NATURAL RESOURCES DEFENSE COUNCIL

January 12, 2009

To: Consumer Product Safety Commission
Office of the Secretary
Submitted by email: phthalates-info@cpsc.gov

Re: Section 108: Phthalates in Children's Products, Request for Information.

These comments are submitted by Natural Resources Defense Council (NRDC), who on behalf of our 1.2 million members and online activists, uses law and science to ensure a safe and healthy environment for all living things. NRDC has no financial interest in phthalates, PVC, or children's toys or childcare articles.

The CPSC has requested information and comments on Section 108 of the Consumer Product Safety Improvement Act (CPSIA), "PROHIBITION ON SALE OF CERTAIN PRODUCTS CONTAINING SPECIFIED PHTHALATES".

Since CPSC last analyzed the toxicity of phthalates in toys, there have been over 500 studies published on phthalates and their toxicity. While we are pleased that the CHPA has been asked to consider cumulative effects when considering the toxicity of the Tier 2 phthalates in toys, we recognize the CHAP will have to consider a voluminous amount of information in a relatively short period of time. We have summarized and appended here the studies we think are most relevant to CSPC and the CHAP in evaluating the cumulative effects of phthalates. Most of these studies were conducted by independent scientists and published in peer-reviewed journals.

NRDC's comments pertain to the last two sections of CPSC's request for information: a. Toxicity of Phthalates and Phthalate Alternatives and b. Exposure to Phthalates and Phthalate Alternatives. A summary of the main points of our comments is followed by a brief description of each.

Toxicity of Phthalates and Phthalate Alternatives.

1. DiNP is a male reproductive toxin which acts through a mode of action similar to other phthalates such as DEHP, DBP or BBP.

2. There is evidence in humans that phthalates cause male reproductive harm similar to that observed in animal studies.

3. Reproductive outcomes in females are also impacted by phthalate exposure.

4. Phthalates have additive effects with one another and with other anti-androgenic chemicals. Therefore cumulative exposures to all anti-androgenic chemicals should be considered when evaluating toxicity.

5. Exposure to phthalates has been associated the neurobehavioral changes.

6. Exposure to phthalates in dust has been associated with the development of allergic symptoms and worsening asthma.

7. Exposure to phthalate has been associated with the alterations in the development of endocrine tissues and may cause reproductive cancers.

8. Phthalates have been associated with disturbances in metabolism and thyroid dysfunction.

9. Di-iso butyl phthalate, an alternative to DBP, has a toxicity profile similar to DBP.

Exposure to Phthalates.

1. Children are highly exposed to phthalates.

2. There is widespread exposure to the phthalate, DiNP.

3. Air fresheners are one source of exposure to phthalates.

4. Toys contain multiple phthalates, including DiNP.

5. Dust and Food are also likely to be sources of exposure to phthalates.

6. Phthalates can be absorbed across the skin.

Toxicity of Phthalates and Phthalate Alternatives.

In animal studies, there is clear and solid scientific evidence that certain phthalates are capable of disrupting testis function in prenatal and peri-pubertal rats. Exposures to phthalates such as BBP, DBP and DEHP have been shown to cause changes in hormone levels, birth defects of the penis (hypospadias) and testicles (cryptorchidism), alter the onset of puberty, and later in life result in poor semen quality and infertility.[1] It is generally accepted that exposures during critical periods of development are most harmful and that these effects are irreversible and permanent.

Numerous government agencies have reviewed the scientific data on phthalates, including the state of California which recognizes four of the phthalates listed in Section 108 as being reproductive and developmental toxins.[2] Those phthalates are DEHP, BBP, DBP and DiDP which were listed after review by the National Toxicology Program's Committee on the Evaluation of Risks to Human Reproduction (NTP CERHR).

Since the NTP CERHR evaluations of seven phthalates were completed in 2000[3], there have been many important new studies published on the toxicity of phthalates, including the importance of considering cumulative effects and the reproductive toxicity of DiNP. New research has also shown cause for concern beyond reproductive outcomes to include neurobehavioral outcomes, allergic and respiratory disease, cancer and metabolic disturbances. In addition, there are new human epidemiological studies which have found similar toxicological outcomes to those seen in laboratory animals. Select studies published after 2002 on phthalate toxicity are listed below according to outcomes.

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[1] Foster, P. M. D. (2006). Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. *International Journal of Andrology* **29**, 140-147.
And
Gray, L. E., Jr, et al. (1999). Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlozolinate, p,p#-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate,PCB169, and ethane dimethane sulphonate) during sexual differentiation produces diverse profiles of reproductive malformations in the male rat. Toxicol. Ind.Health 15, 94–118.

[2] California EPA, Safe Drinking Water and Toxic Enforcement Act, List of chemicals known to the State of California to cause cancer or reproductive toxicity.
http://www.oehha.org/Prop65/prop65_list/Newlist.html

[3] Federal Register Notice, October 10, 2000 (Vol. 65, No. 196). "CERHR Phthalates -- Availability of Reports". http://ntp.niehs.nih.gov/index.cfm?objectid=06F3BF5F-D13F-7A42-7E3DF3C0E61AD1F0

1. **DiNP is a male reproductive toxin which acts through a mode of action similar to other phthalates such as DEHP, DBP or BBP.**

In 2000, Earl Gray and colleagues published a study showing DiNP caused male reproductive toxicity in a manner similar to the toxicity of other phthalates such as DEHP, DBP or BBP.[4] Recent research has replicated this work and demonstrates the DiNP acts through a similar mode of action by reducing the production of testosterone.[5] The anti-androgenic effects of DiNP and other phthalates, including DIDP, in pre-pubertal males have also been demonstrated in the Hershberger assay.[6]

2. **There is evidence in humans that phthalates cause male reproductive harm similar to that observed in animal studies.**

In the past 4 years, human studies have found phthalates are associated with many of the same effects that have been observed in laboratory studies, including alterations in sex hormone levels, feminization of male genitalia and alterations in semen quality.

In utero exposure to phthalates including DBP and BBP has been associated with a feminization of male genitalia with a shortening of the ano-genital distance.[7] Post-natal exposure to the phthalate metabolites of DiNP and DBP in breast milk has been associated with alterations in male hormone profiles in baby boys.[8] In adult men, phthalate exposures have been associated with poor sperm quality[9] and DNA damage[10]. Finally, occupational exposures to DBP and DEHP have been associated with alterations in testosterone levels.[11]

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[4] Gray, L. E., Jr., et al. (2000). Perinatal Exposure to the Phthalates DEHP, BBP, and DINP, but Not DEP, DMP, or DOTP, Alters Sexual Differentiation of the Male Rat. *Toxicol. Sci.* **58**, 350-365.

[5] Borch, J., et al.. (2004). Steroidogenesis in fetal male rats is reduced by DEHP and DINP, but endocrine effects of DEHP are not modulated by DEHA in fetal, prepubertal and adult male rats. *Reproductive Toxicology* **18**, 53-6.

[6] Lee, B. M., and Koo, H. J. (2007). Hershberger Assay for Antiandrogenic Effects of Phthalates. *Journal of Toxicology and Environmental Health, Part A* **70**, 1365 – 1370.

[7] Swan, S., et al. (2005). Decrease in Anogenital Distance Among Male Infants with Prenatal Phthalate Exposure. *Environ Health Perspect* **113**, 1056-1061.

[8] Main KM, et al. (2006) "Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in three months old infants." *Environmental Health Perspectives*, 114(2):270-6.

[9] Hauser R, et al. (2006). "Altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites."*Epidemiology*, 17:682-691

[10] Hauser R, et al. "DNA damage in human sperm is related to urinary levels of phthalate monoester and oxidative metabolites." *Human Reproduction*, 22:688-695 (2007).

[11] Pan G, et al. (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*, 114:1643-1648.

3. **Reproductive outcomes in females are also impacted by phthalate exposure.**

Pregnant female rats exposed to DBP had fetal loss and altered ovarian hormone production.[12] The authors of this study suggest these changes were caused by alterations in females sex hormones through a similar mode of action as has been described in males.

Female rats who inhaled DEHP were found to undergo puberty early and have irregular estrous cycles[13].

In humans, DEHP exposure has been associated with shorter pregnancy duration[14] and exposures to BBP, DBP, DEHP and DnOP have been strongly correlated with the occurrence of endometriosis in women[15].

4. **Phthalates have additive effects with one another and with other anti-androgenic chemicals. Therefore cumulative exposures should be considered when evaluating toxicity.**

Recent research has demonstrated that exposures to low dose mixtures of phthalates can cause the same reproductive harm as exposure to high dose exposure to one phthalate. A mixture of five phthalates including DBP, BBP and DEHP was recently shown to cause a reduction in fetal testosterone levels in a cumulative and dose-additive manner[16]. Other studies have shown that other anti-androgenic chemicals, such as some pesticides, are able to act in an additive manner with phthalates to cause harm to male reproductive development[17]. In humans, an interaction between PCBs and DBP that is

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[12] Gray LE Jr, Laskey J, Ostby J. "Chronic di-n-butyl phthalate exposure in rats reduces fertility and alters ovarian function during pregnancy in female Long Evans hooded rats." *Toxicological Sciences.* 93(1):189-95 (2006).

[13] Ma M, et al. (2006). "Exposure of prepubertal female rats to inhaled di(2-ethylhexyl)phthalate affects the onset of puberty and postpubertal reproductive functions." *Toxicological Sciences,* 93(1):164-71.

[14] Latini G, et al. "In-Utero Exposure to Di-(2-ethylhexyl)-phthalate and Duration of Human Pregnancy." *Environmental Health Perspectives,* 111(14):1783-1785 (2003).

[15] Reddy BS, et al. "Association of phthalate esters with endometriosis in Indian women." *British Journal of Obstetrics and Gynaecology,* 113(5):515-20 (2006).

[16] Howdeshell, K. L., et al. (2008). A Mixture of Five Phthalate Esters Inhibits Fetal Testicular Testosterone Production in the Sprague-Dawley Rat in a Cumulative, Dose-Additive Manner. *Toxicol. Sci.* **105**, 153-165.

[17] Rider, C. V., et al. (2008). A mixture of seven antiandrogens induces reproductive malformations in rats. *International Journal of Andrology* **31**, 249-262.

greater than additive has been shown to cause alterations in semen quality[18]. To date, none of these mixture studies have included DiNP, DIDP or DnOP.

The National Academy of Sciences recently reviewed the evidence for cumulative toxicity of phthalates and issued guidance to EPA regarding how to conduct a cumulative risk assessment on phthalates. The NAS states in their report[19]:

> ***"****Phthalates and other agents that cause androgen insufficiency or block androgen receptor signaling, and are thus capable of inducing effects that characterize components of phthalate syndrome, should be considered in a cumulative risk assessment."*

And

> *"A focus solely on phthalates to the exclusion of other antiandrogens would be artificial and could seriously underestimate cumulative risk."*

The NAS committee concluded by stating that there is sufficient data now to proceed with a cumulative risk assessment of phthalates and other anti-androgens.

The CHAP also should follow this guidance and consider cumulative exposures to anti-androgenic chemicals including phthalates when conducting their safety assessment.

5. **Exposure to phthalates has been associated the neurobehavioral changes.**

There are a number of studies which have been published in the past 5 years which indicate exposure to many different phthalates interferes with sexual differentiation of the brain.

Perinatal exposure to DBP and DiNP has been associated with alterations in gene involved in sexual differentiation of the rat hypothalamus resulting in alterations in male sexual behavior[20]. Perinatal DBP exposure has also been associated with alterations in the development of the pituitary gland[21] in both male and female rats. In

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[18] Hauser R, et al. (2005). "Evidence of interaction between polychlorinated biphenyls and phthalates in relation to human sperm motility." *Environmental Health Perspectives*, 113:425-30.

[19] *Phthalates and Cumulative Risk Assessment: The Tasks Ahead.* (2008). National Research Council of the National Academies, Washington, D.C. Available on-line: http://www.nap.edu/catalog.php?record_id=12528&utm_source=dels&utm_medium=gateway&utm_campaign=delsref

[20] Lee HC, Yamanouchi K, Nishihara M. (2006). "Effects of perinatal exposure to phthalate/adipate esters on hypothalamic gene expression and sexual behavior in rats." *Journal Reproduction and Development*, 52(3):343-52.

[21] Lee, K. Y., et al. (2004). Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during the period from late gestation through lactation. *Toxicology* **203**, 221-238.

utero and lactational exposure to DEHP in rats altered levels of brain aromatase[22], the enzyme necessary for conversion of androgens to estrogens, and has also been shown to alter male sexual behavior[23].

6. **Exposure to phthalates in dust has been associated with the development of allergic symptoms and worsening asthma.**

Both laboratory animal and human epidemiological studies have found that exposure to phthalates, presumably through inhalation, is associated with allergic symptoms and worsening of pulmonary function.

In mice, atopic dermatitis has been shown to develop after exposure to DEHP and then challenge with a mite allergen[24]. A similar response was seen in male rat pups exposed to DEHP during lactation[25].

In children, DEHP has been associated with wheezing[26] and worsening of asthma symptoms[27] in those exposed through house dust. BBP in house dust has been associated with the allergic responses of rhinitis and eczema[28] in children. In study of U.S. adult men, exposure to DBP, but not DEHP, (as measured by urinary metabolites) was associated with decrements in pulmonary function testing[29].

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[22] Andrade AJ, et al. (2006). "A dose-response study following in utero and lactational exposure to di-(2-ethylhexyl)-phthalate (DEHP): non-monotonic dose-response and low dose effects on rat brain aromatase activity." *Toxicology*, 227: 185-192.

[23] Moore RW, et al. (2001). "Abnormalities of sexual development in male rats with in utero and lactational exposure to the antiandrogenic plasticizer Di(2-ethylhexyl) phthalate." *Environmental Health Perspectives*, 109(3):229-37.

[24] Takano, H., et al. (2006). Di-(2-ethylhexyl) phthalate enhances atopic dermatitis-like skin lesions in mice. *Environ Health Perspect* **114**, 1266-1269.

[25] Yanagisawa, R., et al. (2008). Effects of maternal exposure to di-(2-ethylhexyl) phthalate during fetal and/or neonatal periods on atopic dermatitis in male offspring. *Environ Health Perspect* **116**, 1136-1141.

[26] Kolarik B, et al. (2008). "The Association between Phthalates in Dust and Allergic Diseases among Bulgarian Children." *Environmental Health Perspectives*, 116: 98-103.

[27] Bornehag CG, et al. (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):1393-7.

[28] Ibid.

[29] Hoppin JA, Ulmer R, London SJ. (2004). "Phthalate exposure and pulmonary function." *Environmental Health Perspectives*, 112(5):571-574 .

7. **Exposure to phthalate has been associated with the alterations in the development of endocrine tissues and may cause reproductive cancers.**

In laboratory animal studies, exposure to the phthalates DBP and BBP has been associated with changes in the mammary gland that could precede the development of cancer. Exposure to BBP has been found to increase the proliferative index in terminal end-buds and change the gene expression profile of mammary tissue[30]. Peri-natal exposure to DBP has been associated with alterations in mammary gland development that appeared irreversible but the study was not carried out long enough to assess cancer development[31]. In vitro studies have shown DBP, BBP and DEHP interfere with tamoxifen induced apoptosis in MCF-7 cells[32], suggesting that phthalates could promote the progression of mammary tumors.

Testicular cancer has also been associated with phthalate exposure. Male rats exposed to DBP in utero develop Leydig cell tumors[33]. The formation of these tumors may result from abnormal clusters of Leydig cells that form inside seminiferous tubules[34]. Furthermore, a large study of rats exposed to DEHP chronically demonstrated these animals developed testicular tumors earlier than they developed hepatocellular tumors and the number of testicular tumors increased with time[35].

8. **Phthalates have been associated with disturbances in metabolism and thyroid dysfunction.**

In addition to their well recognized ability to interfere with the steroidogenesis and the production of sex hormones, certain phthalates have also been associated with alterations in thyroid hormone, which is important for development of the brain and nervous system as well as for maintaining metabolic rates in adults.

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[30] Moral R, et al. (2007). "The plasticizer butyl benzyl phthalate induces genomic changes in rat mammary gland after neonatal/prepubertal exposure." *BioMed Central, Genomics*, 8: 453.

[31] Lee, K. Y., et al. (2004). Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during the period from late gestation through lactation. *Toxicology* **203**, 221-238.

[32] Kim IY,Han SY,Moon A (2004). "Phthalates inhibit tamoxifen-induced apoptosis in MCF-7 human breast cancer cells." *Journal of Toxicology and Environmental Health,* 67:2025-2035.

[33] Barlow, N. J., McIntyre, B. S., and Foster, P. M. (2004). Male reproductive tract lesions at 6, 12, and 18 months of age following in utero exposure to di(n-butyl) phthalate. *Toxicologic pathology* 32, 79-90.

[34] Mahood, I. K., et al. (2006). Cellular origins of testicular dysgenesis in rats exposed in utero to di(n-butyl) phthalate. *International Journal of Andrology* **29**, 148-154.

[35] Voss, C., et al. (2005). Lifelong exposure to di-(2-ethylhexyl)-phthalate induces tumors in liver and testes of Sprague-Dawley rats. *Toxicology* **206**, 359-371.

Exposure to DEHP has been associated with alterations in free T4 and total T3 in adult men[36]. In pregnant women, DBP has been associated with decrements in T4 levels[37].

Using NHANES data in a U.S. national cross-sectional study of adult men, increased waist circumference and insulin resistance was associated with exposure to three different phthalates[38]. Another study of US men found BBP exposure was associated with obesity[39]. One animal study in rats found exposure to DEHP was associated with an increase in serum glucose and decrease in insulin, as well as thyroid and adrenocortical dysfunction[40].

9. **Di-iso butyl phthalate, an alternative to DBP, has a toxicity profile similar to DBP.**

Di-isobutyl phthalate (DiBP) has a similar structural profile to di-butyl phthalate and reportedly can serve as a replacement for DBP in all applications including as a softener of PVC, printing inks and adhesives[41].

In laboratory studies, DiBP has been shown to have anti-androgenic properties[42] and causes a male reproductive harm at the same doses as BBP, DBP or DEHP[43].

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[36] Meeker JD, Calafat AM, Hauser R. (2007). "Di(2-ethylhexyl) phthalate metabolites may alter thyroid hormone levels in men." *Environmental Health Perspectives*, 115(7):1029-34.

[37] Huang PC, et al. (2007). "Associations between urinary phthalate monoesters and thyroid hormones in pregnant women." *Human Reproduction*, 22:2715-2722.

[38] Stahlhut RW, et al. (2007). "Concentrations of urinary phthalate metabolites are associated with increased waist circumference and insulin resistance in adult U.S. males." *Environmental Health Perspectives*, 115: 876-882.

[39] Hatch, E. E., et al. (2008). Association of urinary phthalate metabolite concentrations with body mass index and waist circumference: a cross-sectional study of NHANES data, 1999-2002. *Environ Health* **7**, 27.

[40] Gayathri NS, et al. (2004). "Changes in some hormones by low doses of di (2-ethyl hexyl) phthalate (DEHP), a commonly used plasticizer in PVC blood storage bags & medical tubing." *Indian Journal of Medical Research*. 119:139-44.

[41] Draft DiBP Hazard Assessment, Australian Government, Department of Health and Ageing, NICNAS. April 2007. http://www.nicnas.gov.au/industry/existing_chemicals/phthalate_hazard_assessments/dibp hazard assessment 30-4-07.pdf

[42] Borch, J., et al. (2006). Diisobutyl phthalate has comparable anti-androgenic effects to di-n-butyl phthalate in fetal rat testis. *Toxicol Lett* **163**, 183-190.
And
Saillenfait, A. M., Sabate, J. P., and Gallissot, F. (2008). Diisobutyl phthalate impairs the androgen-dependent reproductive development of the male rat. *Reprod Toxicol* **26**, 107-115.

[43] Howdeshell, K. L., et al. (2008). A Mixture of Five Phthalate Esters Inhibits Fetal Testicular Testosterone Production in the Sprague-Dawley Rat in a Cumulative, Dose-Additive Manner. *Toxicol. Sci.* **105**, 153-165.

Furthermore, DiBP has been shown to cause reproductive harm when combined with other phthalates capable of causing male reproductive developmental toxicity[44].

Because of its toxicity profile and evidence for causing harm when combined with other phthalates, DiBP should not be permitted for use as an alternative in children's toys.

Exposure to Phthalates.

Biomonitoring from the CDC has indicated there is widespread exposure in the general population to phthalates.[45] Biomonitoring from other countries[46] and from non-governmental organizations in the U.S.[47] also have found evidence of widespread exposure. However, there is relatively little information available on how people are being exposed, what the major sources of exposure are and where individual phthalates are used.

We do know that in general, phthalates are found in a wide array of places including automobiles, food, pesticides, in building materials, personal care products, medical devices and pharmaceuticals, and consumer products such as toys, air fresheners, and furniture.

Select studies published after 2002 on phthalate exposure are listed below and the relevant studies are attached.

1. **Children are highly exposed to phthalates.**

Although the CDC data does not collect biological samples from children younger than six years old, in their 2004 study[48] children ages 6-11 were found to have the highest levels of these three phthalates.

It is certain that exposures to phthalate are occurring in children less than six years of age. A pilot study of 19 U.S. toddlers found when compared to the 6-11 year old

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[44] Ibid.

[45] Silva, M. J., et al. (2004). Urinary levels of seven phthalate metabolites in the U.S. population from the National Health and Nutrition Examination Survey (NHANES) 1999-2000. *Environ Health Perspect* **112**, 331-338.

[46] Wittassek, M., et al. (2007). 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* **210**, 35-42.

[47] Environmental Working Group, Human Toxome Project. Data on phthalates available at: http://www.ewg.org/sites/humantoxome/chemicals/chemical_classes.php?class=Phthalates

[48] Silva, M. J., et al. (2004). Urinary levels of seven phthalate metabolites in the U.S. population from the National Health and Nutrition Examination Survey (NHANES) 1999-2000. *Environ Health Perspect* **112**, 331-338.

children, levels of the DBP monoester metabolite, MBP, were three times higher than the geometric mean while levels of the monoester metabolites of BBP and DEHP were similar[49]. A study of preschool children found urine levels of DBP and BBP metabolites were higher than adult levels[50].

Phthalates have also been found in breast milk[51], cord blood[52], and amniotic fluid[53]. This indicates there is on-going and widespread exposure in the population and that children are highly exposed during critical periods of development.

2. There is widespread exposure to the phthalate DiNP.

When the US CDC analyzed a cross section of the U.S. population for the DiNP monoester metabolite, MiNP in human urine, less than 16% of the samples were positive. However, as has been demonstrated for other phthalates such as DEHP, the monoester metabolite may not be the best indicator of exposure and the oxidative metabolites may be better because the urinary levels are higher and less subject to contamination[54].

When the CDC analyzed a pilot group of urine samples they found none of the 129 samples contained the detectable levels of the DiNP monoester metabolite MiNP but three oxidative metabolites, MCIOP, MHINP, and MOINP were detected in 97, 100, and 87% of the urine samples, respectively[55]. Therefore, the prevalence of human exposure to DINP has previously been underestimated by using MINP as the sole DINP urinary biomarker and future biomonitoring studies should use the oxidative metabolites for a more accurate assessment.

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[49] Brock, J. W., et al. (2002). Phthalate monoesters levels in the urine of young children. *Bulletin of environmental contamination and toxicology* **68**, 309-314.

[50] Koch HM, et al.. (2005). "Exposure of nursery school children and their parents and teachers to di-*n*-butylphthalate and butylbenzylphthalate." *International Archives of Occupational and Environmental Health*, 78(3):223-229.

[51] Frederiksen H, Skakkebaek NE, Andersson AM. (2007). "Metabolism of phthalates in humans." *Molecular Nutrition & Food Research*, 51: 899-911.

[52] Latini, G., et al. (2003). Exposure to Di(2-ethylhexyl)phthalate in humans during pregnancy. A preliminary report. *Biology of the neonate* **83**, 22-24.

[53] Silva MJ, et al. (2004). "Detection of phthalate metabolites in human amniotic fluid." *Bulletin of Environmental Contamination and Toxicology*, 72: 1226-1231.

[54] Silva, M. J., et al. (2006). Measurement of eight urinary metabolites of di(2-ethylhexyl) phthalate as biomarkers for human exposure assessment. *Biomarkers* **11**, 1-13.

[55] Silva, M. J., et al. (2006). Oxidative metabolites of diisononyl phthalate as biomarkers for human exposure assessment. *Environ Health Perspect* **114**, 1158-1161.

3. Air fresheners are one source of exposure to phthalates.

In 2007, NRDC did a pilot study of phthalates in air fresheners. We purchased 14 different air fresheners, including aerosols, plug-ins and stand-alone specimens and sent the unopened containers to a commercial laboratory for testing of 15 different phthalates by GC/MS.

At least one phthalate was found in 12 of 14 products and over half of the air fresheners contained more than one phthalate. Phthalates found included DBP, DiBP, DiHP, DEP and DMP and levels ranged from below the level of detection to one specimen that contained 7,300 ppm DEP. A full description of the methodology and results can be found at: http://www.nrdc.org/health/home/airfresheners.asp

4. Toys contain multiple phthalates, not only DiNP.

Independent laboratory analyses have found that DiNP is not the only phthalate in children's toys. The San Francisco Chronicle in an investigative story published November 19, 2006[56], results of their own toy testing. DEHP was found in one product at level 13 times higher than is allowed under the new legislation. Other phthalates were also found to exceed the proposed legal limit. Additional testing done by Environment California found four phthalates - DEHP, DBP, BBP, and DnOP - in several different children's toys at levels far above what will be allowed in this legislation.[57] Some toys that were labeled "phthalate-free" were found to contain phthalates. The San Francisco Department of the Environment continues to conduct toy testing and publishes the results of their findings on their website[58].

5. Dust and Food are also likely to be sources of exposure to phthalates.

Recently published studies have found phthalates in house dust[59]. A study of 11 homes in Northern California found DEHP and BBP were the most abundant analytes found amongst a group of environmental chemicals which included flame retardants, PCBs,

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[56] http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2006/11/19/TOXICTOYS.TMP

[57] Environment California, "The Right Start" report on chemical contaminants in children's toys. Available at: http://www.environmentcalifornia.org/reports/environmental-health/environmental-health-reports/the-right-start-the-need-to-eliminate-toxic-chemicals-from-baby-products

[58] sfenvironment.org/downloads/library/sfe_phthalate_testing_in_**toys**__results.pdf

[59] Hwang, H. M., et al. (2008). Occurrence of endocrine-disrupting chemicals in indoor dust. *The Science of the total environment* **404**, 26-35.
And
Rudel, R. A., et al. (2003). Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. *Environ science & tech* **37**, 4543-4553.

pesticides and other persistent chemicals[60]. Inhalation is likely to be one route of exposure to phthalates and phthalate have been measured in personal air monitors[61].

Market surveys of food, mostly in European countries have found widespread contamination of food with phthalates[62]. DBP, DiBP, DEHP and BBP were all found in foods ranging from spices to grains to dairy products. Of note, the U.S. FDA has approved several phthalates as food additives but there is no current information on phthalate contamination in the U.S. food supply.

6. Phthalates can be absorbed across the skin.

Numerous human studies have correlate phthalate exposure with the use of personal care products such as shampoos, lotions and soaps[63]. In a controlled laboratory experiment, volunteers applied lotion containing known amounts of DEP and DBP to their skin[64]. Within a few hours, levels of these phthalate metabolites peaked in the urine indicating there was rapid absorption across the skin.

The mode of exposure may be relevant for personal care products and items of clothing made from vinyl or containing phthalates.

NRDC looks forward to an open and transparent process as CPSC continues their evaluation of toxicity of phthalates in children's toys. We welcome any opportunity to participate in or comment on selection of the Chronic Hazard Advisory Panel (CHAP) members, give comments at public meetings of the CHAP or respond to any questions or concerns CPSC has on the materials submitted herein.

Respectfully submitted,

Sarah Janssen, MD, PhD, MPH
Natural Resources Defense Council

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