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California Environmental Protection Agency
1001 I Street
Sacramento, CA 95812

Submitted by email on September 9, 2011 to: fkammerer@oehha.ca.gov

Dear Ms. Kammerer:

I am writing to provide comments on the July 2011 Modified Text of the Proposed Regulations to Division 4.5, Title 22, California Code of Regulations, Chapter 54, entitled **Green Chemistry Hazard Traits, Toxicological and Environmental Endpoints and Other Relevant Data,** released by your office for the implementation of SB 509 authored by Senator Simitian.

These regulations represent an essential contribution to the scientific underpinning to the Clearinghouse contemplated in SB 509. With each iteration, the Office of Environmental Health Hazard Assessment (OEHHA) has improved the scientific quality of the product.

In SB 509, allowing for a science-based process to explicitly identify hazard traits was an important policy innovation to ensure that the program would reflect current scientific knowledge about the inherent properties or attributes of chemicals that could be of concern. Many or most other initiatives have focused on either old assessments of the attributes of interest for chemicals or narrow ones, and so the California program will provide an analysis that will be informative globally. Defining the hazard traits and then the methods that provide information relevant for these traits allows for a systematic approach to this innovation, also a widely shared goal.

The definition of hazard traits that are important to human and ecological health turns out to be an increasingly important step in the evolution of chemicals policy, and one that has not yet been taken elsewhere. This is for two reasons.

One reason is related to setting up a data system and data flows to allow the best possible assessments of chemicals in commerce. In designing such a system, as for the Green Chemistry initiative of the State of California, it is important at the outset to identity what the data should be about. Many or most chemicals policy initiatives have jumped into collecting and displaying

data without scientific review at the outset. By defining the hazard traits relevant to the review of chemical safety, the data systems can be designed at the outset to incorporate all of the relevant data as it may be generated over time. This is a more scientifically valid approach than to pick out one or two or a few traits that may seem to be priorities initially but that will be insufficient to support the policy needs of a genuine green chemistry program over the long term.

The second reason that it is important to clearly and scientifically define hazard traits of possible interest is because a transition in testing and assessment methods is beginning to occur. As the National Academy of Sciences (NAS) has recommended and as OEHHA is well aware, there can be significant value in incorporating into the testing and assessment regime new testing methods that test more chemicals more quickly. Such "high-throughput" methods are already creating massive amounts of data about how chemicals may change or perturb processes such as expression of genes. These are very different from the old school animal testing methods because they are conducted in test systems that reflect very narrow bits of biology both in terms of the systems that are tweaked and the duration of the responses.

While a whole animal experiment by its very nature will integrate biological changes over time and over all systems, the high-throughput systems by their very nature will not. The NAS recognized the significant research and development would be needed to understand the best uses of such high throughout (as well as "medium" throughput) systems and to determine what part of an adverse response or perturbation they might reflect. It is equally important to understand what parts of an adverse response that they may not detect.

At this point, such research and development has not yet occurred, and the meaning of the results is only partially understood. Defining hazard traits of interest provides a reference point for the development of novel methods. Perhaps it might be considered to be a scorecard to which the novel methods could be pegged to determine how much of what we might want to know is being produced by new methods.

One important role for the state's scientists as part of this transition will be to provide information for the public to understand this transition and the implications of new methods. Of late there has been significant promotion of new robot-based assays at the federal level. So far, the scientific rationale for what these methods represent has not been forthcoming. Fast methods are valuable only to the extent that they measure the right things and that we understand and can interpret what the results mean. The California state scientists can play a useful role in helping stakeholders in green chemistry and chemical safety to understand and fairly evaluate this transition in testing and assessment, beyond the hype that now seems to rather widespread.

Important Advances in the Proposal

One important concern is chemicals policy is the treatment of hazards that are of great concern for children.

The current version has incorporated "neurodevelopmental toxicity" as a hazard trait. This is an important advance and contributes to the scientific quality of the document. We are all familiar with lead and the enormous toll that lead exposure has taken on the cognitive abilities of children in the US and around the world because of its neurodevelopmental effects. Identifying neurodevelopmental toxicity as a hazard trait will provide a start toward ensuring that such a

thing never occurs again. Whether chemicals might have a similar trait is very important to know. This proposal recognizes that data from studies using accepted protocols for reproductive and development effects will not include any neurodevelopmental effects that may occur. The testing protocols that are deemed acceptable in regimes such as REACH for detecting developmental effects are not designed to and would not detect neurodevelopmental effects if they occurred. Consequently, a chemical can be tested and found to be "negative" for developmental effects without obtaining any information about whether it might cause neurodevelopmental effects. They are not the same thing. Consequently, including neurodevelopmental effects among the hazard traits is an important step forward for children's health.

The proposal also includes hazard traits of concern for children such as those for lung development and immune system effects. This is also an important advance.

The new section that describes additional data relevant to the assessment of chemicals is also an important and valuable addition.

Throughout, the text has been edited to be more consistent and understandable, and this is valuable as well.

Additional Concerns

The draft does not address including concerns for sensitive populations in the design of the clearinghouse. This does, however, appear to be contemplated in the green chemistry legislation. Perhaps this could be considered as a "flag" on chemicals where there may be specific concerns for sensitive populations. It needs to be addressed in some way in the information design process.

One additional need that is perhaps better addressed at a later stage is to design for the identification of chemicals that have demonstrated a level of safety. It would be most beneficial for the Clearinghouse to make it easy to see which chemicals have hazard traits, which are as yet untested, and which have been determined not to have hazard traits after an appropriate level of assessment.

Technical comments

In the definition as follows for adverse effect, where it says, ""Adverse effect" for toxicological hazard traits and endpoints means a biochemical change, functional impairment, or pathologic lesion that negatively affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge," I would recommend deleting the word "environmental" in the final line. This is because it is an adverse change if an environmental exposure would reduce the body's ability to respond to a challenge from, say, an infectious agent. This could be quite adverse and directly related to an environmental exposure.

In the definition as follows for developmental toxicity, where it says:

> **§ 69402.3 Developmental Toxicity**

> (a) The developmental toxicity hazard trait is defined as the occurrence of adverse effects on the developing organism following exposure to a chemical substance prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Developmental toxicity occurs during the postnatal period only if the developing organism shows greater quantitative or qualitative susceptibility to the chemical substance than does the adult organism.

I would suggest rewriting the last sentence to say:

> "Developmental toxicity occurs during the postnatal period if the developing organisms show greater quantitative or qualitative susceptibility to the chemical substance or earlier onset than does the adult organism."

This is because it makes a big difference if an adverse effect occurs at age 2 compared to, say, age 75. It is increasingly recognized that earlier onset of disease can occur as a result of developmental processes.

Closing comments

In closing, it seems important to emphasize the need for the discussion of the regulation to include the question of resources for OEHHA's responsibilities to provide scientific guidance in the implement of the Clearinghouse. Clearly the State will need to select its areas of focus strategically in beginning this process. It would certainly make sense to build on OEHHA's existing strengths including those related to children's environmental health. Perhaps the State could begin by focusing on chemicals of concern for children in building its database.

Finally, I want to note that, as an employee of the University of California, I submit these comments as an individual with relevant expertise. As I am sure you know, only the Regents may provide a position that represents the views of the University.

Very truly yours,

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