Natural Products ASSOCIATION™
Promoting Natural Products for Healthy Lifestyles

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June 9, 2015

Ms. Esther Barajas-Ochoa
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS-19B
Sacramento, California 95812-4010

Sent Electronically to: P65Public.Comments@oehha.ca.gov
Subject: "Notice of Intent to List Chemicals by the Labor Code Mechanism: Aloe Vera, Whole Leaf Extract and Goldenseal Root Powder"

Dear Ms. Barajas-Ochoa:

The Natural Products Association (NPA) is the trade association representing the entire natural products industry. NPA advocates for members who supply, manufacture, and sell natural ingredients or products for consumers. NPA has set numerous industry standards, such as dietary supplement Good Manufacturing Practices (GMPs), as well as a definition of natural for home care and personal care products (e.g. cosmetics). NPA, which represents nearly 2,000 members accounting for more than 10,000 locations of retailers, manufacturers, wholesalers and distributors of natural products, including foods, dietary supplements, and health/beauty aids, has led the charge to keep the natural products industry in business for 78 years. Of particular concern to the NPA membership is California Environmental Protection Agency's Office of Environmental Health Hazard Assessment's (OEHHA's) announcement on April 23, 2015 for public comment by stakeholders to list *Aloe vera* whole leaf extract and goldenseal root powder as chemicals "known to the state to cause cancer". Cosmetic and dietary supplement firms using *Aloe vera* whole leaf extract (non-decolorized) in products would be required to warn consumers in California that this ingredient has been linked to cancer. The same scenario would hold for another commonly used ingredient, goldenseal root powder.

Introduction

OEHHA's announcement states the listings are pursuant to the "labor code mechanism," which is one of four mechanisms available to the state under Prop 65 for listing chemicals. OEHHA is listing these two substances because the International Agency for Research on Cancer (IARC) classified these substances in 2013 as Group 2B, meaning they are "possibly carcinogenic to humans." The

announcement also made it clear that OEHHA "cannot consider scientific arguments concerning the weight or quality of the evidence considered by IARC when it identified these chemicals and will not respond to such comments if they are submitted." Its listing is therefore a "ministerial" act, something performed by an administrative agency according to established procedures or instructions without exercising individual judgment or discretion on the part of the agency. On behalf of NPA, thank you for the opportunity to submit comments to the OEHHA regarding their notice of intent to list *Aloe vera* whole leaf extract and goldenseal root powder in accordance with California's Labor Code listing mechanism.[1] NPA would like to comment on both the process used to list chemicals as well as the listing of these ingredients, which are used in topical formulations and food products for human consumption.

Chemicals identified in worker safety standards as carcinogens and reproductive toxicants must be listed under California's Safe Drinking Water and Toxics Enforcement Act of 1986 ("Proposition 65") without further scientific review. Prop 65 requires the State of California to compile and maintain a list of substances known to cause cancer, reproductive harm, and birth defects and to update the list annually. Listed chemicals may not be discharged into drinking water and businesses may not expose people to them without first providing a clear and reasonable warning. Currently, Prop 65 lists more than 1,000 chemicals. Prop 65 requires that the list of chemicals must include, at a minimum, the substances listed in worker safety standards set forth in California Labor Code sections 6382(b)(1) and Section 6382(d). Those standards refer to substances listed as carcinogens by IARC and substances identified as carcinogens and/or reproductive toxicants by the federal Occupational Health and Safety Administration (OSHA) in its Hazard Communication Standard (HCS), 29 C.F.R. § 1910.1200.[2] California EPA's OEHHA is notifying industry that it intends to list these ingredients because they are thought to be known to the state to cause cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65).[3] This provision of Prop 65 has henceforth come to be known as the "labor code mechanism" for listing chemicals.

<u>The "Labor Code Mechanism," a Ministerial Process for Listing Prop 65 Chemicals, is Antiquated</u>

The "labor code mechanism" is actually one of four mechanisms in Prop 65 for listing chemicals. The others include listing chemicals identified by the State's Qualified Experts, listing chemicals identified by other federal or state authoritative bodies (US FDA and EPA), and listing chemicals formally required to be listed by an agency of the state or federal governments such as prescription drugs.

[1] Health and Safety Code section 25249.8(a).
[2] OSHA standards include chemicals listed by the American Conference of Governmental Industrial Hygienists (ACGIH) and included in the National Toxicology Program Report on Carcinogens. 29 C.F.R. § 1910.1200(d)(3).
[3] Health and Safety Code section 25249.5 et seq.

The other three mechanisms involve some sort of expert evaluation of evidence, whether it comes from the state or a federal agency. NPA's issue with Prop 65's listing mechanism is that it should be done in a manner which incorporates the judgment of qualified experts in toxicological assessment, reviews the available scientific literature, and extrapolates toxicological risk (carcinogenesis, reproductive, birth defects) from animal or non-animal data to humans. A "labor code listing mechanism" is antiquated and runs counter to methods developed in the early 1990s with the adoption of principles developed from evidence-based medicine by the medical community. Californians deserve better as a "ministerial" act is akin to a reflexive action without any input, thought, or evaluation of evidence.

Listing under the "labor code mechanism" is a ministerial act and occurs without the exercise of any discretion or judgment. The individual judgment that is not exercised here is evaluation of the scientific weight and quality of the evidence related to these two ingredients. California's regulatory structure has not adopted a system of evidence-based practice, an interdisciplinary approach adopted by the rest of the medical and scientific community, in its listing of *Aloe vera* whole leaf extract and goldenseal root powder. "The labor code listing mechanism" does not allow for evaluation of any scientific evidence, judgment or experience. Evidence-based toxicology is a process being adopted in federal agencies as a system for transparently, objectively, and consistently evaluating the scientific evidence to answer questions in toxicology such as those posed by Prop 65. Historically, authors of narrative reviews assessing results of toxicological studies have searched, selected and weighed scientific evidence in a non-systematic and non-transparent way, leading to subjective interpretations that are unable to be reproduced.[4] For example, narrative reviews of polychlorinated biphenyls (PCBs) within a year of each other came to different conclusions about the cancer risk posed by these chemicals.[5] This is not an exception as carcinogenic risk reviews for other chemicals have netted opposing viewpoints.[6] Evidence-based toxicology incorporates a systematic review to synthesize the scientific literature, limit bias, and incorporate meta-analysis, to come to a generally accepted peer-reviewed judgment in the minds of scientific experts in the field.[7]

<u>Scientific Basis for Prop 65 Listing Fails to Extrapolate Toxicological Risk in an Animal Model to Humans</u>

[4] Hoffmann, S and Hartung, T. (2006). Toward an evidence-based toxicology. Hum Exp Toxicol 25: 497-513.
[5] Golden, R, Doul, J., Waddell, W., and Mandel, J. (2003). Potential human cancer risks from exposure to PCBs: a tale of two evaluations. Crit Rev Toxicol 33: 543-580.
[6] Ruden, C. (2001). The use and evaluation of primary data in 29 trichlorethylene carcinogen risk assessments. Regul Toxicol Pharmacol 34: 3-16.
[7] Stephens, M., Andersen, M., Becker, R.A., Betts, K. (2013). Evidence-based toxicology for the 21st century: Opportunities and challenges. Alt Anim Exper 30: 74-104.

In their NTP report, which serves as the basis for many of IARC's conclusions, one National Toxicology Program (NTP) study scientist characterized NTP reports as "a hazard identification rather than a risk assessment document."[8] The IARC classification of both *Aloe vera* and goldenseal root powder in 2013 was based upon toxicology studies performed by the NTP. Each year, NTP conducts toxicological evaluations on many substances. It is also no surprise that they reach similar toxicological conclusions after force-feeding animals (rodent models) high levels of the substance during their life-time. NTP also acknowledges that these findings in rodents demonstrate no risk to humans after a risk assessment has been completed. The extrapolation of animal data to humans is what federal agencies and toxicologists do to understand whether a person is at increased risk. In the NTP aloe study report[9] and goldenseal root powder report,[10] the authors state that "[t]he interpretive conclusions represented in NTP Technical Reports are based only on the results of these NTP studies." They also declare that "[e]xtrapolation of these [animal test] results to other species, including characterization of hazards and risks to humans, requires analyses beyond the intent of these reports" and "[s]election [of the substance for NTP study] per se is not an indicator of a substance's carcinogenic potential." In short, NTP does not know how their animal data extrapolates to humans. If a particular cancer is found to develop in a particular species of rodents as a result of daily ingestion of excessive amounts (100,000 times the level experienced by humans) of the substance chronically (daily consumption) over the life-time of the animal, how does that risk relate to human risk? It is difficult to know how to extrapolate data when large quantities of the substance are force-fed, typically by oral gavage dosing, to an animal on a daily basis throughout its life-time. Exposure data from that level of consumption is difficult to translate to what it means for human consumption at the serving levels recommended in the product.

NTP also provides no evaluation on whether the rodent selected for study was the most appropriate animal model, providing the best predictive comparison for applicability and extrapolation to humans. NTP chooses an animal model without any idea as to the type of tumor that may result at the conclusion of their consumption study, and this animal model may not be appropriate to predict

[8] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F344/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 13.

[9] National Toxicology Program (Boudreau, M.D. Study Scientist, et al.). (2011). Toxicology and Carcinogenesis Studies of a Nondecolorized Whole Leaf Extract of Aloe Barbadensis Miller (Alo Vera) in F344/N Rats and B6C3F1 Mice (Drinking Water Study). Natl Toxicol Program Tech Rep Ser 577. National Toxicology Program NIH Publication No. 11-5919. pp. 2.

[10] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F344/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 2.

carcinogenesis in humans. There are some rodents which are prone to develop certain types of tumors in any chronic feeding study and therefore never appropriate for extrapolation of carcinogenesis risk to humans. For example, rats are predisposed to a high incidence of tumors and cancers. Reliance on historical control data to compare uncommon neoplasms against a high background incidence of neoplasms arising from a particular rodent diet is critical. "One significant factor affecting the background incidence of neoplasms at a variety of sites is diet."[11] Because the force-fed gavage diets alone can produce neoplasms, the ministerial listing of chemicals without any regard to judgment, science or scientific inquiry would suggest that components in standard rodent diets should all be listed in Prop 65 as potentially carcinogenic to humans because of their background levels of toxicity in animal models as determined from historical data.

Addition of *Aloe Vera* to the Prop 65 List Will Create Confusion as to Which Ingredient Triggers a Warning Statement

Your notice of intent to list *Aloe vera* whole leaf extract is limited to non-decolorized form of *Aloe barbadensis* Miller, one of approximately 420 species of Aloe plants, but you do not state it explicitly or clearly. This has the effect of creating confusion within the industry because it is not clear about the ingredient referenced in your notice of intent to list *Aloe vera*. The notice should be made more precise in the language and nomenclature you use to describe which Aloe vera products are limited to this listing proposal. You list common synonyms for this plant as Barbados aloe, Mediterranean aloe, True aloe, and Curaçao aloe. Your notice also states that "[w]hole leaf extract of *Aloe vera* is commonly referred to as whole leaf *Aloe vera* juice or Aloe juice" and is "not the same as *Aloe vera* decolorized whole leaf extract, *Aloe vera* gel, *Aloe vera* gel extract, or *Aloe vera* latex, which would not be covered by this proposed listing." Since IARC's conclusions were based on positive tests in rodents using *Aloe vera* non-decolorized (non-charcoal filtered) whole leaf extract, OEHAA correctly clarified that the Prop 65 listing would be similarly restricted; however, there seems to be confusion over which terminology would be acceptable in labeling and which would prompt a clear and reasonable warning statement.

Your notice incorrectly implies that products labeled as *Aloe vera* juice or Aloe juice are carcinogenic, based upon an NTP report that a non-decolorized whole leaf *Aloe vera* extract taken internally by rats was associated with intestinal mucosal hyperplasia and carcinogenicity. The animal toxicity issue is knowing whether the Aloe whole leaf extract in the product has been decolorized and

[11] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F3rr/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 36.

treated with activated charcoal to remove the toxic latex phenolic compounds like anthraquinones. There are toxicology assessments of commercial decolorized, charcoal-filtered *Aloe vera* juice and *Aloe vera* gel drink products demonstrating a lack of gene toxicity or carcinogenicity in subchronic feeding studies of rats.[12,13,14] One study from 2013 indicated that the anthraquinone glycosides from non-decolorized preparations are responsible for colonic carcinomas and toxicity[15] because they are poorly absorbed from the alimentary tract.[16]

Use of whole leaf non-decolorized *Aloe vera* in the 2011 NTP study was unfortunate because it was not indicative of the *Aloe vera* made available by firms for the marketplace. For instance, the aloin content in the majority of *Aloe vera* leaf extract products is made negligible or very low through a decolorization (charcoal filtering with activated carbon) process, which occurs through removal of the hazardous anthrones and anthraquinones found in aloe latex. On the other hand, NTP did not process their aloe source material further. The aloin content of the NTP aloe test material was therefore between 10,000 and 13,000 ppm, forcing NTP to define their material as decolorized. NPA is concerned that the nomenclature alone on *Aloe vera* products may force a firm to warn consumers in California that this ingredient has been linked to cancer when in reality, the product is decolorized and the hazardous anthrones and anthraquinones have been removed through processing steps. Even the OEHHA notice equates decolorized whole leaf *Aloe vera* with *Aloe vera* latex and *Aloe vera* gel. What about products termed "Aloe inner filet"?

Further, while your notice limits the listing to *Aloe vera* whole leaf extract and not decolorized whole leaf extract, you also state that *Aloe vera* latex would not be covered by this proposal. The anthraquinones derived from the latex layer of *Aloe vera* are presently considered and hypothesized to be responsible for toxicity in rodent animal models. Decolorized and charcoal-filtered *Aloe vera* dramatically

[12] Sehgal, I., Winters, W.D., Scott, M., David, A., Gillis, G., Stoufflet, T., Nair, A.R., and Kousoulas, G. (2013). Toxicologic assessment of a commercial decolorized whole leaf aloe vera juice, lily of the desert filtered whole leaf juice with aloesorb. J Toxicol [Epub 802453].

[13] Williams, L.D., Burdock, G.A., Shin, E., Kim, S., Jo, T.H., Jones, K.N., and Matulka, R.A. (2010). Safety studies conducted on a proprietary high-purity aloe vera inner leaf fillet preparation, Qmatrix. Regul Toxicol Pharmacol. 57: 90-98.

[14] Sehgal, I., Winters, W.D., Scott, M., and Kousoulas G. (2013). An In vitro and in vivo toxicologic evaluation of a stabilized Aloe vera gel supplement drink in mice. Food Chem Toxicol 55: 363-370.

[15] Shao, A., Broadmeadow, A., Goddard, G., Bejar, E., and Frankos, V. Safety of purified decolorized (low anthraquinone) whole leaf Aloe vera (L) Burm. F. juice in a 3-month drinking water toxicity study in F344 rats. Feed Chem Toxicol 57: 21-31.

[16] National Toxicology Program (Irwin, R.W. Study Scientist, et al.). (2001). NTP toxicology and carcinogenesis studies of Emodin (Cas No. 518-82-1) feed studies in F344/N rats and B6C3F1 mice. Natl Toxicol Program Tech Rep Ser 493. National Toxicology Program NIH Publication No. 01-3952. pp. 5.

reduce the anthraquinones extracted from the latex layer. Therefore, as long as the commercial material uses decolorized whole leaf extract and charcoal-filtered material, an *Aloe vera* supplement should not have to require a warning statement. OEHHA's notice also does not convey clear instructions for when a warning statement is required. What happens if a product is decolorized or charcoal-filtered and labeled as *Aloe vera* juice, Aloe inner leaf, or Aloe inner filet, or Aloe gel, *Aloe vera* inner leaf juice is often referred to as inner leaf, inner filet or gel? Again NPA foresees industry confusion and requests clarification as to when firms must comply with a warning statement as there are many synonyms in use, and the non-decolorized whole leaf extract, which would contain high levels of anthraquinones, appears the actual ingredient OEHHA would like industry to limit in applying a warning statement.

<u>OEHHA's Listing of *Aloe Vera* Whole Leaf Extract Should Be Based on Anthraquinone Levels in the Product</u>

Presence of high levels of anthraquinones should be the determining factor as to whether an *Aloe vera* product requires a warning statement. If the anthraquinones are the culprit and agent of toxicity, how can labeling a supplement as *Aloe vera* whole leaf extract or *Aloe vera* juice require a Prop 65 warning statement? The vast majority of commercial *Aloe vera* preparations are processed to remove anthraquinones, so it is not clear who is being targeted to provide warning statements on their products. Based upon NTP's 2011 aloe study, their non-decolorized aloe test material contained aloin in the tens of thousands parts per million. In contrast, commercial material sold in the U.S. is far less and on the order of three orders of magnitude less as a result of responsible processing with activated charcoal. It is still unclear as to whether anthraquinone or the aglycone metabolites cause gastrointestinal toxicity. NTP hypothesized that aglycone production (e.g. emodin) resulting from anthraquinone metabolism was carcinogenic. NTP's study data on carcinogenesis of emodin in both rodent species, F344/N rats and B6C3F1 mice, turned out to be equivocal for both species, meaning the data were ambiguous, uncertain, questionable, or open to more than one interpretation.[17]

<u>OEHHA Listing of *Aloe Vera* Non-Decolorized Whole Leaf Extract and Goldenseal Root Powder Should Not Apply to Cosmetics</u>

Cosmetic companies selling topical products containing *Aloe vera* and Goldenseal Root Powder should not have to apply a warning statement. The IARC monograph, which serves as the basis for OEHHA's ministerial listing, is based upon feeding and drinking water studies of ingredient consumption

[17] National Toxicology Program (Irwin, R.W. Study Scientist, et al.). (2001). NTP toxicology and carcinogenesis studies of Emodin (Cas No. 518-82-1) feed studies in F344/N rats and B6C3F1 mice. Natl Toxicol Program Tech Rep Ser 493. National Toxicology Program NIH Publication No. 01-3952. pp. 7-8.

in rodents performed by NTP. These NTP toxicology studies do not involve topical administration. How does OEHHA view feeding study data in relation to topical administration? The two forms of administration are mutually exclusive from one another and the data from one route cannot be extrapolated to the other. It also is unclear how human carcinogenesis relates to the NTP study data from force-feeding rodents with excess amounts of the ingredient of interest. If an *Aloe vera* product involves topical administration or utilizes a decolorized, processed form of the *Aloe vera* ingredient to reduce the latex anthraquinones, it should not be required to be listed based upon the IARC monograph and NTP study data suggesting that decolorized whole leaf extracts are non-toxic.

Questionable Scientific Basis for Listing of Goldenseal Root Powder

In their toxicology and carcinogenesis study of goldenseal root powder, NTP's subchronic (3-month) study indicated hepatocyte hypertrophy in both male and female F344/N rats when force-fed 12,500 ppm goldenseal root powder or greater and cytoplasmic vacuolization of hepatocytes. The liver can enlarge as a result of ingesting common foods including alcohol consumption. The point here is that the authors did not find any carcinogenesis with the 3-month study despite force-feeding rodents large quantities of goldenseal root powder by gavage for 14 weeks straight. What was the result of their chronic 2-year feeding study in F344/N rats?

NTP investigators concluded from their 2-year feed study in rats that administration of goldenseal root powder resulted in "clear evidence of carcinogenic activity of goldenseal root powder in male F344/N rats based on the increased incidences of hepatocellular adenomas and hepatocellular adenomas or carcinomas (combined)." [18] The combination of all adenoma cases with the lone hepatocellular carcinoma case to conclude that there was *clear evidence of carcinogenic activity* is surprising. NTP study investigators suggested that "adenomas and carcinomas were considered part of a continuum of progressive lesions and the number of adenomas was driving the call."[19] Given the life expectancy of F344/N rats to be only between 2 and 3 years, the non-carcinogenic hepatocellular adenomas found at the end of their lifespan in a 2-year carcinogenesis study are unable to become carcinomas. F334/N lab rats are at their last stage of life after a 2-year bioassay of being force-fed large amounts of a substance and any suggestion that these adenomas would progress to carcinomas if they had lived another 1 or 2 years is

[18] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F344/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 13.

[19] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F344/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 13.

not scientific. Dr. Dunnick, the study scientist, noted that "the actual human intake levels are largely unknown, and also that this NTP report is a hazard identification rather than a risk assessment document." Another NTP scientist argued that "the NTP avoids including dose levels in conclusions where carcinogenic effects were seen, as often the total dose range that elicits a carcinogenic response is not known. In cases where there is no evidence of carcinogenicity, the doses are included in the conclusion statements as this is important information."[20]

In other words, NTP refuses to include the human intake levels extrapolated from their 2-year rodent studies which would indicate carcinogenicity because these human intake levels are unknown, but they typically include these human intake levels when there is no evidence of carcinogenicity in an animal model because this is important information to disseminate. It seems like the people of California and citizens of the U.S. are not getting what they paid for with taxpayer dollars used in NTP studies. What is the sense of doing hazard identification when toxicology experts refuse to opine on how their rodent feed study data applies to human consumption of that ingredient for risk assessment? IARC's use of NTP's study findings on *Aloe vera* and goldenseal root powder might be a "golden fleecing of America" when toxicologists spend federal dollars to make conclusions from warning statement, imply warning statements for human consumption, but fail to extrapolate the data to human consumption.

Naturally Occurring Exemption

It is unclear at present whether firms will have to list warnings statements on conventional food, dietary supplement, and cosmetic products containing *Aloe vera* whole leaf extract and goldenseal root powder. Prop 65 provides exemptions to warning requirements. The regulations[21] define exposure to exclude eating food that contains a listed chemical if the chemical occurs naturally in the food. Section 25501 in Title 27 of the California Code of Regulations provides that a chemical occurs naturally if it is a natural constituent of the food or if it is present as a result of absorption from the environment from which the food is raised. Both *Aloe vera* whole leaf extract and goldenseal root powder are components of foods. As such, firms should be exempt from the warning requirements for dietary supplements containing these two ingredients. The lawsuit *Nicolle-Wagner v. Deukmejian* challenged the validity of the naturally occurring regulation on the grounds it was inconsistent with Prop 65.[22] The court upheld the regulation on the grounds that Prop 65 recognized the distinction between natural and non-natural (e.g. artificial). That

[20] National Toxicology Program (Dunnick, J.K. Study Scientist, et al.). (2010). Toxicology and Carcinogenesis Studies of Goldenseal Root Powder (Hydrastis Canadensis) in F344/N Rats and B6C3F1 Mice (Feed Studies). Natl Toxicol Program Tech Rep Ser 562. National Toxicology Program NIH Publication No. 10-5903. pp. 13.
[21] California Code of Regulations, Title 27, Section 25501.
[22] Nicolle-Wagner v. Deukmejian (Superior Court Los Angeles County, no. C733003, filed Aug. 2, 1989).

decision upholding the naturally occurring regulation was appealed, but the California court of appeals affirmed the decision in May 1991.[23]

Cosmetic products containing these two ingredients should be similarly exempt from warning statements because these ingredients occur naturally in food ingredients. The naturally occurring exemption for foods should apply to products other than foods, which contain these two ingredients. Title 27 of the California Code of Regulations (§ 25501) provides that if an ingredient occurs naturally in food and the food is used in another product, such as a cosmetic, the substance is not an exposure to the extent that it occurs naturally. While the state of California did not expand the naturally occurring exemption to all substances that occur naturally in cosmetic ingredients,[24] the exemption in Title 27 of the California Code of Regulations (§ 25501(b)) does apply to cosmetic ingredients when the ingredient occurs naturally in a food ingredient. Therefore, OEHHA should clarify how the listings for these two ingredients would even apply to dietary supplements and cosmetics given that the naturally-occurring exemption would apply. NPA opposes the listing of both of these ingredients on scientific grounds and urges OEHHA to clarify their exempt status as naturally-occurring when used in either dietary supplements or cosmetics.

Summary

In summary, NPA opposes the listing of *Aloe vera* whole leaf extract and goldenseal root powder by California EPA's OEHHA. Since they are both naturally occurring in foods, they are exempt from OEHHA's warning requirements when used in either food (e.g. dietary supplements) or cosmetics, in accordance with Title 27 of the California Code of Regulations. OEHHA should remove these ingredients as proposed ingredients to be listed. If they insist on listing these ingredients, OEHHA should explain at a minimum in a future notice to industry how they would or would not fit under the naturally occurring exemption. It is unclear to NPA and industry how these ingredients would not be exempt from warning statements under the naturally occurring exemption. NPA believes these two ingredients would be exempt from warning statements when used in dietary supplements or cosmetics.

NPA also opposes the current ministerial process under the labor code mechanism for listing chemicals. This system within California's Health and Safety Code, requires OEHHA to add substances deemed human or animal carcinogens by the IARC to Prop 65. The ministerial process under California's Health and Safety Code (Labor Code) does not allow for evaluation, critical review, or judgment of the available scientific evidence. In many cases, it relies on rodent feed studies involving 2-year carcinogenesis bioassays from NTP, which extrapolates neither levels nor risk to humans. In some cases,

[23] Nicolle-Wagner v. Deukmejian (1991) 230 California App. 3d 652 [281 Cal. Rptr. 494].
[24] CTFA. Comments on Proposed Regulations. July 24, 1988, pp. 4-6.

the study can fail to use test material representative of the ingredient sold in commerce. For example, the IARC monograph concluded there was sufficient evidence of carcinogenicity in experimental animals exposed to *Aloe vera* whole leaf extract (non-decolorized). The IARC monograph was based upon a NTP study which failed to use study material representative of *Aloe vera* sold in commerce which is devoid of aloin. The OEHHA notice for comment is also not clear as to which products would be limited by the proposed listing. The OEHHA notice for *Aloe vera* seems to restrict the listing to non-decolorized whole leaf extract, but it uses other synonyms which do not clarify whether the product has been decolorized through commercial processing. NPA feels this will create great confusion in the industry unless precise nomenclature is included in the listing for *Aloe vera*. Because the *Aloe vera* listing is based upon data generated using non-decolorized material, NPA argues that the majority of *Aloe vera*-containing supplements would not have to provide a warning because the vast majority of aloe products have been commercially processed with activated charcoal to remove anthraquinones. The proposed listings should also not apply to cosmetic firms because the data was based upon feeding and drinking studies rather than topical administration. Finally, NPA finds a questionable scientific basis for the listing of goldenseal root powder because it represents *clear evidence of carcinogenic activity*. We hope that you strongly consider each point raised in these comments.

Thank you for your attention to these important matters and the opportunity to submit comments. Should you have any questions, please contact me directly at (202) 223-0101 Ext.101 or via email at Daniel.fabricant@NPAinfo.org.

Best regards,

Daniel Fabricant, Ph.D.
CEO & Executive Director, NPA