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Sept. 15, 2014

To whom it may concern:

I, David A. Eastmond, am writing this statement in support of the Petition to the CPSC to ban or significantly restrict the availability of certain household products containing additive non-polymeric organohalogen flame retardants.

1. I am Professor and Chair of the Department of Cell Biology and Neuroscience, and a Research Toxicologist at the University of California, Riverside. I received B.S. and M.S. degrees from Brigham Young University, in Provo, Utah, and a Ph.D. from the University of California, Berkeley. My research focuses on the mechanisms involved in the toxicity and carcinogenicity of environmental and agricultural chemicals, with a goal to more accurately identify the potential adverse health effects associated with chemical exposures. I was a Jefferson Science Fellow at the US Department of State, and have served as President of the Environmental Mutagen Society and as Chair of the Board of Scientific Counselors for the National Toxicology Program, NIEHS. I have also participated on numerous review panels related to chemical mutagenesis, carcinogenesis and risk assessment, including panels for the US EPA, the US Food and Drug Administration, the International Programme for Chemical Safety, the International Agency for Research on Cancer, the Organisation for Economic Cooperation and Development, Health Canada, and the International Working Group for Genotoxicity Testing. In 2011, I was elected a Fellow of the Collegium Ramazzini, an organization of international scholars working towards solutions to occupational and environmental health problems occurring internationally. I am currently a member of the Carcinogen Identification Committee for the California Environmental Protection Agency and of the Chemical Assessment Advisory Committee of the US EPA. I have attached my CV and list of publications.

2. Organohalogens are often used as flame retardants in consumer products, without adequate toxicological information to assess whether or not they may be harmful to human or environmental health. To address this lack of knowledge on health effects, two of my graduate students, Virunya Bhat and Kristi Capsel, performed, under my supervision, a hazard screen of approximately 90 brominated and chlorinated flame retardants, ~85 of which are non-polymeric compounds. The list of studied chemicals includes a large number of organohalogen flame retardants (OFRs) in use or available for potential use in consumer products. The objective of the hazard screen was to determine which of these OFRs should be considered toxic, and therefore used with caution, or not used at all. The results of this study have been presented at several scientific meetings, and we are in the process of preparing a peer-reviewed journal article describing our results.

3. Using the Chemical Abstract Services (CAS) registry numbers as primary identifiers, we performed an extensive search for toxicity information on these 85 non-polymeric OFRs. Whenever possible, we searched for and used, if found, the results of existing hazard screens or

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toxicity reviews, such as those from the U.S. EPA Design for the Environment program, the Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency, the World Health Organization/International Programme on Chemical Safety, the Agency for Toxic Substances and Disease Registry, the International Agency for Research on Cancer, Health Canada/Canadian Environmental Protection Agency and/or Clean Production Action. Additionally, we searched for peer-reviewed toxicity data in public databases such as Pubmed and Toxnet. Because often we could not identify peer-reviewed data in these databases, we also used other information sources, which included non-peer reviewed information or unpublished data, such as the U.S. EPA Toxic Substance Control Act Test Submissions, the Registry of Toxic Effects of Chemical Substances, the European Chemicals Agency database, and the U.S. EPA High Production Volume data submissions. We gave preference to *in vivo* data via any exposure route, rather than *in vitro* data, due to the lack of guidelines or current consensus on appropriate method(s) to determine human relevance or to extrapolate the results of *in vitro* assays when characterizing *in vivo* hazard potential. In the cases in which we could not identify any empirical data, we used Structure-Activity Relationship (SAR) models.

4. We used three related hazard screening tools: the U.S. EPA's Design for the Environment (DfE) program, the Clean Production Action's GreenScreen™, and the Washington State Department of Ecology's Quick Chemical Assessment Tool (QCAT®). All three provide a framework for identifying problematic characteristics of chemicals and then grading the chemicals according to the level of concern. Because most OFRs lacked sufficient information to use the DfE tool or run a GreenScreen™, our hazard screening was based mainly on the QCAT® methodology (Stone, 2010, 2012), with some modifications to account for the overall lack of publicly available toxicity information for the majority of chemicals.

5. The QCAT® prioritizes 9 out of the 18 hazard categories included in the more comprehensive GreenScreen™ and US EPA DfE approaches: acute mammalian toxicity, five human health hazards (carcinogenicity, reproductive toxicity, developmental toxicity, mutagenicity/genotoxicity and endocrine disruption) and three environmental hazards (acute aquatic toxicity, persistence, and bioaccumulation). These hazard endpoints are considered to pose significant threats to sensitive populations such as children, and provide a good indication of the risks associated with exposure to chemicals (Stone, 2010). The QCAT® grading process is similar to that established for the GreenScreen™. The main difference is that assigning a QCAT® score requires less information than for a GreenScreen™, meaning that the QCAT® can be performed even on chemicals for which not enough data are available to conduct a GreenScreen™, but it is not as thorough an evaluation of potential hazards posed by chemical alternatives as the GreenScreen™. However, if a chemical is found to be a poor alternative using the QCAT methodology, it will also be a poor candidate using the GreenScreen™ methodology. There remains a chance that a chemical not rejected by QCAT® could still prove to be unsatisfactory if a more complete review is done using methods like the GreenScreen™.

6. To perform our hazard assessment, we assigned concern levels for each hazard category, such as Low, Moderate, or High, based on the available information. Examples are provided below.

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a. Acute Mammalian Toxicity: We assigned the hazard scores based preferentially on the most potent empirical oral, inhalation, and/or dermal LD_{50} (the dose that is lethal to 50% of a population of test animals) values. When empirical LD_{50} data were not identified, SAR predictions (rat oral LD_{50}) were used to assign the score.
b. Carcinogenicity: Cancer bioassays were found for 8 of the studied OFRs, resulting in all of these OFRs being listed as carcinogens by authoritative bodies (i.e. "High" concern). Since most of the screened OFRs did not have empirical carcinogenicity data, the ISS and Oncologic QSAR models (OECD Toolbox, 2012) were used to identify a structural alert for carcinogenicity. If a structural alert was identified, we assigned a hazard score of "Moderate".
c. Reproductive toxicity: Two chemicals listed by an authoritative source as reproductive toxicants were rated as "High" concern. For a limited number of OFRs for which a two-generation reproduction study was identified, we assigned concern levels based on NOAEL values identified from these studies. Less than one-third of the OFRs screened had data to assess reproductive toxicity. We did not conduct SAR modeling of reproductive toxicity, due to the lack of guidelines for the use of SAR modeling tools for this hazard category.
d. Developmental toxicity: The same two chemicals listed by an authoritative source as reproductive toxicants were also listed as developmental toxicants, and thus rated as "High" concern. When developmental toxicity studies were identified, we assigned concern levels based on NOAEL values from these studies. For most of the OFR, we used VEGA Caesar (2012) and/or U.S. EPA (2011) Toxicity Estimation Software Tool (T.E.S.T.) software to predict developmental toxicity potential due to the lack of empirical data. If predicted positive, we assigned a hazard score of "Moderate".
e. Mutagenicity/Genetic Toxicity: One OFR, TCEP (tris(2-carboxyethyl) phosphine, CAS#115-96-8), was listed by an authoritative source as a Global Harmonization System (GHS) category 1B germ cell mutagen (i.e. "High" concern). For the other OFRs, the scores were based, when possible, on empirical data, most commonly *Salmonella* reverse mutation assays. A few chemicals were negative in *Salmonella* assays but positive in other assays of genetic toxicity. In this case, we applied a hazard score of "Moderate". When mutagenicity data were not identified, we used the ISS Quantitative Structure-Activity Relationship (QSAR) model (OECD Toolbox, 2012) to identify molecular functional groups or substructures considered to be structural alerts for *in vivo* or *in vitro* mutagenicity.
f. Endocrine disruption: A few OFRs were listed as known or suspected endocrine disruptors by authoritative sources. Most of the other OFRs lacked empirical data specifically assessing endocrine disruption. Due to the current lack of SAR models to

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predict endocrine disruption, no further modeling was done. This hazard category was the most prevalent one for data gaps.

g. Acute aquatic toxicity: Those chemicals classified as toxic to aquatic organisms by an authoritative source were designated as "High" concern. For the others, the score was based on empirical LC_{50} (the lethal concentration to 50% of the organisms tested) or EC_{50} (the concentration that affects 50% of the organisms) values when identified. When empirical data were not identified, we used the U.S. EPA (2011) ECOSAR software to predict acute aquatic toxicity.

h. Persistence: OFRs that have been classified as POP (Persistent Organic Pollutants) or PBT (Persistent, Bioaccumulative and Toxic) were designated as "High" concern. Most screened OFRs did not have empirical data available for these parameters. For these, the hazard score for persistence was based on the most conservative EPISuite model estimates for half-life in soil, water and sediment.

i. Bioaccumulation: For the OFRs that were not listed or classified as a POP or PBT, the hazard score for bioaccumulation was based on octanol-water partition coefficients (K_{ow}) and bioaccumulation or bioconcentration factors, which were predicted using U.S. EPA (2011) EPISuite software when empirical data could not be identified.

7. Data gaps posed the greatest challenge in this study, and as indicated above, we often had to rely on QSAR modeling. It should be noted that QSAR models are often based on SMILES structures, which are sometimes not unique for every chemical, and the models are likely not calibrated specifically for OFRs. Therefore, we interpreted the modeling results with caution and did not rely solely upon them to denote chemicals of "High" concern. I would like to emphasize that the QCAT® methodology we used is generally health-protective. While it may not find all substances of concern, when it does, that result is defined according to independently established criteria and would be sufficient to warrant concern prompting further investigation or a search for a suitable alternative with a lower degree of concern.

8. On the basis of these data and model results, we assigned each chemical both an initial and a final grade based on QCAT® criteria, where:

"A" means few concerns / preferable,
"B" means the chemical raises slight concerns / improvement possible,
"C" means the chemical raises moderate concern / use but search for safer alternatives,
"D" means the chemical is of high concern / avoid
"F" means the chemical is toxic/do not use.

Chemicals received an automatic F if they were assigned a "High" score for any of the 5 priority human health endpoints. The initial grade considers only the concern levels based on empirical data and model results. The final grade assigned by the QCAT® model includes penalties for excessive data gaps.

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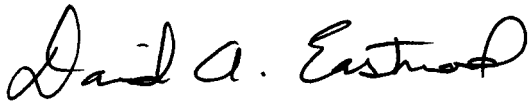
9. The results of our on-going hazard screen are presented in draft form in the attached summary table. Italicized hazard scores denote that QSAR model results and/or low confidence empirical data served as the basis of the score. As the table shows, the initial grades for all of the evaluated organohalogen flame retardants were C or worse: 9 OFRs received C grades, 26 received D grades, and the remaining 48 received F grades. In the final grading step, 5 OFRs received D grades, and the remaining 78 received F grades. Five polymers and 3 OFRs with inadequate chemical information to allow for scoring were excluded from these tallies. These low grades were due to empirical data suggesting high hazard, SAR model predictions, and/or excessive data gaps. Carcinogenicity was the most prominent potential health hazard identified based on empirical data. Endocrine disruption exhibited the most prevalent data gaps.

10. In conclusion, all of the non-polymeric OFRs that we have screened using the QCAT® and related methodologies were found to be either of high concern or toxic based on the criteria described above. The results of our screening show that critical toxicological data are lacking for many OFRs, and that those for which data are available have the potential to pose significant hazards for human or environmental health.

Sincerely,



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