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Protecting Public Health from Phthalates Will Require Consideration of Cumulative Risks

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Thank you for this new opportunity to present the views of the Environmental Working Group (EWG) on the urgent need for a cumulative human health risk assessment for phthalates. EWG is a non-profit health and environmental research and advocacy organization based in Washington DC. For the past seven years we have been conducting our own studies on phthalates that include biomonitoring and product research. In addressing this Committee on the first meeting in December, we argued that a rapidly expanding body of research points to the need for a cumulative risk assessment for phthalates. Such as assessment is essential to protect public health, especially the health of baby boys, the population most vulnerable to phthalates (Frederiksen 2007; Jarosinska 2007; Swan 2006).

A cumulative risk assessment for phthalates is both necessary to protect human health and feasible based on our review of the scientific literature:

- **People are exposed to many phthalates at any given time.** 84% of the U.S. population is contaminated with at least six different phthalates at any given time, according to EWG's analysis of biomonitoring data from the Centers for Disease Control and Prevention (CDC) (CDC 2005). EPA's current practice is to set health standards (reference doses, or RfD's) for phthalates based on an implicit assumption that people are exposed to just one phthalate at a time. This assumption is false and results in health standards that may not adequately protect health of the vulnerable populations.

- **Studies show that phthalates cause harm via a common mechanism of action, and that their impacts to health would be additive.** Studies from different laboratories indicate that phthalates disrupt male sexual differentiation and produce adverse reproductive effects by the same mechanism of action that targets the steroid hormone synthesis pathway (Clark 2007; Hallmark 2007; Howdeshell 2007; Hutchison 2008; Supornsilchai 2007; Svechnikova 2007). The fact that these chemicals do not act independently of each other points to the need for dose additive risk assessment (Sexton 2007).

- **Studies of health effects in people also find impacts linked to multiple phthalates, supporting data that indicates a common mechanism of action.** Epidemiology studies consistently linked multiple phthalates to a broad range of health effects, starting with birth defects in baby boys and reproductive problems in men, and extending to thyroid and immune disruption (Heudorf 2007; Wormuth 2006).

- **Methods are available to conduct a cumulative risk assessment for phthalates.** EPA has already established methods for cumulative risk assessments beginning about 20 years ago with their assessment of dioxin (U.S. EPA 2004). Congress mandated the assessment of cumulative risks for pesticides in food with the passage of the Food Quality Protection Act in 1996. Development of appropriate weighting factors or toxic equivalency factors to account for differing potencies of individual phthalates will facilitate the application of cumulative risk assessment for this family of chemicals (DiGangi 2002; Sexton 2007)

Both EPA and Congress repeatedly emphasized the importance of moving from individual risk assessments for single contaminants or chemicals to analyzing and safeguarding against combined risks due to simultaneous exposure to chemical mixtures (Callahan 2007; Gilman 2003; U.S. EPA 1997, 2000, 2003). The stage is now set and the methods are in place for a thorough review of phthalates by the EPA (Kortenkamp 2008; Wittassek and Angerer 2007).

Over the past eight years a series of scientific studies unambiguously demonstrated that the U.S. population faces chronic exposures to numerous phthalates (DiGangi 2002; Schettler 2006). Over that same period epidemiology studies consistently linked these chemicals to birth defects in baby boys, reproductive problems in men, and thyroid problems in both men and women (Duty 2005; Duty 2003; Hauser 2006; Hauser, Meeker 2007; Huang 2007; Lottrup 2006; Marsee 2006; Meeker 2007; Stahlhut 2007; Swan 2005). Furthermore, immune system effects of phthalates have also been suggested, which could be associated with illnesses such as allergy, asthma, and contact dermatitis (Bornehag 2004; Takano 2006; Wormuth 2006), all of which are on the rise in children.

This human health evidence joins dozens of laboratory studies proving phthalates to be reproductive toxicants with potent anti-androgenic effects that target nearly every aspect of male reproductive system development (Frederiksen 2007; Gray 2006; Matsumoto 2008). All of this research clearly and undeniably points in a single direction: EPA's review of the cumulative risks of phthalates is urgently needed to ensure adequate protection of public health. Key reasons for conducting such a cumulative risk assessment are detailed below.

Exposure to multiple phthalates is ubiquitous and virtually unavoidable. Only a cumulative human health risk assessment can account for the constant exposure of the public to complex mixtures of phthalates (Calafat 2006; Howdeshell 2007; Rider 2008; Silva, Barr 2004; Wittassek and Angerer 2007; Wittassek, Wiesmuller 2007). Reports of research groups all over the world indicate that most industrial consumer products contain phthalates or traces of phthalates (Frederiksen 2007; Sathyanarayana 2008; Schettler 2006). People are exposed to phthalates through all imaginable routes: by ingestion, inhalation, dermal absorption, and even by direct intravenous transfer from medical devices (Heudorf 2007)! Scientists at the Centers for Disease Control and Prevention (CDC) detected phthalates in urine samples from all but 12 of 2,790 people tested (CDC (Centers for Disease Control and Prevention) 2005) with six or more phthalates found in 84% of people tested.

Cumulative risk assessment is especially important for endocrine disruptors such as phthalates. Phthalates have long been known to be toxic to the male reproductive system of test animals. A series of studies published over the last several years link this family of chemicals to reproductive damage in baby boys and adult men (Hauser 2007; Hauser 2006; Lottrup 2006; Main 2006; Marsee 2006; Sharpe 2005; Swan 2005). Exposure to phthalates affects levels of various hormones, which include reproductive hormones such as testosterone, luteinizing hormone, and follicle-stimulating hormone (Main 2006) as well as thyroid hormones

(Huang 2007; Meeker 2007), which confirms the endocrine disrupting properties of these chemicals (Kortenkamp 2008).

Baby boys and pregnant women are two groups especially vulnerable to hormone-disrupting effects of phthalates. Alarmingly, these are precisely the groups whose high level exposure to multiple phthalates has been extensively documented (Adibi 2008; Sathyanarayana 2008; Silva, Barr 2004). Phthalates cross the placenta into amniotic fluid (Silva, Reidy 2004); they are also transferred from the mother to the infant with breast milk (Main 2006). A child's exposure to these potent anti-androgenic chemicals starts from the prenatal stage and continues through the formative early years. As a result, the exposure of children to phthalates generally exceeds that of adults (Heudorf 2007). Infants, with their small body size, and different behavioral patterns from adults, are most at risk from phthalates.

Hypothyroidism patients may also represent a vulnerable group at heightened risk from phthalate exposure. An estimated 8 millions of Americans suffer from underactive thyroid (Thyroid Foundation Of America 2004). Thus, thyroid patients, pregnant women, and baby boys are all groups at risk from numerous sources of endocrine-disrupting phthalates in consumer products. Only a cumulative risk assessment can adequately protect the health of these sensitive populations.

A cumulative human health risk assessment is supported by additive anti-androgenic activity of multiple phthalates. Individual risk assessments for the most common phthalates have already been carried out by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction. Seven phthalates (butyl benzyl phthalate (BBP), di-*n*-butyl phthalate (DBP), di-(2-ethylhexyl) phthalate (DEHP), diisodecyl phthalate (DIDP), diisononyl phthalate (DINP), di-*n*-hexyl phthalate (DnHP), di-*n*-octyl phthalate (DINP) were selected for NTP-CERHR evaluation because of their high production volume, significant human exposures, use in children's products, and published evidence of reproductive or developmental toxicity (NTP-CERHR 2003a, b, c, d, e, f, 2006).

Although different phthalates are processed in the human body into a broad array of distinct metabolites (Silva 2007), studies from different laboratories indicate that phthalates disrupt male sexual differentiation and produce adverse reproductive effects by the same mechanism of action that targets the steroid hormone synthesis pathway (Clark 2007; Hallmark 2007; Howdeshell 2007; Hutchison 2008; Supornsilchai 2007; Svechnikova 2007). The fact that these chemicals do not act independently of each other points to the need for dose additive risk assessment (Sexton 2007). In reality, the situation is likely to be even more complex with the human exposure to multiple anti-androgenic and endocrine disrupting chemicals (Gray 2006; Hotchkiss 2004; Kortenkamp 2008; Rider 2008). At the very least, we need to address the cumulative impact of phthalates, since newly developed methods allow scientists and risk assessors to enumerate and account for different sources of phthalate exposure (Silva 2007; Wittassek and Angerer 2007).

Ongoing biomonitoring research facilitates cumulative risk assessment for phthalates. First, current efforts on the state and federal levels promote environmental health tracking systems that combine information about sources, doses, and health effects of environmental hazards. For phthalates, collecting a comprehensive exposure dataset will represent a major breakthrough in our understanding of the potential risks of these ubiquitous chemicals. Second, large-scale prospective biomonitoring studies at the CDC already started to provide valuable data on exposure to multiple environmental agents, especially endocrine disrupting chemicals and developmental toxicants (Calafat 2006; Calafat 2007; Needham 2008). Finally, advances in

biomedical sciences and a variety of innovative technologies provide new quantitative tools for assessing the effects of cumulative environmental exposure. These technologies should be harnessed to promote public health (Sexton 2007) and protect the most vulnerable populations (DeFur 2007). Using these methods, we can now assess and manage the risks posed by phthalates taking into account their multiple sources, multiple routes of exposure, and multiple toxicological end-points.

In conclusion, a national-level policy of cumulative risk assessment for phthalates will provide the necessary guidance to companies, states and consumers, allowing for case-specific responses and rectifying the current lack of regulatory oversight for this entire family of chemicals.

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