the DCHP exposures calculated using the biomonitoring-based approach. DCHP exposures were not calculated using the scenario-based approach.

Table 5.6-24. DCHP Daily Intakes Estimated from Biomonitoring Studies

Exposure Study	Biomonitoring Study	Biomonitoring Study Description	Metabolite Measured	Daily Intake (µg/kg/day)			
				Min	Percentile		Max
					50th	95th	
Adults							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs; n=289 (56% women); spot	MCHP	<LOD	0.026	0.25	2.3
General Population							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-60 yrs (excluding women 20-40); n=192; spot	MCHP	<LOD	0.012	0.25	2.3
Women Only							
United States							
Kohn et al., 2000	Blount et al., 2000 (NHANES III)	1988-1994; 20-40 yrs; n=97; spot	MCHP	<LOD	0.051	0.24	0.45

LOD = Limit of detection
- Biomonitoring Study Description = Sampling year; Age range; Sample number; Sample type (spot/first-morning void/24-hr)
- See Tables 5.6-3, 5.6-4, 5.6-5, and 5.6-6 for the calculation parameters used.

5.7. POPULATIONS WITH HIGH PHTHALATE EXPOSURE

This section summarizes the available literature that addresses population groups with potential high exposures to phthalates. High exposure populations to phthalates have been addressed in documents including, but not limited to, those prepared by National Research Council (NRC), ATSDR, NTP-CERHR, CDC, and authors of several review journal articles. Populations, other than those in the occupational (manufacturing and processing) sector, identified as ones potentially highly exposed were women of child-bearing age, newborns, infants and children, patients receiving dialysis regularly on a kidney machine, and patients receiving blood transfusions, such as hemophiliacs. Minority populations with potentially higher exposures mentioned in the literature have been Hispanics and blacks. In addition, it has been reported in the ATSDR toxicological profiles on selected phthalates that persons living near industrial facilities or hazardous waste sites with higher than average levels of phthalates could also have higher than average exposures. EWG (2000) has also noted that males may potentially be a population with a more sensitive toxic endpoint due to trends shown in male reproductive health that are similar to results found in animal studies.

The NRC (2008) has reviewed scientific literature on the human health effects of phthalates. NRC (2008) stated that the physiology, developmental stages, and the age appropriated behaviors of infants and children may increase their exposure to phthalates. NRC (2008) noted that exposures may occur through ingestion, inhalation, dermal absorption, and parental administration, but the relative contributions of the exposures to the total body burden at the various ages are not known. NRC (2008) referred to highly exposed persons as those having urinary metabolites concentrations that often exceed the 95th percentile of the general population (see Table 5.7-1). Other populations noted by NRC (2008), Shea (2003), and Green et al. (2005) as potentially highly exposed are neonates receiving medical treatment such as transfusions. Medications that contain phthalates in their coatings or delivery systems may contribute to high exposures in pregnant women, children, and persons taking the coated medications (NRC, 2008; Hauser et al., 2005).

ATSDR (1995; 1997; 2001; 2002) addressed populations with potentially high exposures in toxicological profiles for DnOP, DBP, DEP, and DEHP. For each phthalate, they noted that populations living near hazardous waste sites and workers in industries that produce or use plastics had potentially higher than average exposures. For the industrial workers, inhalation exposures are expected to be high especially from the materials processed at high temperatures. For DnOP, DBP, and DEHP, persons receiving medical treatments (dialysis, pre-term infants) involving the use of PVC tubing was reported as a group with potentially high exposures. For DBP, consumers of certain cosmetics, such as nail polish, may result in higher exposures from the use of these products. Women who work in nail and hair salons are presumed to get the highest exposures (EWG, 2000). ATSDR reported that many plastic articles used in the home and businesses contain DBP. Therefore, indoor concentrations may be higher than outdoor concentrations and populations working indoors may be exposed to the higher levels of DBP. At the time of the ATSDR report, the authors noted that sufficient information was not available to quantify the difference in indoor and outdoor exposures.

Table 5.7-1. Urinary Phthalate Metabolite Concentrations after Exceptional Exposures and Comparison Medians from Available NHANES or European Union Data

Exposure	Metabolite	Concentrations in Urine (µg/L)	Metabolite NHANES or EU	Medians [95th %] (µg/L)	Reference
Enteric-coated medication taken orally for 3 mo (n=1 male)	MBP MEP MEHP MBZP	16, 868 444 3 9	MBP MEP MEHP MBZP	19.3 [95][1] 171 [3,050][1] 4.3 [38][1] 16 [122][1]	Hauser et al., 2004
Intravenous tubing for platelet donation, maximum measured 4 h after donation (n=1 male)	MEHP MEHHP MEOHP MECPP	388 822 729 577	MEHP MEHHP MEOHP MECPP	7.6 [34][2] 21 [77][2] 16.7 [58][2] 26.9 [99][2]	Koch et al., 2005b
Neonatal intensive care unit, 33 samples from infants exposed for over 2 wk (n=6)	MEHP MEHHP MEOHP	129[3] 2, 221[3] 1, 697[3]	MEHP MEHHP MEOHP	4.4 [30][4] 32.9 [210][4] 22.6 [142][4]	Calafat et al., 2004b
Infants in neonatal intensive care unit (n=54)	MEHP MEHHP MEOHP MBP MBZP	22 (75th %=71)[3] 267 (75th %=644)[3] 256 (75th %=628)[3] 18 (75th %=45)[3] 41 (75th %=131)[3]	MEHP MEHHP MEOHP MBP MBZP	4.4 [30][4] 32.9 [210][4] 22.6 [142][4] 32.4 [157][4] 37 [226][4]	Weuve et al., 2006
Plastisol workers after shift (n=25)	MEHP MECPP	56[5] 104[5]	MEHP	4.3 [38][1]	Gaudin et al., 2008

Source: NRC (2008)

[1] U.S. males over 25 years old from NHANES 2001-2002 (CDC, 2005).
[2] German adults 20-29 years old (Wittassek et al., 2007).
[3] Median values, unless otherwise stated.
[4] U.S. children 6-11 years old from NHANES 2001-2002 (CDC, 2005). No data are available on neonates.
[5] Medians before shift. 16 µg/L (MEHP) and 38 µg/L (MECPP), which were slightly higher than in controls.

Animal and human studies show that exposures occur from the developing fetus through early infancy, childhood and beyond (NRC, 2008). Studies have shown that phthalates can cross the placenta, have been measured in amniotic fluid, and are present in human milk and in urine at all ages (NRC, 2008, Shea, 2003). Shea (2003) stated that neonates can have high exposures to DEHP and MEPH (toxic monoester metabolite) when undergoing blood product replacement, exchange transfusions, and extracorporeal membrane oxygenation.

NRC (2008) reported that except for MEP (metabolite of diethyl phthalate), in the U.S. population, urinary metabolites in children, males, Hispanic and Blacks are somewhat higher than for adults overall. Matsumoto et al. (2008) also noted this difference. Concentrations of MEHP, MBzP and MBP were higher in the youngest age (6-11 years old) and decreased with age. Non-Hispanic blacks had higher levels than non-Hispanic whites and Mexican Americans Matsumoto et al. (2008). This assessment of concentrations is based on data from the CDC Third National Report on Human Exposures to Chemicals. Of the 12 phthalates tested by the CDC, eleven were concentrated more highly in children than in adults (also see Table 5.2-2 in

Section 5.2, Biomonitoring). Concentrations were also higher in females than males. NRC (2008) noted that higher metabolite concentrations in children than for adults could be attributed to differences in exposure or possible differences in metabolism. CDC (2005) also noted a similar finding in the 1999-2000 and 2001-2002 NHANES subsamples. In the CDC biomonitoring study results, six of the eight highest measured levels of DBP were in the urine of women of child bearing age (EWG, 2000). Their data indicated that BDP exposures for up to 3 million women of childbearing age may be 20 times higher that exposures for the rest of the population (EWG, 2000).

5.8. UNCERTAINTY AND DATA LIMITATIONS

This section discusses the uncertainties and data gaps that exist in the exposure and dose assessments conducted on phthalates. It is evident that extensive research has been done to study and understand the risks posed by phthalates to humans and the environment. Several countries (Europe, Canada, U.S., and others) have implemented regulations and bans for specific uses of phthalates in recent years. It is, however, critical to realize that most procedures utilized to measure or estimate exposure/dose are associated with some amount of uncertainty, along with data limitations. In addition, there is considerable variability in the methodologies used for such calculations. Thus, it would be noteworthy to discuss and highlight some of the issues with variability and uncertainty regarding phthalate exposures.

Studies conducted by the NTP-CERHR of the U.S. Department of Health and Human Services highlighted critical data needs for individual phthalates. The NTP-CERHR (2000) study mentioned the need to extend and improve the physiologically-based pharmacokinetic (PBPK) model to include parameters for pregnant women and their fetuses as it relates to DBP exposure assessment. They also suggested quantifying the window of prenatal exposure to better estimate the postnatal male exposure effects. The NTP-CERHR DEHP(2006) document stated that both methods for calculating dose (probabilistic and dose reconstruction) have uncertainties. The former tends to over-estimate doses due to conservative model estimates. The dose reconstruction method (back calculation method) for estimating DEHP dose has uncertainties as it assumes a steady state exposure and does not differentiate between peak and background levels. Another simplification is the assumption that the metabolite excretion fraction is constant across populations of different age, race, and sex. The authors of this study also recommended that creatinine-adjusted DEHP metabolite concentrations should not be compared among populations with varying age groups. They suggested conducting follow-up studies of DEHP exposed human populations (particularly premature infants) to better understand the exposure process.

The Committee on the Health Risk of Phthalates (NRC, 2008) identified research needs and data gaps in exposure assessments. They include 1) identification of the most important sources of phthalate exposure and migration pathways that connect the sources to the general population, 2) identification of the full spectrum of phthalate metabolites (especially DEPH and DINP) and the determination of the most important metabolite to be used as a biomarker for human exposures, 3) improvement in the understanding of metabolism and how it would affect and change children and adults over their lifetime, 4) determination of the relationship between maternal urinary phthalate metabolite concentrations and those in the fetal compartments with an emphasis on

understanding the pharmacokinetics of phthalates, 5) characterization of human exposure to other anti-androgens and other factors that contribute to disturbed androgen action, and 6) the use of existing databases, such as NHANES, to assess exposure to multiple phthalates and other chemicals that may contribute to common biologic outcomes.

The CPSC (2001) study identified several uncertainties associated with determinations of exposure, hazard, and dose response. Those associated with exposure included: 1) lack of information about the specific portion of toys containing DINP, 2) lack of information about other consumer products containing DINP, and 3) uncertainties about the exact amount of time spent by the child using toys in their mouth that contain DINP. Uncertainties with hazard and dose response included: 1) methodology to extrapolate an effect from a lifetime exposure in rodents to a two to- three year exposure in young children, 2) lack of toxicological data of exposure of phthalates to children in their infancy and toddler years, and 3) lack of information about exposures to mammals that are not rodents.

Babich et al. (2004) also highlighted limitations and uncertainty involved in the human risk assessment of DINP. They concluded that DINP did not pose a cancer risk to humans mainly because of the lack of relevant information of peroxisome proliferation and related effects in humans. Their research indicated that data in human systems are limited and also, the epidemiological studies are limited in sample size and follow up routines. They also said that the estimates of average daily dose (ADI) lacked sufficient data on children and immature animals. Finally, all of their estimates were based only on oral exposure of DINP from soft toys and that the exposure information from other sources and routes was unavailable.

Kamrin (2009) provided a well reviewed write-up about the general uncertainties associated with most exposure assessments of phthalates. He pointed out that the two main methods used to assess overall human exposure to phthalates are modeling and biomonitoring and both are associated with data gaps and uncertainties. The accuracy of the modeling approach depends on the knowledge of concentrations of each phthalate in each source along with their spatial and temporal variations. Since, this type of data is difficult to quantify, uncertainties in exposure estimates are significant. Furthermore, as phthalates are found everywhere, contamination of samples from the environment may lead to overestimates of exposure. Wormuth et al.(2006) noted that results from modeling studies had high variabilities which were a result of different studies adapting different approaches and/or assumptions. Examples included the variability in choosing percentiles when trying to determine exposure estimates. Thus, using conservative estimates for each parameter would result in the overestimation of the real exposure. Another caveat of the modeling procedure lies in the overestimation of average daily doses. This occurs when annual exposures are overestimated based on infrequent but high magnitudes of exposure for particular items (like spray paints) within specific age groups of a population (Wormuth et al., 2006)

Usually, studies involving phthalates associate uncertainty factors with lowest observable adverse effect levels (LOAEL) and no observed adverse effect levels (NOAEL). Kamrin, (2009) highlighted the fact that these factors vary significantly from one study to another depending on the geographical location or association with a particular agency. Uncertainties also exist in the cumulative exposure assessments of phthalates. Kamrin (2009) pointed out that the mere

addition of exposure values from individual phthalates to come up with an overall exposure estimate is not appropriate. This is so because there are significant differences in the properties and behavior of phthalates. In addition, the effect of different phthalates in humans is different and thus, such lumped estimates might be unrealistic.

Besides the existence of such generic uncertainties in all phthalate exposure/dose estimates, individual studies have specific data gaps and limitations. Adibi et al. (2003) pointed out limitations in their statistical estimates which included small sample sizes, occurrences of extreme values which skewed results, and the fact that their study focused on pregnant women in New York and Krakow (Poland) and thus was limited in terms of race, ethnicity, gender, and age. Similar limitations in statistical measures were found in the CPSC Risk Assessment of DEHP in children's products (CPSC, 1983a). Some of these were: 1) uncertainties in extrapolating from high to low dose from animals to humans, 2) large variations of data while conducting non-linear data fits, and 3) lack of confidence limits on data due to large variability. They also pointed out that there existed large variation in plasticizer emission levels based on data collected from two different approaches. (Barr et al., 2005) attempted to use multiple regression to adjust for large variations in urinary creatinine concentrations. The main sources of uncertainty in their study included: 1) measurements taken from a specific sub-population, 2) lack of information on dietary variables, and 3) the absence of upper bound confidence intervals in the data.

6. CONCLUSIONS

o-DAPs are mainly used to soften and increase the flexibility of plastic consumer products such as shower curtains, medical devices, upholstery, raincoats, and soft squeeze toys (NTP-CERHR DBP, 2003). They can also be found in food wrappings, wood finishes, and upholstery (Hubinger and Havery, 2006). Additional applications include floor and wall coverings, windows and siding, solvents in inks, waxes and polishes, and coatings. Since phthalates have such wide-ranging applications in industry, they have become highly prevalent in the environment and can now be found in food, water, dust, and air. Consequently, exposure to animals and humans is a cause of concern.

The majority of the recent biological monitoring studies show that phthalate metabolites have been detected in virtually all humans tested (Fromme et al., 2007). Most of these biomonitoring studies analyzed urine samples from the general population for phthalate metabolites as biomarkers of the parent phthalates. In the U.S. specifically, it is estimated that more than 75% of the population has measurable levels of several phthalate metabolites in their urine (Stahlhut et al., 2007). For some metabolites, the detection frequency is as high as 100% across all demographic groups. In NHANES 1999-2000, the monoester metabolites of DEP, DBP, BBP, and DEHP were detected most frequently. The metabolites of DCHP, DnOP, and DINP were detected in less than 16% of the samples. Significant differences in metabolite concentrations were seen across various demographic groups. Additionally, children 6-12 years of age had higher concentrations of the DBP, BBP, and DEHP metabolites, whereas higher concentrations of the DEP metabolite were observed in adults (Silva et al., 2004).

Exposure to phthalates occurs through multiple routes, including oral (ingestion), dermal, inhalation, and intravenous (Blount et al., 2000). Many studies have attempted to quantify human exposures, however, this task is both impressive and subject to error (Shea, 2003). In general, there are two different approaches to estimating exposure. The indirect method estimates exposure from phthalate concentrations in products and environmental media, whereas the direct method estimates exposure from biological monitoring results.

Toys and Baby Equipment

Abundant phthalate concentration data are available for toys and baby equipment. The phthalates DEHP, DIDP, and DINP, and to a lesser extent DnOP, have been historically present in toys and/or teethers. The phthalates BBP and DBP have also been found in some toys, but only in trace amounts, probably as byproducts or impurities present during manufacture (Stringer et al., 2000). Review of available testing data from multiple countries show that phthalates were present in toys at levels up to 73% for DINP (CDTSC, 2008), 44% for DEHP (Bouma and Schakel, 2002), and 20.1% for DIDP (Stringer et al., 2000). For teethers specifically, maximum phthalate concentrations were 22.4% for DEHP (NTP–CERHR DEHP, 2000) and 40% for both DIDP and DINP (CPSC, 2001).

Oral exposure occurs through sucking, chewing and biting toys and dermal exposure occurs through skin contact with the toys and other child-care products. Inhalation exposure is not expected from these articles. For DEHP, calculated oral exposures ranged from <1 to 526 µg/kg/day, with the highest exposure calculated for heavy mouthing of a pacifier. Daily dermal exposures for DEHP ranged from 9 to 12.4 µg/kg/day, as calculated by ECB (ECB DEHP, 2008). For DIDP, the highest oral exposure calculated was 19 µg/kg/day (as reported in ECB DIDP, 2003), which was over than the 5000 times higher than the lowest value. Dermal exposure was estimated at 1 µg/kg/day by ECB (ECB DIDP, 2003). For DINP, the highest oral exposure calculated was 320 µg/kg/day, calculated based on mouthing times for teethers and other objects intended for mouthing (as reported in NTP-CERHR DINP, 2003). CPSC (1998a) report the 95th percentile oral exposure value of 94.3 µg/kg/day for DINP. Dermal exposure for DINP was estimated at 1 µg/kg/d by ECB (ECB DINP, 2003).

Medical devices

Currently, DEHP is the most commonly used phthalate in a variety of PVC medical devices, including blood storage bags, IV solution storage bags, umbilical catheters, examination gloves and tubing sets for hemodialysis, mechanical ventilation, nasogastric feeding, and ECMO (NTP-CERHR DEHP, 2006; Green et al., 2005). The DEHP content of PVC medical devices can range from 20 to 40 % by weight (Health Canada, 2002). Patients undergoing medical procedures involving the use of DEHP-containing devices may be exposed to DEHP via the intravenous, inhalation, or ingestion routes (Schettler, 2006; Matsumoto et al., 2008; Health Canada, 2002). DEHP exposure is of special concern in infants undergoing intense medical treatments, given the extensive use of DEHP-containing medical devices in NICUs (Calafat et al., 2004b; Green et al., 2005). It has been suggested that exposure to infants in NICUs may be 2 to 3 orders of magnitude higher than exposure to the general population (NTP-CERHR DEHP, 2006). In general, DEHP exposure levels in all age groups subjected to certain medical procedures are believed to be higher than those of the general population (NTP-CERHR DEHP, 2006).

FDA (2001) estimated aggregate exposures to DEHP for neonates and adults resulting from the use of multiple medical devices. The upper-bound daily dose for NICU infants receiving IV administration of sedatives, TPN administration and replacement transfusion was estimated to be 3 mg/kg/d, based on a body weight of 4 kg. Adults undergoing ECMO may be exposed to over 4 mg DEHP/kg/d from PVC tubing in the ECMO device, multiple blood transfusions, and IV administration of drugs.

Personal Care Products

BBP, DBP, DEHP, DIDP, and DINP concentrations were detected in personal care products, including cosmetics, deodorant, hair products, nail products, and perfume. Of the products reviewed, the personal care products with the highest phthalate concentrations were nail care products and perfume. Products with the highest reported concentrations were predominantly from Europe and Asia.

Dermal exposure to phthalates in personal care products has been evaluated by various researchers based on measured or estimated levels of phthalates (mainly DEHP, DMP, DEP, DBP, and BBP) in the products. Total mean daily exposure levels to phthalates from use of multiple cosmetic products ranged from 0.0003 µg/kg/d for DEHP to 24.88 µg/kg/d for DEP (Koo and Lee, 2004). Dermal exposure to phthalates from use of baby care products was investigated by Sathyanarayana et al. (2008) who found increased urinary concentrations of MEP, MMP, and MiBP in infants younger than 8 months following use of infant lotion, powder and shampoo.

Clothing, Gloves and Footwear

Limited information is currently available regarding exposure to phthalates from clothing, gloves and footwear. The only clothing items found with phthalate concentration data were disposable diapers, plastic gloves, and boots for a Halloween costume. In the CPSC (2001) report, dermal exposures ranged from 0.45 µg/kg/d for adults wearing rainwear to 340 µg/kg/d for children wearing "jelly" sandals. Estimates of dermal exposure from gloves were reported by ECB (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008) as 0.7 µg/kg-bw/d for DIDP and DINP and 6.7 µg/kg-bw/d for DEHP. In the study by Wormuth et al (2006), gloves accounted for over 10% of the exposure to DINP and for 5 to 7% of the total exposure to DIDP in teenagers and adults. Oral (from sucking or chewing fabrics) and inhalation exposures have been addressed by only one current study (Jensen and Knudsen, 2006). In the study by Jensen and Knudsen (2006), oral intake for children sucking or chewing a textile piece was reported as 15.4 µg/kg-bw, while inhalation exposure to DEHP was reported to be very small (6.44×10^{-6} µg/kg-bw/d).

Cars and Related Products

Plasticized PVC materials found in car and public transportation interiors (i.e. seat fabrics, dashboard, and interior trim) can be a source of phthalate exposure to drivers and passengers. Only limited information on the concentrations of phthalates in cars and car related products is available. For car interiors, Fujii et al. (2003) estimated a DBP concentration of 7,700 mg/m^3 and a DEHP concentration of 2.0×10^6 mg/m^3 from vehicle emission test chambers. In contrast, DINP was detected in air at a very low concentration, 2.00×10^{-5} mg/m^3 (ECB DINP, 2003). Inhalation exposure to DIDP, DINP and DEHP for adults was estimated as 0.8 µg/kg-bw/day, 1.7 µg/kg-bw/d and 0.9 µg/kg-bw/day, respectively by the ECB (ECB DIDP, 2003; ECB DINP, 2003; ECB DEHP, 2008). Also, inhalation exposure levels of 1.9 µg/kg-bw/d, 3.9 µg/kg-bw/d, and 2 µg/kg-bw/d were estimated in children for DIDP, DINP and DEHP, respectively.

Phthalates also have been detected in wastewater from car washes and disposable wastes from cars. The EU Risk Assessment on BBP (ECB BBP, 2007) reported a BBP concentration of 0.15 mg/L from car wash wastewater. Additionally, the ECB report on DEHP, (ECB DEHP, 2008) reported a DEHP concentration of 0.07 mg/m^3 from waste volume collected from car shredders.

Building Materials

In general, all six phthalates have been detected at relatively high concentrations in various building materials (ECB DINP, 2003; Clausen et al., 2004; NTP-CERHR DnOP, 2003). BBP had the highest measured concentration of 67,900 mg/kg for paints (Wormuth et al., 2006). Both DEHP and DBP also were detected at relatively high concentrations in paint, at 18,200 mg/kg and 10,000 mg/kg, respectively. For adhesives, glues, and sealants, all phthalates except DnOP had a concentration of 55,000 mg/kg. Concentrations of DBP (5,100 mg/m^3) and DEHP (940 mg/m^3) in PVC-coated wall paper were estimated using emission test chambers data (Fujii et al., 2003). Clausen et al. (2004) reported that about 2.3 mg of DEHP was sorbed to flooring material based on laboratory tests, while DnOP was detected at 0.08 mg/kg in floorings in Germany (NTP-CERHR DnOP, 2003).

Phthalates from surface materials in indoor environments are known to off-gas and are present in residential indoor air (Jaakkola and Knight; 2008, Wormuth et al., 2006; Fujii et al., 2003). Phthalates migrate from PVC tile, vinyl flooring, wallpaper, paint, adhesives, glues, sealing compounds, and synthetic leather to house dust, and, as a result, inhalation of particles and/or ingestion of dust containing phthalates is a plausible route of exposure, especially among children (Jaakkola and Knight, 2008; Jensen and Knudsen , 2006; Wormuth et al., 2006). Jensen and Knudsen (2006) estimated the average daily intake of phthalates for a child exposed to DEHP from all indoor sources to be 10 to 20 μg/kg-bw/d, but as a worst case estimate, intake was as much as 50 to 250 μg/kg-bw/day for a child crawling on vinyl flooring. Dust ingestion was identified as a significant route of exposure, with estimated intakes of 39.3 to 54.1 μg/kg-bw/d (NTP-CERHR DEHP, 2006). Indoor air exposure to DEHP, DEP, DBP, BBP, and dicyclohexyl phthalate was found to be minimal and was deemed insignificant (NTP-CERHR DEHP, 2006, Schettler 2006, Otake et al., 2004). Dust ingestion was identified as a significant source of exposure for infants and toddlers for several of phthalates (DiBP, BBzP, DEHP, and DIDP) (Wormuth et al., 2006). Indoor air inhalation of DMP contributed to nearly all the exposure for infants, toddlers, and children and 70-90% for adults and teenagers. Other phthalates (such as DiBP, BBzP, and DEHP) had little to no contribution to inhalation exposure from indoor air (Wormuth et al., 2006).

Pharmaceuticals

Some oral dosage medications have enteric coatings which generally consist of various polymers that contain plasticizers, including phthalates such as DBP (Hauser et al., 2004). Available studies have measured phthalate levels in urine of patients taking medications with enteric coatings (Hauser et al., 2004 and Hernández-Díaz et al., 2009), however, phthalate concentrations in the urine prior to taking the medication was not measured, as well as phthalate levels in the medication itself. Therefore, there are no phthalate concentration data points available at this time to report.

Hernández-Díaz et al. (2009) concluded that select medications might be a source of high exposure to some phthalates. For mesalamine users, urinary concentrations of MBP

(metabolite of DBP) were 50 times higher than the mean for nonusers. Users of didanosine, omeprazole, and theophylline products also had mean urinary concentrations of MEP (metabolite of DEP) significantly higher than the mean for nonusers. In the Hauser et al. (2004) study, the patient in the case study was determined to have urinary MBP level two orders of magnitude higher than the U.S. population 95th percentile. Hauser et al. (2004) linked this unusually high urinary MBP concentration with the use of the medication Asacol, which contains DBP. Hauser et al. (2004) states that further research is necessary to determine the proportional contribution of medications, as well as personal care and consumer products, to a person's total phthalate burden.

Adult Toys and Gels

Two surveys were conducted by the Danish Environmental Protection Agency to investigate the presence of chemicals, including phthalates, in adult toys and pleasure gels (Nilsson et al., 2006 and Tønnig et al., 2006, respectively). Nilsson et al. (2006) measured DEHP, DINP and DnOP concentrations in 15 different sex toys made of soft vinyl, natural latex, rubber, and thermoplastic rubber. DEHP was detected in 8 of the 15 samples with a maximum concentration at 702,000 mg/kg. DINP and DnOP were detected in two samples each at maximum concentrations at 600,000 mg/kg and 239,000 mg/kg, respectively. None of the six phthalates of interest were identified in the 15 gel and 7 massage oils/cream products screened (Tønnig et al., 2006).

Migration testing on select adult toys showed that migration increased significantly when an oil-based lubricant was used instead of a water-based lubricant. Using the migration testing results, the maximum internal dose for DEHP was for a soft vinyl toy, in which the internal dose was estimated as 0.0017 mg/kg body weight/day for normal use and 0.047 mg/kg body weight/day for worst-case use. For DnOP, Nilsson et al. (2005) assumed a worst case uptake of approximately 0.05 mg/kg body weight/day, based on results for DEHP.

Other Products

Other products containing phthalates include modeling clay/ceramics, a variety of different air fresheners, and stain removers. The product with the highest phthalate concentration was polymer modeling clay with a DnOP concentration of 97,500 mg/kg (Stopford et al., 2003). Polymer modeling clay also contains BBP at a maximum concentration of 39,800 mg/kg. Schettler (2006) measured BBP, DEHP, and DnOP concentrations in indoor air after baking polymer modeling clay. The highest phthalate concentration detected these indoor air samples was DnOP at 6.67×10^6 mg/m^3. The EU (ECB DEHP, 2008) estimated a DEHP concentration of 0.55 mg/kg released to soil when formulating ceramics.

The indoor air surrounding a variety of air fresheners was analyzed to determine DEHP concentrations (SCHER, 2006). The different types of air fresheners included air sprays, electric diffusers, gels, incense, liquid fresheners, and scented candles. The air freshener with the highest DEHP air concentration was incense at 1.25×10^6 mg/m^3. One study

reported that air fresheners contain up to 0.55 mg/kg DEHP. The Danish EPA (Jensen and Knudsen, 2006) estimated a DBP air concentration of 22,500 mg/m^3 resulting from the use of stain removers.

Currently, there are limited data on consumer phthalate exposures resulting from the use of air fresheners, polymer clay, and stain removers. The incidental ingestion of phthalates from polymer clay was estimated to range from 127 to 250 µg/d, depending on the type of polymer clay used (Stopford et al., 2003). Schettler (2006) reported higher maximum inhalation exposures following the baking of polymer clay (2,667 µg for BBP, 6,670 µg for DnOP, and 4,993 µg for DEHP). Inhalation exposure to DBP resulting from the use of stain remover was estimated as 3.19×10^{-6} mg/kg-bw/d, based on an estimated DBP air concentration of 22.5 µg/m^3 (Jensen and Knudsen, 2006).

Food and Food-Related Uses/Products

Phthalates may be found in food and food-related products, including beverages, food, food packaging, and utensils used for food consumption. All six phthalates were found in beverages (milk and alcohol). The highest concentration of phthalates was 80 mg/L milk for DEHP, while all other phthalates were at much lower levels (HSDB DEHP, 2009). Phthalates concentrations observed in food were considerably higher than those in beverages. Food items examined in studies included butter, cheese, oil, peanut butter, pork, and infant formula. Phthalates were measured in various food products sold in glass jars with plastic gaskets in Denmark at very high concentrations (DIDP at 173 mg/kg in garlic oil, and DINP at 99 mg/kg in peanut butter) (Pederson et al., 2008). The total phthalate concentration (expressed as DEHP) found in retail cheese from Norway, Spain, and the U.K. was estimated at 114 mg/kg ECB DINP (2003). The highest levels of phthalates in foods have been detected in the fatty foods such as oils, dairy, infant formula, meat, meat products, and fish (Fromme et al., 2007b; Wormuth et al., 2006; Shea, 2003). Fatty foods and oily foods are believed to be contaminated primarily because of their lipophilic characteristic (Wenzl, 2009).

Food packaging mainly includes plastic wraps and water containers. All phthalates except DIDP and DINP were detected in food packaging. ATSDR (2001) indicated a very high concentration of DBP (5,860 mg/kg) in miscellaneous food packaging items. These included packaging for pudding, ice-lolly, waffles, eggs, and vegetable burger mix. The HSDB DEHP (2009) information showed concentration of 3,680 mg/kg for DEHP. Among food utensils, only DBP was detected at 15 mg/kg in coffee filters based on the HSDB DEHP report.

Food is likely to be the largest single exposure source of phthalates in the general population (Schettler, 2006; Chen et al., 2007; Shea, 2003; Wormuth, et al., 2006). Exposure estimates and dietary intakes for phthalates as related to food are primarily for DEHP, BBP, and DBP. In addition, it appears from the available data, that levels of DEHP are usually higher in food than for the other phthalates (Schettler, 2006). Foods have been found to be contaminated with phthalates during growth, production, processing, or packaging (Shea, 2003; Kamrin, 2009). Possible sources of some phthalates found in food are cellulose-based food wraps and latex adhesives used in food

processing in which the phthalate has migrated into the food (NTP-CERHR DnOP, 2003). The levels of selected phthalates in food, infant formula, and human milk have been shown in food surveys worldwide. However, according to Schletter (2006), the phthalate levels found in food are widely variable; the data are often old and may not reflect current dietary intake and exposure levels.

Wormuth et al. (2006) provided the percent contribution of food to total phthalate exposure in consumer groups as follows: DBP, 60% in infants and toddlers, >95% in teenagers and adults; DnBP, 40-90% for all consumer groups, DEHP, 50-98% for all consumer groups. For DIDP, food contributes to 55-70% of the exposure for teenagers and adults. Food is a major source (73%) of BBP exposure in children (73%), teenagers (> 20%) and adults (60%). Data on levels of DINP, DIDP, and DnOP in food are limited, therefore exposure estimates are few. Schettler (2006) reported maximam daily intakes for several phthalates in food as follows: 0.48 µg/kg/day for DBP, 4.9 to 18 µg/kg/day for DEHP, and 0.11 to 0.29 µg/kg/day for BBP.

Cumulative Exposures

Cumulative exposures have been widely estimated for the general population, women, men, children, and infants of various ages from countries around the world utilizing two different methods. One method, the biomonitoring-based approach, calculates exposures based on phthalate or phthalate metabolite levels in urine, while the second method calculates exposures based on environmental concentrations in media and human behaviors (i.e., scenario-based approach). In general, the biomonitoring approach is often preferred since it provides a direct and accurate measurement of the magnitude of exposures; however, this approach does not provide information on the relative contribution of different sources or routes of exposure, as can be determined in the scenario-based approach. One researcher (Wormuth et al., 2006) compared exposures calculated using both methods and determined exposures were similar, however, caution should be taken, as this was only one study (Kamrin, 2009).

The exposure values used in estimating cumulative exposure based on biomonitoring data were not all calculated using the same methods. Factors which can influence the calculations include which metabolite was measured in the urine samples, if exposures were calculated from spot urine samples or 24-hr urine samples, the method used to extrapolate the phthalate metabolite concentrations in the spot samples into daily values (creatinine-based or urine volume-based), the metabolite conversion method, and other model specific factors (i.e., creatinine excretion values).

The scenario-based approach to estimating cumulative exposure involves summing together exposures calculated from all exposure routes (oral, dermal, and inhalation) and sources. Example exposure sources include food, water, outdoor air, soil, indoor air, toys, personal care products, and other consumer products. Underestimation could occur if not all sources of exposure are known. Also, the addition of several reasonable worst-case values (e.g., 95th percentile exposure values) could lead to unreasonable over estimation of exposures (ECB DEHP, 2008). Additionally, modeling results may be

misleading when they are influenced by infrequent, but high magnitude exposures, such as spray paint (Kamrin, 2009).

The various scenario-based estimates reviewed each used different concentration data and country-specific use patterns. Another major difference in the estimates from the different studies is the sources/pathways of exposure included in the estimates. For example, some studies only provided cumulative exposure for the environmental routes (i.e., food, water, and air) or only consumer products. Other variances between calculation methods include the use of internal or external exposures and factors such as breathing rates and body weights. As such, comparisons between the different studies should be made with caution.

Populations with High Phthalate Exposures

Populations, other than those in the occupational (manufacturing and processing) sector, identified as potentially highly exposed include women of child-bearing age, newborns, infants and children, patients receiving dialysis regularly on a kidney machine, and patients receiving blood transfusions, such as hemophiliacs. Minority populations with potentially higher exposures mentioned in the literature have been Hispanics and blacks. Persons living near industrial facilities or hazardous waste sites with higher than average levels of phthalates may also have higher than average exposures. EWG (2000) has also noted that males may potentially be a population with a more sensitive toxic endpoint due to trends shown in male reproductive health that are similar to results found in animal studies.

NRC (2008) reported that except for MEP (metabolite of diethyl phthalate), in the U.S. population, urinary metabolites in children, males, Hispanic and Blacks are somewhat higher than for adults overall. Matsumoto et al. (2008) also noted this difference. Concentrations of MEHP, MBzP and MBP were higher in the youngest age (6-11 years old) and decreased with age. Non-Hispanic blacks had higher levels than non-Hispanic whites and Mexican Americans Matsumoto et al. (2008). This assessment of concentrations is based on data from the CDC Third National Report on Human Exposures to Chemicals. Of the 12 phthalates tested by the CDC, eleven were concentrated more highly in children than in adults. Concentrations were also higher in females than males. NRC (2008) noted that higher metabolite concentrations in children than for adults could be attributed to differences in exposure or possible differences in metabolism. CDC (2005) also noted a similar finding in the 1999-2000 and 2001-2002 NHANES subsamples. In the CDC biomonitoring study results, six of the eight highest measured levels of DBP were in the urine of women of child bearing age (EWG, 2000). Their data indicated that BDP exposures for up to 3 million women of childbearing age may be 20 times higher that exposures for the rest of the population (EWG, 2000).

Uncertainty and Data Limitations

Extensive research has been done to study and understand the risks posed by phthalates to humans and the environment. However, the methods used to assess human exposure to

phthalates are associated with data gaps, variabilities, and uncertainties. In particular, there are numerous uncertainties associated with determining exposure, hazard, and dose response for populations of different age, race, and sex.

Parameters representing exposure patterns and behaviors for the various exposure groups and the associated product use need to be better characterized. Using conservative estimates for each parameter may result in the overestimation of the real exposure. The dose reconstruction method (back calculation method) for estimating phthalate dose has uncertainties associated with it, as the method assumes a steady state exposure and does not differentiate between peak and background levels. The conversion from body fluid phthalate concentrations to exposure levels is based on data collected from adults and it is not clear how applicable these data are to other age groups, especially infants and children. In addition, biomonitoring data indicate that there is significant variability in levels, and thus exposures, over time and among populations (Kamrin, 2009).

Different researchers have used different factors to calculate the exposure levels that correspond to the measured phthalate concentrations (Kamrin, 2009). Researchers in the U.S. have selected factors that result in significantly lower exposure estimates for some phthalates, generally by a factor of about 5 for mean values, than those reported by researchers in Germany and Korea. However, there appears to be a closer agreement across countries of 95th percentile values than of the means. In addition to differences in exposure values due to different measurement approaches, exposures to some phthalates appear to be higher in Germany and Korea than in the U.S. (Kamrin, 2009).

Additionally, there are considerable uncertainties associated with the existing toxicological data on phthalates and the extrapolation from laboratory results for rodents to different human populations, such as young children, and to lifetime or other exposure durations.

There also are uncertainties associated in quantifying the levels phthalates contained in each consumer product, including the accuracy of the concentrations of each phthalate in each source along with their spatial and temporal variations. The choice of metabolite appears to have a significant influence on the exposure estimate with exposure values potentially varying significantly when they are based on different metabolites (Kamrin, 2009).

The key research needs and data gaps in phthalate exposure assessments were identified by the Committee on the Health Risk of Phthalates (NRC, 2008). They included 1) identification of the most important sources of phthalate exposure and migration pathways that connect the sources to the general population, 2) identification of the full spectrum of phthalate metabolites (especially DEPH and DINP) and the determination of the most important metabolite to be used as a biomarker for human exposures, 3) improvement in the understanding of metabolism and how it would affect and change children and adults over their lifetime, 4) determination of the relationship between maternal urinary phthalate metabolite concentrations and those in the fetal compartments with an emphasis on understanding the pharmacokinetics of phthalates, 5)

characterization of human exposure to other anti-androgens and other factors that contribute to disturbed androgen action, and 6) the use of existing databases, such as NHANES, to assess exposure to multiple phthalates and other chemicals that may contribute to common biologic outcomes.

7.0 REFERENCES

Adibi, J., F. Perera, W. Jedrychowski, D. Camann, R. Jacek, R. Whyatt. 2003. Prenatal exposures to phthalates among women in New York City and Krakow, Poland. *Environmental Health Perspectives.* **112(**14)1719-1722. (also, cited in Calafat and McKee, 2006).

Albro, P.W., B. Moore. 1974. Identification of the metabolites of simple phthalate diesters in rat urine. *J Chromatog.* **94**:209-218. (cited in Kohn et al., 2000; Marsee et al., 2006)

Anderson, W.A., L. Castle, M. Scotter, C. Springall. 2000. A biomarker approach to measuring human dietary exposure to phthalates, risk assessment and communication for food safety. (Abstract) Presented at the first joint CSL/JIFSAN symposium on food safety and nutrition 20-22 June 2000, Central Science Laboritory, Sand Hutton, York, UK. (cited in ECB BBP, 2007)

Anderson, W.A., L. Castle, M.J. Scotter, R.C. Massey, C. Springall. 2001. A biomarker approach to measuring human dietary exposure to certain phthalate diesters. *Food Addit. Contam.* 18(12): 1068-1074. (cited in Chen et al., 2008; Calafat and McKee, 2006; Fromme et al., 2007b; Itoh et al., 2005 and 2007; Koch et al., 2003b; Koch et al., 2007; Marsee et al., 2006; SCENIHR, 2008; Wittasset et al., 2007b)

ATSDR. 1990. Di-n-butylphthalate. Toxicological Profile. U.S. Department of Health and Human Services, Public Health Service. Agency for Toxic Substances and Disease Registry.

ATSDR. 1995. Toxicological profile for diethyl phthalate. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. June 1995.

ATSDR. 1997. Toxicological profile for di-n-octylphthalate. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. September 1997.

ATSDR. 2001. Toxicological profile for di-n-butyl phthalate. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. September 2001.

ATSDR. 2002. Toxicological profile for di(2-ethylhexyl)phthalate. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. September 2002.

Axford I.P., A.O. Earls, R.P. Scott, J.H. Braybrook.1999. Interlaboratory validation of laboratory-based agitation methods for the determination of phthalate plasticizer migration from PVC toys and childcare articles laboratory of the government chemist, Teddington, Middlesex, UK. June 1999 (cited in Babich, 2002).

Babich M.A. 1998. Preliminary hazard assessment of diisononyl phthalate (DINP) in children's products. U.S. Consumer Product Safety Commission, Bethesda, MD 20814. March 10, 1998 (cited in CPSC 2002a).

Babich, M., S. Chen, M. Greene, C. Kiss, W.K. Porter, T.P. Smith, M.L. Wind, W.W. Zamula. 2004. Risk assessment of oral exposure to diisononyl phthalate from children's products. *Regulatory Toxicology and Pharmacology.* **40**(2)151–167.

Barr, D.B., M.J. Silva, K. Kato, J.A. Reidy, N.A. Malek, D. Hurtz, M. Sadowski, L.L. Needham, A.M. Calafat. 2003. Assessing human exposure to phthalates using monoesters and their oxidized metabolites as biomarkers. *Environmental Health Perspectives*. **111**(9)1148-51.

Barr, D.B., L.C. Wilder, S.P. Caudill, A.J. Gonzalez, L.L. Needham, J.L. Pirkle. 2005. Urinary creatinine concentrations in the U.S. population: implications for urinary biological monitoring measurements. *Environmental Health Perspectives.* **113**(2)192-200.

Barry Y.A., R.S. Labow, W.J. Keon, M. Tocchi, G. Rock. 1989. Perioperative exposure to plasticizers in patients undergoing cardiopulmonary bypass. *The Journal of Thoracic and Cardiovascular Surgery.* **97**:900-905 (cited in FDA, 2001).

Becker, K., M. Seiwert, J. Angerer, W. Heger, H.M. Koch, R. Nagorka, E. Robkamp, C. Schluter, B. Seifert, D. Ullrich. 2004. DEHP metabolites in urine of children and DEHP in house dust. *International Journal of Hygiene and Environmental Health.* **207**: 409-417. (cited in Calafat and McKee, 2006; Wittassek et al., 2007b; SCENIHR, 2008)

Blount, B.D., M.J. Silva., S.P. Caudill, L.L. Needham., J.L. Pirkle, E.J. Sampson., G.W. Lucier, R.J. Jackson, J.W. Brock. 2000. Levels of seven urinary phthalate metabolites in a human reference population. *Environmental Health Perspectives*. **108**(10). (also, cited in Kohn et al., 2000; David, 2000; Fromme et al, 2007b; Calafat and McKee, 2006; SCENIHR, 2008; ECB BBP, 2007; SCHER, 2008)

Bogen, K.T. 1994. Models based on steady-state *in vitro* dermal permeability data underestimate short-term *in vivo* exposures to organic chemicals in water. *Journal of Exposure Analysis and Environmental Epidemiology.* **4**:457-476 (cited in CPSC, 2001).

Bommer J., E. Ritz, K. Andrassy. 1985. Side effects due to materials used in hemodialysis equipment. *Advanced Nephrology*. **14**:409-438 (cited in ECB, 2008).

Bornehag, C.G., J. Sundell, C. Weschler, T. Sigsgaard, B. Lundgren, M. Hasselgren, L. Hägerhed-Engman. 2004. The association between asthma and allergic symptoms in children and phthalates in house dust: a nested case–control study. *Environmental Health Perspectives.* **112**(14)1393-1397.

Bosgra, S., P. Bos, T. Vermeire, R. Luit, W. Slob. 2005. Probabilistic risk characterization: an example with di(2-diethylhexyl) phthalate. *Regulatory Toxicology and Pharmacology.* **43(**1)4-13 (cited in Fromme et al., 2007).

Bosnir, J., D. Puntaric, A. Galic, I. Skes, T. Dijanic, M. Klaric, M. Grgic, M. Curkovic, Z. Smit. 2007. Migration of phthalates from plastic containers into soft drinks and mineral water. *Food Technology and Biotechnology.* **45**(1)91-95.

Bouma, K., D.J. Schakel. 2002. Migration of phthalates from PVC toys into saliva stimulant by dynamic extraction. *Food Additives and Contaminants*. **19**(6)602-610.

Brandon, E., A.G. Oomen, C.J.M. Rompelberg, C.H.M. Versantvoort, J.G.M. van Engelen, A.J, A.M. Sips. 2006. Consumer product *in vitro* digestion model: bioaccessibility of contaminants and its application in risk assessment. *Regulatory Toxicology and Pharmacology.* **44**:161-171.

Brock, J.W., S.P. Caudill, M.J. Silva, L.L. Needham, E.D. Hilborn. 2002. Phthalate monoesters levels in the urine of young children. *Bulletin of Environmental Contamination and Toxicology.* **6**(3)309-314 (cited in NRC, 2008; Calafat and McKee, 2006; ECB BBP, 2007).

Buchta, C., C. Bittner, P. Hocker, M. Macher, R. Schmid, C. Seger, M. Dettke. Donor exposure to the plasticizer di(2-ethylhexyl)phthalate during plateletpheresis. *Transfusion* 2003. **43**:1115-20 (cited in NTP-CERHR, 2006).

Calafat, A.M., R.H. McKee. 2006. Integrating biomonitoring exposure data into the risk assessment process: phthalates [diethyl phthalate and di(2-ethylhexyl) phthalate] as a case study. *Environmental Health Perspectives*. **114**(11)1783-1789.

Calafat, A.M., A.R. Slakman, M.J. Silva, A.R. Herbert, L.L. Needham. 2004a. Automated solid phase extraction and quantitative analysis of human milk for 13 phthalate metabolites. *Journal of Chromatography B*. **805:**49-56.

Calafat, A., L. Needham, M. Silva, G. Lambert. 2004b. Exposure to di-(2-ethylhexyl) phthalate among premature neonates in a neonatal intensive care unit. *Pediatrics.* **113**(5)e429-e434.

Castle L., A. Mayo, J.Gilbert. 1989. Migration of plasticizers from printing inks into food. *Food Additives and Contaminants.* **6**(4) 437-443.

California Department of Toxic Substances Control (CDTSC). 2008. Detailed Results of Phthalate Testing in Children's Toys. Available online at http://www.sfenvironment.org/our_programs/interests.html?ssi=2&ti=3&ii=135

CEFIC-ECPI Affairs (cited in European Union Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). 1998. Phthalate migration from soft PVC toys and child-care articles. Opinion expressed at the CSTEE third plenary meeting Brussels, 24 April 1998.

Centers for Disease Control and Prevention (CDC). 2001. National Report on Human Exposure to Environmental Chemicals. Atlanta, Georgia.

Centers for Disease Control and Prevention (CDC). 2003. Second National Report on Human Exposure to Environmental Chemicals. NCEH Pub. No. 02-0716. National Center for Environmental Health Division of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, GA. (cited in ECB, 2007).

Centers for Disease Control and Prevention (CDC). 2005. Third National Report on Human Exposure to Environmental Chemicals. NCEH Pub. No. 05-0570. National Center for Environmental Health Division of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, GA [online]. Available at http://www.cdc.gov/exposurereport/report.htm (accessed July 15, 2008) (cited in NRC, 2008; Calafat and McKee, 2006; Fromme et al., 2007b; SCENIHR, 2008; SCHER, 2008).

Chan, P., M. Meek. 1994. Di-*n*-butyl phthalate: Evaluation of risks to health from environmental exposure in Canada. *Environmental Carcinogenesis Ecotoxicology Reviews.* **C12**:257-68 (also, cited in NTP-CERHR DBP, 2000).

Chen, S.B. 1998a. Laboratory Sciences Report on the migration of diisononyl phthalate from polyvinyl chloride children's products. U.S. Consumer Product Safety Commission, Washington, DC. November, 1998 (also, cited in CPSC, 1998; Babich, 2002; CPSC, 2001).

Chen S.B. 1998b. Migration of diisononyl phthalate from a Danish polyvinyl chloride teether. U.S. Consumer Product Safety Commission, Bethesda, MD. July 24, 1998 (cited in Babich, 2002).

Chen S.B. 2002. Screening of toys for PVC and phthalates migration. U.S. Consumer Product Safety Commission, Bethesda, MD. June 20, 2002 (cited in Babich, 2002).

Chen, M., J. Chen, C. Tang, I. Mao. 2007. The internal exposure of Taiwanese to phthalate-an evidence of intensive use of plastic materials. Environment International 34:79-85.

Chen, M.L., J.S. Chen, C.L. Tang, I.F. Mao. 2008. The internal exposure of Taiwanese to phthalate - an evidence of intensive use of plastic materials. *Environment International.* **34**(1)79-85.

Clark , K., I. Cousins, D. MacKay. 2003. Assessment of critical exposure pathways. In: C.A. Staples, ed. The Handbook of Environmental Chemistry. New York: Springer-Verlag (cited in NTP-CEHR 2008-DEHP).

Clausen, P.A., V. Hansen, L. Gunnarsen, A. Afshari. 2004. Emission of di-2-ethylhexyl phthalate from PVC flooring into air and uptake in dust: emission and sorption experiments in FLEC and CLIMPQA. *Environmental Science and Technology*. **38**(4)2531-2537.

Consumer Product Safety Commission (CPSC). 1982. Phthalates in consumer products. Final report to Consumer Product Safety Commission, Washington D.C. by Arthur D. Little, Inc. July 7, 1982. C-84560.

Consumer Product Safety Commission (CPSC). 1983a. Risk assessment on di (2-Ethylhexyl) Phthalate in children's products. U.S. CPSC, Washington, DC 20207. August 1983 (also, cited in Babich, 2002).

Consumer Product Safety Commission (CPSC). 1983b. Memorandum to Peter W. Preuss from Bharat Bhooshan. 1983. Di(2-ethylhexyl)phthalate (DEHP) migration from polyvinyl chloride consumer products – summary of results and findings. August 24, 1983.

Consumer Product Safety Commission (CPSC). 1998a. Appendix B, Statistical analysis for prediction of DINP intake by young children. U.S. CPSC, Bethesda, MD 20814. December 1998.

Consumer Product Safety Commission (CPSC). 1998b. The risk of chronic toxicity associated with exposure to diisononyl phthalate (DINP) in children's products. U.S. CPSC, Bethesda, MD 20814. December 1998 (also cited in Babich, 2002).

Consumer Product Safety Commission (CPSC). 2001. Chronic hazard advisory panel on diisononyl phthalate (DINP). Directorate of Health Sciences, Bethesda, MD 20814 (also cited in Babich, 2002).

Consumer Product Safety Commission (CPSC). 2002a. Updated risk assessment of oral exposure to Diisononyl Phthalate (DINP) in children's products. Michael A. Babich, Ph.D. Directorate for Health Sciences, U.S. Consumer Product Safety Commission. Bethesda, MD 20814. August 26, 2002.

Consumer Product Safety Commission (CPSC). 2002b. Memorandum to Marilyn L. Wind from S.B. Chen. Screening of toys for PVC and phthalates migration. June 20, 2002.

Consumer Product Safety Commission (CPSC) BBP. 2009. Memorandum to Michael A. Babich, Ph.D., Project Manager, Phthalates Section 108 of CPSIA. Toxicity review of Benzyl-*n*-butyl Phthalate (Benzyl Butyl Phthalate or BBP) May 11, 2009. pp.1-36.

Consumer Product Safety Commission (CPSC) DBP. 2009. Memorandum to Michael A. Babich, Ph.D., Project Manager, Phthalates Section 108 of CPSIA**.** Toxicity review of Di-*n*-butyl Phthalate (Dibutyl Phthalate or DBP). pp.1-35.

Consumer Product Safety Commission (CPSC) DEHP. 2009. Memorandum to Michael A. Babich, Ph.D., Project Manager, Phthalates Section 108 of CPSIA. Toxicity review of Di-(2-ethylhexyl) Phthalate (DEHP). August 25, 2009. pp. 1-239.

Consumer Product Safety Commission (CPSC) DIDP. 2009. Memorandum to Michael A. Babich, Ph.D., Project Manager, Phthalates Section 108 of CPSIA**.** Toxicity review of Di(isodecyl) Phthalate. May 20, 2009. pp.1-25.

Consumer Product Safety Commission (CPSC) DnOP. 2009. Memorandum to Michael A. Babich, Ph.D., Project Manager, Phthalates Section 108 of CPSIA. Toxicity review of Di-n Octyl Phthalate (DnOP). May 20, 2009. pp.1-87.

Corley J.H., T.E. Needham E.D. Sumner, R. Mikeal. 1977. Effect of various factors on the amount of plasticizer in intravenous solutions packaged in flexible bags. *American Journal of Hospital Pharmacy*, Mar; **34**(3)259-264 (cited in FDA, 2001).

Cousins, I., D. Mackay. 2000. Correlating the physical-chemical properties of phthalate esters using the 'three solubility' approach. *Chemosphere*. **41**(2000)1389-1399.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment). 1997a. Letter from the Dutch authorities (BR/HA/I – 97/46666). Reaction to Danish notifications n°8017/18/19-97.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment). 1997b. Fax from Professor Jansson with documentation from ARTSANA on migration of PAE from their toys.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment. 1997c. Table prepared by Prof. Jansson on PAE emissions from toys. It contains overview of data made available by the different EU M. States.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment). 1997d. Document from LGC (Laboratory for the Government Chemist – UK) on the subjects of (i) development project to validate methodology for migration of phthalate plasticiser from PVC toys and (ii) brief review of European standardisation activities on plasticisers in PVC articles (1990-1997) and (iii) phthalate leaching
from soft PVC toys.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment). 1998a. Phthalate migration from soft PVC toys and child-care articles. Opinion expressed at the CSTEE third plenary meeting Brussels, 24 April 1998.

CSTEE (EU Scientific Committee on Toxicity, Ecotoxicity and the Environment).1998b. Recent plasticiser migration studies on toys carried out at three laboratories in Germany – LGA, TÜV Rheinland and Dr Budde – submitted by CEFIC-ECPI.

David, R.M. 2000. Exposure to phthalate esters. *Environmental Health Perspectives.* **108**:A440.

David, R.M. 2004. Commentary regarding the article by Koch et al.: An estimation of the daily intake of di(2-ethylhexyl) phthalate (DEHP) and other phthalates in the general population. *International Journal of Hygiene and Environmental Health.* **206:**77-83 (2003).

Deisinger, P.J., L.G. Perry, D. Guest, 1998. In vivo percutaneous absorption of ^{14}C DEHP from ^{14}C DEHP plasticized polyvinyl chloride film in male Fisher 344 rats. *Food and Chemical Toxicology.* **36**(6)521-7 (cited in CPSC, 2001).

Dine, T., M. Luyckx, B. Gressier, C. Brunet, J. Souhait, S. Nogarede, J. Vanpoucke, F. Courbon, Y. Plusquellec, G. Houin. 2006. A pharmacokinetic interpretation of increasing concentrations of DEHP in haemodialysed patients. *Medical Engineering and Physical* 2000; **22**:157-65 (cited in NTP-CERHR, 2006).

Division of Environmental Health and Risk Management (DEHRM). 2003. Measuring the bioavailability of human dietary intake of PAH, phthalates and aromatic hydrocarbons (cited in Fromme et al., 2007b).

Doull J., R. Cattley, C. Elcombe, B.G. Lake, J. Swenberg, C. Wilkinson, G. Williams, M. van Gemert. (1999). A cancer risk assessment of di(2-ethylhexyl)phthalate: application of the new U.S. EPA Risk Assessment Guidelines. *Regulatory Toxicolology and Pharmacology.* **29**(3)327-57 (cited in FDA, 2001; ECB, 2008; Huber et al., 1996).

Duty, S.M., M.J. Silva, D.B. Barr, J.W. Brock, L. Ryan, Z. Chen, R.F. Herrick, D.C. Christiani and R. Hauser. 2003. Phthalate exposure and human semen parameters. *Epidemiology.* **14**(3)269-277.

Duty, S.M., A.M. Calafat, M.J. Silva, J.W. Brock, L. Ryan, Z.Y. Chen, J. Overstreet, R. Hauser, 2004. The relationship between environmental exposure to phthalates and computer-aided sperm analysis motion parameters. *J. Androl*. 25:293-302. (as cited in Calafat and McKee, 2006)

Earls, A.O., C.A. Clay, I.P. Axford, R.P. Scott, J.H. Braybrook.1998. Laboratory-based agitation methods for the determination of phthalate plasticizer migration from PVC toys and childcare articles. Laboratory of the Government Chemist, Teddington, Middlesex

TW11 0LY, UK. September 1988. LGC technical report number LGC/1998/DTI/009 (cited in Babich, 2002).

Eigenberg, D.A., H.P. Bozigian, D.E. Carter. 1989. Distribution, excretion, and metabolim of butylbenzyl phthalate in the rat. *J. Toxicol. Environ Health*. 17:445-456. (cited in Kohn et al., 2000; Marsee et al., 2006)

Elsisi, A.E., D.E. Carter, I.G. Sipes, 1989. Dermal absorption of phthalate diesters in rats. *Fundamental and Applied Toxicology.* **12**:70-77 (cited in CPSC, 2001).

EUROPA. 2005. Permanent ban of phthalates. Commission hails long-term safety for children's toys. Available at http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/838 (accessed July 15, 2008).

European Chemicals Agency (ECHA) BBP. 2009. Data on manufacture, import, export, uses and releases of Benzyl Butyl Phthalate (BBP) as well as information on potential alternatives to its use.

European Chemicals Agency (ECHA) DBP. 2009. Data on manufacture, import, export, uses and releases of Dibutyl Phthalate (DBP) as well as information on potential alternatives to its use.

European Chemicals Agency (ECHA) DEHP. 2009. Prioritisation and annex XIV background information bis(2-ethylhexyl)phthalate, EC number: 204-211-0, CAS number: 117-81-7.

European Chemicals Bureau (ECB) BBP. 2007. European Union Risk Assessment Report on Benzyl Butyl Phthalate (BBP). European Commission, Joint Research Centre, Institute of Health and Consumer Protection (IHCP), Toxicology and Chemical Substances (TCS), European Chemicals Bureau (ECB). Volume 76. EUR 22773 EN.

European Chemicals Bureau (ECB) BBP Summary. 2008. Benzyl Butyl Phthalate (BBP): Summary Risk Assessment Report. European Commission, Joint Research Centre, Institute for Health and Consumer Protection, Toxicology and Chemical Substance (TCS), European Chemicals Bureau. EUR 22773 EN/2**.**

European Chemicals Bureau (ECB) DBP. 2003-04. European Union Risk Assessment Report on Dibutyl Phthalate. European Commission, Joint Research Centre, Institute of Health and Consumer Protection (IHCP), Toxicology and Chemical Substances (TCS), European Chemicals Bureau (ECB).Volume 29. EUR 19840 EN.

European Chemicals Bureau (ECB) DBP Summary. 2003-04. Dibutyl phthalate - with addendum 2004. Summary Risk Assessment Report. European Commission, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. Special Publication I.01.66.

European Chemicals Bureau (ECB) DEHP. 2008. European Union Risk Assessment Report on Bis(2-Ethylhexyl) Phthalate (DEHP). European Commission, Joint Research Centre, Institute of Health and Consumer Protection (IHCP), Toxicology and Chemical Substances (TCS), European Chemicals Bureau (ECB). Volume 80. EUR 23384 EN.

European Chemicals Bureau (ECB) DEHP Summary. 2008. Bis (2-ethylhexyl) phthalate (DEHP) Summary Risk Assessment Report. European Commission, Joint Research Centre, Institute for Health and Consumer Protection, Toxicology and Chemical Substance (TCS), European Chemicals Bureau. EUR 23384 EN/2.

European Chemicals Bureau (ECB) DIDP. 2003. European Union Risk Assessment Report on 1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate (DIDP). European Commission, Joint Research Centre, Institute of Health and Consumer Protection (IHCP), Toxicology and Chemical Substances (TCS), European Chemicals Bureau (ECB). Volume 36. EUR 20785 EN.

European Chemicals Bureau (ECB) DIDP Summary. 2003. 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate (DIDP) Summary Risk Assessment Report. European Commission, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. Special Publication I.03.103

European Chemicals Bureau (ECB) DINP. 2003. European Union Risk Assessment Report on 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP). European Commission, Joint Research Centre, Institute of Health and Consumer Protection (IHCP), Toxicology and Chemical Substances (TCS), European Chemicals Bureau (ECB). Volume 35. EUR 20784 EN.

European Chemicals Bureau (ECB) DINP Summary. 2003. 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP). Summary Risk Assessment Report. European Commission, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. Special Publication I.03.101.

EWG (Environmental Working Group). 2000. Does a common chemical in nail polish pose risk to human health. Beauty secrets: phthalates. Washington DC: Environmental Working Group. Available at: http://www.ewg.org.

Exponent, Inc. 2007. Review and risk analysis of child exposure to Di-isononyl Phthalate in toys. Prepared for Toy Industry Association Inc. Exponent, Bellevue, WA. Doc No. BE03157.001 01F1 0407 RK20.

Faouzi, M.A., F. Khalfi, T. Dine, M. Luyckx, C. Brunet, B. Gressier, F. Goudaliez, M. Cazin, J. Kablan, A. Belabed, J.C. Cazin. 1999. Stability, compatibility and plasticizer extraction of quinine injection added to infusion solutions and stored in polyvinyl

chloride (PVC) containers. *Journal of Pharmacology Biomedical Analysis*. **(5):**923-30. (cited in FDA, 2001).

Federal Register. 2007. "Air Fresheners; TSCA Section 21 Petition; Notice" Federal Register 72, Number 245 (21 December, 2007): 72885-72896. Available online at http://www.epa.gov/EPA-AIR/2007/December/Day-21/a6176.htm (accessed November 2009).

Fiala, F., I. Steiner, K. Kubesch. 2000. Migration of Di-(2-ethylhexyl)phthalate (DEHP) and Diisononyl Phthalate (DINP) from PVC articles. Deutsche Lebensmittel-Rundschau **2(**51-57). (Also cited in Babich, 2002)

Flaminio L.M., R. Bergia, L. De Angelis, M. Ferazza, M. Marinovich, G. Galli, C.L. Galli. 1988. The fate of leached Di-(2-ethylhexyl) Phthalate (DEHP) in patients on chronic haemodialysis. The *International. Journal of Artificial Organs.* (**11)**428-434 (cited in ECB, 2008).

Food and Drug Administration (FDA). 2001. Safety assessment of Di(2-ethylhexyl)phthalate (DEHP) released from PVC medical devices. Center for Devices and Radiological Health, U.S. FDA, Rockville, MD.

Foster, P.M.D., M.W. Cook, L.V. Thomas, D.G. Walters, S.D. Gangolli. 1983. Differences in urinary metabolic profile from di-n-butyl phthalate-treated rats and hamsters. A possible explanation for species differences in susceptibility to testicular atrophy. *Drug Metab Despos.* 11:59-61. (cited in Kohn et al., 2000; Marsee et al., 2006)

France. 2001. Risk Assessment, 1,2-Benzenedicarboxylic acid, Di-C8-10-branched alkyl esters, C9 rich and di"isononyl" phthalate CAS # 68515-48-0 and CAS # 28553-12-0; EINECS # 271-090-9 and EINECS # 249-079-5. May (cited in Babich, 2002).

Freire, M.R. De A., I. Santana, F. Reyes. 2006. Plasticizers in Brazilian food-packaging materials acquired on the retail market. *Food Additives and Contaminants.* **23**(1):93-99.

Fromme, H., G. Bolte, H.M. Koch, J. Angerer, S. Boehmer, H. Drexler, R. Mayer, B. Liebl. 2007a. Occurrence and daily variation of phthalate metabolites in the urine of an adult population. *International Journal of Hygiene and Environmental Health*. **210**(2007)21-33.

Fromme H, L. Gruber M. Schlummer, G. Wolz, S. Böhmer, J. Angerer, R. Mayer, B. Liebl, G. Bolte. 2007b. Intake of phthalates and di(2-ethylhexyl)adipate: results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data. *Environ Int.* Nov;33(8):1012-20. Epub 2007 Jul 3.

Fujii, M., N. Shinohara, A. Lim, T. Otake, K. Kumagai, Y. Yanagisawa. 2003. A study on emission of phthalate esters from plastic materials using a passive flux sampler. *Atmospheric Environment*. **37:**5495-5504.

Fujimaki, K., J. Yoshinaga, C. Watanabe, S. Serizawa, H. Shiraishi, Y. Mizumoto. 2006. Estimation of intake level of di (2-ethyhexyl) phthalate (DEHP) in Japanese pregnant women based on measurement of concentrations of three urinary metabolites. Nippon Eiseigaku Zasshi 61, 340–347. (cited in Matsumoto et al., 2008)

Ganning A.E., U. Brunk, G. Dallner. 1984. Phthalate esters and their effect on the liver. *Hepatology*. **4**:541-547 (cited in ECB, 2008).

Gaudin, R., P. Marsan, A. Robert, P. Ducos, A. Pruvost, M. Levi, and P. Bouscaillou. 2008. Biological monitoring of occupational exposure to di(2-ethylhexyl) phthalate: Survey of workers exposed to plastisols. *International Archeological Occupational of Environmental Health.* **81**(8)959-966.

Gesundheidsbescherming (cited in EU Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). 1997. Table prepared by Professor Jansson on PAE emissions from toys. It contains overview of data made available by the different EU M. States (cited in ECB DIDP, 2003).

Gibson, T.P., W.A. Briggs, B.J. Boone. 1976. Delivery of di-2-ethylhexyl phthalate to patients during hemodialysis, *J. Lab. Clin. Med*. **87**:519-524 (cited in ECB, 2008).

Gray, L.E., J. Ostby, J. Furr, M. Price, D.N.R. Veeramachaneni, L. Parks. 2000. Perinatal exposure to phthalates DEHP, BBP, and DINP, but not DEP, DMP, or DOTP, alters sexual differentiation of the male rat. *Toxicological Sciences.* **58**:350-365.

Green, R., R. Hauser, A.M. Calafat, J. Weuve, T. Schettler, S. Ringer, K. Huttner, and H. Hu. 2005. Use of di(2-ethylhexyl) phthalate-containing medical products and urinary levels of mono(2-ethylhexyl) phthalate in neonatal intensive care unit infants. *Environmental Health Perspecivet*. **113**(9)1222-1225 (cited in NRC, 2008).

Greene, M.A. 1998. Statistical methods for prediction of DINP intake by young children. U.S. Consumer Product Safety Commission, Washington, D.C. December 1998 (cited in CPSC 1998b).

Greene, M. 2002b. Oral DINP Intake Among Young Children. U.S. CPSC, Bethesda, MD 20814. June 18, 2002.

Greenpeace (1997) Chemical leaching from soft PVC toys. Excerpts from the Greenpeace publication: Children's toys made of plasticized PVC, 1997, summary (cited in ECB DEHP 2008)

Haishima, Y., R. Matsuda, Y. Hayashi, C. Hasegawa, T. Yagami, T. Tsuchiya. 2004. Risk assessment of di(2-ethylhexyl)phthalate released from PVC blood circuits during hemodialysis and pump-oxygenation therapy. *International Journal of Pharmaceutics* , 2004. **274**:119-29 (cited in NTP-CERHR, 2006).

Hanawa, T., N. Endoh, F. Kazuno, M. Suzuki, D. Kobayashi, M. Tanaka, K. Kawano, Y. Morimoto, S. Nakajima, T. Oguchi. Investigation of the release behavior of diethylhexyl phthalate from polyvinyl chloride tubing for intravenous administration based on HCO60. *International Journal of Pharmaceutics,* 2003. **267:**141-149 (cited in NTP-CERHR, 2006).

Hatanaka H., Y.Yasui, S. Matsushita. 1994. Direct determination method of phthalic acid esters in vodka by HPLC. *Journal of the Food Hygienic Society of Japan* **35**(1) 51-55.

Hauser, R., S. Duty, L. Godfrey-Bailey, A.M. Calafat. 2004. Medications as a source of human exposure to phthalates. *Environmental Health Perspectives.* **112**(6)751-753 (cited in NRC, 2008).

Hauser, R., P. Williams, L. Altshul, A.M. Calafat. 2005. Evidence of interaction between polychlorinated biphenyls and phthalates in relation to human sperm motility. *Environmental Health Perspectives.* **113**(4)425-430 (cited in NRC, 2008).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Butyl Benzyl Phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Dibutyl Phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Di(2-ethylhexyl)phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Diisodecyl Phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Diisononyl Phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Di-N-Octyl Phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Hazardous Substances Data Bank (HSDB). Hazardous substances data bank query for Bis(2-ethylhexyl)phthalate. National Library of Medicine's TOXNET system. Available online at http://toxnet.nlm.nih.gov (accessed on August 13, 2009).

Health Canada. 1998. Updated risk assessment on Diisononyl Phthalate in vinyl children's products. Consumer Products Division, Product Safety Bureau, Environmental Health Directorate, Health Protection Branch. Ottawa, Ontario. November 14, 1998 (cited in Babich, 2002).

Health Canada. 2002. DEHP in medical devices: an exposure and toxicity assessment. Medical Devices Bureau, Therapeutic Products Directorate, Health Products and Food Branch. Ottawa, Canada, 2002.

Hernández-Díaz, S., A.A. Mitchell, K.E. Kelley, A.M. Calafat, R. Hauser. February 2009. Medications as a potential source of exposure to phthalates in the U.S. population**.** *Environmental Health Perspectives*. **117**(2).

Hileman B. 2000. Alert on phthalates. *Chemical Engineering News.* **78**(32), August 7, 2000 (cited in ECB, 2008).

Hill, S.S. 1997. Analysis of contaminants in oxygen from PVC tubing in respiratory therapy, chromatographic components in electrochemical sensors, and a model for the degradation of electrical cable insulation. Ph.D. Thesis. University of Connecticut (cited in FDA, 2001).

Hines, E.P., A.M. Calafat, M.J. Silva, P. Mendola, S.E. Fenton. 2009. Concentrations of phthalate metabolites in milk, urine, saliva, and serum of lactating North Carolina women. *Environmental Health Perspectives.* **117**(1)86-92.

Högberg, J., A. Hanberg, M. Berglund, S. Skerfving, M. Remberger, A.M. Calafat, A.F. Filipsson, B. Jansson, N. Johansson, M. Appelgren, H. Häkansson. 2008. Phthalate diesters and their metabolites in human breast milk, blood or serum, and urine as biomarkers of exposure in vulnerable populations. *Environmental Health Perspectives.* **116**(3)334-339.

Hoppin, J.A, J.W. Brock, B.J. Davis, D.D. Baird. 2002. Reproductibility of urinary phthalate metabolites in first morning urine samples. *Environmental Health Perspectives*. **110**(5)515-518. (also, as cited in Calafat and McKee, 2006; Fromme et al., 2007b; ECB BBP, 2007)

Hoppin, J.A., R. Ulmer, S.J. London. 2004. Phthalate exposure and pulmonary function. *Environmental Health Perspectives.* **112**(5)571-574.

Huang, P.C, P. Kuo, Y. Guo, P. Liao, C. Lee. 2007. Associations between urinary phthalate monoesters and thyroid hormones in pregnant women. *Human Reproduction*. **22**(10)2715-2722.

Huber, W.W., B. Grasl-Kraup, R. Schulte-Hermann. 1996. Hepatocarcinogenic potential of di(2-ethylhexyl)phthalate in rodents and its implications on human risk. *Critical Reviews in Toxicology*. **26**(4)365-480 (also, cited in ECB DEHP, 2008).

Hubinger, J., D. Harvey. 2006. Analysis of consumer cosmetic products for phthalate esters. *Journal of Cosmetic Science.* **57**(2)127-137.

Hüls. 1996. Study of the determination of the bioaccumulation behavior of Di-n-butyl Phatalate in carp (*Cyprinus carpio*) as specified by OECD 305E. Final report BA-002.

International Programme on Chemical Safety (IPCS). 1997. Environmental Health Criteria 189 Di-n-butyl Phthalate ISBN 92 4 157189 6. Geneva: WHO -- World Health Organization, 1997 (cited in NTP-CEHR, 2003 – DBP).

International Programme on Chemical Safety (IPCS). 1999. Concise International Chemical Assessment Document 17 -Butyl Benzyl Phthalate. Geneva, Switzerland:WHO, 1999 (cited in NTP-CEHR, 2003 – BBP).

Itoh, H., K. Yoshida, S. Masunaga. 2005. Evaluation of the effect of governmental control of human exposure to two phthalates in Japan using a urinary biomarker approach. *International Journal of Hygiene and Environmental Health*. **208**(4)237-245.

Itoh, H., K. Yoshida, S. Masunaga. 2007. Quantitative identification of unknown exposure pathways of phthalates based on measuring their metabolites in human urine. *Environmental Science & Technology*. **41:**4542-4547.

IUR (Inventory Updating Report) database. 2006. U.S. Environmental Protection Agency. (http://www.epa.gov/oppt/iur/tools/data/index.html) (accessed on November 2009).

Jaakkola, J.K., T.L. Knight. 2008. The role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis. *Environmental Health Perspectives.* **116**(7)845-853. Institute of Occupational and Environmental Medicine, University of Birmingham, Birmingham, United Kingdom.

Jacobson M.S., S.V. Kevy, R.J. Grand. 1977. Effects of a plasticizer leached from polyvinyl chloride on the subhuman primate: a consequence of chronic transfusion therapy. *Journal of Laboratory and Clinical Medicine.* **89**(1066-1079) (cited in ECB, 2008).

Jaeger, R. J., R.J. Rubin, 1972. Migration of a phthalate ester plasticizer from polyvinyl chloride blood bags into stored human blood and its localization in human tissues. *New England Journal of Medicine.* **287**:1114-1118 (cited in FDA, 2001 and ECB, 2008).

Janssen P, M. van Veen, M. van Apeldoorn, G. Speijers. 1997. Phthalates in teething rings/animal figures for infants. Advisory report 5293. Brussels: EU Committee Scientific on Toxicity Ecotoxicity and the Environment, CSTEE, 1997.

Jensen, A., H. Knudsen. 2006. Total health assessment of chemicals in indoor climate from various consumer products. Survey of Chemical Substances in Consumer Products, No. 75. Danish Ministry of the Environment. Environmental Protection Agency.

Jönsson, B., J. Richthoff, L. Rylander, A. Giwercman, L. Hagmar. 2005. Urinary phthalate metabolites and biomarkers of reproductive function in young men. *Epidemiology*. **16**(4)487-493.

Juberg, Daland R., K. Alfano, R. Coughlin, K. Thompson. 2001. An observational study of object mouthing behavior by young children. *Pediatrics* **107**(1) 135-142.

Kambia, K., T. Dine, B. Gressier, S. Bah, A.F. Germe, M. Luyckx, C. Brunet, L. Michaud, F. Gottrand. Evaluation of childhood exposure to Di(2-ethylhexyl) Phthalate from perfusion kits during long-term prenatal nutrition. *International Journal of Pharmaceutics,* 2003. **262**:83-91 (cited in NTP-CERHR, 2006).

Kamrin, M.A. 2009. Phthalate risks, phthalate regulation, and public health: a review. *Journal of Toxicology and Environmental Health, Part B.* **12**:157-174.

Karle, V.A., B.L. Short, G.R. Martin, D.I. Bulas, P.R. Getson, N.L. Luban, A.M. O'Brien, R.J. Rubin. 1997. Extracorporeal membrane oxygenation exposes infants to the plasticizer, Di(2-ethylhexyl)phthalate. *Critical Care Medicine.* **25**(4)696-703 (cited in FDA, 2001).

Kato, K, M.J. Silva, J.A. Reidy, D. Hurtz, 3rd, N.A. Malek, L.L. Needham, H. Nakazawa, D.B. Barr, A.M. Calafat. 2004. Mono(2-ethyl-5-hydroxyhexyl) Phthalate and Mono-(2-Ethyl-5-oxohexyl) Phthalate as biomarkers for human exposure assessment to di-(2-ethylhexyl) phthalate. *Environmental Health Perspective*. 112:327-30 (cited in SCENIHR, 2008).

Kawasaki, T., K. Uezono, K. Itoh, M. Ueno. 1991. Prediction of 24-hour urinary creatinine excretion from age, body weight and height of an individual and its application. Nippon Koshu Eisei Zasshi. 38(8), 567-574 (in Japanese). (cited in Itoh et al., 2005)

Kluwe, WM. 1982. Overview of phthalate ester pharmacokinetics in mammalian species. *Environmental Health Perspectives*. **45**:3-9. (cited in Kohn et al., 2000; Marsee et al., 2006)

Koch, H.M. J. Angerer. 2007. Di-iso-nonylphthalate (DINP) metabolites in human urine after a single dose of deuterium-labelled DINP. *Int. J. Hyg. Environ. Health*. Published online 19 December 2006; doi:10.1016/j.ijheh.2006.11.2008.

Koch, H.M., B. Rossbach, H. Drexler, J. Angerer. 2003a. Internal exposure of the general population to DEHP and other phthalates – determination of secondary and primary phthalate monoester metabolites in urine. *Environmental Research.* **93**:177-185.

Koch, H.M., H. Drexler, J. Angerer. 2003b. An estimation of the daily intake of di(2-ethylhexyl)phthalate (DEHP) and other phthalates in the general population. *International Journal of Hygiene and Environmental Health.* **206**:77-83.

Koch, H.M., H. Drexler, J. Angerer. 2004a. Internal exposure of nursery-school children and their parents and teachers to di(2-ethylhexyl)phthalate (DEHP). *International Journal of Hygiene Environmental Health*. **207**:15-22.

Koch, H.M., H.M. Bolt, J. Angerer. 2004b. Di(2-ethylhexyl)phthalate (DEHP) metabolites in human urine and serum after a single oral dose of deuterium labelled DEHP. *Arch Toxicol* 78: 123-130.

Koch, H.M., H.M. Bolt, R. Preuss, R. Eckstein, V. Weisbach, J. Angerer. 2005a. Intravenous exposure to di(2-ethylhexyl) phthalate (DEHP): metabolites of DEHP in urine after a voluntary platelet donation. *Archeological Toxicology*. **79**(12)689-693. (cited in NRC, 2008)

Koch, H.M., H.M. Bolt, R. Preuss, J. Angerer. 2005b. New metabolites of di(2-ethylhexyl)phthalate (DEHP) in human urine and serum after single oral doses of deuterium-labelled DEHP. *Arch Toxicol*. **79**:367-76. (cited in SCENIHR, 2008)

Koch, H.M., K. Becker, M. Wittassek, M. Seiwert, J. Angerer, M. Kolossa-Gehring. 2007. Di-n-butylphthalate (DnBP) and butylbenzylphthalate (BBzP) - urinary metabolite levels and estimated daily intakes: pilot study for the German Environmental Survey on children (GerES IV). *Journal of Exposure Science and Environmental Epidemiology* 17: 378-387 . http://dx.doi.org/10.1038/sj.jes.7500526

Kohn, M.C., F. Parham, S.A. Masten, C. J. Portier, M.D. Shelby, J.W. Brock, L.L. Needham. 2000. Human exposure estimates for phthalates. *Environmental Health Perspectives* **108**(10): A440-442.

Könemann, W.H. 1998. Phthalate release from soft PVC baby toys. Report from the Dutch Consensus Group. RIVM-National Institute of Public Health and the Environment. (cited in ECB DEHP, 2008)

Koo, H., B. Lee. 2004. Estimated exposure to phthalates in cosmetics and risk assessment. *Journal of Toxicology and Environmental Health, Part A.* **67**(23-24)1901-1914.

Koo, H., B. Lee. 2005. Human monitoring of phthalates and risk assessment. *Journal of Toxicology and Environmental Health, Part A.* **68**(16)1379-1392.

Kuchen, A., F. Müller, M. Farine, H. Zimmermann, O. Blaser, C. Wüthrich. 1999. Die mittlere tägliche Aufnahme von Pestiziden und anderen Fremdstoffen über die Nahrung in der Schweiz. *Mitt Lebensm.unters Hyg*. **90**:78-107.

Kwapniewski, R., M. Hirata-Koizumi, M. Ema. 2008. Occupational exposure to dibutyl phthalate among manicurists. *Journal of Occupational and Environmental Medicine*. **50**(6)705-711.

Lay, J.O., B.J. Miller. 1987. Plasticizers in pacifiers: Direct determination by FAB-MS. *Analytical Chemistry* **59**:1323A-1325A. (cited in NTP-CERHR DEHP, 2000)

Lewis L.M., T.W. Flechtner, J. Kerkay, K.H. Pearson, S. Nakamoto S. 1978. Bis(2-ethylhexyl) phthalate concentration in the serum of hemodialysis patients. *Clinical Chemistry*. **245**:741-746 (cited in ECB, 2008).

Loff, S., F. Kabs, K. Witt, J. Sartoris, B. Mandl, K.H. Niessen, K.L. Waag. 2000. Polyvinylchloride infusion lines expose infants to large amounts of toxic plasticizers. *Journal of Pediatric Surgery.* **35**(12)775-1781. (cited in FDA, 2001 and NTP-CERHR, 2006)

Loff, S., F. Kabs, U. Subotic, T. Schaible, F. Reinecke, M. Langbein. 2002. Kinetics of diethylhexyl-phthalate extraction from polyvinylchloride-infusion lines. *JPEN Journal of Parenteral and Enteral Nutrition*. **26:**305-9 (cited in NTP-CERHR, 2006).

Maas, R., S. Patch, T. Pandolfo. 2004. Inhalation and ingestion of phthalate compounds from use in synthetic modeling clays. *Bulletin of Environmental Contamination and Toxicology*. **73:**227–234 (cited in Schettler, 2006).

Main, K.M., G.K. Mortensen, M.M. Kaleva, K.A. Boisen, I.N. Damgaard, M. Chellakooty, I.M. Schmidt, A. Suomi, H.E. Virtanen, J.H. Petersen, A. Andersson, J. Toppari, N.E. Skakkebaek. 2006. Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. *Environmental Health Perspectives.* **114**(2)270-276.

Marin, M.L., J. Lopez, A. Sanchez, J. Vilaplana, A. Jimenez. 1998. Analysis of potentially toxic phthalate plasticizers used in toy manufacturing. *Bulletin of Environmental Contamination and Toxicology*. **60**(1)68-73

Marsee, K., T.J. Woodruff, D.A. Axelrad, A.M. Calafat, S.H., Swan. 2006. Estimated daily phthalate exposures in a population mothers of male infants exhibiting reduced anogenital distance. *Environmental Health Perspectives,* 2006. **114**(6):805-809.

Matsumoto, M., M. Hirata-Koizumi, M. Ema. 2008. Potential adverse effects of phthalic acid esters on human health: A review of recent studies on reproduction. *Regulatory Toxicology and Pharmacology.* **50:**37–49.

Mazur, H.I., D.J. Stennett, P.K. Egging. 1989. Extraction of diethylhexylphthalate from total nutrient solution-containing polyvinyl chloride bags. *JPEN Journal of Parenteral and Enteral Nutrition*. Jan-Feb; **13**(1):59-62 (cited in FDA, 2001).

Meek, M., P. Chan. 1994. Bis(2-ethylhexyl)phthalate: Evaluation of risks to health from environmental exposure in Canada. *Environmental Carcinogenesis & Ecotoxicology Reviews.* C12:179-194 (cited in Shea, 2003; SCENIHR, 2008; NTP-CERHR DEHP, 2006).

Ministry of Agriculture, Fisheries and Food (MAFF). 1987. Survey of plasticizer levels in food contact material and in food. Food Surveillance paper No 21. Ministry of Agriculture, Fisheries and Food. London, Her Majesty's Stationary Office. (cited in ECB DBP 2003-04).

Ministry of Agriculture, Fisheries and Food (MAFF). 1996a. Food Surveillance Information Sheet No. 82. London, UK:MAFF (cited in Fromme et al., 2007b; ECB BBP 2007; ECB DINP, 2003; NTP-CERHR BBP, 2003; NTP-CERHR DBP, 2003).

Ministry of Agriculture, Fisheries and Food (MAFF). 1996b. Phthalates in Infant Formulae. Joint Food Safety and Standards Group Food Surveillance Information Sheet, Vol 1999: MAFF - UK, 1996; 7p (cited in NTP-CERHR BBP, 2003; NTP-CERHR DBP, 2003).

Ministry of Agriculture, Fisheries and Food (MAFF). 1998. Phthalates in infant formula-follow-up survey. Food Surveillance Sheet No. 168. (cited in ECB BBP, 2007; NTP-CERHR, 2003)

Mint, A., S.A.M. Hotchkiss, J. Caldwell. 1994. Percutaneous absorption of diethyl phthalate through the rat and human skin. *Toxicology in Vitro.* ***8***(2)251–256. (cited in Wormuth et al., 2006).

Morita M., M. Nakamura, S. Minura. 1973 . Phthalic acid esters (DOP and DBP) in foods. Annual Report of Tokyo Metropolitan Research Laboratory of Public Health. (1972, published in 1973) **24:**357-362.

Müller, A.K., E. Nielsen, O. Ladefoged. 2002. Human exposure to selected phthalates in Denmark. Institute of Food Safety and Nutrition, The Danish Veterinary and Food Administration.

Nässberger L, A. Arbin, J. Östelius. 1987. Exposure of patients to phthalates from polyvinyl chloride tubes and bags during dialysis, *Nephron.* **45**:286-290 (cited in ECB, 2008).

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2008a. Existing chemical hazard assessment report on butyl benzyl phthalate (BBP). Department of Health and Ageing. Government of Australia. June 2008. Available online at http://www.ag.gov.au/cca.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2008b. Existing chemical hazard assessment report on dibutyl phthalate (DBP). Department of Health and Ageing. Government of Australia. June 2008. Available online at http://www.ag.gov.au/cca.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2008c. Existing chemical hazard assessment report on di-isononyl phthalate (DINP). Department of Health and Ageing. Government of Australia. June 2008. Available online at http://www.ag.gov.au/cca.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2008d. Existing chemical hazard assessment report on di-n-octylphthalate (DnOP). Department of Health and Ageing. Government of Australia. June 2008. Available online at http://www.ag.gov.au/cca.

National Institutes of Health (NIH). ChemIDPlus-BBP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Institutes of Health (NIH). ChemIDPlus-DBP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Institutes of Health (NIH). ChemIDPlus-DEHP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Institutes of Health (NIH). ChemIDPlus-DIDP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Institutes of Health (NIH). ChemIDPlus-DINP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Institutes of Health (NIH). ChemIDPlus-DnOP. U.S. National Library of Medicine. ChemIDPlus Lite database of chemicals. Available online at http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (accessed November 2009).

National Research Council (NRC). 2008. Phthalates and cumulative risk assessment: the task ahead. Committee on the Health Risks of Phthalates. Washington, DC: National Academies Press. Available online at http://www.nap.edu/catalog.php?record_id=12528 (accessed November 2009).

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR). 1982. Carcinogenesis bioassay of di-(2-ethylhexyl)phthalate (CAS No. 117-81-7) in F344 rats and B6C3F, mice (feed study). NTP Tech. Rep. Ser. TR No. 217, NTP, Research Triangle Park, NC.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) BBP. 2000. Monograph on the potential human reproductive and developmental effects of Butyl Benzyl Phthalate (BBP). U.S. Department of Health and Human Services. October 2000. NTP-CERHR-BBP-00.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DBP. 2000. Monograph on the potential human reproductive and developmental effects of di-*n* -butyl phthalate (DBP). U.S. Department of Health and Human Services. October 2000. NTP-CERHR-DBP-00.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DEHP. 2000. Monograph on the potential human reproductive and developmental effects of di-(2-ethylhexyl)phthalate (DEHP). U.S. Department of Health and Human Services. October 2000. NTP-CERHR-DEHP-00.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DINP. 2000. Monograph on the potential human reproductive and developmental effects of di-isononyl phthalate (DINP). U.S. Department of Health and Human Services. October 2000. NTP-CERHR-DINP-00.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DnOP. 2000. Monograph on the potential human reproductive and developmental effects of di *n* octyl phthalate (DnOP). U.S. Department of Health and Human Services. October 2000. NTP-CERHR-DNOP-00.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) BBP. 2003. Monograph on the potential human reproductive and developmental effects of butyl benzyl phthalate (BBP). U.S. Department of Health and Human Services. March 2003. NIH Publication No. 03-4487.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DIDP. 2003. Monograph on the potential human reproductive and developmental effects of di-isodecyl phthalate (DIDP). U.S. Department of Health and Human Services. April 2003. NIH Publication No. 03-4485.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DINP. 2003. Monograph on the potential human reproductive and developmental effects of di-isononyl phthalate (DINP). U.S. Department of Health and Human Services. March 2003. NIH Publication No. 03-4484.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DnHP. 2003. Monograph on the potential human reproductive and developmental effects of di-*n*-hexyl phthalate (DnHP). U.S. Department of Health and Human Services. May 2003. NIH Publication No. 03-4489.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DnOP. 2003. Monograph on the potential human reproductive and developmental effects of di-*n*-octyl phthalate (DnOP). U.S. Department of Health and Human Services. May 2003. NIH Publication No. 03-4488.

National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) DEHP. 2006. Monograph on the potential human reproductive and developmental effects of di-(2-ethylhexyl) phthalate (DEHP). U.S. Department of Health and Human Services. March 2006. NIH Publication No. 06-4476.

Nativelle, C., K. Picard, I. Valentin, J.C. Lhugenot, M.C. Chagnon. 1999. Metabolism of n-butylbenzyl phthalate in the female Wistar rat. Identification of new metabolites. *Food Chem Toxico*l 37:905-917. (cited in Kohn et al., 2000; Marsee et al., 2006)

Niino, T., T. Ishibashi, T. Itho, S. Sakai, H. Ishiwata, T. Yamada, S. Onodera. 2001. Monoester formation by hydrolysis of dialkyl phthalate migrating from polyvinyl chloride products in human saliva. *Journal of Health Science*. **47**(3)318-322.

Niino, T., T. Kura, T. Ishibashi, T. Itho, S. Sakai, H. Ishiwata, T. Yamada, S. Onodera. 2003. A simple and reproducible testing method for dialkyl phthalate migration from polyvinyl chloride products into saliva stimulant. *Journal of the Food Hygienic Society of Japan*. **44**(1)13-18.

Nilsson, N.H., B. Malmgren-Hansen, N. Bernth, E. Pedersen, K. Pommer. 2006. Survey and health assessment of chemicals substances in sex toys. *Survey of Chemical Substances in Consumer Products*, **No. 77.**

Ono, K., R. Tatsukawa, T. Wakimoto. 1975. Migration of plasticizer from hemodialysis blood tubing, *Journal of the American Medical Association.* **234**:948-949 (cited in ECB, 2008).

Otake, T., J. Yoshinaga, Y. Yanagisana. 2004. Exposure to phthalates esters from indoor environment. *Journal of Exposure Analysis and Environmental Science.* **14**(7)524-8.

Page, B.D., G.M. Lacroix. 1992. Studies into the transfer and migration of phthalate esters from aluminum foil-paper laminates to butter and margarine. *Food Additives and. Contaminants.* **9**(3) 197-212.

Pan, G., T. Hanaoka, M. Yoshimura, S. Zhang, P. Wang, H. Tsukino, K. Inoue, H. Nakazawa, S. Tsugane, K. Takahashi. 2006. Decreased serum free testosterone in workers exposed to high levels of di- n-butyl phthalate (DBP) and di-2-ethylhexyl

phthalate (DEHP): a cross-sectional study in China. *Environmental Health Perspectives*. **114**(11)1643-1648.

Peck, C.C., P.W. Albro. 1982. Toxic potential of the plasticizer di(2-ethylhexyl) hthalate in the context of its disposition and metabolism in primates and man. *Environmental Health Perspectives*. **45**:11-17. (cited in Kohn et al., 2000; Marsee et al., 2006)

Peck, C.C., D. Odom, H. Friedman, P. Albro, J. Hass, J. Brady, D. Jess. 1979. Di-(2-ethylhexyl)phthalate (DEHP) and mono-2-ethylhexyl phthalate (MEHP) accumulation in whole blood and red cell concentrates. *Transfusion* **19**:137-146 (cited in ECB, 2008).

Pedersen, G.A., L. Jensen, A. Fankhauser, S. Biedermann, J. Petersen, B. Fabech. 2008. Migration of epoxidized soybean oil (ESBO) and phthalates from twist closures into food and enforcement of the overall migration limit. *Food Additives and Contaminants.* **25**(4):503-510.

Petersen, J., T. Breindahl. 2000. Plasticizers in total diet samples; baby food and infant formulae. *Food Additives and Contaminants.* **17:**133-141 (cited in Fromme et al., 2007).

Pfannhauser, W., E. Leitner, H. Siegel. 1995. Phthalates in Lebensmitteln. Forschungsbericht Sektion III: Osterreichisches Bunderministerium fur Gesundheit and Konsumentenschutz, Wien, 1995. (cited in Fromme et al., 2007).

Pindar, A. et al. (1997) (cited in European Union Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). 1998a. Phthalate migration from soft PVC toys and child-care articles. Opinion expressed at the CSTEE third plenary meeting Brussels, 24 April. 1998)

Plonait, S.L., H. Nau, R.F. Maier, W. Wittfoht, M. Obladen. 1993. Exposure of newborn infants to di-(2-ethylhexyl)-phthalate and 2-ethylhexanoic acid following exchange transfusion with polyvinylchloride catheters. *Transfusion*. **33**:598-605 (cited in ECB, 2008; FDA, 2001).

Pollack, G.M., J.F. Buchana, R.L. Slaughter, R.K. Kohli, D.D. Shen. 1985. Circulating concentration of di(2-ethylhexyl) phthalate and its de-esterified phthalic acid products following plasticizer exposure in patients receiving hemodialysis. Toxicological Applications Pharmacology. **79**:257-267 (cited in FDA, 2001 and ECB, 2008).

Rastogi, S.C., J. Vikelsøe, G.H. Jensen, E. Johansen, L. Carlsen. 1997. Migration of phthalates from teethers. Ministry of Environment and Energy, National Environmental Research Institute, Roskilde, Denmark. Research notes from NERI no. 64 (cited in Babich, 2002).

Rastogi S.C. 1998. Gas chromatographic analysis of phthalate esters in plastic toys. *Chromatographia.* **47**:24-726.

Reddy, B., R. Rozati, B.V.R Reddy, N.V.V.S.S. Raman. 2006. Association of phthalate esters with endometriosis in Indian women. *BJOG*: *An International Journal of Obstetrics and Gynaecology*. **113**(5)515-520.

Remer, T., A. Neubert, C. Maser-Gluth. 2002. Anthropometry-based reference values for 24-h urinary creatinine excretion during growth and their use in endocrine and nutritional research. *Am. J. Clin. Nutr*. 75(3): 561-569. (cited in Koch et al., 2007)

Rijk, M.A.H, J. Telman, K. Ehrlert. 1999. Addendum to TNO Report V99.598, "Validation of the method 'determination of diisononylphthalate in saliva stimulant.'" TNO Nutrition and Food Research Institute, Ultrechtseweg, The Netherlands. Report number V99.849 (cited in Babich, 2002).

Rijk, R., K. Ehlert. 1999. Validation of the method "determination of diisononyl phthalate in saliva stimulant." 1999. TNO Nutrition and Food Research Institute, Ultrechtseweg, The Netherlands. May 27, 1999. TNO Report V99.598 (cited in Babich, 2002).

RIVM, 1998. Rijksinstituut voor Volksgesondheid en Milieu (National Institute of Public Health and Environment). Phthalate release from soft PVC baby toys, Report from the Dutch Consensus Group. Könemann W.H. ed. RIVM, Bilthoven, The Netherlands RIVM report 61 3320 002. September 1998 (cited in Babich, 2002 and in CSTEE (1998).

Ringer, S.A., D.K. Richardson, R.A. Sacher, M. Keszler, W.H. Churchill. 1998. Variations in transfusion practice in neonatal intensive care. *Pediatrics*, Feb; **101**(2)194-200 (cited in FDA, 2001).

Rubin R.J., C.A Schiffer. 1976. Fate in humans of the plasticizer di-2-ethylhexyl phthalate, arising from transfusion of platelets stored in vinyl plastic bags. *Transfusion.* **16(**4)330-335 (cited in ECB, 2008).

Sathyanarayana, S. 2008. Phthalates and children's health. Current *Problems in Pediatric and Adolescent Health Care***. 38**:34-49.

Sathyanarayana, S., C.J. Karr, P. Lozano, E. Brown, A.M. Calafat, F. Liu, S.H. Swan, 2008. Baby care products: possible sources of infant phthalate exposure. *Pediatrics*. 260-268.

SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks). 2008. Opinion on the safety of medical devices containing DEHP-plasticized PVC or other plasticizers on neonates and other groups possibly at risk. Adopted after public consultation by the SCENIHR during the 22nd Plenary of 6 February 2008. Health and Consumer Protection, European Commission.

SCHER (Scientific Committee on Health and Environmental Risks). 2005. Opinion on the report "Emission of chemicals by air fresheners tests on 74 consumer products sold in Europe" (BEUC report January 2005). Adopted by the SCHER during the 9th plenary of 27 January 2006. Health and Consumer Protection Directorate- General. European Commission.

SCHER (Scientific Committee on Health and Environmental Risks). 2006. Opinion on the report "Emission of chemicals by air fresheners tests on 74 consumer products sold in Europe" (BEUC report January 2005) Adopted by the SCHER during the 9th plenary of 27 January 2006. European Commission Health & Consumer Protection Directorate-General. Directorate C - Public Health and Risk Assessment. pp.1-19.

SCHER (Scientific Committee on Health and Environmental Risks). 2008. Opinion on phthalates in school supplies. European Commission Health & Consumer Protection Directorate-General. Directorate C - Public Health and Risk Assessment. October 17. pp.1-18.

Schettler, T. 2006. Human exposure to phthalates via consumer products. *International Journal of Andrology*. **29:**134–139. ISSN 0105-6263.

Schmid, P., C. Schlatter. 1985. Excretion and metabolism of di(2-ethylhexyl)phthalate in man. *Xenobiotica.* 15(3): 251-256. (cited in David, 2000; Koch et al., 2003b; Koo and Lee, 2005; Chen et al., 2008; SCENIHR, 2008)

SFED (San Francisco Environment Department). 2008. San Francisco Environment Department website testing results for phthalates in children's toys. August 2008. http://www.sfenvironment.org/our_programs/interests.html?ssi=2&ti=3&ii=135.

Shea, K.M. 2003. Pediatric exposure and potential toxicity of phthalate plasticizers. American Academy of Pediatrics-Technical Report. *Pediatrics.* **111**(6)1467-1747

Shneider B, J. Schena, R. Truog, M. Jacobson, S. Kevy. 1989. Exposure to di(2-ethylhexyl) phthalate in infants receiving extracorporal membrane oxygenation. *New England Journal of Medicine.* 320, 1563 (cited in ECB, 2008; FDA, 2001).

Simoneau, C, H. Geiss, A. Roncari, P. Zocchi, P. Hannaert. 2001. Validation of methodologies for the release of di-isononylphthalate (DINP) in saliva stimulant from toys. European Commission, DG-Joint Research Center, Food Products Unit, Institute for health and Consumer Protection, Ispra, Italy. 2001 EUR 19826 EN (cited in Babich, 2002).

Silva, M.J., D.B. Barr, J.A. Reidy, N.A. Malek, C.C. Hodge, S.P. Caudill, J.W. Brock, L.L. Needham, A.M. Calafat. 2004. Urinary levels of seven phthalate metabolites in the U.S. population from the National Health and Nutrition Examination Survey (NHANES) 1999-2000. *Environmental Health Perspectives*. **112**(3)331-338. (also, as cited in Calafat and McKee, 2006; Fromme et al., 2007b; SCENIHR, 2008)

Silva, M.J., J.A. Reidy, E. Samandar, A.R. Herbert, L.L. Needham, A.M. Calafat. 2005. Detection of phthalate metabolites in human saliva. *Archeological Toxicology*. **79:**647-652.

Silva, M.J., J.A. Reidy, J.L. Preau, Jr., L.L. Needham, A.M. Calafat. 2006. Oxidative metabolites of diisononyl phthalate as biomarkers for human exposure assessment. *Environmental Health Perspectives*. **114**(8)1158-1161. (also, cited in SCENIHR, 2008).

Silva, M.J., J.A. Reidy, K. Kato, J.L. Preau, Jr., L.L. Needham, A.M. Calafat. 2007. Assessment of human exposure to di-isodecyl phthalate using oxidative metabolites as biomarkers. *Biomarkers*. **12**(2)133-144.

Sjöberg P., U. Bondesson, G. Sedin, J. Gustafsson. 1985a. Disposition of di- and mono-(2ethylhexyl)phthalate in newborn infants subjected to exchange transfusions. *Eu. J. Clin. Invest*. 15, 430-436.

Sjöberg P.O., U.G. Bondesson, E.G. Sedin, J.P. Gustafsson. 1985b. Exposure of newborn infants to plasticizers. Plasma levels of di-(2-ethylhexyl) phthalate and mono-(2-ethylhexyl) phthalate during exchange transfusion, *Transfusion* **25:**424-428 (cited in ECB, 2008).

Sørensen, L. 2006. Determination of phthalates in milk and milk products by liquid chromatography/tandem mass spectrometry. *Rapid Communication Mass Spectrom*. **20**:1135-1143.

Spanish Ministry of Health and Consumer Affairs (cited in European Union Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). 1998a. Phthalate migration from soft PVC toys and child-care articles. Opinion expressed at the CSTEE third plenary meeting Brussels, 24 April 1998.)

Stahlhut, R.W., E. van Wijngaarden, T.D. Dye, S. Cook and S. Swan. 2007. Concentrations of urinary phthalate metabolites are associated with increased waist circumference and insulin resistance in adult U.S. males. *Environmental Health Perspectives*. **115**(6)876-882.

Steiner I, K. Kubesch, F. Fiala. 1998a. Migration of DEHP and DINP from PVC articles, preliminary summary. *Austrian Standards Institute* (cited in ECB DEHP, 2008).

Steiner, I., L. Scharf, F. Fiala, J.F. Washuttl. 1998b. Migration of di-(2-ethylhexyl) phthalate from PVC child articles into saliva and saliva stimulant. *Food Additives and Contaminants*. **15**:812-817 (cited in Babich, 2002).

Stopford, W., J. Turner, D. Cappellini. 2003. Determination of the magnitude of clay to skin and skin to mouth transfer of phthalates associated with the use of polymer clays.

Department of Community & Family Medicine, Division of Occupational & Environmental Medicine, Duke University Medical Center. Durham, NC, 2003.

Stringer, R., I. Labunska, D. Santillo, P. Johnston, J. Siddorn, A. Stephenson. 1997. Determination of the composition and quantity of phthalate ester additives in PVC children's toys. Greenpeace Research Laboratories Technical Note, University of Exeter, UK.

Stringer, R., I. Labunska, D. Santillo, P. Johnston, J. Siddorn, A. Stephenson. 2000. Concentrations of phthalate esters and identification of other additives in PVC children's toys. *Environmental Science and Pollution Research International*. **7**(1)27-36.

Swan, S.H. 2006. Prenatal phthalate exposure and anogenital distance in male infants. *Environmental Health Perspectives*. **114**(2)A84-A90. (also, cited in SCENIHR, 2008; Marsee et al., 2006)

Swan, S.H., K.M. Main, F. Liu, S.L. Stewart, R.L. Kruse, A.M. Calafat, C.S. Mao, J.B. Redmon, C.L. Ternand, S. Sullivan, J.L. Teague and the Study for Future Families Research Team. 2005. Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environmental Health Perspectives*. **113**(8)1056-1061. (also, cited in Fromme et al., 2007b; Marsee et al., 2006; SCENIHR, 2008)

Tanaka, A., A. Matsumoto, T. Yamaha. 1978. Biochemical studies on phthalic esters. III. Metabolism of dibutyl phthalate (DBP) in animals. Toxicology. 9:109-123. (cited in Kohn et al., 2000; Marsee et al., 2006)

Teitelbaum, S.L., J.A. Britton, A.M. Calafat, X. Xe, M.J. Silva, J.A. Reidy, M.P. Galvez, B.L. Brenner, M.S. Wolff. 2008. Temporal variability in urinary concentrations of phthalate metabolites, phytoestrogens and phenols among minority children in the United States. *Environmental Research*. **106**(2)257-269. (also, cited in SCHER, 2008).

Thornton, J. 2002. Environmental impacts of polyvinyl chloride building materials. A Healthy Building Network Report.

Tønning, K., P.L. Hansen, K. Pommer, B. Malmgren-Hansen. 2006. Survey and health assessment of chemicals substances in pleasure gel. *Survey of Chemical Substances in Consumer Products,* **No. 76.**

Tsumura, Y., S. Ishimitsu, I. Saito, H. Saki, Y. Kobayashi, Y. Tonogai. 2001. Eleven phthalate esters and di(2-ethylhexyl) adipate in one-week duplicate diet samples obtained from hospitals and their estimated daily intake. *Food Additives and Contaminants.* **18**(5)449-460.

Tsumura, Y., S. Ishimitsu, I. Saito, H. Saki. 2003. Estimated daily intake of plasticizers in 1-week duplicate samples following regulation of DEHP-contaminated PVC gloves in Japan. *Food Additives and Contaminants.* **184**:49-60. (cited in NTP-CEHR, 2008-DEHP).

Tulve, N.S. J. Suggs, T. McCurdy, E. Cohen Hubal, J. Moya. 2002. Frequency of mouthing behavior in young children. *Journal of Exposure Analysis and Environmental Epidemiology.* **12**(4)259-264.

TURI (Toxics Use Reduction Institute). 2006. Five chemicals alternatives assessment study. Prepared by The Massachusetts Toxics Use Reduction Institute, University of Massachusetts Lowell.

Turnbull D., J.V. Rodricks.1989. A comprehensive risk assessment of DEHP as a component of baby pacifiers, teethers, and toys. The Risk Assessment of Environmental and Human Health Hazards: *A Textbook of Case Studies, John Wiley and Sons* (cited in ECB DEHP, 2008)

U.S. Environmental Protection Agency (EPA). 2008. Morgan, M.K., L.S. Sheldon, C.W. Croghan. A pilot study of children's total exposure to persistent pesticides and other persistent organic pollutants (CTEPP). Research Triangle Park, NC.

Van Veen, M.P. 1995. ConsExpo. A program to estimate consumer product exposure and uptake. Report nr. 612810.002. National Institute of Public Health and Environmental Protection, Bilthoven (cited in ECB, 2003).

Vikelsøe, J., G.H. Jensen, E. Johansen, I. Carlsen, L. Carlsen. 1997. Migration of phthalates from teething rings. Environmental Chemistry Department, Danish Environment Testing Agency, Roskilde, Denmark. July 2, 1997. (also cited in Babich, 2002, and cited in ECB DEHP, 2008).

Wenzl, T. 2009. Methods for the determination of phthalates in food. Outcome of a survey conducted among European food control laboratories. Belgium: European Commission. Joint Research Center, Institute for Reference Materials and Measurement.

Weuve, J., B.N. Sanchez, A.M. Calafat, T. Schettler, R.A.Green, H. Hu, R. Hauser. 2006. Exposure to phthalates in neonatal intensive care unit infants: Urinary concentrations of monoesters and oxidative metabolites. *Environmental Health Perspectives*. **114**(9)1424-1431 (cited in NRC, 2008).

Wigle, D.T. (2003). Child health and the environment. New York: Oxford University Press.

Wilson, N.K., J.C. Chuang, C. Lyu, R. Menton, M.K. Morgan. 2003. Aggregate exposures of nine preschool children to persistent organic pollutants at day care and at home. *Journal of Exposure Analysis and Environmental Epidemiology.* **13**:187-202

Wind, M.L. 2002. Memorandum from Marilyn L. Wind, Ph.D., Deputy Associate Executive Director, Directorate for Health Sciences to the Commission. Response to Petition HP 99-1, August 13, 2002.

Wittassek, M., J. Angerer. 2008. Phthalates: metabolism and exposure. *International Journal of Andrology*. **31**(2)131-138.

Wittassek, M., G.A. Wiesmuller, H.M. Koch, R. Eckard, L. Dobler, J. Muller, J. Angerer, C. Schluter. 2007a. Internal phthalate exposure over the last two decades—a retrospective human biomonitoring study. *International Journal of Hygiene and Environmental Health.* **210**(3-4)319-333 (cited in NRC, 2008).

Wittassek, M., W. Heger, H.M. Koch, K. Becker, J. Angerer, M. Kolossa-Gehring. 2007b. Daily intake of di(2-ethylhexyl)phthalate (DEHP) by German children -- A comparison of two estimation models based on urinary DEHP metabolite levels. *International Journal of Hygiene and Environmental Health*. Jan; **210**(1)35-42. Epub 2006 Dec 20.

Wittassek, M., G.A. Wiesmüller, H.M. Koch, R. Eckard, L. Dobler, J. Müller, J. Angerer, C. Schlüter. 2007c. Internal phthalate exposure over the last two decades – A retrospective human biomonitoring study. *International Journal of Hygiene and Environmental Health,* **210(**3-4)319-333. (cited in SCENIHR, 2008).

Wolff, M.S., S.L. Teitelbaum, G. Windham, S.M. Pinney, J.A. Britton, C. Chelimo, J. Godbold, F. Biro, L.H. Kushi, C.M. Pfeiffer, A.M. Calafat. 2007. Pilot Study Of Urinary Biomarkers Of Phytoestrogens, Phthalates, And Phenols In Girls. *Environmental Health Perspective*. Jan;115(1):116-21. (Cited in SCHER, 2008).

World Health Organization (WHO). 1998. Food Safety Issues, GEMS/FOOD International Diary Survey: Infant exposure to certain organochloric contaminants from breast milk – a risk assessment. WHO/FSF/FOS/98.4, Geneva Switzerland (cited in European Union, 2004).

Wormuth, M., M. Acheringer, M. Vollenweider, M. Hungerbuhler. 2006. What are frequently used phthalic acid esters in Europeans? *Risk Analysis*: **26**(3)803-24.

Yano, K, N. Hirosawa, Y. Sakamoto, H. Katayama, T. Moriguchi, K. Asaoka. 2005. Phthalate levels in baby milk powders sold in several countries. *Bulletin of Environmental Contamination and Toxicology.* **74(**373-379).

Zhang, Y., L. Zheng, B. Chen. 2006. Phthalate exposure and human semen quality in Shanghai: a cross-sectional study. *Biomedical and Environmental Sciences*. **19**(3)205-209.

Zhu, J., S. Phillips, Y. Feng, X. Yang. 2006. Phthalates esters in human milk: concentration variations over a 6-month postpartum time. *Environmental Science and Technology*. **40:**5276-5281.