Pulegone

May Not be Listed as a Proposition 65 Carcinogen

Pursuant to the Labor Code Listing Process

Comments of

Flavor and Extract Manufacturers Association

Consumer Healthcare Products Association

International Chewing Gum Association

International Fragrance Association, North America

National Confectioners Association

and

Personal Care Products Council

Submitted to the
Office of Environmental Health Hazard Assessment

by

Gary M. Roberts
F. Jay Murray

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I. Introduction

OEHHA's proposal to add pulegone to the Proposition 65 list of chemicals "known to cause cancer," pursuant to the "Labor Code listing mechanism" found in California Health & Safety Code section 25249.8(a), is not based upon sufficient information and should be withdrawn. Through these comments, the Flavor and Extract Manufacturers Association, the Consumer Healthcare Products Association, the International Chewing Gum Association, the International Fragrance Association, North America, the National Confectioners Association, and the Personal Care Products Council (the "Associations") oppose the Proposition 65 listing of pulegone and submit that OEHHA is obligated to withdraw the February 7, 2014, Notice of Intent to List pulegone.

OEHHA's proposed action is based upon two unexplained conclusions that recently were announced by the International Agency for Research on Cancer (IARC): first, IARC's classification of pulegone as a "Group 2B" carcinogen; and, second, IARC's conclusion that "sufficient evidence of carcinogenicity in experimental animals" exists for pulegone. These two bare conclusions, without sufficient information on their *basis,* are not adequate grounds upon which to list a chemical such as pulegone as a matter of law.

OEHHA cannot proceed to list pulegone at this time for four independent reasons. First, Proposition 65 incorporated the IARC standard for “sufficient evidence” that existed in November 1986, and IARC has changed the "sufficient evidence" standard for carcinogenicity in animals. Because IARC has adopted new, more permissive criteria for sufficient evidence, a current sufficient evidence conclusion

cannot and should not be used, by itself, as the basis for Labor Code listings. As a matter of law, OEHHA must confirm, without controversy, that IARC's conclusion under the new criteria would have been the same under the old criteria adopted by specific reference in Proposition 65. OEHHA has not done this for pulegone. Anything less than this confirming analysis would represent an unauthorized amendment to Proposition 65 or an unauthorized delegation of authority to IARC.

Second, the evidence on which OEHHA relies is not adequate to demonstrate that pulegone is a *"known"* animal carcinogen, and only "known" animal carcinogens may be listed through the Labor Code.

Third, the Director of the Department of Industrial Relations has not yet "identified" pulegone as a hazard, which is necessary for a listing to proceed under section 25249.8(a).

Fourth, OEHHA has not adequately explained or substantiated its conclusion that pulegone warrants listing through the Labor Code listing mechanism. Not all IARC "Group 2B" chemicals may be added to the Proposition 65 list pursuant to the Labor Code listing mechanism. *See Styrene Information and Research Center v. OEHHA*, 210 Cal.App.4th 1082, 1088 (2012). Only "known carcinogens" can be drawn from the Labor Code sources and placed on the Proposition 65 list. *Id.* at 1094. OEHHA has not proffered sufficient evidence to conclude that pulegone has been identified by IARC as a "known carcinogen."

These four independent reasons mandate that OEHHA withdraw its February 7, 2014 Notice and analyze IARC's explanation and reasoning for its conclusions before proceeding in its process to list pulegone under Proposition 65.[1]

When Proposition 65 was enacted by the voters in 1986, IARC's standard for "sufficient evidence" in animals was more stringent than it is today. This higher standard still must apply to current Labor Code listings because it was incorporated by specific reference in Proposition 65. *Palermo v. Stockton Theaters*, 32 Cal.2d 53 (1948). Four significant aspects of IARC's 1986 "sufficient evidence" standard have either been removed or weakened in the current sufficient evidence criteria that IARC applied to pulegone. OEHHA must analyze the IARC Monograph on pulegone to determine whether IARC's evaluation of pulegone readily demonstrates that it would have satisfied the 1986 standard. At this time, nothing is known about the rationale for IARC's action other than pulegone "caused liver tumours in mice."[2] And, that information is not enough to list a chemical pursuant to the Labor Code listing mechanism because not all chemicals that cause liver tumors in mice would have been identified as having "sufficient evidence" of carcinogenicity in animals under the 1986 IARC criteria for assessing animal carcinogenicity.

[1] The Associations also oppose the listing of pulegone because the Labor Code listing mechanism was intended only to form the initial Proposition 65 list, for the reasons expressed by the California Chamber of Commerce in its case, but the Associations recognize that there currently is a controlling Court of Appeal decision on that point. None of the Associations' four grounds noted above in the text for submitting that OEHHA must withdraw the February 7 Notice are inconsistent in any way with the Court's holding in *California Chamber of Commerce v. Brown*, 196 Cal.App.4th 233 (2011).

[2] Grosse, Y, *et al*. "Carcinogenicity of some drugs and herbal products," *The Lancet Oncology* (vol. 14; pp. 807-808; 2013).

II. The IARC "Sufficient Evidence" Standard has Materially Changed Since Proposition 65 was Enacted

The IARC criteria for "sufficient evidence of carcinogenicity in animals" has materially changed from 1986 to today. These material changes are directly relevant to pulegone and combine to create a less stringent standard that moves away from what is a "known carcinogen."

First, the 1986 standard specifically identified liver tumors in mice as indicative of "limited" rather than "sufficient" evidence of carcinogenicity, and that language does not appear in the current criteria. Second, the 1986 IARC criteria for "limited evidence," as opposed to "sufficient evidence" also included animal studies characterized by "inadequate dosage levels . . . [and] poor survival." Again, the current criteria do not articulate this factor. The rat study of pulegone was marred by excessive morbidity and mortality; the only dose at which tumor incidence was elevated in rats greatly exceeded a proper maximum tolerated dose (MTD). Third, the IARC criteria put more emphasis on malignant tumors in 1986. The “sufficient evidence” criteria was “there is an increased incidence of malignant tumours.” There is no mention of benign tumors or combined malignant and benign tumors. In contrast, the “sufficient evidence” criteria applied to pulegone in 2013 was “a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms.” For pulegone specifically, under the current criteria, it would be appropriate to combine hepatocellular adenoma and carcinoma. But, this would not have been true under the 1986 criteria. Fourth, the 1986 criteria require tumor increases in "multiple species or strains . . . or multiple

experiments," and the current criteria permit a finding of sufficient evidence if only one experiment in one strain or species is positive in both sexes.

None of these four important changes in the IARC criteria for sufficient evidence has been described by OEHHA as based on "additional knowledge;" indeed, such a description does not appear warranted. For example, additional knowledge has continued to consider mouse liver tumors more inadequate than sufficient,[3] and continues to express concern for exceeding the MTD.[4]

When Proposition 65 was enacted by the voters in November 1986, the IARC standard for "sufficient evidence of carcinogenicity" in "experimental animals" was as follows:

> *Evaluation of carcinogenicity studies in experimental animals*: The evidence of carcinogenicity in experimental animals is assessed by the Working Group and judged to fall in to one of four groups, defined as follows:
> (1) *Sufficient evidence* of carcinogenicity is provided when there is an increased incidence of malignant tumours: (a) in multiple species or strains; or (b) in multiple experiments (preferably with different routes of administration or using different dose levels); or (c) to an unusual degree with

[3] Expert opinion continues to express serious concern as to the relevance of mouse liver tumors. No additional knowledge justifies elevating the importance of liver tumors in the "known" animal carcinogen analysis. Carmichael NG, Enzmann H, Pate I, Waechter F (1997). The significance of mouse liver tumor formation for carcinogenic risk assessment: results and conclusions from a survey of ten years of testing by the agrochemical industry. Environ Health Perspect 105(11):1196-1203. EFSA (2011). European Food Safety Authority; EFSA Statement on the scientific evaluation of two studies related to the safety of artificial sweeteners (question no EFSA-Q-2011-00064, approved on 25 February 2011 by European Food Safety Authority). EFSA J 9(2):2089 [16 pp.]. doi:10.2903/j.efsa.2011.2089. Available at: http://www.efsa.europa.eu/en/efsajournal/pub/2089.htm. Commonwealth of Australia, 2000. National Industrial Chemical Notification and Assessment Scheme (NICNAS), December 2000, Commonwealth of Australia, 134 pp. Holsapple, M.P., Pitot, H.C., Cohen, S.M., Boobis, A.R., Klaunig, J.E., Pastoor, T., Dellarco, V.L., Dragan, Y.P., 2006. Mode of action in relevance of rodent liver tumors to human cancer risk. Toxicol. Sci. 89, 51–56. Billington R, Lewis R.W, Mehta J.M, Dewhurst I (2010). The mouse carcinogenicity study is no longer a scientifically justifiable core data requirement for the safety assessment of pesticides Crit Rev Toxicol 40(1):35-49. Cohen S.M., Klaunig J., Meek M.E., Hill R.N., Pastoor T., Lehman-McKeeman L., Bucher J., Longfellow D.G., Seed J., Dellarco, V. 2004. Evaluating the human relevance of chemically induced animal tumors. Toxicol. Sci. 78: 181–186.

[4] The Associations have not identified additional knowledge that has elevated the significance of tumors observed in excess of the MTD or in the context of poor survival. U.S. EPA (2005) Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. March, 2005, p. 2-16.

> regard to incidence, site or type of tumour, or age at onset. Additional evidence may be provided by data on dose-response effects.
> (2) *Limited evidence* of carcinogenicity is available when the data suggest a carcinogenic effect but are limited because: (a) the studies involve a single species, strain or experiment; or (the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) the neoplasms produced often occur spontaneously and, in the past, have been difficult to classify as malignant by histological criteria alone (e.g., lung adenomas and adenocarcinomas and liver tumours in certain strains of mice).[5]

In contrast, the standard for "sufficient evidence of carcinogenicity" in "experimental animals" that IARC applied to pulegone in 2013, is different from the 1986 standard in several material respects:

> *Carcinogenicity in experimental animals*: Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multi-stage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.
>
> The evidence relevant to carcinogenicity in experimental is classified into one of the following categories:
>
> ***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

[5] *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 41, p. 18 (1986).

> A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.
>
> ***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g., (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or neoplasms of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.[6]

These two different standards for what constitutes "sufficient evidence" make it clear that certain animal carcinogenicity results considered "sufficient" in 2013 would have been considered "limited" rather than "sufficient" in 1986. Accordingly, OEHHA must wait to review the IARC analysis in the Monograph in order to determine whether it may list pulegone through the Labor Code mechanism. *Cf. Western Crop Protection Ass'n v. Davis*, 80 Cal.App.4th 741, 746-749 (2000).

The Associations request that OEHHA withdraw the February 7 Notice and wait to review and analyze the IARC Monograph before proceeding to finally determine whether the proposed listing of pulegone is appropriate. Doing so is especially critical for pulegone because the available animal carcinogenicity data plainly constitute only "limited evidence," not "sufficient evidence," under the applicable 1986 criteria. Moreover, OEHHA's own 2008 proposal concerning Labor Code mechanism-based listings noted that OEHHA would await the "published" IARC Monograph document.[7]

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[6] *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 106, p. 26 (2013) (cited by OEHHA in the February 7, 2014 Notice of Intent to List pulegone).

[7] OEHHA, "Request for Public Participation, Notice of Public Workshop, Proposition 65 Regulatory Update Project. Labor Code Mechanism Regulatory Concept." May 16, 2008.

Pulegone has been tested for carcinogenicity in one NTP study of B6C3F1 mice and F344/N rats.[8] Normally, "sufficient evidence" only would arise under the 1986 criteria if malignant tumors were increased in multiple species, multiple strains or multiple experiments (preferably with different routes of administration or using different dose levels). The NTP Technical Report found no evidence of carcinogenic activity in male rats. In female rats, the NTP Technical Report noted that there were "increased incidences of urinary bladder neoplasms." These increased urinary bladder neoplasms, however, only were observed at the 150 mg/kg/day dose, a dose at which the NTP was forced to stop administration of pulegone at 60 weeks, rather than the planned 102 weeks, and a dose for which none of the female rats survived to the conclusion of the study. At 60 weeks, this female dose group weighed 79% of controls, making the dose of pulegone administered well above a proper maximum tolerated dose.[9] Furthermore, IARC may well have further discounted the bladder tumors in female rats as secondary to renal disease, rather than as attributable to the carcinogenicity of pulegone.[10] Given these data, it is highly unlikely that the IARC Monograph, when published, will support a "sufficient evidence" finding under the 1986 criteria.

Similarly, the liver tumors in female mice were benign and only significantly increased at an excessively high dose that dramatically exceeded the MTD. The average body weight of female high-dose mice was 75% of the control mean during weeks 53 to 101 of the study. It is unknown how much weight IARC attributed to an increase in tumors at a dose that exceeded the MTD or even whether IARC considered

[8] NTP Technical Report 563, August 2011.
[9] US EPA, "Guidelines for Carcinogen Risk Assessment," March, 2005, pp. 2-16 to 2-18.
[10] S.M. Cohen, *et al*., "Investigations of rodent urinary bladder carcinogens: Collection, processing, and evaluation of urine and bladders." Toxicol. Pathol. 35, 337-347 (2007); M.S. Da Rocha, *et al*., "Mode of action of pulegone on the urinary bladder of F344 rats." Toxicol. Sci. 128(1):1-8 (July 2012).

the high dose in this study to be scientifically valid testing since the NTP missed so badly in its dose selection.

In sum, the IARC Monograph is likely to reveal that the pulegone animal data would not have satisfied the 1986 IARC "sufficient evidence" criteria for a variety of reasons, including: (1) the inherent lack of confidence that experts place in mouse liver tumors, (2) the dose level dramatically exceeding the MTD in rats and female mice, and (3) the lack of dose response in male mice.[11] While OEHHA may have an opinion on the relevance of these factors with respect to pulegone, IARC's opinion won't be known until the IARC Monograph is published. The IARC Monograph discussing pulegone has not yet been published; pulegone will be discussed in volume 108, and volume 106 is the most recent volume that has been published.[12] OEHHA may not substitute its scientific judgment for that of IARC with respect to a proposed Labor Code listing.

Supplement 7 to the IARC Monographs reflects chemical assessments performed by IARC in March 1987, shortly after Proposition 65 was passed. This Supplement contains numerous examples of chemicals that induced liver tumors in mice but were then judged by IARC to only have "limited" rather than "sufficient" evidence of carcinogenicity. Addressing these chemicals alphabetically, aldrin is the first such example. In 1987, under the IARC criteria then in place, aldrin was noted to have only "limited" rather than "sufficient" evidence of carcinogenicity in animals even though, in mice, it "produced malignant liver neoplasms."[13] Liver neoplasms also resulted in only a "limited" evidence classification for cholrdane/heptachlor.[14]

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[11] The Associations fully incorporate their April 10, 2012, comments in support of these comments.
[12] *See* http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php (accessed March 4, 2014).
[13] IARC Monographs, Supplement 7, p. 88 (1987).
[14] *Id*. at 146-47.

One of the best examples of a chemical that produced liver tumors in mice and then was judged by IARC to have “limited” rather than “sufficient” evidence of carcinogenicity is trichloroethylene, which also was reviewed in Supplement 7 to the IARC Monographs.[15] Trichloroethylene was classified by IARC as Group 3, and the evidence for carcinogenicity to animals was considered “limited.” This example is especially instructive because IARC concluded that trichloroethylene produced not only hepatocellular carcinomas in male and female mice, but also lung tumors in male and female mice: “In mice, [trichloroethylene] produced hepatocellular carcinomas and lung tumours in both males and females.”[16] IARC’s criteria at the time the evaluation of trichloroethylene was conducted led IARC to conclude that there was only “limited” evidence of carcinogenicity. Under IARC’s current criteria, it is clear that trichloroethylene would be assigned “sufficient” evidence based on the same data.

III. California Law Prohibits the Listing of Pulegone Based on Section 25249.8(a) at this Time

OEHHA cannot add pulegone to the Proposition 65 list of "known carcinogens" at this time. First, California law requires that section 25249.8(a)[17] listings be based on the 1986 IARC "sufficient evidence" criteria. It is not possible now to determine for pulegone whether these criteria have been met because the IARC Monograph for pulegone has not yet been published. Second, even if one assumes that it is permissible to use the current IARC criteria, California law only permits "known carcinogens" to be added to the Proposition 65 list. OEHHA's Notice of Intent to List pulegone does not establish that pulegone has been identified as a "known carcinogen,"

[15] *Id.* at 364-366.
[16] *Id.* at 364
[17] All references to section 25249.8(a) are to the California Health and Safety Code.

and, indeed, that determination is not possible at this time because the IARC Monograph for pulegone has not yet been published. Third, because section 25249.8(a) refers to Labor Code section 6382(b)(1) rather than directly to IARC, one must infer that there was a purpose to the Labor Code reference, namely, awaiting a hazard ruling from the Director of the Department of Industrial Relations.

A. Section 25249.8(a) specifically incorporated the 1986 IARC standard for "sufficient evidence" and only permits new listings based on "additional knowledge," not changed criteria

Section 25249.8(a) specifically refers to certain Labor Code provisions. These Labor Code provisions, in turn, specifically refer to certain IARC and federal HCS standards and provisions. When a statute specifically refers to another statute or rule, the referenced provision that is incorporated into California law is what existed at the time of incorporation, absent a clear intent to the contrary. *Palermo*, 32 Cal.2d at 58-59.[18] Under California law, OEHHA must utilize the 1986 IARC criteria for sufficient evidence when supplementing the Proposition 65 list through section 25249.8(a).

1. Section 25249.8(a) specifically incorporated Labor Code section 6382(b)(1) and the 1986 IARC Criteria

The analysis of whether or not there has been a specific incorporation begins with the language of the relevant provisions. Section 25249.8(a) of Proposition 65 states:

> "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 . . . 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

[18] As discussed below, "where the reference is general instead of specific, such as a reference to a system or body of laws or to the general law relating to the subject in hand, the referring statute takes the law or laws referred to . . . as they may be changed from time to time." *Palermo*, 32 Cal.2d at 59.

> 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)."

These are clearly specific references that incorporated the relevant Labor Code provisions as of the date of incorporation. *See People v. Domagalski*, 214 Cal.App.4th 1380, 1385 (1989) ("Without exception, in each case where a statute, or some portion of it, was incorporated by reference to its section designation, the court found the reference to be specific.").

Similarly, the Labor Code reference to "Substances listed as human or animal carcinogens by the International Agency for Research on Cancer (IARC)," was a specific reference to IARC's criteria for carcinogenicity. The 1986 criteria for carcinogenicity were articulated clearly in twelve pages of materials in the "Preamble" to the IARC Monographs. These criteria were comprised of two main sections, "General Principles Applied by the Working Group in Evaluating Carcinogenic Risk of Chemicals for Complex Mixtures," and "Explanatory Notes on the Contents of Monographs on Chemicals and Complex Mixtures."[19] These sections are not legally distinguishable from, and indeed are more specific than, "title IX of the Political Code," which was held to be specifically incorporated (thus limiting it to the language on the date of incorporation), and which at the time of incorporation "contained 11 chapters and 200 sections." *In re Oluwa*, 207 Cal.App.3d 439, 445 (1989) (discussing *Rancho Santa Anita v. City of Arcadia*, 20 Cal.2d 319, 322 (1942)). Title IX of the California Political Code was incorporated by the City of Arcadia into one of its ordinances, and the Court held that subsequent amendments to title IX were not part of the Arcadia ordinance at

[19] See, e.g., IARC Monographs, Volume 41, pp. 15-27.

issue because the incorporation was specific and not general. *Rancho Santa Anita*, 20 Cal.2d. at 320-21. The reference to known carcinogens identified by IARC is no less specific.

The Ballot Pamphlet makes the incorporation of the 1986 IARC criteria for carcinogenicity even more plain. "At a minimum, the Governor must include the chemicals *already listed* as *known carcinogens* by two organizations of the most highly regarded national and international scientists: the U.S.'s National Toxicology Program and the U.N.'s International Agency for Research on Cancer."[20]

In contrast, the cases where a "general reference" has been found have been much less specific, such as "all the provisions of law in force regulating elections," and have been found to be "reference to a system or body of laws or to the general law relating to the subject at hand." *In re Oluwa*, 207 Cal.App.3d at 445 (discussing general law and *Kirk v. Rhoads*, 46 Cal. 398, 402 (1873)).[21] Moreover, the Associations did not identify a "general reference" to an *external* (i.e., non-California) body of law where a Court held that changes outside California could directly impact California law.

Section 25249.8(a) has been held to anticipate change because it says that the initial Proposition 65 list must be "revised and republished in light of additional knowledge at least once per year." *California Chamber of Commerce*, 196 Cal.App.4th at 258. The Associations anticipate that this phrase might be considered by some to permit changes to the IARC criteria that can be established to have resulted from "additional knowledge." There are at least two reasons why the "additional knowledge"

[20] Ballot Pamphlet, Argument in Favor of Proposition 65, page 54 (1986) (emphasis added).
[21] *See also In re Jovan*, 6 Cal.4th 801, 807-812, 816-819 and Court decisions (finding the phrase "plus enhancements," along with the overall context of various legislative enactments and Court decisions, to be a general reference to a body of law designed to align youth and adult sentencing, and thereby allowing a court to use a statutorily approved adult prison term as the basis to detain a youth who threatened a witness against him).

phrase cannot support OEHHA moving forward on pulegone. First, allowing IARC to change the *criteria* for what constitutes a "known carcinogen" in California would be an impermissible delegation of legislative authority, as discussed below. Second, OEHHA has made no determination that the changes in the IARC criteria relevant to pulegone were based on "additional knowledge," as opposed to changes in policy. It is arbitrary and capricious for OEHHA to assume, or to conclude without providing a reasoned explanation, that every aspect of the current IARC criteria for sufficient evidence of carcinogenicity in animals is the result of "additional knowledge" rather than changes in IARC policy.

2. Only specific incorporation of the 1986 IARC criteria avoids impermissible delegation of authority to IARC

The Associations submit that Proposition 65 did not and could not delegate to IARC the power to redefine what constitutes a "known carcinogen." Since IARC does not specifically identify "known" animal carcinogens, nor did it do so in 1986, the IARC standard for "sufficient evidence" at the time of the ballot measure must be used to list chemicals pursuant to section 25249.8(a). Any other result would impermissibly delegate to IARC authority to redefine what is "known to the state to cause cancer."

OEHHA should resist here an approach to Proposition 65 that raises grave doubts about the electorate's ability to delegate the definition of a "known carcinogen" to IARC in the same way that the Court in *Palermo* resisted an interpretation of California law that would have delegated "to the treaty-making authority of the United States the right and power thus directly to control our local legislation with respect to future acts." *Palermo*, 32 Cal.2d at 59-60. ""[T]he attempt to make *future* regulations of another jurisdiction part of the state law is generally held to be an unconstitutional delegation of

legislative power." *Brock v. Superior Court*, 9 Cal.2d 291, 297 (1937) (emphasis in original).

Impermissible delegation is a particularly strong concern when the purported delegation is to another jurisdiction. In *People v. Kruger*, (1975) 48 Cal.App.3d Supp. 15, defendant was convicted of unlawfully possessing on board his vessel an amount of yellowfin tuna in excess of 15% of his total catch in violation of the California Administrative Code pursuant to Title 50, Code of Federal Regulations, Section 280.7-b-2, which regulated yellowfin tuna. *Id.* at 16. The relevant state law provided that the State Fish and Game Commission "'may prohibit the taking or processing of tuna in the same manner as taking or possessing tuna is prohibited by federal law or by rules or regulations adopted pursuant to the Tuna Conventions Act of 1950.'" *Id.* at 18. The State Commission then adopted the following regulation: "'The regulations adopted pursuant to Title 50, Code of Federal Regulations…Sections 280.1 through 281.12, issued under…16 USC (s) 951, and adopted and filed on June 11, 1968, *and as such regulations may be revised or amended in the future*, relating to the taking and possession of yellowfin tuna are hereby adopted and made part of this Title 14…." *Id.* at 18 (emphasis added). The Court reversed judgment against defendant because, among other reasons, the "prospective incorporation" of statutes not yet in existence "has never been approved." *Id.* at 19. The Court cited to *Brock*, reciting the rule that "'It is, of course, perfectly valid to adopt Existing statutes, rules, or regulations of Congress or another state, by reference, but the attempt to make Future regulations of another jurisdiction part of the state law is generally held to be an unconstitutional delegation of legislative power.'" *Id.* (quoting *Brock v. Superior Court*, 9 Cal.2d 291, 297 (1937)) (emphasis through capitalization in original).

3. Specific incorporation of the 1986 IARC criteria does not conflict with recent cases addressing section 25249.8(a)

Both courts of appeal that have grappled with section 25249.8(a) have noted the *Palermo* rule: "where a statute adopts by specific reference the provisions of another statute, regulation or ordinance, such provisions are incorporated in the form in which they exist at the time of the reference and not as subsequently modified." *Styrene Information and Research Center,* 210 Cal.App.4th at 1097 (*quoting Palermo*, 32 Cal.2d at 58-59); *see also California Chamber of Commerce v. Brown*, 196 Cal.App. 4th 233, 256-258 (2011).

The Court in *California Chamber of Commerce* did not express a definitive view on whether section 25249.8(a) was a statute of specific reference or one of general reference. *Id.* at 257-258. Instead, the Court stated that *Palermo* did not compel it to hold that Proposition 65 incorporated only the 1986 "lists of identified substances" referenced in the federal Hazard Communication Standard (29 C.F.R. § 1910.1200), which was referenced in the California Labor Code, because "section 25249.8, subdivision (a) anticipates change, by mandating annual revision and republication of the Proposition 65 list." *Id.* at 258. Although section 25249.8(a) may anticipate change based upon new data becoming available, it clearly stated that only chemicals "known to cause cancer" were to be identified.

Plaintiff-Appellants in *Styrene Information and Research Center* and *California Chamber of Commerce* both argued that section 25249.8(a) of the California Health and Safety Code incorporated the specific chemicals that had been identified by IARC as known carcinogens in 1986, and nothing more. Both Courts rejected the proposition that section 25249.8(a) reflected a static, chemical-specific incorporation of the known

carcinogens identified in the Labor Code. As the *Styrene Information and Research Center* Court summarized: "We agree with [*California Chamber of Commerce v.*] *Brown* that the Labor Code method of populating the Proposition 65 list is not frozen in time but may be updated as the lists identified by the HCS are updated." *Styrene Information and Research Center,* 210 Cal.App. 4th at 1097. The issue of IARC's changed substantive standard for "sufficient evidence" was not before the Court in either of these two cases, and that issue is now presented by OEHHA's Notice of Intent to List pulegone. Neither of these two cases rules on the extent to which *Palermo* applies to section 25249.8(a).

4. OEHHA has failed to identify any basis for concluding that pulegone is within the scope of Labor Code section 6382(d)

Labor Code section 6382(d) cannot provide a basis for OEHHA's listing of pulegone at this time.[22] This section, which also is incorporated into Proposition 65 by section 25249.8(a), states:

> "Notwithstanding Section 6381, in addition to those substances on the director's list of hazardous substances, any substance within the scope of the federal Hazard Communication Standard (29 C.F.R. Sec. 1910.1200) is a hazardous substance subject to this chapter."

The federal Hazard Communication Standard ("HCS") makes clear in a section titled "scope and application" that it applies only to chemicals which are "known to be present in the workplace in such a manner that employees may be exposed under normal conditions of use or in a foreseeable emergency." 29 C.F.R. § 1910.1200(b)(2) (1987); *see also* 29 C.F.R. § 1910.1200(b)(2) (2013) (same). OEHHA has presented no

[22] OEHHA's Notice does not explain which aspect of the "Labor Code listing mechanism" it believes provides a sufficient basis for placing pulegone on the Proposition 65 list of "known" carcinogens. Moreover, the Notice refers to section 6382(d) as well as section 6382(b)(1). Thus, these comments address section 6382(d).

finding or evidence that pulegone is present in the workplace in such a manner that employees may be exposed under normal conditions or use or in a foreseeable emergency. Thus, OEHHA cannot rely on section 6382(d) of the Labor Code to support its February 7 Notice.

B. OEHHA must conclude that IARC identified pulegone as a "known carcinogen" to support a section 25249.8(a) listing, but it has not done so

Because OEHHA proposes to list pulegone simply on the basis of IARC's bare conclusion that sufficient evidence of carcinogenicity exists, with no information on how IARC reached that conclusion, OEHHA does not have sufficient information to conclude that IARC has identified pulegone as a "known carcinogen." Accordingly, the Notice of Intent to List pulegone should be withdrawn.

The California courts addressing Proposition 65 listing issues have consistently stated that chemical listings must be limited to "known carcinogens" (and known reproductive toxicants). "Although we concluded in *Deukmejian* that both human and animal carcinogens must be included on the Proposition 65 list, we cautioned that the standard remains *known* carcinogens." *Styrene Information and Research Center*, 210 Cal.App.4th at 1094 (emphasis in original). Courts also have held that not all "hazardous chemicals" identified in the Labor Code, and indeed not all "possible carcinogens" are necessarily "known carcinogens." *Id*. at 1096 - 1101.

The information in the Proposition 65 ballot pamphlet, noted as useful guidance by the Court in *Styrene Information and Research Center* and other courts, also supports withdrawing the pulegone Notice of Intent to List because OEHHA has made no finding that pulegone is a "known carcinogen." "There are certain chemicals that are

scientifically known -- not nearly suspected, but known -- to cause cancer and birth defects. Proposition 65 would: Warn us before we are exposed to any of these dangerous chemicals…." *Styrene Information and Research Center*, Cal.App. 4th at 1098 (quoting ballot pamphlet). "Proposition 65 singles out chemicals that are scientifically known to cause cancer or reproductive disorders …. Proposition 65's new civil offenses focus only on chemicals that are *known to the state* to cause cancer or reproductive disorders. Chemicals that are only suspect are not included …." *Id.* at 1099 (quoting ballot pamphlet (emphasis in original)).

Additional ballot materials emphasize that only "known carcinogens" would be drawn from the IARC identifications: "At a minimum, the Governor must include the chemicals already listed as known carcinogens by … the U.N.'s International Agency for Research on Cancer." Proposition 65 Ballot Pamphlet, Argument in Favor of Proposition 65, page 54, (1986).

C. OEHHA cannot list pulegone based upon Labor Code section 6382(b)(1) before it has been evaluated by the Director of the Department of Industrial Relations

Section 6382(b)(1) specifically references both IARC, the ultimate basis that OEHHA cites for the Notice, *and* section 6382(a) of the Labor Code. Section 6382(b)(1) provides a list of chemicals that the Director of Industrial Relations "shall . . . presume[] . . . to be potentially hazardous . . . and shall be included on the list [of hazardous substances]; provided, that the director shall not list a substance . . . from the listings in subdivision (b) if he or she finds, upon a showing pursuant to the procedures set forth in Section 6380, that the substance as present occupationally is not potentially hazardous to human health." Cal. Labor Code §6382(a). The Director of Industrial Relations has

not added pulegone to the list of chemicals considered hazardous.[23] Proposition 65 could have referred specifically and directly to one or more of IARC's lists of human and animal carcinogens, but it did not do so. By referring to the California Labor Code rather than directly to IARC, one should infer that the intent of Proposition 65 was to await action by the Director of Industrial Relations, because that action may or may not find that a chemical is hazardous, as provided in section 6382(a), and Proposition 65 was designed to limit its focus to hazardous chemicals. This inference is further supported by the language in section 25249.8(a) that refers to substances "*identified by*" reference in Labor Code section 6382(b)(1), rather than simply saying those substances *referred* to in Labor Code section 6382(b)(1). For all of these reasons, Proposition 65's section 25249.8(a) incorporated the IARC chemicals identified by the Director of Industrial Relations as hazardous, not all IARC chemicals.

IV. Listing Pulegone Before Analyzing the Relevant IARC Monograph Is an Abuse of Discretion

An agency decision is not valid when it "has not proceeded in the manner required by law" and when it "is not supported by the findings, or the findings are not supported by the evidence." *Exxon Mobil Corp. v. OEHHA*, 169 Cal.App.4th 1264, 1276 (2009). Section 25249.8(a) only permits chemicals that are "known" to cause cancer to be added to the Proposition 65 list. OEHHA has not articulated a sufficient basis to conclude that pulegone has been identified by IARC as "known" to cause cancer. OEHHA has not explained why all chemicals identified under the current IARC standard for "sufficient evidence" in animal studies are "known" to cause cancer, nor has it explained why pulegone specifically has been identified as "known" to cause cancer.

[23] *See* 8 Cal.Code of Regs. § 339.

V. Conclusion

The proposed basis for listing pulegone, bare conclusions announced by IARC with no explanation or analysis, is legally and factually inadequate, and this would be true in every such case. In the case of pulegone, however, the legal and factual insufficiency of OEHHA's proposed action is all the more compelling because the one study in animals cited as support for IARC's conclusion was marred by its greatly exceeding the maximum tolerated dose. Similarly, mouse liver tumors cannot be an important or primary basis for cancer hazard identification through the Labor Code listing mechanism. Accordingly, the Associations request that OEHHA withdraw the Notice of Intent to List pulegone.

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