



April 17, 2017

Ms. Michelle Ramirez
Office of Environmental Health Hazard Assessment
Proposition 65 Implementation
P.O. Box 4010, MS-12B
Sacramento, California 95812-4010
Via email: P65Public.Comments@oehha.ca.gov; Michelle.Ramirez@oehha.ca.gov

Re: Comments on OEHHA's request for information on coumarin

Dear Ms. Ramirez,

The American Herbal Products Association (AHPA) hereby submits comments on OEHHA's March 3, 2017 request for relevant information on the carcinogenic hazards of the chemical coumarin (the March 3 Notice). The March 3 Notice states that OEHHA has selected the chemical coumarin, identified as CAS No. 91-64-5, for review by the Carcinogen Identification Committee (CIC) of OEHHA's Scientific Advisory Board for possible listing under Proposition 65 as a chemical known to the State of California to cause cancer.

AHPA is the national trade association and voice of the herbal products industry. AHPA is comprised of domestic and foreign companies doing business as growers, processors, manufacturers and marketers of herbs and herbal products. AHPA serves its members by promoting the responsible commerce of products that contain herbs. Many AHPA members do business in California and thus are subject to Proposition 65.

OEHHA should note coumarin is naturally occurring in some food plants

Under California's Proposition 65 certain warnings are required in the presence of an "exposure" to a chemical listed by the state in conformity with this law. But the law also specifies in relevant part:

"Human consumption of a food shall not constitute an 'exposure' for purposes of [Proposition 65's warning provision] to a listed chemical in the food to the extent that the person responsible for the exposure can show that the chemical is naturally occurring in the food. ... For the purposes of this section, a chemical is 'naturally occurring' if it is a natural constituent of a food...." 27 CCR § 25501(a)(1).

The law's treatment of naturally occurring chemicals in a food is relevant to the current matter because coumarin is, in fact, a "natural constituent" of some plants that come into the food supply. To cite just three examples, coumarin is reported to be a natural constituent of lavender oil (*Lavandula angustifolia* syn. *L. officinalis*), of some species of cinnamon, such as *Cinnamomum cassia*, and of sweet woodruff (*Galium odoratum* syn. *Asperula odorata*). The two former species are identified as sources of "essential oils, oleoresins (solvent-free), and natural extractives (including distillates) that are generally recognized as safe for their intended use" under U.S. federal regulations (21 CFR § 182.20); the latter is identified in federal regulation as a natural flavoring substance that may be safely used in alcoholic beverages (21 CFR § 172.510).

AHPA therefore requests that all further communications on the matter of consideration for adding coumarin to the Proposition 65 list of chemicals clearly state that coumarin is a natural constituent of some food plants, and provide a representative list of such plants. AHPA notes that OEHHA has, on several previous occasions, provided such clarifying language; for example:

- December 4, 2015: Chemicals Listed Effective December 4, 2015 as Known to the State of California to Cause Cancer: Aloe Vera, Non-Decolorized Whole Leaf Extract and Goldenseal Root Powder. This communication restated, as is noted below in the April 23, 2015 notices of intent to list these two substances and in relevant part, that "*Aloe vera*, non-decolorized whole leaf extract consists of the liquid portion of the *Aloe vera* leaf and is a natural constituent of the *Aloe barbadensis* Miller plant;" and that "Goldenseal root powder is a natural constituent of the goldenseal plant (*Hydrastis Canadensis*)." As in the April 23, 2015 notices, each of these statements included a footnote that referenced 27 CCR § 25501(a)(1), stating that "Regulations concerning naturally-occurring chemicals in foods can be found in Title 27, Cal. Code of Regs., section 25501(a)(1)."
- April 23, 2015: Notice of intent to list *Aloe vera*, whole leaf extract. This notice stated in relevant part: "*Aloe vera*, whole leaf extract, consists of the liquid portion of the *Aloe vera* leaf and is a natural constituent of the *Aloe barbadensis* Miller plant." This statement included a footnote that referenced 27 CCR § 25501(a)(1), clearly indicating OEHHA's understanding that this particular statutory provision has relevance to this specific "chemical."
- April 23, 2015: Notice of intent to list goldenseal root powder. This notice stated in relevant part: "Goldenseal root powder is a natural constituent of the goldenseal plant (*Hydrastis canadensis*)." This statement also included a footnote that referenced 27 CCR § 25501(a)(1), again clearly indicating

OEHHA's understanding that this particular statutory provision has relevance to this specific "chemical."

- March 27, 2015: Chemical Listed Effective March 27, 2015 as Known to the State of California to Cause Cancer: Beta-Myrcene. This communication itself made no mention of the fact that β -myrcene is a natural constituent of certain foods. It did, however, provide a link to public comments received by OEHHA in response to its February 2014 notice of intent to list β -myrcene and to OEHHA's responses to these public comments; the latter document is identified as, "Response to Comments Pertaining to the Notice of Intent to List β -Myrcene as Causing Cancer under Proposition 65; Office of Environmental Health Hazard Assessment California Environmental Protection Agency; March 2015." Two of the received comments raised issues related to the natural occurrence in certain foods of β -myrcene; OEHHA provided several responses to clarify the relevance of 27 CCR § 25501(a)(1), including confirming that "...food products in which β -myrcene occurs naturally would not require warning, e.g. carrots and hops...."
- February 7, 2014: Notice of intent to list pulegone. This notice stated in relevant part: "Pulegone is a natural constituent of various plants, including mint and other herbs, and of their essential oils," thus establishing OEHHA's understanding that this chemical is naturally occurring in these plants, which are readily recognized as food plants.
- February 7, 2014: Notice of intent to list beta-myrcene. This notice stated in relevant part: "Natural constituent of food plants, such as hop, bay, verbena, lemongrass, citrus, pomegranate, and carrot, and of their juices and essential oils," thus establishing OEHHA's understanding that this chemical is naturally occurring in these food plants.
- February 10, 2012. Request for relevant information on pulegone, identified at that time as a chemical being considered for listing under Proposition 65. This communication included information in its description of pulegone and in relevant part, as follows: "A constituent of pennyroyal, mint, and peppermint, and a component of certain essential oils. Used in flavoring food, drinks, and dental products, as a fragrance, and in herbal medicines." This description clearly established pulegone as naturally occurring in numerous ingredients recognized as used in food.
- February 10, 2012. Request for relevant information on beta-myrcene, identified at that time as a chemical being considered for listing under Proposition 65. This communication included information in its description of β -myrcene and in relevant part, as follows: "Component of certain essential oils, such as hop, bay, verbena, and lemongrass oils. Used to produce aroma and

flavor chemicals, as a flavoring agent in food and beverages, and as a fragrance in cosmetics, soaps, and detergents.” This description clearly established β -myrcene as naturally occurring in numerous ingredients recognized as used in food.

AHPA presents the above list as examples of OEHHA’s normal procedure to call attention, at all stages of communications on consideration for adding a chemical that is naturally occurring in a food to the Proposition 65 list – i.e., at the earliest stage of requesting relevant information, the later stage at which OEHHA’s issues a notice of intent to list the chemical, and the final communication when the agency notifies the public that a listing has occurred. AHPA does not, however, present this list as exhaustive and there may be other examples of this same normal procedure.

AHPA notes with significant concern that OEHHA did not, in issuing the March 3 Notice to request relevant information on coumarin, make any mention of the fact that this chemical is a natural constituent of some foods. AHPA notes that this oversight is inconsistent with OEHHA’s normal procedure to clearly identify chemicals that are natural constituents of one or more foods. AHPA therefore repeats its request that all further publications issued by OEHHA on this matter bring attention to this point.

Further compounding this issue is that there is an entire class of chemical compounds identified as “coumarins,” and these compounds are widely present in many plants that are used as or in human food. Should the specific chemical “coumarin, CAS No. 91-64-5” come to be added to the Proposition 65 list of chemicals, it is essential that OEHHA clearly communicate that the listing would have no regulatory impact whatsoever on any other chemical that is accurately classified as “a coumarin.”

Extant scientific publications provide inconsistent conclusions

Research has been conducted in rodent models administered very high amounts of pure or nearly pure coumarin, presumably from synthetic sources, either orally or by gavage for nearly the entire lifetime of the study animals. One such example is as follows:

National Toxicology Program. September 1993. Toxicology and carcinogenesis studies of coumarin (CAS No. 91-64-5) in F344/N rats and B6C3F₁ mice (gavage studies). Technical Report Series No. NTP TR 422. NIH Publication No. 93-3153. National Toxicology Program: Research Triangle Park, NC. *This research recorded “clear evidence of carcinogenic activity of coumarin in B6C3F₁ mice.”*

Other studies have evaluated the carcinogenic potential of coumarin in humans. For example:

- Lake BG. 1999. Coumarin Metabolism, Toxicity and Carcinogenicity: Relevance for Human Risk Assessment. *Food Chem Toxicol* 37:423-453. *This author provides an estimate of “total daily human exposure from dietary sources together with fragrance use in cosmetic products” of 0.06 mg/kg/day; compares relative rodent and human coumarin metabolic processes; and concludes that “exposure to coumarin from food and/or cosmetic products poses no health risk to humans.”*
- Felter SP *et al.* 2006. A safety assessment of coumarin taking into account species-specificity of toxicokinetics. *Food Chem Toxicol* 44:462-475. *The authors present “a quantitative human health risk assessment that integrates both cancer and non-cancer effects, which confirms “the safety of coumarin exposure from natural dietary sources as well as from its use as a perfume in personal care products;” they state further, “No carcinogenic responses have been reported in humans.”*

AHPA offers these three references as relevant to the March 3 Notice and its request for relevant information on the carcinogenic hazards of the chemical coumarin. AHPA has not, however, attempted a complete literature review, such that these references must be accepted as only a partial list of relevant articles. In AHPA’s view OEHHA’s scientific staff has the ultimate responsibility to identify and compile all relevant scientific evidence on the carcinogenic hazard of coumarin, including evidence that concludes or otherwise suggests that there is no such hazard in humans, for presentation to the Carcinogen Identification Committee.

AHPA greatly appreciates the opportunity to comment on this important regulatory issue. Please feel free to contact me if any clarification is needed on any of the issues raised in these comments.

Sincerely,

Michael McGuffin

President, AHPA

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