June 13, 2011

Ms. Odette Madriago, DTSC Chief Deputy Director
Department of Toxic Substances Control
P.O. Box 806
Sacramento, CA
95812-0806

Re: Regulatory Concept Options Paper Concerning De Minimis/Unintentionally Added Chemicals AND Chemical/Product Identification and Prioritization

Dear Ms. Madriago:

The Grocery Manufacturers Association (GMA) represents the world's leading food, beverage and consumer products companies. The association promotes sound public policy, champions initiatives that increase productivity and growth and helps to protect the safety and security of consumer packaged goods through scientific excellence. The GMA Board of Directors is comprised of chief executive officers from the Association's member companies. The $2.1 trillion consumer packaged goods industry employs 14 million workers and contributes over $1 trillion in added value to the nation's economy.

GMA supports California's Green Chemistry Initiative (GCI) and advocated for the passage of AB1879 and SB509 as key elements in establishing authority to identify, assess, and manage high priority chemicals and to establish a portal for chemical safety information. We appreciate the opportunity to submit this letter in response to DTSC's May 5, 6 regulatory concept options paper concerning "*De Minimis* and Unintentionally-Added Chemicals", AND "Chemical and Product Identification & Prioritization". In keeping with goals of California's Green Chemistry Initiative of significantly reducing adverse health and environmental impacts of chemicals used in commerce, as well as the overall costs of those impacts to the state's society, by *encouraging* the redesign of consumer products, manufacturing processes, and approaches, GMA submits that a science-based process must be employed to identify, prioritize, and evaluate chemicals of concern used in products by considering not only hazard but also potential for exposure and use of the product by targeted subpopulations.

***De Minimis* and Unintentionally-Added Chemicals**[1]

Per the statute, the goal of California's Green Chemistry Initiative is to create a program that will significantly reduce adverse health and environmental impacts from chemical uses of concern.

[1] DTSC's Regulatory Concept Options Paper concerning *De Minimis*/Unintentionally-Added Chemicals - (http://dtsc.ca.gov/PollutionPrevention/GreenChemistryInitiative/upload/GRSP_SaferAlt_Reg-Concepts.pdf)

The focus of the regulations then should be on implementing a science-based process to identify and prioritize those product/chemical use combinations that contribute MOST to exposure for a targeted subpopulation (or for a targeted environmental endpoint). This leads to two important approaches to achieve that goal. First, the focus of DTSC selections of priority products would be directed at the *intentional use* of chemicals of concern that serve an intended function in the final product, and for which product manufacturers have direct responsibility and control. Second, by focusing on intentionally-added chemicals of concern in priority products above a 0.1% *de minimis* in products, DTSC would effectively prioritize uses of potential concern.

Regarding the 0.1% *de minimis* threshold, *de minimis* provisions are standard in a variety of chemical and product safety laws:

(i) Europe's REACh chemical law applies a 0.1% *de minimis* level as a default in products. REACh's 0.1% *de minimis* applies broadly, even to designated Substances of Very High Concern that become banned in Europe.
(ii) The European cosmetic law also includes a 0.1% *de minimis* level for carcinogens and reproductive toxicants.
(iii) This same level is also used in worker and transportation regulations in Europe and North America. The European Classification, Labelling and Packaging (CLP) law, which addresses over 3000 hazardous substances, contains a 0.1% *de minimis* default. The law also allows European authorities the flexibility to scientifically adjust the *de minimis* lower or higher on the basis of likelihood of harm.

Establishing a 0.1% *de minimis* for the whole product is consistent with other national and international laws and should be adopted. As analytical capabilities improve, detection limits will continue to lower detecting presence of a chemical at insignificant levels.

<u>OPTIONS</u>

For the *De Minimis* level, GMA supports Option 1A in which a default of 0.1% (w/w) is set. DTSC should be given the latitude to adjust as necessary dependent on likelihood of harm. That adjustment could consider aggregate exposure from use of the priority chemical in multiple products. Trying to determine what a "safe" *de minimis* is for every chemical/product combination would lead to paralysis of the program and delay pending implementation plans.

Regarding the concentration of a Priority Chemical (PC) in a Priority Product, user accessibility of the component part of the product containing the PC must be considered. The PC concentration should be calculated based on the accessible part. In the case of formulated products, the concentration would be based on the amount of the PC in the mixture (excluding the packaging). GMA supports Option 2A. In terms of Option 2B, any discussion of cumulative exposure and effect should be separated from *de minimis* level considerations primarily because chemicals within a mixture have to be evaluated based NOT ONLY on similarities of mode of action/biological pathway/human health and environment endpoints BUT ALSO on similarities of toxicokinetic profiles and relevant routes of exposure.[2] A simple aggregation of

[2] 1986: EPA Guidelines on Chemical Mixtures; 2000: Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures

concentrations of different chemicals in specific products does not address the complexities of the toxicokinetic/toxicodynamic profiles of chemical mixtures and would lead to gross overestimates of potential for adverse impacts.

The *de minimis* exemption should be permitted for all Priority Chemicals (Options 3A and 4A) to help create a workable and manageable program that addresses real concerns. By not allowing for a *de minimis* exemption for intentionally- and unintentionally-added ingredients, an effective prioritization process to identify chemical product use combinations of potentially significant concern would be undermined. Without an effective prioritization process, DTSC cannot assure that its efforts will be focused on achieving meaningful reductions in adverse health and environmental impacts.

Exemption should be self-implementing (Option 5A) and avoid any unnecessary, unauthorized and bureaucratically burdensome notification process. For compliance and enforcement reasons, manufacturers could be required to maintain records supporting their actions.

Chemical and Product Identification & Prioritization[3]

In order to "significantly reduce" adverse impact to health and the environment, it is essential to identify and prioritize those chemical/product use scenarios that are of real concern and contribute MOST to the adverse impact on health and the environment, and for which a viable alternative would significantly improve the overall profile to health and the environment and avoid unintended consequences.

GMA recommends that the initial Green Chemistry Initiative focus be science-based and identify chemicals known or reasonably anticipated to be CMRs in humans or PBTs based on authoritative sources such as IARC, NTP's RoC, EU REACH SVHC, EPA's TRI, Canada's CEPA-Toxic designations and others. A tiered approach in identifying "chemicals of concern (CoC)" would help maximize limited resources by focusing on those chemicals of known or presumed hazards first. In order to prioritize chemical uses of concern that are reasonable and foreseeable, a relative ranking approach is suggested, similar to the approach used in setting priorities in Canada's Chemical Management Program under CEPA.

Key steps include:

(i) For each of the chemicals on the initial set of CoCs, identify product uses from publicly available information (e.g., manufacturers' websites, government chemical/product information, Household Product Database, PCPC's International Cosmetic Ingredient Dictionary and Handbook, etc.)
(ii) Group products based on similar use profiles.
(iii) Identify the Sentinel Product(s) for each product group that represents the greatest plausible exposure scenario(s). This step provides a surrogate for use in ranking calculations.
(iv) The exposure scenario from different source contributions (i.e., every Chemical/Sentinel Product) is modeled using upper bound exposure values (rather than averages) and is specific to targeted subpopulations (age/gender)). (e.g., Chemical Exposure Priority Setting Tool)

[3] DTSC's Regulatory Concept Options Paper concerning Chemical/Product Identification and Prioritization - http://dtsc.ca.gov/PollutionPrevention/GreenChemistryInitiative/upload/Regulatory-Concepts-Chems-Prods-5-03-2011.pdf

(v) Secondary exposure through the environment is also included in the health ranking exercise.

The Ranking model generates relative quantitative ranking from high to low considering hazard and exposure. These steps will help identify the top priorities worth further consideration. The focus should remain on chemicals "used" in products to perform a certain function, and for which the product manufacturers would be directly responsible rather than unintentional constituents present at incidental levels.

OPTIONS

Section I: Chemical List Tiering and Sequencing

GMA does not support inclusion of targeted product categories or lists of priority chemicals within regulations, but rather supports the establishment of a science-based process to select these. Thus, GMA supports Options 1(1)C AND 1(2)A to develop a CoC list and Priority Chemical (PC) list, respectively, using criteria and a process set forth in regulations. Specifically, *authoritative bodies* would reflect government agencies or scientific organizations that have engaged in an open and deliberative scientific process in characterizing chemicals, that are objective, that base decisions on best available science weighted for quality accordingly, and that publish their evaluation.

Basing any priorities on available alternatives (as proposed in Option 1(2)B) would effectively initiate the Alternatives Assessment (AA) process which statutorily comes only AFTER identification and prioritization of chemical uses of concern. Establishing priorities based on available alternatives, which is not authorized in the statute, would defeat the purpose of reducing significant adverse impact to human health and the environment and the prioritization process. GMA does NOT believe that availability of safer alternatives should preclude or be part of chemical/product use prioritization scheme. Rather, once product-chemical use combinations go through a relative ranking exercise, only those identified as top priorities should be subjected to AA. This process will avoid expending resources on incremental improvements in the overall profile of a particular chemical product use combination that offer negligible opportunity for significant reduction in adverse impact to public health and/or the environment, and focus instead on those combinations for which meaningful reduction in significant impacts can be made.

Regarding factors in Option 1(2)C, many would be used in the prioritization process. However, these "chemical groupings" cannot be done in isolation, devoid of any consideration of product usage by target subpopulations. Ultimately, it is the way the product is used (which defines frequency, magnitude, nature, and route of exposure) and the chemical characteristics and potency that inform the level of concern.

Regarding some of the *non-conventional endpoints* highlighted by OEHHA[4] (as proposed in Option 1(1)A), potency cut-offs MUST be established to classify a chemical as "hazardous", and

[4] **OEHHA must address the importance of reliable information and data quality and make use of existing systems.** The OEHHA Proposed Regulation on hazard traits/toxicological endpoints for the Toxics Information Clearinghouse defines well-

the extent of hazard whether it is of high concern versus moderate versus insignificant concern. GMA supports this concept of setting cut-off values in helping prioritize chemicals as to level of concern. However, the process MUST also consider data quality (e.g., validated protocols), reliability, relevance to human health/environment (*in vitro/in vivo* correlation), and weight of evidence considerations in hazard identification/characterization. For making product safety decisions, one needs confidence that a test reliably measures an effect that is predictive of an adverse effect (with an acceptable degree of confidence). For example, *in vitro* studies may have limited potential to predict toxicity and adverse effects unless the methodology has been validated and an *in vitro/in vivo* correlation and relevance to human health has been demonstrated. OEHHA also identified "emerging hazard traits"[5], such as endocrine disruption

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conducted studies as "studies published in the open literature or conducted by or submitted to a local, state, national or international government agency, using methods and analyses which are scientifically valid according to generally accepted principles". There are several concerns with this definition. First, it is an altogether different term and definition than the "Reliable Information" concept used by DTSC in its Proposed Regulation. Second, it does not establish a discriminating method for determining the reliability of data. Third, it does not identify how data should be weighed when assessing chemical hazards. And fourth, it does not support a method for consistent presentation of information in the Clearinghouse.

Consistent definition on reliable information/data quality. The notion of "reliable information" and study quality is not addressed in the OEHHA draft other than marginally via the "well-conducted scientific studies" concept. Neither peer review alone nor submission to/conduct by an authoritative body are sufficient metrics of study quality. The OECD methodology for determining the quality of data in chemical dossiers, described in Chapter 3 of their Manual for Investigation of HPV Chemicals (OECD Secretariat, July 2007 http://www.oecd.org/document/7/0,3746,en_2649_34379_1947463_1_1_1_1,00.html), 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 Clearinghouse. It has been applied to all studies in the US and OECD HPV programs and is required for every study on all chemicals submitted under REACh (over 4300 high volume and high hazard chemicals were submitted to REACh 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. This topic must be addressed in a harmonized way by both OEHHA and DTSC in their Regulations.

Scientifically sound approach to weighing data. OEHHA needs to clearly identify how data should be weighed when assessing chemical hazards, recognizing that certain types of data are less appropriate than others, even if authoritative bodies develop them. 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. *In vitro* studies and QSARs are generally recognized as appropriate tools for prioritizing chemicals and identifying the need for more complex biological system testing, but have limits in their ability to predict risk or even identify classification of toxicological properties as OEHHA proposes. There are significant efforts underway nationally and internationally to develop alternative methods, reducing the need for unnecessary animal testing and GMA supports those programs. However, the predictability of many QSAR and *in vitro* methods to human health is still being evaluated. Results from such a QSAR or *in vitro* method should only be considered for assigning hazard traits to a chemical 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 (Guidance Document No. 69 on the Validation of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models, http://www.oecd.org/dataoecd/55/35/38130292.pdf) and regulatory acceptability (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) of QSAR models and alternative test methods for predicting biological effects and toxicity. All testing methods in OEHHA's proposed regulation should be based on national and international standard protocols or validation by an appropriate authoritative body.

[5] To date, a universal definition of what an "endocrine active substance" or "endocrine disrupter" is has yet to be agreed upon. Endocrine disruption 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 this 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

and epigenetics, which require further scientific clarification and consensus. Developing a unique to California classification system that goes beyond generally accepted systems such as GHS becomes quite resource intensive and is contrary to the objectives of the green chemistry statutes. For these reasons, any criteria and process set forth in the regulations to develop a list of CoC and PC must account for establishing appropriate potency cut-off values for any unique endpoint not currently in the GHS or EPA's Design for the Environment list of hazards.

GMA also supports the concept of including opportunities for notice and comment for public input to priority decisions. Such an iterative opportunity ensures decisions are made with the best information.

Section II: Product List and Tiering and Sequencing

Product grouping and prioritization should not be divorced from chemical prioritization. GMA supports Options II(1)C AND II(2)A in conjunction with Options 1(1)(C) and 1(2)(A) in establishing a process in the regulations laying out the criteria by which chemical product uses of concern are identified and prioritized for further evaluation. Listing certain product categories may indeed miss important sources of contribution, that would otherwise address most serious chemical concerns for targeted subpopulations (or for environmental endpoints) by identifying the most likely sources of those chemicals. As mentioned above, GMA suggests a relative ranking approach to identifying/prioritizing chemical product uses of concern.

Regarding available alternatives, GMA reiterates that considering alternatives at this initial stage would in fact invoke the process prematurely before critical chemical product uses of concern have been identified/prioritized based on likelihood of harm, which goes against that statutory requirements.

Section III: Prioritization Criteria

As mentioned previously, many of the factors listed in DTSC's Options document are relevant to identifying and prioritizing chemical product uses of concern. However, regarding the menu of other factors, neither viable alternatives NOR externalized costs should be part of that process. The statute is clear that these are considered subsequently in the Alternatives Assessment process. Additionally, cumulative exposures/effects of chemical mixtures are not currently well

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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." (EPA (2009). Endocrine Disruptor Screening Program; Policies and Procedures for Initial Screening.) EPA, which is leading the world in developing validated protocols for Endocrine Disruption, has determined that it can't classify an agent as an endocrine disrupter based on Tier 1 screening assays in its Endocrine Disruptor Screening Program. Positive results in the screening raise their priority for Tier 2 testing, but standing alone do not support a definitive classification. It's clear that this is a field of science that is in relative infancy compared with other toxicology endpoints. In addition, the relationship of certain human diseases to the endocrine system is poorly understood and scientifically controversial. Uniform and universally accepted test procedures and criteria must be established in order to evaluate the validity and quality of potential adverse endocrine effects and to identify chemicals as having or not having such traits.

On epigenetics, scientific consensus is far beyond reach. It 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. The nascent field of epigenetics is under extensive scientific investigation with a "normal" baseline undefined at this time. Thus, OEHHA should be able to show that scientific consensus exists that these areas are in fact hazard traits that are endpoints for toxicity testing, or should be establishing the process for reaching consensus and validation where none exist, but should not be unilaterally establishing endocrine disruption or epigenetics hazard traits, nor relying on non-validated test methods for their determination.

understood and should not be used as a prioritization factor. As mentioned previously, the toxicokinetic/toxicodynamic profiles of different chemicals may vary and consequently would modulate the extent to which different chemicals would impact the organism, and does not necessarily make clear synergistic/agonist or inhibitory/antagonistic behavior between chemicals.

GMA supports the more balanced approach of the first subsection of Option III(3)(C) as appropriate for prioritization criteria to identify chemical product uses of concern to target subpopulation or environmental endpoints - "Threat to human health and the environment, considering both hazard and exposure". However, we do not support the rest of Option III(3)(c). Any emphasis on externalized cost or availability of alternatives would fall outside the scope for prioritization as prescribed for in the statute. Per the statute, a process must be established to identify and prioritize those chemicals or chemical ingredients in consumer products that may be considered a chemical of concern. This process MUST include:

(1) The volume of the chemical in commerce in this state
(2) The potential for exposure to the chemical in a consumer product
(3) Potential effects on sensitive subpopulations, including infants and children

by using available information from other nations, governments, and authoritative bodies that have undertaken similar chemical prioritization processes.

Section IV. Decision-Making Process

GMA supports a quantitative relative ranking approach to identifying and prioritizing chemical product uses of concern to specified target subpopulations as explained previously. We do not support qualitative processes, which are inherently subjective. As such, a sieving process as suggested in Option IVC, in combination with a framework as suggested previously (built on the "sentinel product" concept considering both chemical and product uses together) AND application of thresholds as suggested in Option IVB, would produce a robust and scientifically sound "relative ranking" of prioritized uses of concern for further evaluation. Once again, any consideration of alternatives should be postponed until AFTER the priority-setting process.

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In summary, it is critical to have a science-based process that identifies and prioritizes the most important risks to human health and environment. Doing so ensures a workable, pragmatic, and targeted approach that will significantly reduce adverse impact to public health and the environment from CoC used in consumer products.

If you have any questions or comments, please feel free to contact me by phone at 916-447-9425 or email at JHewitt@gmaonline.org. We look forward to our continued work together on this important public policy initiative.

Sincerely,

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cc. Patty Zwarts, Deputy Secretary for Policy, CalEPA
George Alexeeff, Acting Director OEHHA
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