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COMMENTS FROM THE NATURAL RESOURCES DEFENSE COUNCIL ON THE DEPARTMENT OF TOXIC SUBSTANCES CONTROL DRAFT STAGE 1 ALTERNATIVES ANALYSIS GUIDANCE

We appreciate this opportunity to submit comments on behalf of the Natural Resources Defense Council (NRDC), a non-profit organization with over 2.4 million members and activists, 380,000 of whom are Californians. NRDC has no financial interest in any of the chemicals or products that may be affected by the subject matter of these comments.

We commend the Department on the Alternatives Analysis (AA) Guidance document, which provides resources and elaborates on the particulars of the AA framework and first stage requirements under the Safer Consumer Products (SCP) regulations. SCP's mission is to reduce toxic chemicals in consumer products, and a strong, comprehensive alternatives analysis process is critical to achieving this mission and avoiding 'regrettable substitutions' and risk trade-offs. The central problem of regrettable substitution is painfully apparent in cases where companies replace one toxic flame retardant with another^{1,2}, or replace bisphenol-A (BPA) with similar endocrine-disrupting chemicals³. Through a robust AA process, potential replacements for chemicals of concern are first evaluated and then a safer replacement is made, avoiding regrettable substitutes and reducing adverse effects on human health and the environment.

The Safer Consumer Products Program has the potential to deliver better health and a cleaner environment for all California families. Moving forward, the realization of this vision depends on the type and number of Priority Products identified, the integrity of the alternatives analysis process, and the concrete steps the Department takes to protect the public.

Our comments are summarized here and discussed in more detail below.

- 1. The Guide follows through on the Department's obligations pursuant to Section 69505 of the Safer Consumer Products regulations. As envisaged by the regulations, the Guide is advisory, non-binding, and provides resources to assist stakeholders in performing an alternatives analysis under the SCP regulation.**
- 2. The Commons Principles are a strong foundation for alternatives analysis.**
- 3. Though there are other relevant factors to consider, the goal of the alternatives analysis is to find a safer replacement. The Guide should be more specific that reduction of adverse impacts must be prioritized.**
- 4. Data from current high-throughput, predictive and computational toxicology methods cannot reliably show that a potential replacement is "safe."**
- 5. Other minor comments**

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DETAILED COMMENTS

- 1. The Guide follows through on the Department’s obligations pursuant to Section 69505 of the Safer Consumer Products regulations. As envisaged by the regulations, the Guide is advisory, non-binding, and provides resources to assist stakeholders in performing an alternatives analysis under the SCP regulation.**

Section 69505 requires that “[b]efore finalizing the initial Priority Products list, the Department shall make available on its website guidance materials to assist persons in performing AAs under this article.” The finalized Guide would satisfy the Department’s obligations under this section. As the draft Guide notes, the Guide creates no new legal obligations, is informational in content, and does not alter the regulatory and statutory requirements. We support the Department’s approach to the Guide and believe that it provides useful advice and guidance on resources, approaches, methods, tools, and examples to help meet the regulatory and statutory requirements for AAs.

- 2. The Commons Principles are a strong foundation for alternatives analysis.**

We agree that the Commons Principles included in DTSC’s Guide (p. 11-12) are a useful reference for responsible entities and provide an excellent foundational set of principles for an alternatives analysis. The principles complement the SCP tenets and AA framework. For example, the principle of hazard reduction is embedded within the SCP regulation’s preference for ‘inherent protection’ over risk reduction through exposure controls (Section 69506).

The Commons Principles are also shared with the nine different AA frameworks reviewed by the National Academies in their report “A Framework to Guide the Selection of Chemical Alternatives⁴.” The fact that the principles are common to all the frameworks reflects the consensus amongst the community of practice that these principles are central to a successful alternatives analysis in order to: (1) guide an informed scientific review process for evaluating alternatives to chemicals of concern and (2) ensure that a safer alternative is chosen and regrettable substitutes are avoided. Briefly, the principles are:

- Reduce hazard
- Reduce exposure
- Use the best available information
- Ensure transparency in methods, criteria, and data used
- Identify and mitigate trade-offs

- 3. Though there are other relevant factors to consider, the goal of the alternatives analysis is to find a safer replacement. The Guide should be more specific that reduction of adverse impacts must be prioritized.**

The overall goal of SCP is to reduce toxic chemicals in consumer products. As part of this process, the SCP regulations Section 69501(a) describe the purpose of the AA: “to determine how best to eliminate or reduce potential exposures to, or the level of potential adverse impacts posed by, the Chemical(s) of Concern in Priority Products.” Adverse impacts means adverse public health and/ or adverse environmental impacts (Section 69501.1(a)(5)). This means that any alternative that presents *greater* adverse impacts than the chemical of concern is not an acceptable alternative and must be screened out of consideration, even if an alternative looks better for other relevant factors.

Therefore, when an alternative presents various trade-offs amongst a number of relevant factors, reduction of adverse impacts should be the primary consideration, with other factors a secondary consideration. So while DTSC's Guide is right that "[b]ecause the regulations explicitly favor alternatives that are 'safer,' most responsible entities will compare health and environmental factors first, placing these factors at the top of the hierarchy" (p. 61), we believe the regulations *require* that hierarchy. The Guide should be amended to make that clear, for example by changing "most responsible entities will..." to the more directive statement, "responsible entities should."

4. Data from current high-throughput, predictive and computational toxicology methods cannot reliably show that a potential replacement is "safe."

As described on pp. 56-57 of the Guide, recent advances in computational and biological tools allow for the rapid evaluation of chemical toxicity at the molecular and cellular levels, generating data that can provide valuable information on the potential hazards of materials. However, as we explain below, due to the significant limitations of these methods as they currently exist, these types of data on their own are not sufficient to demonstrate the absence of hazard. **The Guide should note clearly that these types of data can be used to support hazard determinations, but not a conclusion of lack of hazard.**

Background

High-throughput chemical toxicity testing has been implemented in large-scale agency projects, including the Toxicity Forecaster (ToxCast™) and Tox21 projects at EPA and NIEHS. While some initial data indicate that the methods may have promise^{5,6}, the ability of these methods to predict chemically-induced perturbations at the tissue, whole organism, and population levels has yet to be determined. A report of the National Academies released this summer details some of the concerns associated with the use of the predictive toxicology methods⁷. The committee warned that:

"In vitro assays, alternative animal models, and other emerging technologies described here and in more detail later in the committee's report hold promise, but some important limitations or considerations should be noted:

- a. *In vitro* assays for predicting acute toxicity have focused primarily on non-mechanistic indicators of toxicity, such as cytotoxicity; they were not developed with a quantitative linkage to any phenotype (acute or chronic).
- b. Existing assays do not cover the full range of exposure or toxicity routes, and do not include first pass metabolism.
- c. Most current *in vitro* assays do not account for important pharmacokinetic characteristics, such as metabolism, that can influence *in vivo* toxicity.
- d. Cellular systems commonly use immortalized cancer cell lines, which might fail to detect chemical activity or effects that might occur in normal (non-tumor) differentiated cells.
- e. Cells can have different levels of activity or responsiveness, depending on whether they are primary cells, differentiated cells, or immortalized cells and on how many times they have been cultured, so assay reproducibility can be a problem. "

Data cannot be used to demonstrate absence of hazard

The limitations highlighted by the National Academies report demonstrate that interpretation of data from emerging tools is not straightforward. While these tests are useful in demonstrating what pathways or mechanisms of toxicity a test agent may trigger, the lack of response in these assays could mean, for example, that the test dose or vehicle was inappropriate, that the test agent triggers another portion of the pathway, or that the test agent triggers an entirely different toxicity pathway outside the

model. Failure to test positive in these screening assays does not mean that a chemical is “safe,” non-toxic or even necessarily a “low priority” for a more thorough assessment. For example, studies found that some chemicals known to disrupt steroidogenesis or thyroid did not show these effects in the high-throughput assays^{8,9}. The Guide should make clear that data from these methods can neither be used to exonerate a test chemical, or dismiss evidence of hazard from reliable whole animal or human data such as animal bioassays, epidemiologic studies, or case reports.

Data can be used to support affirmative hazard determinations

However, these data can be useful to support evidence of hazard/ adverse effects from other types of studies including toxicology and epidemiology. Because high-throughput assays are simply traditional *in vitro* and mechanistic tests conducted at a much larger scale, positive results can be used in the same way that positive results from these types of tests have always been used—as a parallel stream of data to support hazard trait assignments and/ or increase the level of concern for an alternative’s potential to cause adverse effects. This is particularly true for the estrogen receptor and androgen receptor endocrine pathways where the high-throughput assays have better coverage^{5,6,8,9}. For example, if an alternative showed high activity in the estrogen receptor pathway assays, then the alternative could be flagged for the “endocrine activity” hazard trait based on this data. These high-throughput assays are like little needles pinpointing a small number of specific pathways, sprinkled throughout the very large haystack of biological space. If you reach in and get poked, then you’ve identified one potential pathway the test agent perturbs. But if nothing pokes out, it is hard to draw any conclusion from that result. The International Agency for Research on Cancer (IARC) gives explicit guidance on the use of mechanistic data to support hazard assessments (for cancer) which responsible entities may find useful¹⁰. The IARC Monograph pre-ambule was developed with considerable international scientific comment and input, and has proven effective and scientifically defensible over the past decade of well over a hundred chemical reviews.

In summary, because we know that these emerging methods do not comprise comprehensive toxicity evaluations for numerous reasons, negative/ no-activity results cannot be used to indicate that a chemical does not pose a hazard. On the other hand, positive results can be used to inform hazard trait assignments and/ or upgrade the level of concern for an alternative.

5. Other minor comments

On pg. 55 of the Guide, the ChemHAT tool is from the BlueGreen Alliance (not GreenBlue Alliance).

In the example conceptual models on pp. 45-46, there should be an arrow showing direct human exposure from the indoor dust contaminated with the flame retardant “chemical X” or “chemical A.” Contaminated indoor dust is a well-known pathway for human exposure to flame retardant chemicals and other chemicals, especially for children^{11,12}. The U.S. Environmental Protection Agency (EPA) recently published an initial assessment document related to the flame retardant chemical hexabromocyclododecane (HBCD)¹³. This document includes a conceptual model which may be a useful example for the Department to refer to in that it shows human and environmental exposure pathways and receptors for HBCD, clear indications of which exposures will be included or not included in the assessment, and the hazard endpoints of concern. A conceptual model with all these features would also be useful in the context of an alternatives analysis.

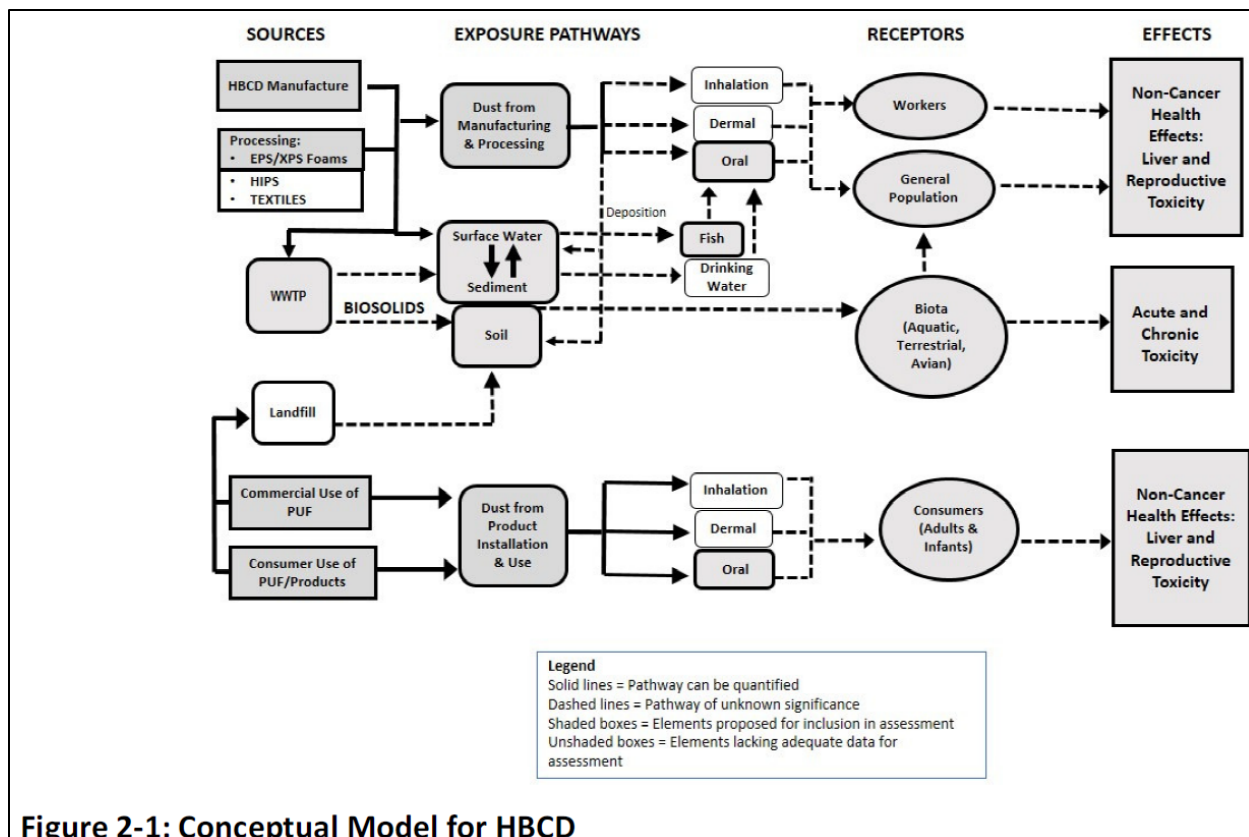


Figure 2-1: Conceptual Model for HBCD

Conceptual model for the flame retardant HBCD from US EPA's initial assessment document¹³.

CONCLUSION

The Safer Consumer Products program is the first in the nation to put forward an alternatives analysis framework in order to avoid regrettable substitutions. Indeed, it is only with strong, comprehensive and health-protective alternatives analysis that the Department can ensure that replacements for chemicals of concern are safer for human health and the environment. We look forward to seeing robust implementation of the principles and processes outlined in the Guide, as this is a critical step in achieving the aspiration of SCP: a paradigm shift towards safer chemicals that will benefit consumers, families, communities and our environment.

Thank you for your consideration of these comments. Please feel free to contact us with any questions.

Respectfully submitted,

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