Green Chemistry Alliance

Committed to Product Sustainability in the Global Economy

February 15, 2011

Ms. Fran Kammerer
Staff Counsel
Office of Environmental Health Hazard Assessment
1001 I Street
Sacramento, CA 95812

RE: Proposed Regulation for Green Chemistry Hazard Traits (12/17/10)

Dear Ms. Kammerer:

On behalf of the Green Chemistry Alliance (GCA) and its stakeholders, we respectfully submit the following comments and concerns relative to the Office of Environmental Health Hazard Assessment's (OEHHA) Proposed Regulation for Green Chemistry Hazard Traits ("regulation") released on December 17, 2010.

While GCA and its members appreciate the additional background OEHHA has provided for the proposed regulation since the August draft regulation was released, GCA remains highly concerned over the breadth and direction of the regulation.

The enacting legislation, SB 509 (Simitian, 2008), requires OEHHA "to evaluate and specify the hazard traits and environmental and toxicological endpoints and any other relevant data that are to be included in the clearinghouse." This directive is simple and clear. However, the proposed regulation goes beyond the authority provided for in statute, by establishing a chemical classification system that is not only unique to California but also inconsistent with some of the key principles of chemical hazard assessment that are employed worldwide. It would also establish a unique California system of hazard trait nomenclature that will substantially increase the cost and timing of populating and deploying the Toxics Information Clearinghouse, and make it unnecessarily difficult to leverage existing information on chemicals.

Of all of GCA's concerns or questions, the overarching and recurring issue seems to revolve around how the information in the regulation will be applied. The proposed Green Chemistry Hazard Traits regulation is generally unclear and disconnected from the Department of Toxics Substances Control's (DTSC) proposed regulations for safer products, and DTSC's own vision for the Toxics Information Clearinghouse (TIC). Since the OEHHA regulations will be a critical touchstone for DTSC's safer alternatives process, scrutiny needs to be employed in the development of

applicable, definable and scientifically sound hazard traits and endpoints in order to inform the prioritization process. The proposed Green Chemistry Hazard Traits regulation does not accomplish this critical task.

The underlying statutes clearly envision a coordinated approach between DTSC and OEHHA and with the change in Administration it is important that incoming leaders at both DTSC and OEHHA have the opportunity to provide the Brown Administration's input regarding the approach envisioned by OEHHA's proposed Green Chemistry Hazard Trait regulation. The OEHHA regulation will define content for the Toxics Information Clearinghouse (TIC) and identify considerations for "Chemicals of Concern" listings. Without clarity on the regulatory structure into which the hazard traits must fit, there is too much uncertainty regarding both their operative impact and sufficiency.

Given DTSC's Revised Proposed Safer Consumer Products Alternatives Regulation has not been submitted to the Office of Administrative Law (OAL) and all indications are the proposed regulations will be the subject of further review and amendments, GCA urges OEHHA to withdraw their Green Chemistry Hazard Traits proposed regulation until the regulatory approach that DTSC is charged with undertaking becomes more clear. In order to help ensure clarity and consistency, it is critical that OEHHA coordinate more closely with DTSC as the overall regulatory development process moves forward.

In the meantime, GCA respectfully submits the attached comments and concerns regarding the Proposed Green Chemistry Hazard Trait Regulation (December 17, 2010). For questions or further information or questions regarding the Green Chemistry Alliance, its members, or our comments please contact John Ulrich (916) 989-9692 or Dawn Koepke (916) 930-1993. Thank you!

Sincerely,

John Ulrich
Co-Chair
Chemical Industry Council of California

Dawn Sanders Koepke
Co-Chair
McHugh & Associates

Cc: The Honorable Linda Adams, Secretary, CalEPA
The Honorable Joan Denton, Director, OEHHA
The Honorable Leonard Robinson, Acting Director, DTSC
Office of the Governor

**** The Green Chemistry Alliance*** *(GCA) has its roots in a group of business trade associations and companies that lobbied effectively during the closing weeks, days and hours of the 2008 California legislative session in support of bi-partisan measures to create a new science based framework for chemicals management. The driving force behind the legislation was a broad based desire for state regulators, rather than the legislators alone, to exercise their expert scientific and engineering judgment and experience when determining appropriate regulatory actions affecting chemicals of concern in consumer products. In the wake of this groundbreaking legislation, the GCA was formalized for the purpose of constructively informing the implementation effort such that the promulgated regulations remain true to the objective and scientific ideals of the authorizing legislation. GCA has strongly advocated for crafting regulations to enable the full and successful implementation AB 1879 (Feuer, 2008) and SB 509 (Simitian, 2008), which will enhance public health and environmental protection, promote innovation while still respecting confidential business information, and further the principles of sustainable development.*

Green Chemistry Alliance Signatories

Alliance of Automobile Manufacturers
American Apparel & Footwear Association
American Chemistry Council
American Cleaning Institute
American Forest & Paper Association
Amway
Association of Global Automakers, Inc.
Association of Home Appliance Manufacturers
BASF
The Boeing Company
California Aerospace Technology Association
California Chamber Commerce
California Grocers Association
California Healthcare Institute
California League of Food Processors
California Manufacturers & Technology Assoc
California New Car Dealers Association
California Paint Council
California Restaurant Association
Can Manufacturers Institute
Chemical Industry Council of California
Chevron
Citizens for Fire Safety Institute
Consumer Healthcare Products Association
Consumer Specialty Products Association
Dart Container Corporation
Defoamer Industry Trade Association
Del Monte
Dow Chemical Company
DuPont
Ecolab
Ellis Paint
ExxonMobil
Fashion Accessories Shippers Assoc
Florida Chemical Company, Inc.
Goodrich Corporation
Grocery Manufacturers Association
Honeywell
Independent Lubricant Manufacturers Association
Industrial Environmental Association
Information Technology Industry Council
International Fragrance Association of North America
International Sleep Products Association
Johnson & Johnson
Kern Oil & Refining Company
Koch Companies Public Sector
Metal Finishing Associations of Northern & Southern California
National Aerosol Association
National Paint & Coatings Association
National Shooting Sports Foundation (NSSF)
Northrop Grumman
OPI Products Inc.
Personal Care Products Council
Phoenix Brands
Plumbing Manufacturers Institute
Procter & Gamble
Reckitt Benckiser
Rio Tinto
Rubber Manufacturers Association
SABIC Innovative Plastics
Silicones Environmental Health and Safety Council
Solar Turbines
Sporting Arms and Ammunition Manufacturer's Institute (SAAMI)
Synthetic Amorphous Silica & Silicate Industry Association
TechAmerica
Toy Industry Association
Travel Goods Association
United Technologies
Western Growers
Western Plant Health Association
Western States Petroleum Association
Western Wood Preservers Institute

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Guide to GCA Comments regarding
The Proposed Green Chemistry Hazard Traits Regulation

(December 17, 2010)

EXHIBITS INCORPORATED BY REFERENCE

1) GCA OEHHA Pre-Draft Hazard Trait Regulation Comment Letter – September 13, 2010

EXECUTIVE SUMMARY

The Green Chemistry Alliance (GCA) is highly concerned about the novel approach OEHHA has proposed for hazard trait determination, which amounts to a California-specific process of classifying chemicals. Not only are major aspects of OEHHA's ~~is this~~ approach unauthorized by the implementing statute, in many instances it represents scientifically questionable deviations from well established, internationally agreed upon systems and principles for determining chemical hazards.

Additionally, OEHHA's Notice of Proposed Regulation suggests that the Proposed Regulations will "not impose new duties on OEHHA or any other state agency other than the need to periodically review and update the regulation to keep up with changing scientific knowledge and methodologies" (page 5). Even evaluating the information to put in to the Toxics Information Clearinghouse (TIC) will require resources. OEHHA should not underestimate the costs associated with this Proposed Regulation.

Attachment 1 will discuss the legal and technical issues associated with the regulation. This will include consideration of the following overarching issues:

Independent Scientific Peer Review – The scientific portions of the proposed regulation have not yet been subjected to independent external scientific peer review. Although public comments have been solicited by OEHHA, the public comment process is not equivalent to independent external scientific peer review. Under California Health and Safety Code Section 57004, all CalEPA organizations, including OEHHA, are required to conduct an external scientific peer review of the scientific basis for any rule proposed for adoption, and a final regulation cannot be issued until such a scientific peer review has been completed. Given that this proposed regulation would create a create a novel, California-only method of hazard classification or designation, it is imperative that the scientific basis of the regulation be thoroughly and comprehensively peer reviewed to establish that the proposed rule is based upon sound scientific knowledge, methods, and practices.

Existing Systems – A new California-only chemical classification system as proposed under the proposed regulation is inefficient, duplicative, and will make it unnecessarily difficult to leverage existing information on chemicals. A non-standard approach will slow the development of the TIC database as there will be a substantial agency effort required to convert the information to the unique California system, both initially and on an ongoing basis. Given that there are existing systems currently in use worldwide, it is not clear why OEHHA has chosen to develop a California-unique system. Most importantly, OEHHA has failed to discuss why existing systems are inadequate and why there is a need for a unique and costly system.

Classification – The classification proposal should be abandoned entirely. SB 509 gives OEHHA neither the mandate nor the authority to create a novel California classification system. DTSC has responsibility for what actually gets placed into the TIC, not OEHHA. The classification system is a significant overstep of OEHHA's authority.

List of "icities" – There is no need to break out systemic toxicity or target organ toxicity by specific systems as proposed in the draft regulation when the goal is hazard identification. Notwithstanding GCA's contention that OEHHA lacks the statutory authority to create a classification system, the critical issue for chemical hazard classification should be identifying the most relevant sensitive system(s) affected by chemical exposure. Thus, it is more than adequate to describe a chemical's hazard by listing the sensitive target organ effects, which is the method used by every other hazard classification system currently in use. Apart from identifying target organs of toxicity, cancer hazard and reproductive toxicity hazard are usually

considered separately. Furthermore, as virtually every chemical at some dose will produce toxicity in some organ system, the proposed classification approach, taken at its face, would lead to every chemical substance being classified. This is not the intent of the Green Chemistry Hazard Traits thrust.

Emerging Traits – OEHHA should seek scientific consensus on the description of emerging traits and in doing so define the appropriate validated study protocol for the endpoint(s) prior to including them in the regulation. OEHHA should not unilaterally establish definitions for new hazard traits, nor rely on non-validated test methods for ascertainment of such traits. This is of particular concern when it is suggested that unvalidated *in vitro* study protocols could be used as a basis for identifying such hazard trait listings.

Endpoint Lists – Each of the toxicological and environmental traits in the OEHHA proposal is accompanied by a list of possible endpoints. However, the listings are not all actual hazard traits or endpoints. In some cases, the endpoints listed are considered to be adaptive changes that may or may not lead to adverse effects in organisms. The fact that certain changes may not lead to disease or an adverse outcome could lead to erroneous classification of a chemical.

Other Relevant Information – The proposed regulation fails to include any concept of potential exposure which is a critical part of prioritizing chemicals to be reviewed in the hazard risk assessment process. Thus, use category and production volume information reported via U.S. EPA's Inventory Update Rule (IUR) should be included as part of "other relevant information" in order to at least provide some measure of potential for human exposure.

Attachment 2 reviews many of the outstanding issues that are not resolved by the proposed regulation. In many cases, OEHHA has indicated that a particular task is DTSC's responsibility. GCA is concerned over a possible disconnect between the Hazard Trait regulation, DTSC Safer Consumer Products Alternatives Regulation and TIC. These are critical components of the Green Chemistry enabling legislation that must be discussed and resolved prior to finalizing this proposed regulation. Each of the hazard traits identified and evaluated in this regulation will affect the other steps in the overall Green Chemistry Initiative. It is for this reason that it is critical for a more coordinated and cohesive effort to be undertaken between DTSC and OEHHA prior to OEHHA moving forward on this regulation. This attachment will review the specific issues and concerns related to these points, including:

Data Quality – *In vitro* studies and QSARs are generally recognized as appropriate tools for prioritizing chemicals, but not for making definitive declarations about toxicological properties as proposed. OEHHA needs to clearly identify how certain types of data should be weighed when assessing chemical hazards, recognizing that certain types of data are less defensible than others, even when developed by authoritative bodies. OEHHA should recognize that assessments should use the best available data from validated test methods and related hazard characterization tools within a scientific hierarchy that affords greater weight to measured data from validated methods compared to analog data and modeled data. It is inappropriate and scientifically unsound to rely on data from non-validated methods alone. OEHHA should look toward the robust study format used in the Organization for Economic Cooperation and Development's (OECD's) chemical hazard assessment program and OECD harmonized templates as the internationally accepted model for providing information on study results, study quality and reliability.

Potency – The proposal is defective as there is no indication of potency for traits which exhibit a hazard. Without some indication of potency, every substance, whether synthetic or naturally occurring, could be considered toxic, even the "greenest" of substances. The concept of dose-response is a standard part of hazard assessment. GCA recommends OEHHA look toward

existing systems, particularly the OECD's robust summaries, to understand how other bodies have handled this critical issue.

Weight of Evidence – The proposed regulation provides insufficient consideration to weight of evidence. As framed, the proposed classification would proceed with weight given only to positive data. There are inadequate procedures for considering negative data. A scientifically sound weight of evidence process depends on looking at both positive and negative data and the reproducibility of results. Without considering these, the format proposed by OEHHA is skewed and not scientifically supportable. OEHHA must implement a weight of evidence approach considering both the positive and negative evidence that may be available about substances under evaluation in the TIC. Such information must also consider potency – the current proposal ignores this critical information.

Exhibit 1, GCA comments to OEHHA dated September 13, 2010 regarding Pre-Draft Hazard Trait Regulation Comment Letter –is included and incorporated by reference.

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ATTACHMENT 1

GCA OVERARCHING CONCERNS

Independent Scientific Peer Review

The scientific portions of the proposed regulation have not yet been subjected to independent external scientific peer review. Although public comments have been solicited by OEHHA, the public comment process is not equivalent to scientific peer review, and does not substitute for scientific peer review.[1] Under California Health and Safety Code Section 57004 (HSC 57004), all CalEPA organizations, including OEHHA, are required to conduct an external scientific peer review of the scientific basis for any rule proposed for adoption, and a final regulation cannot be issued until such a scientific peer review has been completed. HSC 57004 recognizes the ramifications any science based regulations may have, and therefore imposes the general peer-review requirements which must be satisfied. OEHHA's proposed regulation would create a novel, California-only method of hazard classification or designation. Therefore, it is imperative that the scientific basis of the regulation is thoroughly and comprehensively peer reviewed by external scientific experts to establish that the proposed rule is based upon sound scientific knowledge, methods, and practices. In accordance with HSC 57004, the most appropriate body for conducting the external scientific peer review is the National Academy of Sciences (NAS), since the proposed regulation represents scientifically questionable deviations from well established, internationally agreed upon systems for evaluating and describing chemical hazards.,. In addition, the NAS is best suited to conduct the required external scientific peer review because of its global stature and proven track record for tackling complex toxicology and risk assessment issues. Moreover, adoption of a novel California-specific method of hazard trait identification could have global ramifications, since the California economy represents 13-14% of the US GDP and is the world's eighth largest economy. For all of these reasons, scientific peer review of the OEHHA proposal is critical to establish that the proposed rule is based upon sound scientific knowledge, methods, and practices.

Existing Systems

The Initial Statement of Reasons states that in complying with its statutory obligation under Government Code subsection 11346.5(a)(13), "OEHHA has determined that no reasonable alternative considered by OEHHA, or that has otherwise been identified and brought to the attention of OEHHA, would be more effective in carrying out the purpose for which this action is proposed, or would be as effective and less burdensome to affected private persons than the proposed action." This is simply not the case.

Several existing hazard trait and toxicological end-point regimes currently in existence nationally and internationally are widely in use and could be easily leveraged by California in harmony with existing practice. The hazard criteria proposed by the US Occupational Safety and Health Administration (OSHA) to modify its existing Hazard Communication Standard (HCS) to conform with the United Nations' (UN) Globally Harmonized System of Classification and Labeling of Chemicals (GHS; *74 FR 50279*, September 30, 2009) constitute one set of hazard traits that will be widely used in commerce in the US and across the globe. Perhaps more applicable to the

[1] The differences between public comment and independent scientific per review are explained in EPA's Peer Review Handbook, 3rd Edition (2006), pg 14.
http://www.epa.gov/peerreview/pdfs/peer_review_handbook_2006.pdf

development of the Toxics Information Clearinghouse (TIC), the OECD Harmonized Templates for Reporting Chemical Test Summaries are standard data formats for reporting studies done on chemicals to determine their properties or effects on human health and the environment.[2] These templates are the basis for the International Uniform Chemical Information Database (IUCLID) which is the standardized format for reporting chemical test data in the USEPA and OECD High Production Volume Chemical Challenge Programs, and the European REACH chemical management program.

GCA is concerned that having a new California-only system as proposed under the draft regulation is inefficient, duplicative, and will make it unnecessarily difficult to leverage existing information on chemicals. For conventional hazard traits, OEHHA should harmonize as much as possible with existing international and national systems that already identify the information elements necessary to study and characterize chemicals. If California wants to create a system that can be populated quickly and efficiently, these systems should be leveraged. Tens of thousands of tests for thousands of chemicals have been or will be performed and interpreted through these systems. Leveraging these existing systems will provide a framework for things like the use of categories, tiered testing, acute vs. chronic toxicity, judging study quality/reliability, and weight of evidence approaches, all of which are inadequately addressed at all in OEHHA's proposed regulation.

If California proceeds with a non-standard approach, not only will the database take years to develop and populate, but there will be a substantial Agency effort (time, resources, cost) required to convert the information in the tens of thousands of available studies to the unique California system both initially and on an ongoing basis. Given that there are existing systems currently in use worldwide, it is not clear why OEHHA has chosen to develop a unique system. OEHHA has failed to discuss why existing systems are inadequate and why there is a need for a unique system. Moreover, instead of creating a novel, California-unique designation of toxicities and endpoints that will require significant state resources to populate even with existing information, OEHHA could offer a far more cost efficient solution by leveraging existing data already provided to the world's governments and create a master portal that provides easy access to existing information sources. Such an approach would avoid a California-unique approach that makes no sense and would be a drain on an already fragile economy.

Classification

The classification proposal should be abandoned entirely. SB 509 gives OEHHA neither the mandate nor the authority to create a novel California classification system. DTSC has responsibility for what actually gets placed into the TIC, not OEHHA. The classification system is a significant overstep of OEHHA's authority into DTSC's responsibilities. Moreover, the entire classification provision is pejorative, unrealistic, and unhelpful. The OEHHA proposal does not bring clarity to chemical information. Indeed, it increases opacity on all dimensions.

ARTICLE 1 – GENERAL

Section 69401.2 – Definitions

(b) "Authoritative organization" – This definition fails to account for the concept of "deliberative review" in coming up with scientific findings versus creation of derivative lists. Referencing "other states" is particularly concerning, where there are generally no authoritative

[2] http://www.oecd.org/site/0,3407,en_21571361_43392827_1_1_1_1_1,00.html

processes in place. However, on page 4 (of 24) the wording suggests that "authoritative organizations" are limited to those listed.

(c) "Chemical substance" – this definition is broadly expansive and different from DTSC's proposal.

(e) "Hazard Traits" – this definition lacks clarity in that it does not actually define what a hazard trait is, but states (in a circular fashion) the types of hazards. Hazards are, in the context of chemicals, inherent properties that lead to adverse effects in humans and wildlife. In the context of the present regulation, they are toxicities. The definition should be amended accordingly.

(f) "Mechanistic similarity" – this definition is sweeping and imprecise and is not consistent with the terms usually applied within the toxicological community. This definition should be expanded to include not only a similar mode of action/toxicological effect, but also considerations on the toxicokinetic profile of the chemical (such as in their absorption, distribution, metabolism, and excretion (ADME) profile, for example, or in their Physiologically-based, Pharmacokinetic (PBPK) models). The toxicokinetic profile is important to establish whether the same level of concern is warranted for a chemical with a similar mode of action.

(g) "Other relevant data" – this definition lacks clarity and consistency with the authorizing statute (SB 509) in that OEHHA has narrowly interpreted the scope of the definition. The statute states that the office shall specify "any other relevant data that are to be included in the clearinghouse." These other relevant data are not restricted to only hazard traits, but could be any relevant data about a chemical in the TIC. Potential exposure is but one example. Is it permitted in commerce in the United States? Is it widely used in commerce in the US? What kind of applications is the chemical used for? Information addressing these questions is very relevant and useful to be captured by the TIC, and easily accessible towards that end.

Much more than hazard information alone is needed for people searching for alternatives, whether they are product manufacturers, DTSC staff, or lay citizens. EPA is finalizing changes to its Inventory Update Rule (IUR) which will collect 2010 chemical information. The Toxics Information Clearinghouse should include information reported by industry to IUR. Use categories, chemical functional uses and production volume will be reported by industry in mid-2011 and should be integrated into the "Other Relevant Information" section of the TIC.

Further, while there is important physical-chemical information that should be included in the TIC, to try to characterize this information as "exposure potential hazard traits" is unscientific and contrary to well established chemical management practices. This information rightly belongs in the "other relevant information" segment of the TIC.

(h) "Toxicological endpoint" – this definition lacks clarity because it is not specific to toxicity and the potential to cause harm. This definition should be revised as such, and additional definitions for other hazard trait endpoints should be defined as necessary.

(i) "Well-conducted scientific study" – this definition lacks clarity and consistency in that it might arbitrarily exclude any study which is not published in the open literature, or submitted to a government agency. Furthermore, this definition is different and inconsistent with DTSC's "reliable information" definition, which attempts to address the critical need of understanding

the quality and reliability of a study. GCA recommends that OEHHA withdraw the "well-conducted scientific studies" terminology and replace it with the following definition:

> *"Reliable information" is from studies or data generated according to valid accepted testing protocols in which the test parameters documented are based on specific testing guidelines or in which all parameters described are comparable to a guideline method. Where such studies or data are not available, the results from accepted models and quantitative structure activity relationship ("QSAR") approaches validated in keeping with OECD principles of validation for regulatory purposes may be considered. The methodology used by the Organization for Economic Cooperation and Development (OECD) in Chapter 3 of the Manual for Investigation of HPV Chemicals (OECD Secretariat, July 2007) shall be used for the determination of reliable studies."* [3]

ARTICLE 2 – TOXICOLOGICAL HAZARD TRAITS

Section 69402.2 – Evidence for Carcinogenicity Hazard Trait

This entire section is unnecessary and unauthorized by the statute (SB 509) in that the state is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints. Furthermore, this section of the regulations is duplicative of the office's function of identifying carcinogens under Proposition 65. This section should be eliminated.

Section 69402.4 – Evidence for Developmental Toxicity Hazard Trait

This entire section is unnecessary and unauthorized by the statute (SB 509) in that the state is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints. Furthermore, this section of the regulations is duplicative of the office's function of identifying developmental toxicants under Prop. 65. This section should be eliminated.

Section 69402.6 – Evidence for Reproductive Toxicity Hazard Trait

This entire section is unnecessary and unauthorized by the statute (SB 509) in that the state is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints. Furthermore, this section of the regulations is duplicative of the office's function of identifying reproductive toxicants under Prop. 65. This section should be eliminated.

ARTICLE 3 – OTHER TOXICOLOGICAL HAZARD TRAITS

List of "icities"

OEHHA has justified its position on use of the long list of toxicities as hazard traits by stating that each trait was chosen in part because of listings within a textbook of toxicology, where discussions are broken out by target organ systems. Regardless of the fact that toxicology textbooks may organize information based on target organs, it is a generally accepted method for hazard identification to describe hazards in terms of either durations of exposure (*i.e.* toxic effects seen after acute exposure, toxic effects see after chronic exposures) or local versus systemic toxicity. Then, under the hazard trait of "systemic toxicity," the target organs would be identified (*i.e.* liver, kidney, heart, etc.). It is unnecessary to break out systemic toxicity or target organ toxicity by specific systems (*e.g.* cardiovascular, gastrointestinal, liver, renal, etc.) when

[3] http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html

the goal is hazard identification. Instead, listing target organ effects is more than adequate to describe a chemical's hazard. This is especially true since the critical issue for chemical hazard classification should be identifying the most sensitive system(s) affected by chemical exposure, not simply a laundry list of toxicity. Thus, when the goal is hazard identification, GCA argues that there is no need to break out systemic toxicity or target organ toxicity by specific systems as proposed in the draft regulation (e.g., cardiovascular, gastrointestinal, liver, renal, etc.).

It is also important to consider that none of the prominent national or international systems list the vast number of "icities" contained in the OEHHA proposal. On the human heath side for instance, chemicals are characterized for "acute toxicity" and "chronic toxicity" (sometimes "systemic toxicity"). Organ systems impacted are noted, but there is no presumption of separate and distinct test for every organ system that the OEHHA proposal implies. The structure presented by OEHHA could be misinterpreted in such a way. Noting which organ system(s) is most sensitive is more than adequate to describe a chemical's hazard. Said differently, a single test can cover many different "icities," and the TIC should be structured in a way that makes that more apparent to users.

Emerging Traits

With regard to "emerging" traits, endocrine disruption (Section 69403.3) and epigenetics (Section 69403.4), for example, are mechanisms of potential toxicity, not toxic end-points themselves and thus not hazard traits. As such, OEHHA should not unilaterally establish these or other new hazard traits.

Section 69403 – General

The regulations should be clarified and made consistent with the general practice of organizing toxicological hazards among acute toxicities and repeat dose toxicities.

Section 69403.3 – Endocrine Toxicity

Endocrine toxicity is a new emphasis within chemical risk assessment and toxicity testing. It is standard practice in toxicology and risk assessment to describe toxic effects on endocrine organs as part of the systemic toxicity of chemicals, or as part of the hazard trait of reproductive toxicity or developmental toxicity, since toxicity to these systems is related to effects on endocrine systems. OEHHA fails to discuss the fact that many of the endpoints listed in this section have not been validated as unique endpoints for identifying endocrine toxicity of chemicals. Moreover, the listing of endocrine toxicity as a unique hazard trait is somewhat redundant when reproductive and developmental toxicity are listed.

Section 69403.4 – Epigenetic Toxicity

Epigenetic toxicity as defined by OEHHA is overly broad as it could include adaptive as well as adverse effects on organisms. The omission of a discussion of adaptive changes versus adverse effects of chemicals is a flaw that affects all steps in the process of identifying hazard traits. The changes listed should be manifested in standard toxicity testing as endpoints of systemic toxicity and would include changes in either biological function or tissue structure (pathological or histopathological changes). If such changes do not manifest in acute or repeat dose toxicity studies, then they may be adaptive changes only and not relevant for chemical hazard assessment. OEHHA fails to provide any scientific basis for including "epigenetic toxicity" as a separate discrete hazard trait apart from systemic toxicity.

Section 69403.5 – Genotoxicity
This section should be clarified to specify what constitutes an adverse outcome with respect to genotoxicity.

Section 69403.8 – Immunotoxicity

Section (b) states "Endpoints include" but then the list of items appear to be more of a mix of overall endpoint outcomes, syndromes and measurable effects/observations. It appears confusing to have allergic sensitization alongside changes in circulating immune cells. Moreover there is no context in their relative significance. Alteration in cytokine production and release are observations that might be relevant as entry points in the assessment of sensitization, immunostimulation/suppression or autoimmunity. Data could be from humans or laboratory animals but no distinction is made here. In any case, there has to be tiered approach in terms of what experimental data you would need in order to be able to determine whether sufficient or insufficient to conclude upon immunotoxicity. This also makes (c) awkward to interpret – why are only two items cited here - is there some other more specific text that provides the context for what evidence is needed to substantiate structural/mechanistic similarity? Only the definition for mechanistic similarity is provided.

Section 69403.12 – Ocular Toxicity

This section should be clarified to specify what constitutes an adverse effect (not change) with respect to genotoxicity.

Ocular toxicity is an endpoint commonly addressed through testing for eye irritation and damage in standard acute toxicity tests in animals. As a result, ocular effects are included as a hazard trait within many classification systems. Since testing for eye irritation, for example, is commonly included within standard toxicity testing batteries, it is unclear why OEHHA has chosen to deviate from the standard approach to identifying hazards to the eye.

Section 69403.14 – Reactivity in Biological System

This section should be clarified to specify what constitutes an adverse outcome with respect to reactivity in biological systems.

Reactivity in biological systems is an overly broad trait that is not useful for hazard evaluation since all chemicals could be considered to "react" with biological systems simply by being absorbed into a cell. The endpoints mentioned in the OEHHA proposal appear to fit more easily within other hazard trait categories as underlying mechanisms or modes of action.

Section 69403.15 – Respiratory Toxicity

This section should be clarified to specify what constitutes an adverse effect (not change) with respect to reactivity in biological systems.

Respiratory toxicity is also a standard endpoint of systemic toxicity that would be monitored in most acute as well as repeat dose toxicity studies. As already discussed above for other endpoints of systemic toxicity, it is not clear why OEHHA has chosen to isolate changes in respiratory function apart from systemic toxicity when most other toxicity classification and hazard identification systems would include such endpoints within the scope of defining chemical hazard in terms of systemic toxicity. Also, some of the endpoints listed in the proposal have not been validated as indicators of adverse effects as opposed to adaptive changes (*e.g.* increased inflammatory cytokine expression.)

Section 69403.16 – Evidence for Toxicological Hazard Traits

This entire section is unnecessary and unauthorized by the statute (SB 509) in that the office is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints. Furthermore, while it will be critical that only high quality information is included in the Toxics Information Clearinghouse (TIC), it is the purview of the Department of Toxic Substances Control to establish the criteria for inclusion of any particular study, or other data or information in the TIC.

ARTICLE 3 & 4 – TOXICOLOGICAL & ENVIRONMENTAL HAZARD TRAITS

Endpoint Lists

Each of the toxicological and environmental traits in the OEHHA proposal is accompanied by a list of possible endpoints that could demonstrate that a chemical has the respective trait. However, the hazard traits and endpoints listed are not actual hazard traits or endpoints. Rather, much of what is listed in the draft are preludes in multiple-step pathways that may or may not lead to disease or an adverse outcome (i.e., these are actually mechanisms and not endpoints; examples include epigenetic adverse perturbations and electrophilic potential). This will not further the Green Chemistry goals or provide the certainty necessary to make prioritization decisions or weigh chemical alternatives.

ARTICLE 4 – ENVIRONMENTAL HAZARD TRAITS

Section 69404.1 – Domesticated Animal Toxicity

This section is unnecessary in that it is making a distinction with respect to the inherent toxicity of a chemical based on the route of exposure of that chemical, which is not an inherent property. Furthermore, it is one more example of the development of a California-unique system that does not mesh with other established systems and associated data/criteria. This section should be eliminated and any data which might be included in the TIC that is relevant to domesticated species should be generally included with all other data for animals and wildlife.

Section 69404.2 – Eutrophication

This proposed hazard trait section is unnecessary, lacks clarity and should therefore be eliminated. Eutrophication is a complex process that is influenced by a number of physical, biological and chemical factors within the ecosystem. It is not an inherent property of a chemical, and therefore, should not be considered a hazard trait of a chemical.

Section 69404.3 – Impairment of Waste Management Organisms

This proposed hazard trait is unnecessary and should therefore be eliminated. While there are specific internationally accepted standardized tests to determine the potential for a chemical to impact organism in biological waste treatment systems, it is just another facet of environmental toxicity. The regulations would be clearer if generally accepted terminology was used rather than California developing new terminology.

Section 69404.4 – Loss of Genetic Diversity, Including Biodiversity

This proposed hazard trait is unnecessary and should be removed. The potential for a chemical to adversely affect the community structure of an ecosystem is no different than the environmental toxicity of a chemical. Moreover, it is not possible to objectively quantify the effect a chemical may have on a particular ecosystem since the health of any ecosystem will be the subject of a great number of factors. For this and all subsequent traits that have a field data component, there is a major problem in that potential effects in the field exist in the context of multiple stressors and it is frequently not possible to parse out the causative stressor(s) responsible for the observed effect. Use of field data will require additional confirmatory data, e.g., from lab studies, etc., in order to be indicative of a particular hazard trait in most instances. This includes data on things like wildlife reproductive impairment based on field data.

Section 69404.10 – Evidence for Environmental Hazard Traits

This entire section is unnecessary and unauthorized by the statute (SB 509) in that the office is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints. Furthermore, while it will be critical that only high quality information is included in the Toxics Information Clearinghouse (TIC), it is the purview of the Department of Toxic Substances Control to establish the criteria for inclusion of any particular study, or other data or information in the TIC.

ARTICLE 5 – EXPOSURE POTENTIAL HAZARD TRAITS

Article 5 is unnecessary and lacks clarity. The state is proposing to establish that certain physical-chemical properties of a chemical are hazards. This notion has no basis in science and there is no precedent anywhere in the world.

The “exposure potential hazard trait” concept should be stricken from this regulation. Exposure potential is not a hazard. Rather hazard is an intrinsic trait that requires adequate exposure to demonstrate the hazard, i.e., hazards can only be manifest when the exposure are sufficiently high. One would not expect to demonstrate a hazard from exposure to a single molecule of a substance. This concept is embodied in the Prop 65 statutory language and Safe Harbor levels that OEHHA has set for hazardous substances.

While exposure potential is certainly germane to risk, it is so only in the context of a particular chemical having a specific hazard associated with it. The appropriate manner in which to incorporate consideration of exposure potential is therefore directly in the consideration related to each specific hazard trait, as identified in earlier sections of the Proposed Regulation, where such consideration may be relevant as “other relevant data.” To label these considerations of exposure as hazard traits is both misleading and ripe for abuse.

Some individual items within this section (*e.g.* bioaccumulation, environmental persistence) are important chemical properties that are often reported and for which there may be substantial data to populate the TIC. While it is fair to consider these properties as “other relevant data” and include them in the TIC as such, they should not be considered stand-alone hazard traits.

Additionally, the following sections in Article 5 are currently subject to existing regulations set forth by the U.S. EPA's National Ambient Air Quality Standards, U.S. EPA’s Stratospheric Protection Division's Regulations, and/or California Air Resources Board’s (CARB's) Greenhouse Gas Rules.

- Section 69405.1 Ambient Ozone Formation;
- Section 69405.4 Global Warming Potential;
- Section 69405.7 Particle Size or Fiber Dimension; and
- Section 69405.8 Stratospheric Ozone Depletion Potential.

SB 509 states: "The department shall not duplicate or adopt conflicting regulations for product categories already regulated or subject to pending regulation consistent with the purposes of this article." Therefore, if Article 5 is not deleted, an exemption from each of the sections referenced above should be included for products subject to current and draft regulations.

Section 69405.1 – Ambient Ozone Formation

Ozone formation is not a hazard trait and should therefore be removed from the regulation. By definition of the reference cited in OEHHA's draft regulation[4] "Ozone, the tri-atomic form of oxygen, is a gaseous atmospheric constituent. In the troposphere, ozone is created both naturally and by photochemical reactions involving gases resulting from human activities." The formation of ozone may amount in measurable concentrations that reach an effect level for organisms that are exposed; however ozone formation in itself is not a hazard trait.

Section 69405.2 – Bioaccumulation

As noted above, bioaccumulation is not a hazard trait and should be removed from the regulation as such. Although bioaccumulation has been defined by various credible entities[5], none have defined it as a hazard trait. That said, it is an important inherent chemical property that is often measured and reported. As such, it could be included in the Toxics Information Clearinghouse as "other relevant data."

OEHHA should use the best available science when identifying appropriate bioaccumulation data to be included in the TIC. Recently, the Society of Environmental Toxicology and Chemistry (SETAC) conducted a Pellston workshop on POPs and PBTs that explored the current state of bioaccumulation science.[6] Much of this science was discussed at the May 2010 OEHHA workshop in Berkeley, California on *Indicators of Ecotoxicity Hazards and Exposure Potential*. The SETAC workshop developed the following definition for a bioaccumulative substance: "A substance is considered bioaccumulative if it biomagnifies in food chains." Standard criteria for reporting the extent to which a chemical may bioaccumulate were noted including bioconcentration factor (BCF), bioaccumulation factor (BAF), biomagnification factor (BMF, both laboratory and field), trophic magnification factor (TMF), octanol-water partition coefficient (K_{OW}) and octanol-air partition coefficient (K_{OA}). The workgroup concluded that the most relevant bioaccumulation criterion is the trophic magnification factor (TMF; also referred to as a "food-web magnification factor"); in the absence of data on the TMF, the BMF (either derived in the laboratory or based on field data) is a reliable indicator. They also concluded that "BCF is no longer recognized to be a good descriptor of the biomagnifications capacity of chemical substances." One criterion found in the OEHHA proposed regulation that was not the subject of the SETAC exercise is "inhibition of an efflux transporter;" this concept is not generally accepted by the scientific community as a measure of the potential for a compound to

[4] The Intergovernmental Panel on Climate Change, IPCC Fourth Assessment Report: Climate Change 2007. World Health Organization and United Nations Environment Programme, Annex I Glossary. (The annex is incorrectly cited in the draft regulation; Annex 1 contains the glossary).
[5] From USGS Toxics Substances Hydrology Program website: http://toxics.usgs.gov/definitions/bioaccumulation.html
[6] Gobas, F.A.P.C., W. de Wolf, L.P. Burkhard, E. Verbruggen and KPlotzke. 2009. Revisiting bioaccumulation criteria for POPs and PBT assessment. *Integrated Environmental Assessment and Management*, 5(4):624-637.

bioaccumulate and should be eliminated from the OEHHA proposal. OEHHA should consider including the other six criteria (BCF, BAF, BMF, TMF, K_{OW}, and K_{OA}) in the TIC as "other relevant data" as they are common chemical measures.

As has been stated previously, OEHHA has proposed to classify chemicals as a bioaccumulation hazard if its bioaccumulation factor (BAF) is greater than 1000, or it has a log octanol-water partition coefficient greater than or equal to 5. Bioaccumulation is not a hazard, and OEHHA has neither the mandate nor the authority to be classifying chemicals as such. Therefore, this classification aspect of bioaccumulation should be eliminated.

Section 69405.3 – Environmental Persistence

The identification of classification threshold values for this trait is unauthorized by the statute (SB 509) in that OEHHA is attempting to classify chemicals when it is only authorized to specify hazard traits and endpoints.

Furthermore, persistence is not a hazard characteristic. Persistence is a characteristic whereby the chemical resists photolytic, biological and chemical degradation.[7] Because it is persistent, a material could become measurable in environmental media and depending on the level, it may be present in high enough concentrations to each an effect level for organisms that are exposed; however, persistence in itself is not a hazard trait. OEHHA should include persistence as "other relevant data" as it is a common chemical measure.

Section 69405.4 – Global Warming Potential (GWP)

Global Warming Potential (GWP) is not a hazard trait and should therefore be removed from the regulation. By definition of the reference cited in OEHHA's draft regulation,[8] GWP is "An index, based upon radiative properties of well mixed greenhouse gases, measuring the radiative forcing of a unit mass of a given well mixed greenhouse gas in today's atmosphere integrated over a chosen time horizon, relative to that of CO2. The GWP represents the combined effect of the differing lengths of time that these gases remain in the atmosphere and their relative effectiveness in absorbing outgoing infrared radiation."

Section 69405.6 – Mobility in Environmental Media

Mobility in environmental media is not a hazard trait and should therefore be removed from the regulation. Mobility in air, water or soil/sediment will depend on external conditions, such as temperature, humidity, organic content of soil and sediment. Mobility is not an inherent characteristic of a chemical and it is not a hazard trait.

Section 69405.7 – Particle Size or Fiber Dimension

Particle Size or Fiber Dimension is not a hazard trait and should therefore be removed from the regulation. By themselves, particle size and fiber dimension do not convey hazard, only deposition probability in the respiratory tract, and therefore inclusion of this separate category as a "hazard trait" is inappropriate and misleading. Furthermore, it is unclear if the dimensions cited could encompass all nanomaterials.

[7] Ritter L; Solomon KR, Forget J, Stemeroff M, O'Leary C.. "Persistent organic pollutants". *United Nations Environment Programme*. http://www.chem.unep.ch/pops/ritter/en/ritteren.pdf. Retrieved 2007-09-16.

[8] The Intergovernmental Panel on Climate Change, IPCC Fourth Assessment Report: Climate Change 2007. World Health Organization and United Nations Environment Programme, Annex I Glossary. (The annex is incorrectly cited in the draft regulation; Annex 1 contains the glossary).

Section 69405.8 – Stratospheric Ozone Depletion Potential

Stratospheric Ozone Depletion Potential (ODP) is not a hazard trait and should therefore be removed. According to EPA's Ozone Layer Protection Glossary[9] "Ozone Depletion Potential (ODP): a number that refers to the amount of ozone depletion caused by a substance The ODP is the ratio of the impact on ozone of a chemical compared to the impact of a similar mass of CFC-11. Thus, the ODP of CFC-11 is defined to be 1.0. Other CFCs and HCFCs have ODPs that range from 0.01 to 1.0."

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[9] http://www.epa.gov/ozone/defns.html

ATTACHMENT 2

The Green Chemistry Alliance (GCA) questions OEHHA proceeding with regulatory action related to Green Chemistry Hazard Traits at this time in light of Secretary Adams' announcement of December 23, 2010 that she has directed the Department of Toxic Substances Control (DTSC) to take additional time to develop regulations for the California Green Chemistry Initiative.[10] OEHHA's actions in this regard seem to fly in the face of the Secretary's decision and signal a very troubling lack of coordination in CalEPA among OEHHA, DTSC and the Secretary. This apparent lack of coordination with the DTSC proposed regulations and DTSC's vision for the Toxics Information Clearinghouse (TIC) signifies the need for additional time and action by the Secretary, DTSC and OEHHA to employ the vision of developing and implementing the very best program possible, one that is workable and addresses key policy concerns.[11]

To develop and implement a program that is firmly grounded in science, one that is workable and one that addresses key policy concerns greater coordination between the CalEPA, DTSC and OEHHA is critical. The novel approach OEHHA has proposed for hazard trait determination oversteps its statutory authority. Further, in many instances the proposed approach represents scientifically questionable deviations from well established, internationally agreed upon systems for evaluating and describing chemical hazards.

Given the lack of coordination thus far and recent change in Administration, it is important that incoming leaders and DTSC and OEHHA have the opportunity to provide the Brown Administration's input regarding the path forward for the overall Green Chemistry Initiative. The OEHHA regulation will both define content for the Toxics Information Clearinghouse (TIC) and be considerations in defining "Chemicals of Concern," per the laws. Without clarity on the regulatory structure into which the traits must fit, there is too much uncertainty regarding both their operative impact and sufficiency.

GCA strongly urges OEHHA to first undertake the necessary coordination with DTSC and the CalEPA Secretary and then to revise the proposed regulation to adopt a structure that allows existing chemical toxicity information and hazard trait determinations to be utilized in a scientifically rigorous manner to more quickly and cost effectively fulfill its mandate under SB 509.

With these points and concerns as a basis, Attachment 2 reviews many of the outstanding issues that are not resolved by the proposed regulation. In many cases, OEHHA has indicated that a particular task is DTSC's responsibility. GCA is concerned that the gray areas between the responsibilities of CalEPA, DTSC, and OEHHA are critical issues that must be discussed and resolved prior to finalizing this proposed regulation. The following points address specific issues and concerns regarding OEHHA's regulation for which OEHHA may or may not have the authority or responsibility to address, but nonetheless must be considered and included as part of the bigger approach for green chemistry.

[10] http://www.dtsc.ca.gov/upload/GRSP-12-23-2010.pdf
[11] ibid

ARTICLE 1 - GENERAL

Classification

It is important to note that DTSC, in its Toxics Information Clearinghouse Feasibility Study Report[12], suggests that the user will make their own judgment as to the hazards, based on the information presented. (p.26)

> *"DTSC will not be conducting any safety assessments and do not want to imply that inadvertently. The Clearinghouse is envisioned to provide access to all of the information; and any determinations and interpretation of the data will be left to the user based on the information in the Clearinghouse."*

Thus, the Hazard Trait Regulation and Clearinghouse should be open to including all information available on a chemical, but remain as objective as possible, without introducing biases and subjectivity through a classification system.

And while GCA objects to OEHHA's classification approach (lack of authority), the approach completely fails to address potency and weight of evidence (see discussion below regarding Section 69403.16 – Evidence for Toxicological Hazard Traits). These two components must be addressed in any classification system and in fact are addressed in OSHA's GHS.

Potency

There is a dose level that produces an effect for every chemical. How will the TIC address the very real issue of potency before declaring that substance possesses a toxicity trait? Potency is a measure of the hazard potential and is a critical part of any hazard identification process.

The OEHHA proposal is deficient in that there is no indication of consideration of potency for the hazard traits for which there is evidence of hazard. Without some indication of potency cutoff values, every substance, whether synthetic or naturally occurring, could be considered toxic. As a case in point, without information about the dose at which a substance causes acute toxicity, will everything in the TIC be marked as acutely toxic?

OEHHA has established a framework that will undoubtedly be misunderstood and certainly misused.

We recommend that OEHHA look at existing systems, particularly the OECD Harmonized Templates for Reporting Chemical Test Summaries (see comments above) to understand how authoritative and respected bodies have handled this critical issue.

Data Quality

OEHHA needs to clearly identify how certain types of data should be weighed when assessing chemical hazards, recognizing that certain types of data are less appropriate than others, even if they are developed by authoritative bodies. Evaluation of chemicals should be based on the best available data. Best practices in toxicology use the following order of preference: 1) measured data on the chemical being evaluated, 2) measured data from a suitable analog, and 3) estimated data from appropriate models.

[12] Toxics Information Clearinghouse Feasibility Study Report. DTSC. April 8, 2010.

In vitro studies and QSARs are generally recognized as appropriate tools prioritizing chemicals and identifying the need for more complex biological system testing, but are limited in their ability by themselves to make decisions about risk or even classification of toxicological properties as OEHHA proposes. There are significant efforts underway nationally and internationally to reduce the need for unnecessary animal testing and GCA supports those programs. However, the validity of many *in vitro* studies to human health is still being evaluated and should be considered for assigning hazard traits to a chemical only after it has been clearly demonstrated that the specific method is scientifically valid and achieves an acceptable level of sensitivity (false negative rate) and specificity (false positive rate). There are multiple validated assays that have false positive rates that exceed validated *in vivo* methods (*e.g. in vitro* micronucleus assays). Additionally, *in silico* (computer simulation) methodology holds great promise, but in its current state, should be applied cautiously and only for select classes of materials and endpoints for which the models have been scientifically justified. Currently most *in silico* and *in vitro* assays only provide an indication of potential hazard and should not be the sole basis of decisions such as assigning or classifying a hazard trait. This is recognized by regulatory bodies worldwide, and is exemplified by OECD's development of internationally harmonized guidance on the validation[13] and regulatory acceptability[14] of QSAR models and alternative test methods for predicting biological effects and toxicity. All testing methods in the proposed regulation should be based on national and international standard protocols or validation by an appropriate authoritative body.

> "*It will always be necessary to evaluate relevance, reliability, sensitivity, and specificity of advanced high-throughput molecular screening and computational profiling methods prior to regulatory acceptance so that regulatory agencies, the regulated community, and the public have sufficient confidence in the decisions based on such methods. While traditional structures for conducting method validation and demonstrating model predictivity may not be practical, approaches such as those discussed by the National Research Council, Committee on Applications of Toxicogenomic Technologies to Predictive Toxicology, Board of Environmental Studies and Toxicology, Board of Life Studies, Division of Earth and Life Studies (2007b) with respect to validation of toxicogenomic technologies as well as practices embodied in the Organization for Economic Cooperation and Development (OECD) principles and guidance for the validation of quantitative structure activity relationships (OECD, 2007) and evidence-based toxicology (Guzelian et al., 2005; Hoffmann and Hartung, 2006) should be considered."*[15]

What kind of quality control and/or contextual information will accompany data and information from *in vitro* and QSAR studies? OEHHA has indicated that this is a DTSC responsibility and that they do not plan to address these issues in their regulation. Is DTSC prepared to develop data quality guidance (and perhaps test methods) for all of OEHHA's various toxicities? How and to what degree are the two agencies coordinating, given that OEHHA's actions directly impact DTSC's 1879 implementation? What implications does DTSC see for the safer alternatives process?

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[13] Guidance Document No. 69 on the Validation of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models (see http://www.oecd.org/dataoecd/55/35/38130292.pdf)

[14] Guidance Document No.34 on the Validation and International Acceptance of new or Updated Test Methods for Hazard Assessment http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono(2005)14&doclanguage=en

[15] Becker, Richard and James Bus. Toxicity Testing in the 21st Century: A View from the Chemical Industry. Toxicological Sciences (2009),doi:10.1093/toxsci/kfp234

The notion of "reliable information" and study quality is not addressed in the OEHHA draft other than marginally via a "well-conducted scientific studies" concept. Peer-review alone is an insufficient metric of study quality. The OECD methodology for determining the quality of data in chemical dossiers described in their Manual for Investigation of HPV Chemicals is a globally accepted way to rate the reliability, relevance and adequacy of existing data; as such, it should be defined into these regulations and required for every study used to populate the TIC. It has been applied to all studies in the US and OECD HPV programs and is required of all chemicals submitted under REACh (4300 high volume and high hazard chemicals submitted as of January 2011). It has been found to be an excellent approach to separate good studies from those that are not of sufficient quality and reliability for science-based regulatory and product stewardship decisions.

Data quality and weighting considerations are critical in ensuring good decision making in Prioritization and Alternative Analysis. Use of poor quality data can result at a minimum in needless action and at worst, unintended consequences. This is particularly important in the context of evaluating potential hazards associated with metabolic products and environmental breakdown products. For example, a study showing that a parent compound can be broken down to toxic metabolites under artificial conditions in a laboratory setting should not serve as the basis for assigning hazard traits unless there is evidence of such process occurring under actual environmental conditions. Weighting consideration are also important in the context of relevance for human health hazard where data collected in a non-standard species of unknown relevance to human physiology should not be given equal weight as compared to a study conducted in a standard laboratory animal species whose physiology is known to be relevant for human health hazard assessment.

If the TIC is populated with all available data and information in the absence of quality and reliability screens; how is any user, technical expert or lay citizen, supposed to identify what's truly relevant for making a decision? Even users with technical backgrounds will require an enormous amount of time to sift through the TIC if there are no quality control measures in place.

Questions of data quality and quantity raise the issue of resources DTSC will need to put toward its data quality and management obligations under SB 509. What are DTSC's plans for populating the TIC, making data quality decisions, etc.? What importance will DTSC put on information generated through validated test guidelines versus other types of studies?

To address these issues and to harmonize with national and international approaches, OEHHA together with DTSC should adopt the robust study summary format used in the OECD's hazard assessment program and OECD harmonized templates as a model for populating the TIC and, as a result, providing internationally accepted information on study quality and reliable information. This has the additional benefit of enabling a quick start-up of the TIC, since information from hundreds of thousands of studies on over 4300 chemicals has now been submitted to REACH and was rated according to this approach. Studies on thousands of additional chemicals will be forthcoming in this format in future years.

ARTICLE 2 – TOXICOLOGICAL HAZARD TRAITS

Section 69402.2 – Evidence for Carcinogenicity Hazard Trait

The lead agency should clearly state that there are a number of modes of action that are causally linked to tumor induction in lab animals that are not relevant to human health and therefore are not appropriate for use as evidence of a carcinogen hazard trait. Examples

include, but are not limited to, high-dose cytotoxicity which stimulates compensatory cell proliferation, certain receptor mediated responses and male rat kidney tumors caused by accumulation of α-2microglobulin.

ARTICLE 3 – OTHER TOXICOLOGICAL HAZARD TRAITS

Emerging Traits

True hazard traits should be measurable by recognized, validated tests. OEHHA should seek scientific consensus on the description of the trait and the appropriate study protocol for the endpoint(s) prior to including it in the regulation. OEHHA should be able to show that scientific consensus exists, or should be establishing the process for reaching that consensus where none exist, but they should not be unilaterally establishing new hazard traits.

Section 69403.3 – Endocrine Disruption

Endocrine disruption (Section 69403.3) is not an endpoint, but rather a mode of action. It has been standard practice in toxicology and risk assessment to describe toxic effects mediated by the endocrine system based on the apical adverse effects that are induced. Thus, a chemically-induced change on a component of the endocrine system that is of sufficient magnitude/duration/nature to cause an adverse effect on an organ system has, in practice, been evaluated as target organ toxicity (which includes assessment of reproductive toxicity or developmental toxicity). The OEHHA document fails to discuss the fact that many of the endpoints listed in their section have not been validated as unique endpoints for identifying endocrine disrupting chemicals.

As OEHHA is well aware, endocrine activity, consistent with the principles expressed in EPA's Endocrine Disruptor Screening Program (EDSP), is not a distinct toxicological hazard per se, but rather a measure of a compound's ability to interact with components of the endocrine system. Interaction with or modulation of endocrine processes may or may not give rise to adverse effects; EPA states, "The fact that a substance may interact with a hormone system, however, does not mean that when the substance is used, it will cause adverse effects in humans or ecological systems." Toxicological tests that evaluate the induction of adverse effects in validated test systems (EPA's EDSP Tier 2 tests), not mechanistic screens, are to be used for hazard identification. As EPA has stated, "At this stage of the science, only after completion of Tier 2 tests will EPA be able to determine whether a particular substance may have an effect in humans that is similar to an effect produced by a naturally occurring EAT, that is, that the substance is an endocrine disruptor." The World Health Organization's definition of an endocrine disruptor is very similar to that of the EPA: "An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations."

Section 69403.4 – Epigenetic Toxicity

Epigenetic toxicity (Section 69403.4) is an even newer concept within toxicology and has been examined as the basis for identifying mechanisms of systemic toxicity. In fact, "epigenetics" is defined as a mechanism of action for potential toxic effects, not an endpoint for toxicity testing. Epigenetic changes such as DNA methylation or histone modification, as listed in the OEHHA Proposal, may not lead to stable expressions of an altered, adverse phenotype, which is what would be needed in order to identify a specific endpoint of hazard or toxicity. The changes listed in Article 3 in association with epigenetic toxicity, however, should be manifested in standard

toxicity testing as endpoints of systemic toxicity and would include changes in either biological function or tissue structure (pathological or histopathological changes). If such changes do not manifest in acute or repeat dose toxicity studies, then they may be adaptive changes only and not relevant for chemical hazard assessment. OEHHA fails to provide any scientific basis for including "epigenetic toxicity" as a separate discrete hazard trait from systemic toxicity.

Section 69403.15 – Respiratory Toxicity

As with many of the "traits" cited in these Proposed Regulations, there is a conspicuous absence in this definition, of language that would clearly differentiate potential exposures at insignificant levels. This poses the possibility of materials being "classified" as having respiratory toxicity hazard where no hazard logically exists. From the perspective of nanomaterials, this is a concern because of the potential interaction with *§ 69405.7 Particle Size or Fiber Dimension* (see below). GCA recommends the addition of language at the end of (c), to clarify intent to deal with significant exposure threats. Specifically, we recommend it to read:

> *(c) Other relevant data include but are not limited to: in vitro evidence for respiratory toxicity; particle size distribution inclusive of respirable particles; respirable fibers; long half-life in the lung; chemical reactivity; redox potential; structural or mechanistic similarity to other chemical substances with the respiratory toxicity hazard trait. In interpreting the above, anticipated exposure must be detectable or significant at levels above background.*

We would also call to your attention the inclusion in this definition of "*particle size distribution inclusive of respirable particles; respirable fibers;"* This is appropriately applied as a consideration relevant specifically to Respiratory Toxicity.

Section 69403.16 – Evidence for Toxicological Hazard Traits

It is a general principle of hazard assessment that all available data must be considered and weighted in order to arrive at a scientifically defensible decision regarding chemical hazard. Since in many cases, dozens of toxicological studies will be available for review on any given chemical, the only valid scientific approach is to consider the weight of the scientific data. Without such an approach, the document can be interpreted to suggest that a single assessment, regardless of its quality could be used to conclude that a chemical possesses "suggestive evidence" of a specific hazard trait. Additionally, with respect to cancer, developmental toxicity and reproductive toxicity hazards, it is likely that for many chemicals there will be multiple hazard assessments available from a variety of sources. As a result, specific discussion of how a weight-of-the-evidence assessment should be, and will be, performed is needed.

Without use of WOE, "sufficient evidence" of a hazard trait could be assigned to a chemical, for example, based on data from two poorly conducted studies even if there were several more reliable studies available that contradicted the results of those two studies. It is not scientifically valid to ignore this weight of the scientific evidence. Yet, while Section 69403.16 Evidence for Toxicological Hazard Traits proposes a framework for evaluating scientific results, it is not a WOE approach. Instead, OEHHA is proposing to simply count the positive studies, OEHHA's proposed approach fails to consider all the relevant information required for a causal determination and falls well short of the scientific standard of practice for weight of evidence evaluation in toxicity determinations. A scientifically sound WOE analysis involves evaluating each study for data quality and reliability and then integrating data from all relevant studies. In contrast to a true WOE process, OEHHA's proposal makes no mention of 1) evaluating negative studies, 2) evaluating the consistency of results across different studies and over time, 3)

evaluating biological plausibility. The framework that OEHHA should employ must provide for a transparent, scientifically-based evaluation of the overall weight of evidence that a there is a relationship between an outcome of concern and exposure to a substance.

ARTICLE4 – ENVIRONMENTAL HAZARD TRAITS

Section 69404.5 – Phytotoxicity

Since this is the first time that in vitro evidence is discussed in the context of environmental hazard trait, it may be important to highlight the fact that *in vitro* approaches are not always predictive of whole organism effects for any number of reasons (*e.g.* whole organism physiology and metabolism capabilities are not always reflected in *in vitro* data). It would be useful to suggest that the text be altered throughout the document to indicate that *in vitro* data can only be used to indicate the hazard trait when it can be conclusively demonstrated that the *in vitro* effect is directly related to an apical, whole-organism effect of interest.

ARTICLE 5 – EXPOSURE POTENTIAL HAZARD TRAITS

Section 69405.7 – Particle Size or Fiber Dimension

According to the Statement of Reasons, the express intent of this is to focus on particles which may pose respiration hazard – clearly airborne nanomaterials can be respirable. However, the trait definition, itself, seems not narrowly tied to respiration. The particle description does not even mention respiration. It should be amended to add something to the effect that particles have to be free in the environment or measurably released. If opportunities for release are minimal or zero, the provision doesn't apply.

The fiber description does mention respirable, but complicates that by also citing "dermal or ingestion exposure" as concerns. This reference to "dermal or ingestion exposure" should be stricken. While getting material on skin or hand and transferring to mouth is often taken into account, size is not a defining property in the likelihood of that happening. This should not be mixed-up with the size-related respiratory hazard consideration.

Would this requirement encompass "regular" molecules? What factors would distinguish which chemicals to provide size/dimensional information on and which not?

Particle size and fiber dimension only impact deposition in the respiratory tract. Particle size or fiber dimension convey hazard only if the substance itself can cause the hazard in that they influence the deposition of the substance in the respiratory tract. Thus, particle size and fiber dimension are appropriately included in Section 69403.15 of Respiratory Hazards which states "Other relevant data include but are not limited to: *in vitro* evidence for respiratory toxicity; particle size distribution inclusive of respirable particles; respirable fibers..."

Beyond the fundamental inconsistency referenced above, the operative elements of this definition are problematic in their own right, and should be revised in the context of any consideration of particle size or fiber dimension taken into account as "other relevant data" in any of the toxicological hazard traits.

# # # # #

EXHIBIT 1

Green Chemistry Alliance

Committed to Product Sustainability in the Global Economy

September 13, 2010

Fran Kammerer
Staff Counsel
Office of Environmental Health Hazard Assessment
1001 I Street
Sacramento, CA 95812

RE: Draft Regulation for Hazard Traits & Environmental and Toxicological Endpoints (8/10/10)

Dear Ms. Kammerer:

On behalf of the Green Chemistry Alliance (GCA)* and its stakeholders, we respectfully submit the following comments and suggestions relative to the Office of Environmental Health Hazard Assessment's (OEHHA) *Draft Regulation for Hazard Traits and Environmental and Toxicological Endpoints* ("regulation") released on August 11, 2010.

In a proactive fashion, GCA members have invested countless hours over the last year and a half developing regulatory text and comments for implementing the broader framework for the Green Chemistry Initiative. This work has been the result of a focused and proactive effort by a broad array of individuals from coast to coast with science, engineering, toxicology, R&D, manufacturing and legal backgrounds and possessing significant expertise in state, national and international chemical management policy. This same group has come together to also provide insight and technical review of the draft regulations relative to hazard traits and endpoints.

Overarching Concerns

The task of chemicals management is a long-term endeavor driven by ever changing developments in science. Regardless of the resources directed toward development of data, there will always be more questions to ask and more data to gather – it is after all the nature of the scientific process.

Of all of GCA's concerns or questions, the overarching and recurring issue seems to be focused on how the information in the draft regulation will be used. It is generally unclear and disconnected from the DTSC proposed regulations and DTSC's vision for the Toxics Information Clearinghouse (TIC). The OEHHA regulations will be a critical launching point for the safer alternatives process, in particular; therefore, scrutiny needs to be employed in the development of applicable and definable hazard traits and endpoints in order to inform the prioritization process.

Although OEHHA staff has indicated a weight-of-evidence approach is envisioned for the regulation, it must be more clearly and specifically incorporated into the draft. A robust weight-of-evidence approach will give stakeholders confidence in the studies and data relied upon and feeding into the complex DTSC safer alternatives process.

GCA comments, which follow in Attachment 1, include the following items of significance:

- **Existing Systems -** a new California-only system as proposed under the draft regulation is inefficient, duplicative, and will make it unnecessarily difficult to leverage existing information on chemicals. A non-standard approach will slow the development of the TIC database and there will be a substantial agency effort required to convert the information to the unique California system, both initially and on an ongoing basis.

- **List of "icities" -** there is no need to break out systemic toxicity or target organ toxicity by specific systems as proposed in the draft regulation when the goal is hazard identification - the critical issue for chemical hazard classification should be identifying the most sensitive system(s) affected by chemical exposure.

- **Emerging Traits -** OEHHA should seek scientific consensus on the description of emerging traits and the appropriate study protocol for the endpoint(s) prior to including them in the regulation. OEHHA should not unilaterally establish definitions for new hazard traits.

- **Endpoint Lists -** Each of the toxicological and environmental traits in the OEHHA proposal is accompanied by a list of possible endpoints. However, the listings are not actual hazard traits or endpoints, but rather preludes in multiple-step pathways that may or may not lead to disease or an adverse outcome.

- **Other Relevant Information - U**se category and volume information reported via U.S. EPA's Inventory Update Rule ((IUR) should be included as part of "other relevant information."

- **Data Quality -** *In vitro* studies and QSARs are generally recognized as appropriate tools for prioritizing chemicals, but not for making definitive declarations about toxicological properties as proposed. OEHHA needs to clearly identify how certain types of data should be weighed when assessing chemical hazards, recognizing that certain types of data are less reliable than others, even when developed by authoritative bodies. OEHHA should look toward the robust study format used in the OECD's hazard assessment program and OECD harmonized templates as a model for providing information on study results and study quality.

- **Potency -** The proposal is defective as there is no indication of potency for traits which exhibit evidence of hazard. Without some indication of potency, every substance, whether synthetic or naturally occurring, will be labeled as toxic, even the "greenest" of substances. GCA recommends OEHHA look toward existing systems to understand how other bodies have handled this critical issue.

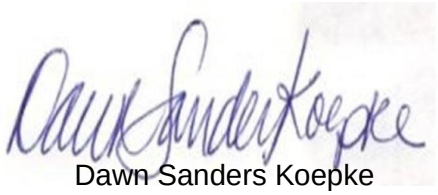
- **Classification -** The classification proposal should be abandoned entirely. SB 509 gives s OEHHA neither the mandate nor the authority to create a novel California classification system. DTSC has responsibility for what actually goes into the TIC, not OEHHA. ***The classification system is a significant overstep of OEHHA's authority.***

The Green Chemistry Alliance and its members appreciate the work OEHHA has invested in developing this draft regulation; however, GCA remains highly concerned over the breadth and direction of the draft regulation. GCA remains committed to working with OEHHA and other stakeholders to finalize reasonable and effective regulations that reflect the intent and specific requirements of SB 509 relative to the identification of hazard traits and endpoints.

GCA respectfully submits the attached comments regarding the draft *Hazard Trait, Endpoints, and Other Relevant Data* regulation (August 10, 2010). For further information or questions regarding the Green Chemistry Alliance, its members, or our comments please contact John Ulrich (916) 989-9692 or Dawn Koepke (916) 930-1993. Thank you!

Sincerely,

John Ulrich
Co-Chair
Chemical Industry Council of California



Dawn Sanders Koepke
Co-Chair
McHugh & Associates

**** The Green Chemistry Alliance*** *(GCA) has its roots in a group of business trade associations and companies that lobbied effectively during the closing weeks, days and hours of the 2008 California legislative session in support of bi-partisan measures to create a new science based framework for chemicals management. The driving force behind the legislation was a broad based desire for state regulators, rather than the legislators, to exercise their expert scientific and engineering judgment and experience when determining appropriate regulatory actions affecting chemicals of concern in consumer products. In the wake of this groundbreaking legislation, the GCA was formalized for the purpose of constructively informing the implementation effort such that the promulgated regulations remain true to the objective and scientific ideals of the authorizing legislation. GCA has strongly advocated for crafting regulations to enable the full and successful implement AB 1879 (Feuer, 2008) and SB 509 (Simitian, 2008), which will enhance public health and environmental protection, promote innovation while still respecting confidential business information, and further the principles of sustainable development.*

Green Chemistry Alliance
Signatories

Alliance of Automobile Manufacturers
American Apparel & Footwear Association
American Chemistry Council
American Cleaning Institute
American Forest & Paper Association
Amway
Association of Home Appliance Manufacturers
Association of International Automobile Manufacturers
BASF
The Boeing Company
California Aerospace Technology Association
California Chamber Commerce
California Grocers Association
California Healthcare Institute
California League of Food Processors
California Manufacturers & Technology Assoc
California New Car Dealers Association
California Paint Council
California Restaurant Association
California Retailers Association
Can Manufacturers Institute
Chemical Industry Council of California
Chevron
Citizens for Fire Safety Institute
Consumer Healthcare Products Association
Consumer Specialty Products Association
Dart Container Corporation
Defoamer Industry Trade Association
Del Monte
Dow Chemical Company
DuPont
Ecolab
Ellis Paint
ExxonMobil
Fashion Accessories Shippers Assoc
Florida Chemical Company, Inc.
Fragrance Materials Association
Goodrich Corporation
Grocery Manufacturers Association
Honeywell
Hyundai-Kia America
Independent Lubricant Manufacturers Association
Industrial Environmental Association
Information Technology Industry Council
International Sleep Products Association
Johnson & Johnson
Kern Oil & Refining Company
Koch Companies Public Sector
Metal Finishing Associations of Northern & Southern California
National Aerosol Association
National Paint & Coatings Association
National Shooting Sports Foundation (NSSF)
Northrop Grumman
OPI Products Inc.
Personal Care Products Council
Phoenix Brands
Plumbing Manufacturers Institute
Procter & Gamble
Reckitt Benckiser
Rio Tinto
SABIC Innovative Plastics
Silicones Environmental Health and Safety Council
Solar Turbines
Sporting Arms and Ammunition Manufacturer's Institute (SAAMI)
TechAmerica
Toy Industry Association
Travel Goods Association
United Technologies
Western Growers
Western Plant Health Association
Western States Petroleum Association
Western Wood Preservers Institute

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Attachment 1

Existing Systems

The Green Chemistry Alliance (GCA) is concerned that having a new California-only system as proposed under the draft regulation is inefficient, duplicative, and will make it unnecessarily difficult to leverage existing information on chemicals. For conventional hazard traits, OEHHA should harmonize as much as possible with existing international and national systems that already identify the information elements necessary to study and characterize chemicals (e.g., OECD and EPA test methods and guidelines, OECD SIDS, GHS[1]).

- Tens of thousands of tests for thousands of chemicals have been or will be performed and interpreted through these systems.
- If California wants to create a system that can be populated quickly and efficiently, these systems should be leveraged.
- Using such systems will provide a framework for things like the use of categories, tiered testing, acute vs. chronic toxicity, judging study quality/reliability, and weight of evidence approaches that are not addressed at all in OEHHA's discussion draft.
- If California proceeds with a non-standard approach, not only will the database be slow to be populated, there will be a substantial agency effort required to convert the information to the unique California system both initially and on an ongoing basis. In a resource strapped economy, that makes no sense.

List of "icities"

GCA argues that there is no need to break out systemic toxicity or target organ toxicity by specific systems as proposed in the draft regulation (*e.g.,* cardiovascular, gastrointestinal, liver, renal, *etc.*) when the goal is hazard identification. This is especially true since the critical issue for chemical hazard classification should be identifying the most sensitive system(s) affected by chemical exposure.

None of the prominent national or international systems list the vast number of "icities" in the OEHHA proposal. On the human heath side for instance, chemicals are characterized for "acute toxicity" and "chronic toxicity" (sometimes "systemic toxicity"). Organ systems impacted are noted, but there is no presumption of separate and distinct test for every organ system that the OEHHA proposal implies. The structure presented by OEHHA could be misinterpreted in such a way. Noting which organ system(s) is most sensitive is more than adequate to describe a chemical's hazard. Said differently, a single test can cover many different "icities," and the TIC should be structured in a way that makes that more apparent to users.

Emerging Traits

In the case of "emerging" traits such as endocrine disruption and epigenetics (and scores of other novel traits identified in the environment section), OEHHA should seek scientific consensus on the description of the trait and the appropriate study protocol for the endpoint(s) prior to including it in the regulation. OEHHA should be able to show that scientific consensus

[1] It should be noted that authors of the REACh legislation relied on these systems heavily, as do all countries of the OECD.

exists, or should be establishing the process for reaching that consensus where none exist, but they should not be unilaterally establishing new hazard traits.

Endpoint Lists

Each of the toxicological and environmental traits in the OEHHA proposal is accompanied by a list of possible endpoints that could demonstrate that a chemical has the respective trait. However, the hazard traits and endpoints listed are not actual hazard traits or endpoints. Rather, much of what is listed in the draft are preludes in multiple-step pathways that may or may not lead to disease or an adverse outcome (i.e., these are actually mechanisms and not endpoints; examples include epigenetic adverse perturbations and electrophilic potential). This will not further the Green Chemistry goals or provide the certainty necessary to make prioritization decisions or weigh chemical alternatives.

Other Relevant Information

Hazard information provided in the abstract is not terribly useful for people searching for alternatives, whether they are product manufacturers, DTSC staff, or lay citizens. EPA recently released a proposed rule for changes to its Inventory Update Rule (IUR) beginning with 2010 information collection. The Clearinghouse could include information reported by industry to IUR after this rulemaking is complete. Use categories and volume as reported by industry in the next round (2011) of the IUR should be integrated into the "Other Relevant Information" section of the TIC.

Further, while there is some interesting physical-chemical information that might be included as "other relevant information" in the TIC, to identify and classify chemicals based on "exposure potential" is unscientific and contrary to well established risk assessment principles.

Data Quality

In vitro studies and QSARs are generally recognized as appropriate tools prioritizing chemicals and in identifying the need for higher tier testing, not for making definitive declarations about toxicological properties as OEHHA proposes. The validity of many *in vitro* studies to human health is still in question, and they should not be the sole source of information used to assign a hazard trait to a chemical.

Additionally, *in silico* (computer simulation) QSAR is still in its infancy and should not be relied upon for definitive decisions. These methods have not been validated. All testing methods in the Draft should require validated methods. In decision-making a priority for *in vivo* rather than *in vitro* should be established in the regulation.

OEHHA needs to clearly identify how certain types of data should be weighed when assessing chemical hazards, recognizing that certain types of data are less reliable than others, even if they are developed by authoritative bodies.

- What kind of quality control and/or contextual information will accompany data and information from *in vitro* and QSAR studies? OEHHA has indicated that this is a DTSC responsibility and that they do not plan to address these issues in their regulation.

- Is DTSC prepared to develop data quality guidance (and perhaps test methods) for all of OEHHA's various toxicities?

- How and to what degree are the two agencies coordinating, given that OEHHA's actions directly impact DTSC's 1879 implementation? What implications does DTSC see for the safer alternatives process?
- The notion of study quality is not addressed in the OEHHA draft. Peer-review alone is an insufficient metric of study quality. The OECD methodology for determining the quality of data in chemical dossiers described in their *Manual for Investigation of HPV Chemicals* is a globally accepted way to rate the reliability, relevance and adequacy of existing data; as such, it should be required for every study used to populate the TIC. It has been applied to all studies in the US and OECD HPV programs and to those submitted under REACh. It has been found to be an excellent approach to separate good studies from those that are not of sufficient quality and reliability for science-based regulatory decisions.
- Data quality and weighting considerations are particularly important in the context of evaluating potential hazards associated with metabolic products and environmental breakdown products. For example, a study showing that a parent compound can be broken down to toxic metabolites under artificial conditions in a laboratory setting should not serve as the basis for assigning hazard traits unless there is evidence of such process occurring under actual environmental conditions.
- If the TIC is populated with ***ALL*** data and information in the absence of quality and reliability screens; how is any user, technical expert or lay citizen, supposed to identify what's truly relevant for making a decision? Even users with technical backgrounds will require an enormous amount of time to sift through the TIC if there are no quality control measures in place.
- Questions of data quality and quantity raise the issue of resources DTSC will need to put toward its data quality and management obligations under SB 509. What are DTSC's plans for populating the TIC, making data quality decisions, etc.? What importance will DTSC put on information generated through validated test guidelines versus other types of studies?
- OEHHA should look toward the robust study summary format used in the OECD's hazard assessment program[2] and OECD harmonized templates[3] as a model for providing information on study quality.

Potency

There is some dose level that produces an effect for every chemical. How will the TIC address the very real issue of potency before declaring that substance possesses a toxicity trait?

- The OEHHA proposal is deficient in that there is no indication of potency for the hazard traits for which there is evidence of hazard. Without some indication of potency cutoff values, every substance, whether synthetic or naturally occurring, will be labeled as toxic. As just one example, without information about the dose at which a substance causes acute toxicity, will everything in the TIC be marked as acutely toxic?

[2] See section 2.4.3 Robust Study Summaries in the *OECD Manual for the Investigation of HPV Chemicals.* See http://www.oecd.org/dataoecd/13/18/36045056.pdf.
[3] See http://www.oecd.org/document/0,3343,en_2649_34365_36206733_1_1_1_1,00.html.

- OEHHA has established a framework that will undoubtedly be misunderstood and certainly misused.
- We recommend that OEHHA look toward existing systems (see comments above) to understand how other bodies have handled this critical issue.

Classification

The classification proposal should be abandoned entirely. SB 509 gives OEHHA neither the mandate nor the authority to create a novel California classification system. DTSC has responsibility for what actually goes into the TIC, not OEHHA. The classification system is a significant overstep of OEHHA's authority into DTSC's responsibilities. Moreover, the entire classification provision is pejorative, unrealistic, and unhelpful. The OEHHA proposal does not bring clarity to chemical information. Indeed, it increases opacity on all dimensions, as evidenced by the following:

- It combines lack of information and no effect (i.e., nontoxic) into "unclassifiable." This is not reflective of the real world and is of no utility to TIC users.
- It muddies the waters by lumping distinctions made in existing systems (e.g., IARC as just one example) for no apparent reason, actually *decreasing* information available on chemicals.
- Clearly there are chemicals where the scientific data has demonstrated that the chemical lacks certain hazard traits, including some of the most important concerns such as carcinogenicity and reproductive and developmental toxicity.
- Without identifying a class for hazard traits that recognizes the lack of activity for a chemical, rather than the lack of data, the system used to classify chemicals is flawed.
- It would be impossible to identify "non-toxic" chemicals using OEHHA's proposed classification scheme. Even the "greenest" of chemicals will be classified as hazardous or "unclassifiable."
- Finally, it appears that, a chemical is categorized as having many of the toxicities listed until such time as OEHHA or DTSC determines otherwise. Furthermore, the language within (i – page 28) could conceivably allow anyone using any study design of their choosing to publish something saying chemical X has hazard trait Z, and unless DTSC or OEHHA determined otherwise, it would be so. This approach will heighten controversy and fear while doing little to advance public health or environmental protection.

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