May 10, 2010

Information Quality Guidelines Staff
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Re: Request from the Phthalate Esters Panel of the American Chemistry Council for correction of EPA's Action Plan for Phthalate Esters (December 2009)

To Whom It May Concern:

The Phthalate Esters Panel (Panel)[1] of the American Chemistry Council submits this Request for Correction to EPA under the *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity, of Information Disseminated by the Environmental Protection Agency* (Guidelines).[2] This Request seeks the correction of numerous factual errors contained in the Agency's Phthalates Action Plan issued in December 2009.[3]

As set forth in EPA's Guidelines, information is objective when it is "presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased."[4] In its Phthalates Action Plan, however, EPA presents information on phthalates that is not accurate and fails to meet the requisite standard of objectivity.

As outlined in the introduction of the Phthalates Action Plan, the Plan "is intended to describe the courses of action the Agency plans to pursue in the near term to address its concerns." The accuracy of the information presented in the Plan is commensurate to the scientific integrity of EPA's potential subsequent actions and the regulatory message these actions convey to the market place and general public. The request for correction therefore is of utmost significance to the members of the Phthalates Ester Panel.

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1 The Panel members are: BASF Corporation, Eastman Chemical Company, ExxonMobil Chemical Company, and Ferro Corporation. Teknor Apex Company, a major user of the materials, is an associate member.

2 EPA, Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity, of Information Disseminated by the Environmental Protection Agency, EPA/260R-02-008 (Oct. 2002).

3 http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/phthalates_ap_2009_1230_inal.pdf

4 Guidelines at 15.

The remainder of this letter delineates each instance of factual error and a recommend-dation for corrective action. The inaccurate statements are presented in italics followed by the Panel's explanation of the inaccuracy and recommendation of corrective action.

The most sensitive health outcomes following exposure to some phthalates in animal studies are the phthalate syndrome effects, which consist of changes in the fetal development of the reproductive system.[5]

Explanation of Inaccuracy – "Phthalate syndrome" is not an accepted scientific term or diagnosis. Reproductive development effects have been observed in rats, but not mice, at relatively high doses. Data on the potential relevance of these effects in rats to humans are conflicting, particularly at environmentally relevant exposures. Much of the controversy surrounding phthalates and male development is based on the research of Dr. Shanna Swan and her colleagues. These researchers initially published an article in 2005 suggesting that maternal exposure to certain phthalates resulted in a reduction in the anogenital index (not distance) in male children. Dr. Swan was among the authors of a commentary on this research in 2006 and she authored an additional article in 2008 that, in part, reanalyzed the data presented in the earlier publications. More recently, Dr. Swan and her colleagues published a report suggesting reduced male play behavior in the same male children.

The methodologies used by Dr. Swan to generate her data and the statistical analysis she has employed to present her results are considered by most to be controversial and require further, independent verification. The information available from the publications, and from Dr. Swan, has not been sufficient to allow a comprehensive assessment of the potential significance of her results. As a consequence, the National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction (CERHR) did not incorporate the results of the Dr. Swan's research into their 2005 evaluation of DEHP. In evaluating the research, the CERHR report concluded –

> However there were no data presented on the reliability of the measurement of anogenital distance [AGD] or other variables that may be associated with anogenital distance. Methods used to determine independent or combined effects of various phthalates (creation of summary score) were not appropriate for that purpose. A weakness of the study is that potential confounding by clinic, education, and calendar time was not assessed.[6]

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5 Phthalates Action Plan at 4.

6 CERHR, Expert Panel Report on Update on the Reproductive and Developmental Toxicity of Di(2-ethylhexyl) Phthalate (November 2005), page 54.

Recommendation for Corrective Action: Remove discussion of Phthalate Syndrome.

Several human studies have reported associations of exposure of some phthalates with adverse reproductive outcomes and developmental effects similar to those in the rat, although no casual link has been established (Swan et al., 2005, Huang et al., 2009).[7]

Explanation of Inaccuracy – The beginning of this statement, "several human studies have reported associations of exposure with adverse reproductive outcomes," is not accurate. The reports cited in this statement – Swan *et al.* (2005) and Huang *et al.* (2009) – do not make any claims that reproductive outcomes are affected by phthalates. No adverse reproductive effects in humans are attributable to phthalates. Furthermore, the paper by Huang *et al.* (2009) does not report any adverse effects in male infants – the population of concern.

Recommendation for Corrective Action: Remove the phrase *"with adverse reproductive outcomes"* from the statement.

The reproductive developmental effects observed in humans include shortened anogenital distance observed in newborn boys; and shortened pregnancy, lower sex and thyroid hormones, and reduced sperm quality in adults.[8]

Explanation of Inaccuracy – The Phthalates Action Plan does not provide a citation for the specific references used to support this statement. The sources EPA is presumably referencing are small, clinical studies that require independent verification. The Action Plan fails to indicate that the observed effects are quite controversial and are contradicted by other research. The suggestion of shortened anogenital index (not distance) by Swan *et al.,* (2005) was determined to be "novel" by the NTP-CERHR whose relevance in humans "has not been established." The anogenital distances reported by Swan and her colleagues, moreover, appear to be within the normal population distribution reported by Thankamony *et al.,* (2009)[9] and may be more reflective of the differences in age between Swan's groups than of exposures to certain phthalates. Reports of shortened pregnancy are contradicted by suggestions of

[7] Phthalates Action Plan at 4.

[8] *Id.* at 4.

[9] Thankamony A *et al.* Anogenital Distance from Birth to 2 Years: a Population Study. *Environ Health Persp* 117(11): 1786-1790 (2009).

longer pregnancies in other studies (Wolff *et al.*, 2008; Adibi *et al.*, 2009),[10,11] as have the suggestions of lower sex hormones (Rais-Bahrami *et al.*, 2004)[12] and reduced sperm quality (Herr *et al.*, 2009).[13]

Recommendation for Corrective Action: Revise statement to read *"The reproductive developmental effects reported in humans include shortened anogenital index in newborn boys, lower sex and thyroid hormones, and reduced sperm quality in adults, although other studies have failed to find an association with phthalate exposure."*

In addition, recent studies in animals evaluating the cumulative effects of mixtures of several active phthalates on testosterone production, fetal mortality, and male and female reproductive development later in life showed all mixtures were cumulative for all endpoints (Rider et al., 2008, 2009; Howdeshell, et al., 2007, 2008a, 2008b; Gray et al., 2006; Hotchkiss et al., 2004).[14]

Explanation of Inaccuracy – The results of cumulative exposure studies have been mixed. The research conducted by Gray and his coworkers have suggested dose-additivity in laboratory animals at relatively high-dose levels (~150 mg/kg body weight), but Foster *et al.*[15] were unable to produce additivity at lower doses (~100 mg/kg). More recent studies have suggested response additivity whereby substances may have the same effect by different mechanisms. These studies also have been conducted at high doses that are not reflective of environmental exposures.

Christensen *et al.,* (2009) acknowledge that "our developmental rat model would not have produced any responses, had we combined all mixture components at [low, environmentally relevant exposure levels.]"[16] This finding is supported by

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[10] Wolff MS *et al.* Prenatal phenol and phthalate exposure and birth outcomes. *Environ Health Persp* 116(8): 1092–1097 (2008).

[11] Adibi JJ *et al.* Maternal urinary metabolites of di-(2-ethylhexyl) phthalate in relation to the timing of labor in a US multi-center pregnancy cohort. *Am J Epidemiol* 69(8): 1015–1024 (2009).

[12] Rais-Bahrami K *et al.* Follow-up study of adolescents exposed to di(2-ethylhexyl) phthalate (DEHP) as neonates on extracorporeal membrane oxygenation (ECMO) support. *Environ Health Persp* 112: 1339-40 (2004).

[13] Herr C *et al.* Urinary di(2-ethylhexyl) phthalate (DEHP) – metabolites and male human markers of reproductive function. *Intl J Hyg Environ Health* 212(6): 648-653 (2009).

[14] Phthalates Action Plan at 4.

[15] Foster PMD *et al.* Antiandrogenic effects of a phthalate combination on *in utero* male reproductive development in the Sprague-Dawley rat: additivity of response?, Poster presentation at Society of Toxicology Annual Meeting (2002).

[16] Christiansen S *et al.* Synergistic disruption of external male sex organ development by a mixture of four antiandrogens. *Environ Health Persp* 117(2): 1839-1846 (2009).

earlier studies of up to 25 chemicals at environmental dose levels by Chapin *et al.,* (1989)[17] and Heindel *et al.,* (1995).[18]

The absence of a cumulative effect at environmental relevant levels is further supported by the evaluation conducted by Benson (2009) who concluded that "it is unlikely that humans are suffering adverse developmental effects from current environmental exposure to these phthalate esters.

Recommendation for Corrective Action: Revise statement to read "*In addition, recent studies in animals evaluating the cumulative effects of mixtures of several active phthalates on testosterone production, fetal mortality, and male reproductive development later in life have suggested dose additivity at relatively high-dose levels (Rider et al., 2008, 2009; Howdeshell, et al., 2007, 2008a, 2008b; Gray et al., 2006; Hotchkiss et al., 2004). Similar effects have not been observed at environmentally-relevant exposure levels."*

For example, inhalation exposure for adults and children could be of concern in vehicle interiors, particularly in summer due to elevated temperatures in vehicles given the vapor pressure range of these chemicals.[19]

Explanation of Inaccuracy – EPA fails to cite any references to support this assertion. Moreover, the suggestion in the Phthalates Action Plan of concern about phthalate exposure from off-gassing from vehicle interiors is contradicted by the available data. Limited measured data are available from a survey conducted in 2000.[20] Samples (n = 3) were collected from car interiors and analyzed for selected phthalates. The concentrations of DINP and DIDP did not exceed 20 nanograms per cubic meter (ng/m^3). A study conducted in 2001 by Australia's Commonwealth Scientific and Industrial Research Organization (CSIRO)[21] identified nine contaminants in the interior air of three new automobile. None of the contaminants were phthalates.

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17 Chapin RE *et al.* Toxicology studies of a chemical mixture of 25 groundwater contaminants. III. Male reproduction study in B6C3F1 mice. *Fund Appl Toxicol*. 13(3): 388-98 (1989).

18 Heindel JJ *et al.* Assessment of the reproductive toxicity of a complex mixture of 25 groundwater contaminants in mice and rats. *Fund Appl Toxicol* 25(1): 9-19 (1995).

19 Phthalates Action Plan at 6.

20 Research Institute for Chromatography. Report: Overview of Phthalate Measurements in Air. Research Institute for Chromatography, Ref. ECPI\2000-12-S, Kortrijk, Belgium (2000). (Cited in ECB. European Union Risk Assessment Report – 1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate, 2003). Available at http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/didpreport041.pdf.

21 Available at http://www.csiro.au/files/mediaRelease/mr2001/newcars.htm.

More recently, Buters *et al.,* (2007) tested the health effects of emissions from two vehicles (one new, one used) under conditions simulating being parked in sunshine.[22] The researchers identified about 50 contaminants, none of which were phthalates. They report that "phthalates" were low in both the new and used vehicle. Importantly, the study employed halogen lamps to mimic environmental sunshine exposure and sampled the interior air at 65 degrees C (150 degrees F).

Contrary to EPA's suggestion, in fact, the phthalates used in car interiors have very low vapor pressures and would not be expected to result in inhalation exposure.

Recommendation of Corrective Action: Remove discussion of potential exposure due to vehicle interiors.

Due to their pervasive use and release, as well as its propensity for global transport, phthalates are found in most environmental media, for example ambient air, surface water, soil, sediment, etc (EC, 2003a-b; 2008a-b; NTP-CERHR, 2003 a-e; 2006).[23]

Explanation of Inaccuracy – It is not clear what EPA is using as its source in suggesting that phthalates have a "propensity for global transport." The references cited in the Phthalates Action Plan suggest, in fact, that phthalates are rapidly broken down in the environment. As noted elsewhere in the Action Plan, phthalates are not considered to be either persistent or bioaccumulative. Notably, none of the phthalates are candidates for listing under the UN Stockholm POPs Convention, the international instrument under which chemicals whose properties for global transport would be expected to be addressed. None are listed under EPA's Resource Conservation and Recovery Act Waste Minimization Persistent, Bioaccumulative and Toxic (PBT) Chemical List.[24]

Phthalate esters are readily biodegradable, and therefore not persistent, based on "ready" biodegradation testing that involves stringent methods of assessing the potential for the biodegradation of a substance. Passing a ready biodegradation test indicates that the substance will be rapidly biodegraded in the environment. Phthalates also have been shown to rapidly biodegrade in test systems that used the natural microbial consortia found in soil and water.

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22 Buters JTM *et al.* Toxicity of Parked Motor Vehicle Indoor Air. *Environ. Sci. Technol.* 41(7): 2622-29 (2007).

23 Phthalates Action Plan at 7.

24 http://www.epa.gov/osw/hazard/wastemin/priority.htm.

Recommendation for Corrective Action: Remove "*as well as its propensity for global transport*" from the statement.

Among other provisions, the Consumer Product Safety Improvement Act of 2008 (CPSIA) banned the use of six phthalates in toys and child care articles at concentrations greater than 0.1 percent: DEHP, DBP, BBP, DINP, DIDP and DnOP.[25]

Explanation of Inaccuracy – The Phthalates Action Plan misstates the requirements of the CPSIA. Three phthalates - DEHP, DBP, and BBP - have been permanently prohibited by Congress in concentration of more than 0.1% in "children's toys" or "child care articles." The other three phthalates - DINP, DIDP, and DnOP - have been prohibited only in child care articles and toys that can be placed in a child's mouth pending scientific review by a group of outside experts and the Commission.

A more complete review of the requirements can be found at http://www.cpsc.gov/about/cpsia/sect108.html.

Recommendation for Corrective Action: Change to read, *"Among other provisions, the Consumer Product Safety Improvement Act of 2008 (CPSIA) banned the use of DEHP, DBP, and BBP in children's toys and child care articles at concentrations greater than 0.1 percent. The act also imposes an interim prohibition on DINP, DIDP, and DnOP in toys and child care articles that can be placed in a child's mouth."*

As part of a statute concerning chemicals in children's products generally, Washington prohibits a manufacturer, wholesaler, or retailer from manufacturing, knowingly selling, offering for sale, or distributing for sale or for use in the state a children's product or product component containing phthalates (DEHP, DBP, BBP, DINP, DIDP, DnOP) individually or in combination, at a concentration exceeding 0.1% by weight (CRS, 2008).[26]

Explanation of Inaccuracy – This is not an accurate statement. Washington's Department of Ecology (DOE) withdrew the proposal to implement the Children's Safe Products Act (CPSA) that would have adopted several enacted sections of the CPSA and clarified the requirements as they pertained to electronic components. DOE determined that the phthalate standards established by the state's CPSA were preempted by the passage of the federal Consumer Product Safety Improvement Act.[27]

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[25] Phthalates Action Plan at 8.

[26] *Id.* at 10.

[27] Washington DOE, Notice from Laurie Davies, Program Manager – Solid Waste and Financial Assistance, WSR 08-23-040 (November 5, 2008). Available from http://www.ecy.wa.gov.

Recommendation for Corrective Action: Remove the discussion of the Washington statute.

Please feel free to contact me at steve_risotto@americanchemistry.com or 703-741-5501 if you have any questions on this submission.

Sincerely,

Steve Risotto

Stephen P. Risotto
Senior Director, Phthalate Esters