

## Peer Review of Green Chemistry Safer Products Alternatives Regulations

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Thank you for the opportunity to peer review California's green chemistry safer products alternatives regulations. The revised scope of work provided to me, dated 14 September 2010, requests a written review from my professional viewpoint and field of expertise of the scientific basis of the proposed regulations for the Safer Consumer Product Alternatives, with emphasis on those provisions relating to chemicals of concern, priority products, and alternatives analysis and "the big picture" of the regulations and green chemistry.

My detailed comments in response to this scope of work are set out below. Please note that I am submitting this peer review on my own behalf and the views expressed in it do not represent the views of my employer, Johns Hopkins University and the Johns Hopkins Bloomberg School of Public Health.

### *I. Introduction and Conceptual Overview*

As requested, I have reviewed the proposed regulations and other materials provided to me. The scope of work asks for discussion about whether the scientific basis of the proposed regulatory plan of action and presents three discussion points for detailed examination. These are:

- A peer review of the use of chemical properties, toxicological information, volume of chemicals in commerce, and adverse impact to sensitive subpopulations, the public, and the environment to prepare lists of (a) Chemicals Under Consideration and (b) Priority Chemicals.
- A peer review of the use of consumer product marketing, potential for exposure to Priority Chemicals, environmental contamination, in preparing lists of (a) Products Under Consideration and (2) Priority Products.
- A peer review of the human health and environmental impacts of the Priority Chemical in the Alternatives Assessment to develop safer consumer products.

In addition, the scope of work invites comments about "the big picture," presenting an opportunity to offer comments regarding whether, taken as a whole, the scientific portion of the proposed rule is based upon sound scientific methodology, reasoning, methods and practice.

In carrying out this peer review, I considered these discussion points, and comments about the big picture, in light of the green chemistry principles and purpose of the regulations

because based on the materials you provided to me it is clear that the purpose of regulatory program is to support the implementation of these principles. The way that information and data is collected, organized, evaluated and deployed in decision-making is thus instrumental to establishing a science-based regulatory scheme as well as carrying out the underlying purposes of the law on which these regulations are based.

According to the Green Chemistry Safer Products Alternatives Regulations (pages 8 and 9), the green chemistry principles embodied in these proposed regulations state that:

- Green chemistry principles and life cycle analysis should be considered throughout implementation;
- Adverse public health and environmental impacts, which can result along the continuum of a product's life cycle, starting with production and ending with disposal (end of life management), should be reduced or eliminated;
- Adverse public health and environmental impacts should be reduced or eliminated by encouraging redesign of products and manufacturing (or in other steps in the continuum of a product's life cycle); and
- Chemical and product prioritization should seek to give priority to those chemicals and products posing the greatest public health and environmental threats, are most prevalently used, and pose greatest potential for harmful exposures.

## ***II. Specific Peer Review Questions***

The proposed regulations divide the regulations into a three-step process that is science-based, continuous, and iterative (page 9). In carrying out this peer review, it is first helpful to describe (in a simplified fashion) the regulatory process. As a first step, an evaluation and prioritization of consumer products in California is carried out. At the end of this process, a list of Priority Products, containing Priority Chemicals, will be identified. In the second step, an alternatives assessment is carried out for all Priority Chemicals and Priority Products. In step three, regulatory responses, if appropriate, are undertaken.

Step 1 of this process is further divided into several decision-making points. These are set out (in a simplified schematic) in Appendix 1 and are further discussed in this peer review. In summary, this process involves the following actions. Starting with a list of all of the consumer products in California, identify the "Chemicals of Concern" (COC) in these products. Second, prioritize and evaluate this COC list to construct a list of "Chemicals Under Consideration (COC)." Third, starting with the COC list, further prioritize and evaluate this list to create a list of Priority Chemicals (PC)." Fourth, using this PC list, prioritize and evaluate consumer products and establish a list of "Priority Products (PP)".

For PPs, steps 2 and 3 of this process are activated. In other words, PPs must undergo an alternatives assessment and any selected alternative is possibly subject to a regulatory response.

It is important to again emphasize that this process is intended to be iterative and science-based. I take that to mean that information gathered in any phase of the regulatory process will be used, to the extent appropriate, in other parts of the process. As applied to these comments, the iterative intent of the regulations means that comments addressed to a

specific part of this regulatory program are likely applicable to other parts. This is particularly relevant to comments regarding how scientific information and data will be used for evaluation, prioritization and decision-making.

With this background in mind, I would like to turn to the specific questions set out in the peer review.

- A. *Question 1: A peer review of the use of chemical properties, toxicological information, volume of chemicals in commerce, and adverse impact to sensitive subpopulations, the public, and the environment to prepare lists of (a) Chemicals Under Consideration and (b) Priority Chemicals.*

This first discussion question specifically requests a peer review of sections 69302.3 and 69302.4 of proposed regulations. Section 69302.3(a) lists 14 chemical and physical properties to consider in carrying out the required analysis, and also includes a “catch-all” category (see 69302.3(a)(15)) specifically for nanomaterials. While this list seems to be comprehensive and the addition of a catch-all provision for nanomaterials is appropriate, there are at least two issues that need attention. First, there is no indication of how these chemical and physical properties will be weighed or considered in the analysis. Since this section is a crucial first step in prioritization, it would be valuable if an algorithm were developed to show how these characteristics will be used. Second, it is possible that other characteristics should be added to this list. To that end, it would be useful to add another catch-all category for this purpose and a petitioning provision for adding to this list. Adding provisions for petitions is discussed later in this document.

Section 69302.3(b) lists adverse public health impacts. It contains 26 factors that cover a broad range of health endpoints and specific toxicities, and also includes a catch-all provision that is meant to include any hazard traits not listed among these factors. It also lists a catch-all provision that is meant to address health impacts in sensitive subpopulations. There are several issues that could use clarification. As in section 69302.3(a), there is no indication about how these many hazard traits will be weighed or considered in this analysis. It would be valuable if an algorithm were developed for this purpose. Since these evaluations are meant to be iterative and science-based, one possible approach to developing an algorithm for these hazard traits as well as the list of chemical and physical highlights could be based on the products in which they exist, and their intended and actual uses. Second, section 69302.3(b)(26) – adverse impacts on sensitive subpopulations – should be expanded. (Additional comments about sensitive subpopulations are set out later in this document.) Finally, these hazard traits are intended to be evaluated from exposures that might result from “single, intermittent or frequent use.” These terms are not defined in the regulations, and are essential to help understand how exposure will be assessed. A more complete explanation of these concepts would be valuable.

It is also not clear whether this definition takes aggregate exposure into consideration. One well-accepted definition of aggregate exposure is found in the federal Food Quality

Protection Act and US EPA's implementation of it. Aggregate exposure is defined "as the combined exposures to a single chemical across multiple routes (oral, dermal, inhalation) and across multiple pathways (food, drinking water, residential)." EPA, General Principles For Performing Aggregate Exposure And Risk Assessments (2001). (Available at [www.epa.gov/pesticides/trac/science/aggregate.pdf](http://www.epa.gov/pesticides/trac/science/aggregate.pdf) ).

Section 69302.3(b) focuses for the most part on apical endpoints, reflecting past and current approaches to hazard evaluation and risk characterization. The National Academy of Sciences National Research Council (NAS/NRC) has recommended that regulatory testing move toward an approach based on pathways and perturbations, and toxicology is advancing in that direction. According to a recent committee report by the NAS/NRC:

"The committee considered recent scientific advances in defining a new approach to toxicity testing. Substantial progress is being made in the elucidation of cellular-response networks—interconnected pathways composed of complex biochemical interactions of genes, proteins, and small molecules that maintain normal cellular function, control communication between cells, and allow cells to adapt to changes in their environment. For example, one familiar cellular-response network is signaling by estrogens in which initial exposure results in enhanced cell proliferation and tissue growth in specific tissues. Bioscience is enhancing our knowledge of cellular-response networks and allowing scientists to begin to uncover how environmental agents perturb pathways in ways that lead to toxicity. Cellular response pathways that, when sufficiently perturbed, are expected to result in adverse health effects are termed *toxicity pathways*. The committee envisions a new toxicity-testing system that evaluates biologically significant perturbations in key toxicity pathways by using new methods in computational biology and a comprehensive array of in vitro tests based on human biology."

National Research Council, Toxicity Testing in the Twenty-First Century: A Vision and A Strategy (2007) [quoting page 2 of the Executive Summary]. (Available on-line at [http://www.nap.edu/catalog.php?record\\_id=11970](http://www.nap.edu/catalog.php?record_id=11970) )

As in vitro knowledge about these cellular response networks becomes available, the safer products alternatives regulatory program should take advantage of this knowledge for prioritization and evaluation. The regulations should include provisions so that incorporation of these advances in toxicology can be used.

Section 69302.4 addresses how the list of priority chemicals will be prepared, based on the selection of Chemicals under Consideration (section 69302.3). This analysis will focus on both potential for exposure and potential harm resulting from exposure. The proposed regulations (Section 69302.4) call for prioritization of chemicals "that pose the greatest public health and environmental threats, are most prevalently distributed in commerce and contained in products used by consumers, and for which there is the greatest potential for consumers or environmental receptors to be exposed to the chemical in quantities that can result in public health or environmental harm."

This section states that the initial list of Priority Chemicals shall consider only a subset of chemicals that includes (1) carcinogens and reproductive toxins (or both) that are now contained in certain lists set out in the definition section of these proposed regulations; (2) chemicals that are mutagens according to certain European Union regulations; and (3) chemicals listed by EPA as bioaccumulative toxic chemicals. It is unclear what role, if any, scientific data played in selection of chemicals on this list.

According to this section of the proposed regulations, “market data” regarding the chemicals shall be considered. In collecting such data for purposes of exposure analysis, it would be very useful if the Department could obtain data that would show intended audiences for the products containing these chemicals. It is likely that certain products will be marketed to, and more heavily used, in subpopulations or groups that might therefore be at potentially greater risk due to potentially higher exposure. According to this section of the regulations, the Department also intends to use for evaluation reliable information demonstrating exposures. Data collected by the US Centers for Disease Control and Prevention biomonitoring and health tracking programs are scientifically reliable and likely to be useful for this purpose. (See <http://www.cdc.gov/exposurereport/> and <http://www.cdc.gov/nceh/tracking/biomonitoring.htm> ).

- B. Question 2: A peer review of the use of consumer product marketing, potential for exposure to Priority Chemicals, environmental contamination, in preparing lists of (a) Products Under Consideration and (2) Priority Products.*

This second discussion question specifically requests a review of section 69303.3 and 609303.4 (Products Under Consideration and Priority Products). In terms of the scientific information and approaches to be used, there is considerable overlap between this section and section 69302.3. As a result, many of the comments set out above are relevant to this section and will not be repeated here.

This section focuses on identifying products that will be targeted for further regulatory action based on their potential exposure and harm, examined over the life cycle of the product. According to the regulations, the term life cycle is very broad, and includes all events beginning with the product’s design through and including the product’s ultimate disposition (See 69301.2(a)(44)). With this life cycle concept in mind, it seems appropriate to conclude that many, perhaps most, products will not begin their life in California although almost all will be disposed of in California’s environment (e.g., in landfills). It could be useful for the Department to look more closely at the “back end” of the life cycle with a particular emphasis on where these products will be disposed. In addition, a cumulative exposure and risk analysis approach could be appropriate. This approach would involve determining what toxic compounds now exist in unacceptable amounts in California’s environment, including at waste sites, and treating new additions of these compounds cumulatively from an exposure and risk perspective. The Department, for example, could consider the amounts of most common toxic compounds that are listed in California’s hazardous waste inventory. The US Agency for Toxic Substances and Disease Registry (ATSDR) publishes a list of toxic substances at Superfund sites. This list is based

on national data but it is possible that California specific lists exist or could be constructed. (see <http://www.atsdr.cdc.gov/cercla/07list.html> ).

This section specifically requires that the evaluation of harm resulting from potential exposures consider sensitive subpopulations. A detailed discussion of the meaning of sensitive subpopulations and suggestions for amending this concept in these regulations is set out below and should be incorporated into this portion of the peer review. In addition, it is possible that certain population subgroups, including sensitive subpopulations, could be the targeted users of Priority Products. The Department should be sure that its data collection and evaluation efforts, especially efforts involving the collection and evaluation of market data, obtain this critical information.

C. *Question 3: A peer review of the human health and environmental impacts of the Priority Chemical in the Alternatives Assessment to develop safer consumer products.*

This discussion question specifically requests a peer review of section 69305.5(b), (c) and (d) of proposed regulations. Subpart (b) essentially uses all of the same factors contained in 69302.2(a), (b) (c) and (d)(1). This approach seems appropriate given that the alternative must be compared to the Priority Product it is meant to replace using the same methodologies. It could be challenging to carry out this side by side comparison if, for example, the Priority Product and its Alternative create equivalent risks in different portions of the life cycle.

### **III. The Big Picture**

The peer review scope of work invites comments on other parts of the regulations and the regulatory scheme regarding whether, taken as a whole, the scientific portion of the proposed rule is based upon sound scientific methodology, reasoning, methods and practice. The following comments are offered in furtherance of this goal.

1. *Expand the petitioning and citizen input processes.* To ensure that the best and most advanced scientific information and methodologies are available to the Department, the petitioning and citizen input process should be greatly expanded. There should be numerous opportunities to comment and offer suggestions, especially during the critical steps that lead up to the designation of a consumer product as a Priority Product.
2. *Add the NTP's Center for the Evaluation of Risks to Human Reproduction list of reproductive toxicants as a reliable and/or authoritative source* (see <http://cerhr.niehs.nih.gov/> ).
3. *Substantially change the definition of "sensitive subpopulations" (section 69301.2(a)(72)).* The term "pregnant women" should be replaced with the term "women of childbearing age." Women of childbearing age is the correct term because a healthy pregnancy is dependent to a large extent on the health of women before conception. In addition, the term "individuals with a history of serious illness" should be expanded to include persons who have a pre-existing medical condition or chronic illness that is under control, such as diabetics and asthmatics, and persons who have a compromised immune system. All of these

subgroups could be differentially susceptible to harm from exposure to Priority Chemicals and Priority Products.

This definition should also include environmental justice communities that are differentially susceptible or differentially exposed to Priority Chemicals and Priority Products. EPA's National Environmental Justice Advisory Committee (NEJAC) set out a conceptual model that is useful and should be considered in revising this definition. (See <http://www.epa.gov/compliance/ej/resources/publications/nejac/nejac-cum-risk-rpt-122104.pdf>) The model defines several key concepts, such as stressors, and conceives vulnerability broadly. EPA's NEJAC defines four important characteristics of vulnerable populations:

1. More susceptible or sensitive to disease outcomes;
2. Differentially exposed to environmental conditions that could render these populations more vulnerable;
3. Differentially prepared to address deleterious conditions, such as exposures to infectious diseases; and
4. Differential responses to the same level of infection or exposure (as non-vulnerable populations) that may worsen response.

Appendix 1 -- SIMPLIFIED SCHEMATIC OF THE PROCESS TO EVALUATE CONSUMER PRODUCTS AND DETERMINE A LIST OF PRIORITY PRODUCTS

