Endocrine disrupting chemicals in indoor and outdoor air
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**Abstract**

The past 50 years have seen rapid development of new building materials, furnishings, and consumer products and a corresponding explosion in new chemicals in the built environment. While exposure levels are largely undocumented, they are likely to have increased as a wider variety of chemicals came into use, people began spending more time indoors, and air exchange rates decreased to improve energy efficiency. As a result of weak regulatory requirements for chemical safety testing, only limited toxicity data are available for these chemicals. Over the past 15 years, some chemical classes commonly used in building materials, furnishings, and consumer products have been shown to be endocrine disrupting chemicals — that is they interfere with the action of endogenous hormones. These include PCBs, used in electrical equipment, caulking, paints and surface coatings; chlorinated and brominated flame retardants, used in electronics, furniture, and textiles; pesticides, used to control insects, weeds, and other pests in agriculture, lawn maintenance, and the built environment; phthalates, used in vinyl, plastics, fragrances, and other products; alkylphenols, used in detergents, pesticide formulations, and polystyrene plastics; and parabens, used to preserve products like lotions and sunscreens. This paper summarizes reported indoor and outdoor air concentrations, chemical use and sources, and toxicity data for each of these chemical classes. While industrial and transportation-related pollutants have been shown to migrate indoors from outdoor sources, it is expected that indoor sources predominate for these consumer product chemicals; and some studies have identified indoor sources as the predominant factor influencing outdoor ambient air concentrations in densely populated areas. Mechanisms of action, adverse effects, and dose–response relationships for many of these chemicals are poorly understood and no systematic screening of common chemicals for endocrine disrupting effects is currently underway, so questions remain as to the health impacts of these exposures.

1. Background

The rapid development of new building materials, furnishings, and consumer products over the past 50 years has resulted in a corresponding increase in new chemicals in the built environment (Weschler, 2009). Indoor concentrations are largely uncharacterized, but they have likely increased over time as a wider variety of chemicals are used and air exchange rates in buildings decrease to improve energy efficiency (Weschler, 2009). Chemical concentrations are often highest indoors because many of the sources are indoors and because of limited degradation indoors compared with outdoors. Furthermore, people spend about 90% of their time indoors (Klepeis et al., 2001; Schweizer et al., 2007; US General Accounting Office, 1999), so indoor concentrations can be more relevant to human exposure assessment than ambient concentrations.

In this article we review six classes of semivolatile chemicals in indoor and outdoor air, including polychlorinated biphenyls (PCBs), brominated flame retardants (e.g. PBDEs), pesticides, phthalates, alkylphenols (e.g. nonylphenol, alkylphenol ethoxylates), and parabens (see Fig. 1 for examples of chemical structures). We summarize available data on major sources and indoor and outdoor concentrations, describe the relative importance of inhalation and dust as routes of exposure, and provide a brief discussion of potential health effects.

In general, as a result of weak regulatory requirements for chemical safety testing, only limited toxicity data are available for many common commercial chemicals (US Government Accountability Office, 2005). For example, US EPA found that of the almost 3000 chemicals produced at more than 1 million pounds per year (high production-volume chemicals (HPV)), fewer than 7% had a complete set of six basic toxicity tests and 43% had none of the six tests (US Environmental Protection Agency, 1998). Data on exposure to the HPV chemicals are similarly sparse. In light of these data gaps, the European Union recently initiated a regulatory program that requires chemical manufacturers to produce toxicity and
Exposure information on commercial high production chemicals – the Registration, Evaluation and Authorization of Chemicals (REACH) Program (Lahl and Hawxwell, 2006).

Over the past 15 years, some chemicals used in building materials, furnishings, and consumer products have been shown to be endocrine disrupting chemicals (EDCs) – that is they interfere with the action of endogenous hormones. The greatest concern associated with exposure to EDCs is the potential for adverse effects on reproduction and development, because they have been shown to disrupt normal endocrine signaling in in vitro and in vivo animal studies (Colborn et al., 1993). For example, nonylphenol and methyl paraben bind to the estrogen receptor and initiate transcription of estrogen-responsive genes (Bonefeld-Jorgensen et al., 2007; Routledge et al., 1998; Soni et al., 2005); PCBs and PBDEs have been shown to interfere with thyroid hormone homeostasis and as a consequence affect in utero neurological development in humans and rodents (Arisawa et al., 2005; Longnecker et al., 2003; Morse et al., 1996; Turyk et al., 2007; Winnke et al., 2002; Zhou et al., 2002), and dibutyl phthalate interferes with androgen production in utero (Gray et al., 1998). Exposure during development (in utero, infants and children) is of special concern, because developing tissues are exquisitely sensitive to endocrine signals and disruption of these signaling pathways can result in permanent alterations in tissue structure and function (Colborn et al., 1993; Henley and Korach, 2006; Markey et al., 2003; National Research Council, 1999; Rogan and Ragan, 2007).

For example, in utero exposure to phthalates such as dibutyl phthalate has been shown to affect masculinization of the male rat fetus at doses of 100 mg/kg per day (LOAEL) (Mylchreest et al., 2000), to affect testicular testosterone levels at 50 mg/kg per day (LOAEL) (Lehmann et al., 2004), and to affect mammary gland and spermatocyte development at 1.5–3.0 mg/kg per day (LOAEL) in maternal diet (Lee et al., 2004); while testicular toxicity in adult animals is observed only at much higher doses (e.g. LOAEL ~700 mg/kg per day) (European Union, 2004; Marsman, 1995; National Toxicology Program (NTP), 2000b).

While laboratory data on biological effects of EDCs raise concerns, they also leave many questions unanswered. Major uncertainties in understanding health risks of EDCs include the following:

- No routine chemical screening identifies chemicals that act by known endocrine mechanisms.

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Fig. 1. Molecular structures of selected chemicals from each class.

- **PCB (2,2′,5,5′-Tetrachlorobiphenyl, PCB 52)**
- **Brominated flame retardant (2,2′,4,4′-tetrabromodiphenylether, BDE 47)**
- **Chlordane**
- **Di-butyl phthalate**
- **4-nonyl phenol (branched)**
- **Methyl paraben**

[Chemical structures depicted in the text]
Mechanisms by which chemicals may interfere with biological signaling are still incompletely described.

The implications of disrupting these biological signals are not well understood and so the toxicological implications are unknown.

Major exposure sources and pathways are not characterized.

Thus, while human data to support environmental endocrine disruption are extremely limited at this time, this lack of evidence is likely attributable to the broadness and complexity of the subject. In the meantime, information on chemical uses and air concentrations can aid in understanding major exposure sources and pathways in order to suggest opportunities for exposure reduction and aid in the design of human studies.

2. Sources, measured air concentrations, and potential health effects

2.1. Polychlorinated biphenyls

Polychlorinated biphenyl (PCB) use in the US began in 1929 and peaked in the 1970s (Agency for Toxic Substances and Disease Registry, 2000; Vorhees, 2001). The mixtures of 209 possible PCB congeners based on the number and position of chlorine atoms were valued for their low flammability and vapor pressure and used extensively through the 1970s in a wide range of consumer products such as flame retardants, paints, plastics, adhesives, lubricants, sealants, hydraulic and heat transfer fluids, capacitors, transformers, vacuum pumps and gas transition turbines (Agency for Toxic Substances and Disease Registry, 2000; Jamshidi et al., 2003; Turyk et al., 2007).

Restriction of their use in the US began in the late 1970s through the US EPA Toxic Substance Control Act (US Environmental Protection Agency, 2008; Vorhees, 2001) though they remain major global pollutants detected in the atmosphere as well as in human blood and breast milk (Arisawa et al., 2005; Centers for Disease Control and Prevention, 2005; Longnecker et al., 2007; Turyk et al., 2007).

PCB concentrations in air tend to be highest in urban areas and lower in rural or remote areas (Hamer et al., 2004; Jamshidi et al., 2006; Motelay-Massei et al., 2005; Shen et al., 2006), with congener composition varying from city to city, indicating that local sources may have a substantial influence on regional values (Shen et al., 2006) (see Fig. 2). There is evidence of geographic variation in PCB homolog compositions according to latitude, where relative contributions of tetra-CBs seem to increase with increasing latitude, while penta-CB and hexa-CB contributions decrease with increase in latitude (Shen et al., 2006).

In Fig. 2, concentrations of a single PCB congener (IUPAC PCB 52) are plotted to enhance comparability across studies. PCB 52 is among the more volatile of the congeners, so it tends to be readily detected in air. PCB 52 is estimated to comprise 5–10% of the sum of major PCB congeners in two sets of air sampling data (D. Vorhees, S. Harrad, personal communication).

Indoor air exposures to PCBs are considered to be more significant than outdoor exposures as studies have shown indoor air concentrations to be at least 10 and up to 100,000 times higher than outdoor air concentrations (Fig. 2). Buildings constructed between 1950 and 1979 generally have higher concentrations of PCBs in indoor air (Hazarati and Harrad, 2006). Caulking in older buildings (pre 1977) is another important source and its presence in schools is of particular concern. For example, Fig. 2 shows elevated PCB concentrations in several schools and public buildings in Switzerland and Germany where PCB-containing caulk was used (Gabrio et al., 2000; Kohler et al., 2002, 2005). Furthermore, Liebl et al. showed that higher air concentrations of lower chlorinated PCB congeners (as found in PCB contaminated schools) corresponded to increased blood levels of the same PCB congeners (Liebl et al., 2004). In addition, certain floor finishes that were commercially available for residential use during the 1950s and 1960s contained PCBs. Rudel et al. (2008) reported elevated PCBs in indoor air, house dust, and residents’ blood in two homes where the PCB-containing wood finish Fabulon or “bowling alley wax” was reportedly used in the 1960s. Sanding of floors to refinish them increased exposures substantially (Rudel et al., 2008). PCBs may also leach from old electronic products, and so in some cases indoor air concentrations can be reduced by properly disposing of old appliances and fluorescent lighting that is not marked ANo PCB.
Researchers have hypothesized that PCBs enter the atmosphere from environmental media such as soil (Vorhees, 2001), although recent consideration of chiral signatures indicates that volatilization from soil is not a major source of outdoor air PCB concentrations (Jamschidi et al., 2007). Rather, outdoor air concentrations in urban areas seem to be due to venting of indoor air (Jamschidi et al., 2007).

Although most PCB uses were banned many years ago, PCBs can still be found in the environment today due to their thermal stability, resistance to microbial degradation, and chemical inertness (Vorhees, 2001). PCBs tend to bioaccumulate, leading to dietary exposures through fish, meat, dairy and processed foods (La Rocca and Mantovani, 2006). As PCBs become less prevalent, PCB levels in blood seem to be decreasing (Link et al., 2005; Sjodin et al., 2004). A US study found median blood serum levels of PCB-153 of 90 ng/g lipid in 1985–1989 and 35 ng/g lipid in 2000–2002, with median values steadily decreasing over the years in between (Sjodin et al., 2004). Some studies have shown a slow decline in ambient PCB concentrations from the 1980s to 1990s (Vorhees, 2001) though others show no significant decline from 1997 to 2005 (Harrad et al., 2006). While diet is considered to be the major source of exposure, dietary levels seem to be decreasing faster than indoor air concentrations, making inhalation an increasingly important route of exposure (Harrad et al., 2006; Vorhees, 2001).

A study of several North Carolina daycare centers concluded that inhalation of PCBs was the major route of exposure to the children, compared with dietary and non-dietary ingestion (Wilson et al., 2001), and in homes with elevated PCBs in indoor air and house dust, possibly due to Fabulous wood floor finish applied around 1960, residents had blood PCB concentrations in the highest 5% of a representative sample of adults in the US (Rudel et al., 2008).

PCBs are established developmental neurotoxicants in humans, with elevated prenatal PCB concentrations being associated with cognitive deficits in children (Arisawa et al., 2005; Winneke et al., 2002). PCBs are also associated with thyroid toxicity, effects on immune, reproductive, nervous, and endocrine systems, and cancer effects including breast cancer (Agency for Toxic Substances and Disease Registry, 2000; Arisawa et al., 2005; Brody et al., 2007; Turyk et al., 2007; Winneke et al., 2002). Among the 209 PCB congeners, different congeners are associated with different types of effects; mono-ortho-substituted and co-planar congener structures show toxicological effects similar to dioxin (Schecter et al., 1994), while ortho-substituted congeners appear more neurotoxic (Giesy and Kannan, 1998).

2.2. Polybrominated diphenyl ethers

Polybrominated diphenyl ethers (PBDEs) are current use flame retardants found in a variety of consumer products such as plastics, upholstery, construction materials, and electrical appliances (Talsness, 2008). PBDEs are lipophilic and hydrophobic compounds that tend to persist in the environment, bioaccumulate, and be globally transported due to their resistance to chemical, physical and biological transformations (Deng et al., 2007; Vives et al., 2007); thus, PBDEs can be considered persistent organic pollutants, or POPs, many of which are targeted for global elimination (Ballschmiter et al., 2002). There are 209 PBDE congeners, named according to the total number of bromines off the phenyl rings. Generally the lower brominated congeners (mono through penta) are considered to be potentially more harmful to humans (Deng et al., 2007). While PBDEs are fairly evenly distributed between the particulate and the vapor phase in air, as the congeners get heavier (more bromine atoms) they are increasingly likely to be found in the particulate phase (Vives et al., 2007).

PBDEs are sold as three commercial mixtures: penta-bromodiphenyl ether (penta-BDE), octa-bromodiphenyl ether (octa-BDE), and deca-bromodiphenyl ether (deca-BDE) (Allen et al., 2007). The Bromine Science Environment Forum (BSEF) estimated that 67,000 tons of PBDEs were produced worldwide in 2001 (Deng et al., 2007). Deca-BDE is the most widely used, with an estimated 56,100 tons produced worldwide in 2001, compared to 7,500 tons of penta-BDE produced in the same year (Harrad et al., 2006). While penta-BDE and octa-BDE have recently gone out of use due to restrictions posed by certain governments and a voluntary production ban by some major manufacturers, many sources of exposure remain as these PBDEs are prevalent in a number of common commercial products (Allen et al., 2007; Cahill et al., 2007; Deng et al., 2007; Harrad et al., 2006). Traditionally, penta-BDE was dominated by the BDE 47 and BDE 99 congeners and used in polyurethane foam, foam products, bedding, vehicle interiors, and furniture (Allen et al., 2007; Harrad et al., 2006). Octa-BDE contained a mixture of hepta, octa and nona congeners while deca-BDE consists primarily of BDE 209 (Allen et al., 2007). Both octa- and deca-BDE can be found in electronics such as computers and televisions and deca-BDE is also often in textiles (Allen et al., 2007; Harrad et al., 2006). Because PBDEs are additives mixed into polymers, and are thus not chemically bound to plastics or textiles, they tend to leak off products and enter the air and dust (Deng et al., 2007).

PBDEs are considered to be a ubiquitous environmental contaminant found both in the environment (sediment, soil, sewage, air, and wildlife) and in people (tissue, blood, and breast milk) worldwide (Deng et al., 2007; Goel et al., 2006). Though body burdens show regional variation (the highest values are found in the US), they are also increasing exponentially with approximately a 4–6 year doubling rate (Allen et al., 2007; Deng et al., 2007; Goel et al., 2006; Hites, 2004; Vives et al., 2007; Zota et al., 2008). PBDEs have been found in marine mammals and air in remote areas including the Baltic Sea and the northern Atlantic Sea, indicating that the atmosphere is a pathway for transport (Allen et al., 2007; Deng et al., 2007; Hites, 2004; Vives et al., 2007; Wang et al., 2005).

Indoor air concentrations of PBDEs are generally higher than outdoor air concentrations (see Fig. 3) (Hazarati and Harrad, 2006). Levels of PBDEs in offices are generally higher than levels of PBDEs in homes (Harrad et al., 2004, 2006; Saito et al., 2007). Outdoor concentrations vary regionally, with urban higher than rural, and both indoor and outdoor concentrations vary seasonally with higher concentrations in spring and summer (Goel et al., 2006; Harrad et al., 2006; Hazarati and Harrad, 2006).

Occupational exposures are also of concern. Workers at electronic waste recycling plants or automotive shredd/recycling facilities are often subject to substantial occupational exposures (Cahill et al., 2007; Deng et al., 2007). Work environments where older computers are used may also lead to higher exposures (Cahill et al., 2007; Harrad et al., 2006).

While some researchers conclude that indoor air is the primary source of exposure for the general population, others studies assert that dust is the more significant source, especially for toddlers, who have greater hand-to-mouth activity (Allen et al., 2007; Harrad et al., 2006). Diet is also considered to be a potentially important source of PBDE exposure (Harrad et al., 2004; Schecter et al., 2006). Dannerud et al. (2006) estimated a daily total PBDE intake of 51 ng in Sweden, with the highest levels found in fish. Overall, although it is widely agreed that outdoor air is a minor source of PBDE exposure, the relative importance of indoor air, diet and dust exposures is not clear.

Though few studies have been conducted on health effects of PBDEs, they are similar to PCBs in their ability to interfere with thyroid hormone function, and so are likely to cause similar effects on neurodevelopment following in utero exposure (Darras, 2008; McDonald, 2005; Zhou et al., 2002).
2.3. Pesticides

Pesticides are generally classified according to the type of substance they are intended to repel or kill. Accordingly, the many varieties include insecticides, acaricides, fungicides, herbicides, rodenticides, avicides, larvicides, and germicides (Lewis, 2001). Pesticides can be composed of inorganic substances, organometallic compounds, volatile organic compounds, semivolatile organic compounds, and non-volatile organic compounds (Lewis, 2001). Most conventional pesticides are semivolatile organic compounds or non-volatile organic compounds (Lewis, 2001). Major classes of pesticides include organochlorines, such as DDT and chlordane; organophosphates such as chlorpyrifos; carbamates, such as carbayl; and pyrethroids and pyrethrins such as permethrin. There are also many chemicals commonly introduced into products as anti-microbials, for example triclosan and triclocarban, and α-phenyl phenol. Semivolatile pesticides are often detected in both dust and indoor air, while non-volatile pesticides are typically found only in dust (Lewis, 2001). Both have been frequently detected in indoor and outdoor environments in studies from 1992 to the present (Butte and Heinzow, 2002; Lewis, 2001; Rudel et al., 2003).

Pesticides are commonly used on pets, in the garden, and as repellent or disinfectant (Lewis, 2001). They may be added to carpets, paints, furnishings, and building materials during manufacturing and are often available “off the shelf” for use inside and outside homes and public places such as schools, hospitals, and office buildings (Lewis, 2001). In addition, pesticides applied outdoors can be tracked into the home (Lewis, 2001). Diet may also be an important source, especially for infants and children, because of their greater food and beverage consumption per kilogram body weight and their propensity to have less variety in their diets than adults (Clayton et al., 2003). Lu et al. (2006b) found that switching a particular population of children to an organic diet dramatically reduced concentrations of certain pesticides in urine, sometimes to a level below the detection limit. This suggests that dietary exposure predominates, at least for certain pesticides, such as malathion (Lu et al., 2006b), while residential exposure is more important for other pesticides, such as pyrethroids (Lu et al., 2006a).

Pesticide air concentrations are affected by a number of factors. Pesticide use is generally higher in warmer weather, which also increases pesticide volatility (Lewis, 2001). Thus pesticide concentrations vary seasonally (higher in the spring and summer months) and geographically (higher in southern versus northern US) (Lewis, 2001). Air concentrations of specific types of pesticides are also influenced by the varying volatility of the different chemical constituents (Lewis, 2001). Current use pesticides are less persistent than the now banned organochlorines which can still be detected in the environment (Lewis, 2001). However, degradation rates are typically much lower indoors, thus indoor air levels are typically higher than outdoor levels (Butte and Heinzow, 2002; Rudel et al., 2003). Pesticides tend to accumulate on toys, carpets, and dust, sources that can become major routes of exposure for infants and toddlers (Butte and Heinzow, 2002; Lewis, 2001).

Fig. 4 shows measured concentrations for the termiticide chlordane, a persistent organochlorine pesticide which was widely used in and around building foundations until its use was restricted in the US in the mid 1980s (Kilburn and Thornton, 1995). Chlordane concentrations are widely variable indoors; and lower concentrations are seen outdoors compared with indoors, and in rural versus urban areas. Regional levels of pesticides in outdoor air have been shown to be correlated with concentrations in lichen, snow, and spruce needles (Daly et al., 2007; Hageman et al., 2006; Romanic and Krauthacker, 2007; Wang et al., 2006).

Because pesticides include many types of chemicals, it is not possible to generalize about health effects. Many of the banned organochlorines such as DDT, chlordane, and methoxychlor have been identified as EDCs (Kelce et al., 1995; Soto et al., 1994; Soto et al., 1995), and health effect studies for these compounds suggest neurotoxicity, effects on developing reproductive systems, effects on lactation, and cancers, including breast cancer (Brody et al., 2007; Cohn et al., 2007; Kilburn and Thornton, 1995; Rogan and Ragan, 2007). Some pesticides in current use appear to also have effects on the endocrine system, for example various pyrethroids.
have been demonstrated to have weak anti-androgenic, anti-
estrogenic, or estrogenic activity, and chlorpyrifos has been shown
to affect thyroid hormones in animal and human studies (Garey and
Wolff, 1998; Go et al., 1999; Jeong et al., 2006; Kim et al., 2005a,b; Kim et al., 2006), and to affect infant development in human
studies (Rahel et al., 2006). In general, more comprehensive toxicology and health information is available for current use pesticides than for most chem-
icals in commercial use, because tests are required for pesticide
registrations. However, some important gaps persist in the data available on pesticide effects on neurodevelopment (an especially
important endpoint since many pesticides affect neuroendocrine function) (Colborn, 2006).

2.4. Phthalates

Phthalates are common plasticizers in polyvinyl chloride (PVC)
resins (European Union, 2004, 2007; Rudel, 2000). By weight, they
contribute 10–60% of plastic products because of their ability to
increase flexibility and transparency (Rakkestad et al., 2007). Phthalates
are subject to photo degradation, biodegradation, and anaerobic
degradation and thus generally do not persist in the outdoor
environment (Stales et al., 1997; Xie et al., 2007). Photo degradation
half lives of common phthalates range from approximately 0.3 to
15 days (Stales et al., 1997; Xie et al., 2007). In remote regions of the
Norwegian Sea, where cold temperatures, low concentrations, and
lack of nutrients can retard the degradation process, phthalates
have been found despite the lack of a recognized source (Xie et al.,
2007). In this case, atmospheric transport and deposition is likely to
be the major source, with adsorption of phthalates by snow and ice
both slowing down the degradation process and contributing to an
underestimation of the total phthalate load (Xie et al., 2007).

Due to the nature of phthalate sources, phthalates are ubiquitous
in the indoor environment, with indoor air concentrations generally
higher than outdoor concentrations (see Fig. 5) (Rakkestad et al.,
2007; Rudel, 2000; Rudel et al., 2003). Outdoors, urban and suburban
concentrations are higher than rural and remote concentrations
(Fig. 5). Generally, it is agreed that outdoor sources of phthalates,
such as the wearing of tires, are secondary to indoor sources
(Rakkestad et al., 2007).

More volatile phthalates such as diethyl phthalate (DEP),
dimethyl phthalate (DMP) and dibutyl phthalate (DBP) are present
at higher concentrations in air compared with heavier, less volatile
phthalates such as di(2-ethylhexyl)phthalate (DEHP) and benzyl
butyl phthalate (BBP), which are more prevalent in dust (Heudorf
et al., 2007; Rudel et al., 2003). It has been difficult to establish correlations between particular
activities or objects and measured concentrations of phthalates
(Fromme et al., 2004). Higher air temperatures lead to increased air
centrations of phthalates (Uhde et al., 2001), and PVC flooring has been associated with higher concentrations of BBP and DEHP in
house dust, and may also influence indoor air concentrations
(Borneshag et al., 2004, 2005).

Phthalate metabolites have been detected in virtually all human
urine samples tested, indicating widespread exposure (Heudorf
et al., 2007). Most exposure studies have concluded that diet is the
major route of exposure for phthalates, especially DEHP, (Fromme
et al., 2007; Heudorf et al., 2007; National Toxicology Program

![Fig. 4. Chlordane air concentrations (sum of vapor and particulate phases unless otherwise noted) in selected studies.](image-url)
A number of the phthalates have been shown to interfere with androgen production, with the developing male fetus being the most sensitive to this effect. In animal studies, endpoints include effects on the developing male reproductive tract, including disrupted epididymal development, hypospadias, cryptorchidism, retained nipples, and reduced fertility (Henley and Korach, 2006; Mylchreest et al., 2000). Most animal studies show these effects occurring at higher exposure levels than are observed in the general human population, although certain medical procedures such as dialysis can result in much higher levels of exposure and adverse effects from these exposures are a serious concern (European Union, 2008; National Toxicology Program (NTP), 2000c). However, one human study has shown an association between maternal levels of urinary phthalate metabolites and reproductive tract development in male offspring in the general population (Swan, 2006). Associations have also been observed between sperm quality and urinary phthalate metabolite levels in adult men (Duty et al., 2003ab, 2005b). In addition, two studies have reported associations between phthalate levels in house dust and allergic symptoms in children (Bornehag et al., 2004; Kolarik et al., 2008). Thus, while animal studies suggest that current exposure levels in the general population are below levels of health concern, a small number of studies in humans with typical levels of exposure have demonstrated adverse health effects.

### 2.5. Alkylphenols

Alkylphenols, especially nonylphenol ethoxylates and octylphenol ethoxylates, are high production volume chemicals found throughout the world and are important indoor air contaminants (Brody and Rudel, 2003; Rudel et al., 2003; Warhurst, 1995; White et al., 1994). They are used as surfactants in common consumer products such as detergents, disinfectants, surface cleaners, and pesticides; and tris(nonylphenol) phosphate is also used as a plasticizer (Rudel, 2000). General use of alkylphenols began in the 1940s (Warhurst, 1995). Most of the nonylphenol used in commercial products is 4-tert-nonylphenol, which is a mixture of the branched isomers, so it is important that measurement studies quantify the branched rather than the straight-chain isomers (4-n-nonylphenol).

Alkylphenols have been frequently detected in wastewater and aquatic environments (White et al., 1994). Sewage treatment biodegrades less than 40% of nonylphenol polyethoxylates and its metabolites (Warhurst, 1995). During biodegradation, alkylphenol polyethoxylates lose ethoxy groups to become alkylphenols (typically nonylphenol) which are more stable, persistent, and hydrophobic, leading to their accumulation in sewage and rivers.

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**Fig. 5.** Di-n-butyl phthalate air concentrations (sum of vapor and particulate phases unless otherwise noted) in selected studies.
(Warhurst, 1995; White et al., 1994), and their volatilization into ambient air. Nonylphenol is lipophilic and tends to bioaccumulate (Warhurst, 1995). Photochemical degradation of nonylphenol will occur, with a half-life of about 10–15 h in ideal conditions (Warhurst, 1995). The more soluble phenols (such as short chain alkylphenol polyethoxylate) have been found in drinking water and groundwater in the US (Rudel et al., 1998; Swartz et al., 2006; White et al., 1994).

Air concentrations of alkylphenols are rarely reported in the literature. Existing studies show indoor concentrations are generally around 100 ng/m², while outdoor concentrations are about 10 times lower (see Fig. 6). Weschler et al. (1984) measured nonylphenol in the particulate phase of air samples and found mean values substantially lower than those in other studies, indicating that alkylphenols might exist primarily in the gas phase (Weschler, 1984). Studies in outdoor air have demonstrated elevated concentrations above wastewater-impacted surface waters, for example in the lower Hudson River estuary (Dachs et al., 1999).

Major pathways of exposure to these compounds have not been described, and may include dietary and non-dietary ingestion, dermal absorption from product use, and inhalation. A day care study concluded that dietary ingestion was the primary exposure pathway for toddlers to a group of phenolic compounds that included nonylphenol, though inhalation was found to be a secondary route of exposure (Wilson et al., 2001).

4-Nonylphenol and 4-octylphenol have been shown to be estrogen mimics – that is they are able to bind with the estrogen receptor and initiate transcription of estrogen-responsive genes (Bonefeld-Jorgensen et al., 2007; Soto et al., 1991). They are much less potent than the endogenous estrogen 17β-estradiol, however it has also been shown that endogenous estrogen mimics can act in combination, additively, to induce estrogen-receptor-mediated effects, so it is expected that these exposures may add to endogenous background levels to induce effects (Silva et al., 2002). A recent study has also reported that these chemicals can act by additional endocrine mechanisms (Bonefeld-Jorgensen et al., 2007), so assessment of potential health effects is complex. In vivo studies in animals show effects at doses between 3 and 10 mg/kg per day (Lee et al., 1999; Lee and Lee, 1996). Though some information is available for these compounds, limited data on human exposure via dietary ingestion, non-dietary ingestion, and dermal absorption make it difficult to compare human exposures with doses associated with effects in animal studies.

2.6. Parabens

Parabens, characterized by a para-substituted hydroxybenzoate, are commonly used as preservatives and anti-microbial agents (Soni et al., 2001). They can be found in food such as jams, jellies, syrups, beverages, and baked goods (Soni et al., 2001). Parabens are also used in commercial products including shampoo, cream, deodorant, hairspray, and cosmetics, as well as pharmaceuticals (Shen et al., 2007; Soni et al., 2001). In a 1995 study, they were found in 77% of rinse-off and 99% of leave-on cosmetic products (Rastogi et al., 1995). Parabens are absorbed into the body through the skin and gastrointestinal tract (Soni et al., 2001). Though it is generally accepted that they do not bioaccumulate, parabens have been detected in human tissue, including human breast tumors (Darbre et al., 2004; Soni et al., 2001).

Few studies have measured parabens in air. In a 2003 study of 120 homes in Cape Cod, Rudel et al. (2003) detected three parabens (butyl paraben, ethyl paraben, and methyl paraben) in indoor air and house dust (Rudel et al., 2003). Methyl paraben was most frequently detected, with air concentrations in 67% of homes above the reporting limit of 1 ng/m³ (Rudel et al., 2003). The median indoor air concentration of methyl paraben was 2.9 ng/m³ and the maximum was 21 ng/m³ (Rudel et al., 2003). Outdoor concentrations have not been reported in the literature. Because of their widespread use in lotions and other products applied to the skin, there has been interest in the likelihood of dermal absorption of parabens. In a study of human breast tumors, methyl paraben was found in the highest concentration of the six parabens tested (Darbre et al., 2004). This may be due to more common use of methyl paraben in products, or a greater tendency for methyl paraben to be absorbed (Darbre et al., 2004).

Parabens have been shown to be weak estrogen mimics in vitro and in vivo (Kang et al., 2002; Routledge et al., 1998). They appear to be rapidly metabolized when given orally, however little is known

Fig. 6. 4-Nonylphenol air concentrations (sum of vapor and particulate phases unless otherwise noted) in selected studies.
about absorption or toxicity by dermal or inhalation routes. It is expected that most paraben exposure may be associated with dermal application of paraben-containing products, however the relative importance of dermal, ingestion, and inhalation exposure routes remains unknown.

3. Conclusion

Ongoing research shows that indoor environments provide important opportunities for exposure to a wide variety of chemicals in commercial use, including pesticides (Rudel et al., 2008; Rudel et al., 2003; Zota et al., 2008). Indoor environments are well documented as important opportunities for exposure due to the fact that so many chemicals have indoor sources, indoor concentrations of many compounds are much higher than outdoor, and a majority of time is spent indoors (US General Accounting Office, 1999). Therefore, future research on EDCs in air should focus on understanding factors influencing indoor air concentrations and exposure, such as sources, ventilation, and chemical degradation processes to be expected indoors.

In this review, we focused on six chemical families that have been detected in indoor environments and shown to be EDCs. Exposures to these and other EDCs are ubiquitous, although they have not been well characterized. National exposure monitoring programs to track indoor and outdoor chemical concentrations over space and time are a priority – such programs would provide important context for ongoing biomonitoring programs and facilitate design and implementation of health studies.

With approximately 80,000 chemicals registered by the US EPA in commercial use, it is clear that there is little information available on exposure and health effects for many of these compounds (US Environmental Protection Agency, 1998; US General Accounting Office, 2005). In particular, endocrine-mediated effects of these chemicals are of concern, and no program has been implemented to screen chemicals for effects on the endocrine system. New initiatives to develop and use bioassays as integrated measures of estrogenic or other hormonal activity offer great promise for advancing the feasibility of health studies of EDC exposure, since integrated measures circumvent the limitations of a chemical-by-chemical analytical approach. This is a priority research area for both biomonitoring and exposure monitoring EDC research (DeCastro et al., 2006; Kortenkamp, 2006). Beyond research area for both biomonitoring and exposure monitoring EDC a chemical-by-chemical analytical approach. This is a priority exposure, since integrated measures circumvent the limitations of

Acknowledgements

This work was supported by grants from the US National Institute of Environmental Health Sciences (NIH), NIH grant 5R25ES13258-4 and from appropriations of the Massachusetts Legislature administered by the University of Massachusetts-Lowell and the Massachusetts Department of Public Health. The authors declare no competing financial interests.

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