

Department of Environmental Health

University of Cincinnati PO Box 670056 Cincinnati, OH 45267-0056

Kettering 160 Panzeca Way Cincinnati, OH 45267-0056 513-558-5701

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- I, Susan Kasper, am writing this statement in support of the Petition to the CPSC to ban certain household products containing additive monomer organohalogen flame retardants.
- 1. I, Susan Kasper PhD, am an Associate Professor in the Department of Environmental Health at the University of Cincinnati, College of Medicine. I have a Ph.D. and a M.Sc. in Physiology/Endocrinology from the University of Manitoba, Canada. Please see my CV and list of publications attached.
- 2. Research in my laboratory has focused on the mechanisms by which cancers develop and progress to become therapy resistant. This includes the role of chemicals such as organohalogen flame retardants on cancer progression. Many organohalogen flame retardants are Persistent Organic Pollutants (POPs), indicating that they are resistant to degradation and capable of remaining in the environment for many years. Furthermore, they are readily absorbed in the food chain and stored in fatty tissues¹. Most Americans, when tested, were found to have trace levels of flame retardants in multiple tissues, including adipose, liver, muscle, skin and blood². Importantly, organohalogen flame retardants can interfere with normal hormonal function in that they act as "endocrine disrupting chemicals" (EDCs) to either mimic or inhibit the action of naturally occurring hormones ³,⁴. Exposure to organohalogen flame retardants has been linked to developmental defects, altered neurologic function, infertility, and cancer (reviewed in Kopras et al., 2014)⁵. Indeed, exposures to EDCs during the critical time of growth and development can result in genetic modifications that are passed down to subsequent generations⁶.
- 3. For the past few years, we have studied the endocrine disrupting activities of Firemaster® 550 (FM 550), a new-generation flame-retardant mixture and previously the second most commonly detected flame retardant in polyurethane foam in the United States⁷. FM 550 might now be the most commonly used flame retardant in polyurethane foam since the previously most common compound, TDCPP, has been listed as a carcinogen under California Proposition 65 and is therefore slowly being phased out.
- 4. FM 550 is a mixture of two organohalogens (2-ethylhexyl-2,3,4,5-tetrabromobenzoate or TBB and bis(2-ethylhezyl)-2,3,4,5-tetrabromophthalate or TBPH) and organophosphates (isotpropylated triphenylphosphate isomers or ITPs, and triphenyl phosphate or TPP). The organohalogen components TBB and TBPH have been found in indoor dust, outdoor air, marine mammal tissues, wastewater and sewage sludge ^{8,9,10,11,12,13,14}. Stapleton and coworkers determined that exposure to FM 550 components could be measured in tissues of pregnant rat dams and offspring. In pregnant dams, TBB increased serum thyroxine levels and reduced

hepatic carboxylesterase activity; in offspring, exposure to FM 550 in the mother's milk resulted in male cardiac hypertrophy, advanced female puberty, significant weight gain in both males and females, and altered exploratory behaviors^{15,16}. These results demonstrate for the first time that at environmentally relevant levels, FM 550 affects multiple biological processes, including organ development and function, weight gain, and behavior.

- 5. In our lab we are studying the effects of FM 550 on prostate cancer stem cells (CSC). Prostate CSCs comprise less than 0.1% of the total number of tumor cells, but they are central to promoting tumor growth, metastasis, and the emergence of treatment-resistant disease^{17,18}. Using prostate CSC-like cells derived from human patient biopsy specimens, our initial findings imply that three FM 550 components, namely ITP, TBPH and TBB, are capable of stimulating the rapid expansion of prostate cancer stem cells. Moreover, this response is similar to that observed in CSC-like cells treated with the antiandrogens Casodex and hydroxyflutamide. Therefore, FM 550 could act as an endocrine disrupting chemical to promote the expansion of CSCs. Since prostate CSCs are thought to be resistant to androgen deprivation therapy, expansion of this cell type by FM 550 activity could promote resistance to clinical treatment.
- 6. The observation that FM 550 exerts anti-androgenic-like activity in prostate cancer implies a high probability that FM 550 will also exert its anti-androgenic effects on non-cancerous processes. These include the development and function of the male reproductive system (prostate, seminal vesicles, penis, testes, epididymis), spermatogenesis, and male fertility¹⁹ as well as normal ovary development in females²⁰.
- 7. The available data on organohalogen flame retardants indicates a high likelihood that other yet unstudied members of this class of chemicals are also endocrine disruptors, which means they can impair normal cell development, and thus cause substantial personal injury or substantial illness. Therefore, I support this petition to the CPSC to ban consumer products containing organohalogen flame retardants in additive form, where there is a high risk of human exposure.

Yours sincerely,

Susan Kasper, Ph.D. Associate Professor,

Environmental Health,

University of Cincinnati College of Medicine

¹ Bartrons M, Grimalt JO, de Mendoza G, Catalan J. Pollutant dehalogenation capability may depend on the trophic evolutionary history of the organism: PBDEs in freshwater food webs. PLoS One. 2012;7(7):e41829.

² Szabo DT, Diliberto JJ, Hakk H, Huwe JK, Birnbaum LS. Toxicokinetics of the flame retardant hexabromocyclododecane alpha: effect of dose, timing, route, repeated exposure, and metabolism. Toxicol Sci. 2011;121(2):234-44.

³ Stapleton HM, Sharma S, Getzinger G, Ferguson PL, Gabriel M, Webster TF, Blum A. Novel and high volume use flame retardants in US couches reflective of the 2005 PentaBDE phase out. Environ Sci Technol. 2012;46:13432-39.

⁴ Birnbaum LS. When environmental chemicals act like uncontrolled medicine. Trends Endocrin Met. 2013;24:321–3

⁵ Kopras E, Potluri V, Bermudez ML, Williams K, Belcher S, Kasper S. Actions of endocrine-disrupting chemicals on stem/progenitor cells during development and disease. Endocr Relat Cancer. 2014;21(2):T1-12.

⁶ Patisaul HB, Roberts SC, Mabrey N, McCaffrey KA, Gear RB, Braun J, Belcher SM, Stapleton HM. Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster® 550 in rats: an exploratory assessment. J Biochem Mol Toxicol. 2013;27(2):124-36.

 7 Stapleton HM, Sharma S, Getzinger G, Ferguson PL, Gabriel M, Webster TF, Blum A. Novel and high volume use flame retardants in US couches reflective of the 2005 PentaBDE phase out. Environ Sci Technol. 2012;46:13432-39.

⁸ Ma Y, Venier M, Hites RA. 2-Ethylhexyl tetrabromobenzoate and bis(2-ethylhexyl) tetrabromophthalate flame retardants in the Great Lakes atmosphere. Environ Sci Technol. 2012;46:204-8.

⁹ Lam JC, Lau RK, Murphy MB, Lam PK. Temporal trends of hexabromocyclododecanes (HBCDs) and polybrominated diphenyl ethers (PBDEs) and detection of two novel flame retardants in marine mammals from Hong Kong, South China. Environ Sci Technol. 2009;43:6944-9.

 10 La Guardia MJ, Hale RC, Harvey E, Chen D. Flame-retardants and other organohalogens detected in sewage sludge by electron capture negative ion mass spectrometry. Environ Sci Technol. 2010;44:4658-64.

¹¹ Klosterhaus SL, Stapleton HM, La Guardia MJ, Greig DJ. Brominated and chlorinated flame retardants in San Francisco Bay sediments and wildlife. Environ Int. 2012;47:56-65.

¹² Davis EF, Klosterhaus SL, Stapleton HM. Measurement of flame retardants and triclosan in municipal sewage sludge and biosolids. Environ Int. 2012;40:1-7.

¹³ Ali N, Harrad S, Goosey E, Neels H, Covaci A. "Novel" brominated flame retardants in Belgian and UK indoor dust: implications for human exposure. Chemosphere 2011;83:1360-1365.

¹⁴ Ali N, Harrad S, Goosey E, Neels H, Covaci A. "Novel" brominated flame retardants in Belgian and UK indoor dust: implications for human exposure. Chemosphere 2012;83:1360-5.

¹⁵ Springer C, Dere E, Hall SJ, McDonnell EV, Roberts SC, Butt CM, Stapleton HM, Watkins DJ, McClean MD, Webster TF, Schlezinger JJ, Beokelheide K. Rodent thyroid, liver, and fetal testis toxicity of the monoester metabolite of bis-(2-ethylhexyl) tetrabromophthalate (TBPH), a novel brominated flame retardant present in indoor dust. Environ Health Perspect. 2012;120:1711-9.

¹⁶ Patisaul HB, Roberts SC, Mabrey N, McCaffrey KA, Gear RB, Braun J, Belcher SM, Stapleton HM. Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster® 550 in rats: an exploratory assessment. J Biochem Mol Toxicol. 2013;27(2):124-36.

¹⁷ Gu G, Yuan J, Wills M, Kasper S. Prostate cancer cells with stem cell characteristics reconstitute the original human tumor in vivo. Cancer Res. 2007;67(10):4807-15.

¹⁸ Chaffer CL, Weinberg RA. A perspective on cancer cell metastasis. Science. 2011;331(6024):1559-64.

¹⁹ Kopras E, Potluri V, Bermudez ML, Williams K, Belcher S, Kasper S. Actions of endocrine-disrupting chemicals on stem/progenitor cells during development and disease. Endocr Relat Cancer. 2014;21(2):T1-12. ²⁰ Prizant H, Gleicher N, Sen A. Androgen actions in the ovary: balance is key. J Endocrinol. 2014. pii: JOE-14-0296.