Statement of Diana Zuckerman, Ph.D.
President
Cancer Prevention and Treatment Fund/National Research Center for Women & Families
at
the Chronic Hazard Advisory Panel (CHAP) on Phthalates
July 26, 2010

Thank you for the opportunity to testify about phthalates on behalf of the National Research Center for Women & Families and the Cancer Prevention and Treatment Fund.

Our Center is dedicated to improving the health and safety of adults and children, and we do that by scrutinizing medical and scientific research to determine what is known and not known about specific health and safety issues.

In addition, I am a fellow at the University of Pennsylvania Center for Bioethics. I was trained in epidemiology and public health at Yale Medical School; was on the faculty at Yale and Vassar; and directed a longitudinal research project at Harvard. I bring that scientific perspective to my testimony today. I have worked on health policy issues in Congress, the White House, and for nonprofit organizations for 26 years.

The Consumer Product Safety Commission appointed the Chronic Hazard Advisory Panel (CHAP) "to study the effects on children's health of all phthalates and phthalate alternatives used in children's toys and child care articles." We are very pleased that the Federal Register notice made it clear that you are interested in many potential products made with phthalates, including cosmetics, medical devices, food, pesticides, and other exposures that affect children prenatally and after they are born.[1]

As we all know, phthalates have been shown to cause adverse health effects, including birth defects, in laboratory animals.[1] Scientific evidence also links phthalates with health problems in humans.

The 2008 Consumer Product Safety Improvement Act (CPSIA) permanently prohibits the sale of certain children's toys and products containing more than 0.1 percent of three phthalates: Benzyl butyl phthalate (BBP), dibutyl phthalate (DBP) and di-(2-ethylhexyl) phthalate (DEHP). On a provisional basis, the law bans children's toys and products containing more than 0.1 percent of three other phthalates: di-isodecyl phthalate (DIDP), di-isononyl phthalate (DINP) and di-n-octyl phthalate (DnOP).

Our Center urges you to make the provisional bans permanent. Of the 12 topics that the panel is seeking comments on, I will focus on #6: human exposure; #11: the sensitivity of potentially vulnerable populations (fetuses, young children, and expectant mothers); and #12: the cumulative risk from multiple phthalates.

Phthalates are chemicals that are used to make plastic flexible and to add fragrances to soap and other personal products. Unfortunately, these chemicals don't stay only in the products, and phthalates have been found in indoor air and dust, and in human urine, blood, and breast milk.[2, 3] Levels are highest in women and children ages 6 to 11. African Americans have been shown to have higher levels of phthalates than whites.[4]

Human Exposure to Phthalates

Researchers are concerned that phthalates and other endocrine-disrupting compounds could lead to adverse reproductive and developmental effects.[5] In men, this could mean reproductive problems and possibly an increased risk of testicular or prostate cancer. In women, exposure may lead to an increased risk for endometriosis, reproductive and other endocrine-related cancers, or impaired ovarian function or menstrual cycling.

Research indicates that boys exposed to phthalates may be more likely to develop smaller genitals and incomplete descent of the testicles. Boys who are born with undescended testicles are more likely to develop testicular cancer as teenagers or young men.[5] Last year the Environmental Protection Agency (EPA) stated that "Although exposure to phthalates can produce a variety of effects in laboratory animals, for certain phthalates the adverse health effects on the development of the male reproductive system are the most serious."[6] According to the EPA, "The reproductive developmental effects observed in humans include shortened anogenital distance observed in newborn boys; shortened pregnancy, lower sex and thyroid hormones, and reduced sperm quality observed in adults."[6]

Phthalates are believed to also affect girls' hormones, but the health impact is less clear. Studies also show associations between children's exposure to phthalates and the risk of asthma, allergies and bronchial obstruction.[7, 8] Studies by Harvard researchers have shown phthalates may alter human sperm DNA and semen quality.[9]

A 2009 research review published in the *Philosophical Transactions of the Royal Society* concluded that there was little correlation between prenatal and post-natal concentrations of phthalate metabolites.[5] That suggests that both prenatal and post-natal exposures are very important and are independent of each other. We agree with the authors that more research is needed.

A study by Cho *et al,* published in *Environmental Health Perspectives* (EHP) in 2010, found that IQ and Verbal IQ were lower in elementary school children with DEHP metabolites but not DBP metabolites.[10] After controlling for mother's IQ and other demographic traits and developmental covariates, both types of phthalates were associated with lower vocabulary scores. This was maintained for DEHP even after maternal IQ was statistically controlled. Boys with more DEHP and MEHP had lower scores on the Wechsler Intelligence Scale for Children vocabulary score, but girls did not.

A 2010 article by Engel *et al* in EHP found a relationship between third trimester prenatal phthalate concentrations and parents' ratings of children's aggression, conduct problems,

attention problems, depression, and executive function between the ages of 4 and 9 years old.[11] Many of these measures are associated with ADHD hyperactivity disorders

A review published this year of the reproductive toxicity data of phthalates in animals found that "The phenotypic alterations observed in male offspring rats exposed during the prenatal period have remarkable similarities with common human reproductive disorders, including cryptorchidism, hypospadias and low-sperm counts."[12] The authors concluded that "biological changes can also be induced at low, human relevant doses and that different active phthalates can have cumulative effects."[12]

Concerns have also been raised that phthalates may be associated with "an increased prevalence of obesity and type 2 diabetes."[5]

Phthalate Substitutes

According to the EPA, a variety of possible alternatives for phthalates are available and the Agency cites four chemicals already being used in children's products. The chemicals are acetyl tri-n-butyl citrate (ATBC); di(2-ethylhexyl) adipate (DEHA); 1,2-cyclohexanedicarboxylic acid; diisononyl ester (DINCH); and di(2-ethylhexyl) terephthalate (DEHT or DOTP).[6] Numerous other possible phthalate substitutes are available but I am focusing just on the substitutes for children's products and toys.

The EPA also notes that in response to the European ban on phthalates in toys and other children's products, "plasticizers based on isosorbide esters were developed….[And] it is worth noting that isosorbideesters could be prepared under solvent-free conditions, providing an environmentally friendly approach to manufacturing."

Sensitivity of Potentially Vulnerable Populations (fetuses, young children, and expectant mothers)

Fetuses

German researchers have concluded that "The fetus is considered to be the most sensitive stage of life to the potential developmental and reproductive toxicity of the phthalates."[13] In their study published in the *International Journal of Hygiene and Environmental Health*, they concluded, "Given that phthalates and their metabolites are toxic to reproduction and development in animals and fetal stage of life is most sensitive for these effects, in utero exposure to phthalate monoesters may be of significant health relevance."[13] According to the Fourth National Report on Human Exposure to Environmental Chemicals, "Human milk can be a source of phthalate exposure for nursing infants."[14]

Children

Children have the highest exposures to phthalates compared to teens and adults.[14] Last year, a study based on the German Environmental Surveys (GerES IV) found that the general population is "exposed to phthalates to a large extent," and that children are exposed "up to four fold higher level than adults."[15] The study also found that "children are exposed to a multiple mixture of phthalates simultaneously.

Expectant mothers

Studies indicate that "phthalate diesters and their metabolites are measurable in human breast milk, cord blood and other pregnancy-related specimens."[5]

Cumulative Risk

We agree with the EPA that focusing individually on phthalates "would likely underestimate their impact since they appear to produce similar adverse effects."[6] The EPA further states that "taken together, the reproductive effects observed in animal studies and in humans, the human biomonitoring data, and the data on cumulative effects of mixtures support EPA's concern for potential human health hazard following exposure to phthalates."[6] Researchers have stated that chemicals may interact with each other "in what is commonly referred to as the 'cocktail effect.' The human health risks of exposure to chemical mixtures are much understudied,"[5] and that exposure to more than one phthalate adds to risk.[16]

It is unfortunate that peer-reviewed published data are not available to draw definitive conclusions about the risks of the three phthalates banned on an interim basis. The evidence thus far suggests that these phthalates are not safe, and the absence of better research is not justification for lifting the ban.

DIDP (di-isodecyl phthalate)

DIDP is used as a plasticizer in a variety of polyvinyl chloride (PVC) plastic products including toys, coverings on wires and cables, artificial leather, carpet backing, and pool liners.[17] "The NTP [National Toxicology Program] judges the scientific evidence sufficient to conclude that DIDP is a developmental toxicant and could adversely affect human development if the levels of exposure were sufficiently high."[17] For this reason alone, DIDP should be permanently banned from children's products and toys (with the exception of inaccessible component parts). Fortunately, it is not currently used in most toys.[18] However, children certainly can be exposed to DIDP because of its use in pool liners, artificial leather, and possibly from carpet backing.

DINP (di-isononyl phthalate)

Before the provisional ban, DINP was the phthalate that was most often used to soften plastic in some children's products and toys sold in the U.S.[19] DINP is also used in products such as flooring, gloves, straws and garden hoses. DINP is considered an animal carcinogen.[20]

In a research study published in 2007 in *Journal of Chromatography*, Koch *et al* noted that "We also have to regard DINP as an endocrine disruptor/modulator in humans. Effects like nipple retention and testis atrophy are comparable to DEHP and di-n-butylphthalate (DnBP)."[21]

A 2010 article by Danish scientists that was published in *Environmental Health Perspectives* found phthalate metabolites in the urine of all the 4-9 year old children studied, and reported several health concerns related to phthalate levels.[22] Boys and girls with higher concentrations of phthalate metabolites had lower thyroid hormones, lower IGF-1 (insulin-like growth factor), and less growth. This suggests a negative effect on children's growth

and development. Specifically, DINP and DEHP levels were negatively associated with IGF-1 in boys.

In addition, DINP apparently causes the same kind of abnormal (smaller) genitals in male rats as other phthalates such as DEHP and BBP, but is not as potent as some other phthalates, such as DEHP. It is therefore probably safer than DEHP, which is the phthalate that it replaced in 1998.[23] However, that does not mean DINP is safe. In addition to DINP's negative impact on growth and the risk of smaller genitals, DINP would add to the cumulative exposure and cumulative risks that has been associated with exposure to other phthalates.

In summary, DINP is of concern because exposure may result in poor growth and development, especially in boys, and also boys having smaller genitals and having secondary sexual characteristics that are less masculine such as female-like areolas/nipples, and it is considered an animal carcinogen. DINP's risks, therefore, far outweigh its benefits. DINP should be permanently banned from children's products and toys unless independent, well-designed studies in the future clearly prove that DINP is safe. Given the findings thus far, that seems unlikely.

DnOP (di-n-octyl Phthalate)
DnOP is used in floorings, carpet tiles, gloves, garden hoses, wire and cable insulation, adhesives, and as package sealants and bottle cap liners.[20] Neither the International Agency for Research on Cancer (IARC) nor NTP has evaluated DnOP for human carcinogenicity. "There are no known commercial uses for pure DnOP. However, DnOP constitutes approximately 20 percent of the $C_{6–10}$ phthalate mixtures used in PVC products."[6] The EPA reports that children have the highest exposure to several phthalates including DnOP.[6]

Conclusions
Safe alternatives to phthalates are available now and we urge industry to switch to these alternatives. It is disturbing to note that under the Resource Conservation and Recovery Act, phthalates are regulated as a hazardous waste if discarded as a commercial chemical product.[6] This tells us that these products are unsafe. And yet, the chemical industry continues to downplay the risks that phthalates pose to public health and argue that there is not yet conclusive evidence that phthalates are dangerous for pregnant women, children, and adults. Based on existing science, some of it summarized above, we strongly disagree. Since the chemical industry has repeatedly denied the growing evidence regarding the risk of phthalates to human health, their pronouncements regarding specific phthalates are not credible. It is true that there is a lack of conclusive evidence on exactly what exposure levels are especially unsafe for certain specific phthalates. However, there is certainly no conclusive evidence that these phthalates are safe, individually or in combination. Cumulative, long-term effects are of particular concern. The provisional ban on DIDP, DINP and DnOP in children's toys and products should be made permanent and the Consumer Product Safety Commission should be considering bans on other products made with phthalates as well, especially because of the growing evidence supporting concerns about fetal exposure when pregnant women use these products.

Footnotes

[1] Federal Register (2010, June 3). Consumer Product Safety Commission, Notice of Meeting of Chronic Hazard Advisory Panel on Phthalates and Phthalate Substitutes and Opportunity for Public Comment.
[2] Rudel RA, Brody JG, Spengler JD, Vallarino J, Geno PW, Sun G, Yau A (2001). Identification of selected hormonally active agents and animal mammary carcinogens in commercial and residential air and dust samples. *Journal of Air and Waste Management Association* 51(4):499-513.
[3] Kato K, Silva MJ, Reidy JA, Hurtz D, Malek NA, Needham LL, Nakazawa H, Barr DB, Calafat AM (2003). Mono(2-ethyl-5-hydroxyhexyl) phthalate and mono-(2-ethyl-5-oxhexyl) phthalate as biomarkers for human exposure assessment to di-(2-ethylhexyl) phthalate. *Environmental Health Perspectives* 112: 327-330.
[4] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (2005). Third National Report on Human Exposure to Environmental Chemicals.
[5] Meeker, JD, *et al.* (2009). Phthalates and other additives in plastics: human exposure and associated health outcomes, *Phil. Trans. R. Soc B* 364, 2097-2113.
[6] U.S. Environmental Protection Agency (2009). Phthalates Action Plan. Retrieved 7/8/2010 from http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/phthalates_ap_2009_1230_final.pdf
[7] Jaakkola JJ, Knight TL (2008 July). The Role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis. *Environ Health Perspect*, 116(7): 845-53.
[8] Kanazawa A, Kishi R (2009 May). Potential risk of indoor semivolatile organic compounds indoors to human health. *Nippon Eiseigaku Zasshi*, 64(3): 672-82.
[9] Duty SM, *et al.* (2003). Phthalate exposure and human semen parameters. *Epidemiology* 14(3): 269-77. Duty SM, *et al*. (2003). The relationship between environmental exposures to phthalates and DNA damage in human sperm using the neutral comet assay. *Environ Health Perspect* 111(9): 1164-9. Duty SM, *et al*. (2004). The relationship between environmental exposure to phthalates and computer-aided sperm analysis motion parameters. *J Androl* 25(2): 293-302. Duty SM, *et al*. (2005). Phthalate exposure and reproductive hormones in adult men. *Hum Reprod* 20(3): 604-10.
[10] Cho S-C, *et al.* (2010). Relationship between Environmental Phthalate Exposure and the Intelligence of School-Age Children. *Environ Health Perspect* 118: 1027-1032.
[11] Engel SM, *et al.* (2010). Prenatal Phthalate Exposure Is Associated with Childhood Behavior and Executive Functioning. *Environ Health Perspect* 118: 565-571.
[12] Martino-Andrade, A.J. and Chahoud, I. (2010). Reproductive toxicity of phthalate esters, *Mol. Nutr. Food Res.* 54, 148-157.
[13] Wittassek, M., *et al.* (2009). Fetal exposure to phthalates – a pilot study. *Int. J. Hyg. Environ. Health* 212, 492-498.
[14] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (2009). Fourth National Report on Human Exposure to Environmental Chemicals.
[15] Becker, K., *et al.* (2009). GerES IV: Phthalate metabolites and bisphenol A in urine of German children, *Int. J. Hyg. Environ. Health.*
[16] Rider, C.V., *et al.* (2008). A mixture of seven antiandrogens induces reproductive malformations in rats, *International Journal of Andrology* 31, 249-262.
[17] U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (2003, April). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-Isodecyl Phthalate (DIDP).
[18] Kamrin, M.A. (2009). Phthalate Risks, Phthalate Regulation, and Public Health: A Review. *Journal of Toxicology and Environmental Health*, Part B, 12:157-174.
[19] U.S. Consumer Product Safety Commission (1999, Winter). Consumer Product Safety Review, Phthalates in Children's Products.
[20] Department of Health and Human Services, Centers for Disease Control and Prevention (2009). Fourth National Report on Human Exposure to Environmental Chemicals.
[21] Koch, H.M., *et al.* (2007, March). Determination of secondary, oxidized di-iso-nonylphthalate (DINP) metabolites in human urine representative for the exposure to commercial DINP plasticizers, *Journal of Chromatography*. B, Analytical Technologies in Biomedical Life Sciences.

[22] Boas et al (2010 July 9) 2010 Jul 9. Childhood Exposure to Phthalates - Associations with Thyroid Function, Insulin-like Growth Factor I (IGF-I) and Growth. *Environmental Health Perspectives* [Epub ahead of print]. Retrieved from http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.0901331

[23] U.S. Consumer Product Safety Commission (1998, December). Press release: CPSC Releases Study on Phthalates in Teethers, Rattles and Other Children's Products.