

Responses to Comments Received from the American Herbal Products Association (AHPA) Objecting to the Listing of “Areca Nut” and Betel Quid without Tobacco” as Known to Cause Cancer

**1. Comment: AHPA submitted its comments “under protest” and reiterated a request for additional time to provide comments citing a need to explore the basis for the IARC findings concerning the two substances.**

Response: The Office of Environmental Health Hazard Assessment (OEHHA) provided a 30-day public comment period on the proposed listing of “areca nut” and “betel quid without tobacco” as known to cause cancer.<sup>1</sup> In its November 8, 2005 letter to OEHHA Director Dr. Joan Denton, AHPA requested a 60-day extension of the comment period stating that the time was needed in order for it to obtain copies of the International Agency for Research on Cancer (IARC) documents that provided the basis for the listing, and that the comment period was ending four days before Christmas and Hanukkah. As outlined in Dr. Denton’s November 10, 2005 response letter to AHPA, given that OEHHA provided the documents directly to counsel for AHPA on November 10, 2005, and due to the ministerial nature of the potential listing, an extension of time to comment was not granted. AHPA also reiterated its request for more time to comment when providing its comments, but the time period for comments had ended and OEHHA did not re-open the comment period based upon this request.

**2. Comment: OEHHA’s proposal to list these substances through the Labor Code mechanism misapplies Health & Safety Code § 25249.8(a).**

Response: OEHHA disagrees with the commenter. There is no express language in the statute that would support limiting the listing requirement in the law to only the initially published list of known carcinogens or reproductive toxicants. In fact, the language in the statute is mandatory and allows no such limitation.

Health and Safety Code section 25249.8 provides that:

“On or before March 1, 1987, the Governor shall cause to be published a list of those chemicals known to the state to cause cancer or reproductive toxicity within the meaning of this chapter, and he shall cause such list to be revised and republished in light of additional knowledge at least once per year thereafter. Such list *shall include at a minimum* those substances identified by reference in Labor Code Section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d).” (Emphasis added.)

Labor Code section 6382(b)(1) refers to:

“Substances listed as human or animal carcinogens by the International Agency for Research on Cancer (IARC).”

Labor Code section 6382(d) refers to:

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<sup>1</sup> Health and Safety Code section 25249.8(a).

“... any substance within the scope of the federal Hazard Communication Standard (29 C.F.R. Sec. 1910.1200) ...”

Title 29, Code of Federal Regulations, section 1910.1200(d) provides:

“(4) Chemical manufacturers, importers and employers evaluating chemicals shall treat the following sources as *establishing that a chemical is a carcinogen or potential carcinogen* for hazard communication purposes:

- (i) National Toxicology Program (NTP, Annual Report on Carcinogens (latest edition);
- (ii) International Agency for Research on Cancer (IARC) Monographs (latest editions);
- (iii) 29 CFR part 1910, subpart Z, Toxic and Hazardous Substances, Occupational Safety and Health Administration.” (Emphasis added.)

In this case, the substances “areca nut” and “betel quid without tobacco” have been identified by IARC as known to cause cancer in humans, thus meeting the criteria in both of the referenced Labor Code sections. Specifically, in 2004, IARC issued the monograph *Betel-quid and Areca-nut Chewing and Some Areca-nut-derived Nitrosamines* (Volume 85) in its series *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. In this monograph, IARC concluded that, “Areca nut is *carcinogenic to humans (Group 1)*.” In the same monograph, IARC concluded, “*Betel quid without tobacco is carcinogenic to humans (Group 1)*.”

AHPA does not dispute that IARC specifically concludes that these two substances cause human cancer. Instead AHPA disagrees with the clear language of the statute, which requires that such substances be listed under Proposition 65 and wishes to read a limitation to the statutory language that does not exist on the face of the law.

**3. Comment: The Labor Code reference in Health and Safety Code section 25249.8 applies only to the initial list of Proposition 65 chemicals.**

Response: As noted above, Health and Safety Code section 25249.8 specifically requires that the Proposition 65 list contain, “*at a minimum,*” those substances identified by reference via the Labor Code provisions. This express statutory language does not provide discretion for OEHHA to choose not to add such substances to the list. If the drafters of the statute had intended the provision to only apply to the first list published by the Governor, they could have easily added this limitation to the statute.

Further, if the drafters of the law had intended the requirement to apply only once, it would have been logical for them to insert the purported one-time requirement after the first sentence in the paragraph that discusses the initial list. Placement of the provision concerning the Labor Code references following the requirement that the list be updated at least annually, strongly supports OEHHA’s conclusion that the list must contain the

substances referenced through the Labor Code provisions and that this requires periodic additions to the list. This is reflected by the use of the language “such list” in 25249.8(a) in referring to the annually updated list and the minimum list identified by reference in certain Labor Code sections.

The fact that the Labor Code listing process was unused for a period of time does not somehow make it invalid. Similarly, the fact that the IARC was designated as an “authoritative body” by the state’s panel of qualified experts pursuant to Title 22, Cal. Code of Regs., section 12306, does not change the purpose or effect of the express language in the statute. On the contrary, the fact that the state’s qualified experts also chose to designate IARC as an authoritative body simply reflects that IARC has demonstrated expertise in the identification of chemical hazards. The statute does not state a preference for one listing mechanism over another and none of the regulations adopted to implement and interpret the statute require that one method be used to the exclusion of others. On the other hand, as noted above, the provisions in Health and Safety Code section 25249.8 concerning references to the Labor Code are stated in mandatory terms (i.e. “Such list *shall include at a minimum* those substances identified by reference in Labor Code Section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d).” (Emphasis added.) Therefore, OEHHA’s listings under this section are ministerial in nature and are not subject to the procedural requirements adopted for the other listing mechanisms within the regulations.

**4. Comment: OEHHA’s use of the Labor Code listing mechanism is contrary to case law (*AFL-CIO v. Deukmejian*<sup>2</sup>)**

Response: AHPA’s reliance on *AFL-CIO v. Deukmejian*, for the proposition that the provisions of Health and Safety Code section 25249.8 are restricted to only the initial list of substances known to cause cancer or reproductive harm is misplaced. In *AFL-CIO v. Deukmejian*, the court was asked to determine whether the lead agency (at that time the California Health and Welfare Agency) could legally exclude from the initial Proposition 65 list published on February 27, 1987, known animal carcinogens or reproductive toxins that were identified by reference in the Labor Code. The Health and Welfare Agency had listed only the human carcinogens on the initial list and excluded known animal carcinogens or reproductive carcinogens. These were referred to the state’s Scientific Advisory Panel for review. At the time the case was filed, there had only been one (initial) list published, and therefore, the Court’s entire focus in the case was on that first list.

After the court read the statute and reviewed the ballot arguments for and against the initiative, it held that Proposition 65 did not contain any limitation in its express language that would allow exclusion of animal carcinogens or reproductive toxins from the list. The court held that “[A]ll known and probable human carcinogens identified by IARC and NTP are *presumed conclusively* by HCS [federal Hazard Communication Standard] to be carcinogens and must be included on the initial list pursuant to section 25249.8,

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<sup>2</sup> *AFL-CIO v. Deukmejian* (1989) 212 Cal. App 3d. 425

subdivision (a) and Labor Code section 6283, subdivision (d)”<sup>3</sup> (emphasis and bracketed words added). Thus, the court required the lead agency to include on the Proposition 65 list all known animal carcinogens, as well as known human carcinogens that were identified by reference in Labor Code sections 6382 subsections (b)(1) and (d).

More importantly for the present discussion, however, is the finding by the court that “...Thus, the initial list *and subsequent lists* published thereafter, need not include all substances listed under HCS but only known carcinogens and reproductive toxins listed there.”<sup>4</sup> While the Court’s discussion focuses on the content of the initial list, because that is the list that was being challenged in the case, it is clear that the Court considered the listing of chemicals by reference to the Labor Code provisions an ongoing ministerial act that does not allow the Governor or lead agency any discretion. Therefore, OEHHA must, according to both statutory and case law, continue to list chemicals or substances that are identified by reference in Labor Code sections 6382 subsections (b)(1) and (d) as known to cause cancer or reproductive toxicity.

**5. Comment: OEHHA may not delegate to IARC the inherently governmental function of listing chemicals under Proposition 65.**

Response: Health and Safety Code section 25249.8 expressly states that the Proposition 65 list must contain “at a minimum” those substances identified by reference to Labor Code sections 6382 subsections (b)(1) and (d). This provision has been part of Proposition 65 since 1987. The Labor Code section cited in the statute specifically identifies IARC by name. If a governmental function was delegated to IARC through this statutory provision, it was done so by the voters in passing Proposition 65, and the Legislature in drafting Labor Code section 6382, not by OEHHA. OEHHA is merely carrying out a ministerial act required by statute when it lists the substances identified through this provision of law.

Further, “[W]hile the legislative body cannot delegate its power to make a law, it can make a law to delegate a power to determine some fact or state of things upon which the law makes or intends to make its own action depend.”<sup>5</sup> In this instance, the people and the Legislature are relying on an internationally recognized scientific body to identify known carcinogens and reproductive toxins. In turn, that identification triggers other provisions of the law. OEHHA is the intermediary agency that performs the ministerial function of adding to the Proposition 65 list the substances identified as carcinogens and reproductive toxins by IARC pursuant to Health and Safety Code section 25249.8(a) and the referenced Labor Code provisions. Relying on IARC’s scientific findings for purposes of listing substances known to cause cancer or reproductive toxicity appears to fit the definition of a “delegation of power to determine a fact or state of things upon which the law depends”<sup>6</sup> (i.e. the identification of substances that are known to cause

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<sup>3</sup> Id. at page 437

<sup>4</sup> Id. at page 438

<sup>5</sup> *Kugler v Yocum* (1968) 71 Cal. Rptr. 687, 690; *Wheeler v Gregg* (1949) 90 Cal. App. 2d. 348, 363

<sup>6</sup> *Kugler v Yocum* (1968) 71 Cal. Rptr. 687, 690; *Wheeler v Gregg* (1949) 90 Cal. App. 2d. 348, 363

cancer or reproductive toxicity that are subject to the warning requirements and discharge prohibitions of the law).

The case cited by AHPA in its comments, *Pittston Co. v. United States*, 368 F.3d 385 (4th Cir. 2004) is not controlling on this question, and does not support the APHA's contention that OEHHA may not rely on the IARC's scientific findings as the basis for listing chemicals pursuant to Health and Safety Code section 25249.8(a). Aside from the fact that *Pittston Co. v. United States* was decided by a federal court in the Fourth Circuit (California is in the Ninth Circuit), and the fact that the case did not discuss California Law, the California legislative or initiative processes, or Proposition 65, the federal court's holding in the case allows a level of delegation by Congress that is consistent with the provisions of Health and Safety Code section 25249.8(a) that were established by the people of California through the adoption of Proposition 65.

**6. Comment: OEHHA has adopted regulatory provisions in Title 22, Cal. Code Regs. Section 12306, that detail the criteria it applies in order to determine whether a chemical has been formally identified by an authoritative body as causing cancer or reproductive toxicity. These criteria should be applied to the listing of all chemicals identified by IARC.**

Response: The listing processes governed by Title 22, Cal Code of Regs., section 12306 are based upon the provisions of Health and Safety Code section 25249.8(b), not subsection (a), which contains the references to the Labor Code. Following passage of Proposition 65 in 1986, OEHHA's predecessor, the Health and Welfare Agency, determined that it was appropriate to adopt regulations interpreting and making specific the provision of Health and Safety Code section 25249.8(b) concerning authoritative body listings. Pursuant to those regulations, the state's qualified experts, the committees of the Scientific Advisory Panel,<sup>7</sup> have identified various bodies that they consider to be authoritative for purposes of identifying chemicals that cause cancer or reproductive toxicity. The Panel may change these designations if they deem it appropriate to do so.<sup>8</sup> The Science Advisory Panel currently identifies both the IARC and the National Toxicology Program (NTP)<sup>9</sup> as authoritative bodies.

The Health and Welfare Agency apparently determined, and OEHHA agrees, that there is no need to adopt regulations for listings occurring pursuant to Health and Safety Code section 25249.8(a), because the law is clear and specific enough on its face. As noted above, Health and Safety Code section 25249.8 does not state a preference for one listing mechanism over another, and none of the regulations adopted to implement and interpret the statute require that one method be used to the exclusion of others. However, Health and Safety Code, subsection 25249.8(a)'s references to the Labor Code are stated in mandatory terms ("Such list *shall include at a minimum* those substances identified by reference in Labor Code") and are contained in a section separate from the listing

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<sup>7</sup> The Carcinogen Identification Committee and the Developmental and Reproductive Toxicant Identification Committee, established in Title 22, Cal Code of Regs., section 12302

<sup>8</sup> Title 22, Cal. Code of Regs., section 12306(b)

<sup>9</sup> Title 22, Cal. Code of Regs., section 12306(m)

provisions in Subsection (b) so if a preference was implied, it would probably in favor of the mandatory listings made pursuant to Subsection (a), over those made pursuant to Subsection (b).

It should also be noted that Health and Safety Code section 25249.8(e) expressly excludes all of OEHHA's listing activities from the requirements of the Administrative Procedure Act. Therefore, there are no statutorily required notice or comment periods for the listing of chemicals under Proposition 65. OEHHA provides a 30-day public comment period prior to listing of substances identified by reference to the Labor Code, but is not expressly required to do so by statute.

**7. Comment: The Labor Code listing mechanism should be used, if at all, only where a chemical has been listed by the Director of the Department of Industrial Relations (DIR) under HSITA (Hazardous Substances Information and Training Act).**

Response: Because the reference in Health and Safety Code section 25249.8(a) is only to two specific subsections of the Labor Code, rather than a full incorporation of HSITA, it is unlikely that the drafters of the law intended to graft HSITA's requirements or limitations into Proposition 65. It would have been quite simple to refer to HSITA in its entirety if that had been the intent of the drafters of the law. A reference to all of Labor Code section 6382 or even a reference to Labor Code section 6380 et seq., rather than only Labor Code sub-sections 6282(b)(1) and (d), would have accomplished a full incorporation of the DIR list by reference. The fact that only certain subsections of the HSITA relating to the findings of specific scientific entities were included in Proposition 65, argues against a requirement that OEHHA adopt only those substances placed on the DIR list by its director or that OEHHA adopt the entire DIR list. It should also be noted that Health and Safety Code section 25249.8(a) specifically states that it is "*those substances identified by reference*" in the Labor Code that are being discussed, and not those substances identified by the Director of DIR that are established as forming the basis of the Proposition 65 list. This reading of the statute is also consistent with the court's findings in *AFL-CIO v. Deukmejian*, which did not require a wholesale adoption the list establish by the DIR Director and instead allowed a chemical-by-chemical listing process.

As noted by AHPA in its comments, Proposition 65's warning and discharge requirements reach well beyond workplace exposures and include chemicals that may cause environmental and consumer products exposures. The primary focus of Health and Safety Code section 25249.8 is the list of chemicals and not the routes of exposure for those chemicals. The provisions of Health and Safety Code section 25249.8(a) are clear and provide a straightforward incorporation by reference of only those provisions of the Labor Code that refer to the findings of particular scientific entities that identify chemicals as known to cause cancer or reproductive toxicity, and neither require nor allow the imposition of the additional criteria that AHPA would apply to such listings.

**8. Comment: Because IARC’s evaluation was limited to chewing of these plant products, the proposed Listing must also be limited to exposures that occur through chewing of the substance.**

Response: IARC did not limit its identification to only those exposures to the substance that occur through chewing areca nut. This was clearly stated in the IARC Monograph. OEHHA staff has contacted IARC staff, who emphasized that it is areca nut that is identified as “carcinogenic to humans (Group 1).” IARC in many cases has limited its identifications to exposure circumstances. For example, 16 exposure circumstances have been identified as “carcinogenic to humans.” IARC could have identified areca nut chewing as carcinogenic, but did not do so.

The Proposition 65 list includes specific limitations in several listings (e.g., alcoholic beverages, aspirin, carbon black, ceramic fibers). In this case, however, the limitation on the listing proposed by AHPA cannot be justified. IARC clearly states its conclusion that areca nut is carcinogenic. In addition to evaluating the epidemiological data on chewing of areca nut, IARC reviewed data on areca nut and extracts given experimentally to animals via gavage, subcutaneous injection, and in the diet, and reported on cancers induced via these routes. IARC subsequently concluded there was sufficient evidence in experimental animals for the carcinogenicity of areca nut. IARC also reviewed genotoxicity and other relevant data on areca nut extracts and alkaloids and noted positive activity in numerous studies. In developing its conclusion that areca nut is carcinogenic to humans, besides the human evidence, IARC noted sufficient evidence of carcinogenicity in experimental animals, and additional strong supporting evidence.

Proposition 65 allows a mechanism to establish that no warning is required for the exposures to areca nut or betel quid without tobacco, that occur through its member’s products if the exposures are so low as to pose no significant risk.<sup>10</sup> This is a separate issue from whether the substances should be listed, however. The manufacturers and sellers of these products have one year from the date of listing of the substance to make this determination. Alternatively, AHPA may wish to request a Safe Use Determination, pursuant to Title 22, Cal. Code of Regs., section 12204, for products that contain these substances, if in fact they pose no significant risk to California consumers.

**9. Comment: OEHHA lacks authority to list an entire plant or product and must only list “chemicals.”**

Response: As noted above, Health and Safety Code section 25249.8 expressly states that the Proposition 65 list must contain “at a minimum” those *substances* identified by reference to Labor Code sections 6382 subsections (b)(1) and (d). AHPA is correct that this is the only provision within Proposition 65 that uses the term “substances” rather than “chemicals.” The common definition of the term “substance”<sup>11</sup> would certainly include materials such as areca nut or betel quid without tobacco. AHPA states that some

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<sup>10</sup> Health and Safety Code section 25249.10(c) and Title 22, Cal. Code of Regs., section 12701

<sup>11</sup> “a. Something that has mass and occupies space; matter. b. A material of a particular kind or constitution.” *The American Heritage Dictionary*, 2<sup>nd</sup> College Edition, 1989, page 678.

chemical components of areca nut or betel quid may be proper subjects of listing, but plant parts themselves cannot be listed. AHPA notes IARC's discussion of the hypothesis that during the chewing of betel quid, nitrosation of arecoline, the major alkaloid of areca nut, produces NGL [N-nitrosoguvacoline] and MNPN [3-methylnitrosaminopropionitrile]. While the evidence for some areca nut constituents may be adequate for listing under Proposition 65, this does not preclude the listing of areca nut.

“Chemical” is not defined by the Act and several substances that are mixtures of chemicals are on the Proposition 65 list as known to cause cancer or reproductive toxicity under Proposition 65, including: bracken fern, diesel engine exhaust listings;<sup>12</sup> herbal remedies containing plant species of the genus *Aristolochia*, soots, tars and mineral oils, and coke oven emissions;<sup>13</sup> tobacco smoke (for cancer), tobacco smoke (primary) (for reproductive toxicity) and unleaded gasoline (wholly vaporized).<sup>14</sup> The particular components in these mixtures thought to cause the cancer or reproductive toxicity were not identified in the listing. In addition to mixtures, numerous single chemical compounds are on the Proposition 65 list. In the event that future research establishes that a single chemical or chemicals within these mixtures are the only carcinogens or reproductive toxicant in the substance, OEHHA can narrow the listing as appropriate at that time.

**10. Comment: If “Areca Nut” is listed, it will be more difficult for product manufacturers to prove that the substance is “naturally-occurring” in their products.**

Response: Title 22, Cal. Code of Regs., section 12501 concerning naturally occurring chemicals, only applies to chemicals in food and only to the extent that the business can show that the chemicals in the areca nut products do not result from any known human activity.<sup>15</sup> Given that this provision is limited to foods and that areca nut is apparently intentionally added to the products by the manufacturers, it is highly unlikely that this regulation could be used to avoid providing a warning.<sup>16</sup> Further, if the substance were considered a contaminant, the manufacturer would also have to show that it has been reduced to the “lowest level currently feasible.”<sup>17</sup>

**11. Comment: At most, OEHHA should only list specific parts of the Areca Nut under Proposition 65.**

Response: OEHHA has proposed the listing of “areca nut” based upon its identification in the IARC document. The concerns noted in the comment about potential enforcement actions based upon a misunderstanding of the scope of the listing are remote and

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<sup>12</sup> Listed under the Authoritative Bodies mechanism

<sup>13</sup> Listed via the Labor Code

<sup>14</sup> Listed by the State's Qualified Experts

<sup>15</sup> Title 22, Cal. Code of Regs., section 12501(a)(3)

<sup>16</sup> *Bryan Nicolle-Wagner v George Deukmejian* (1991) 230 Cal. App. 3d. 652

<sup>17</sup> Title 22, Cal. Code of Regs. section 12501(a)(4)

speculative at best. To address this concern, however, OEHHA will include further clarification in the Notice announcing the addition of areca nut to the Proposition 65 list, emphasizing that it is the nut and not other elements of the plant (such as the husk) that is being listed under Proposition 65.