CA Department of Public Health
Office of Regulations
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Sacramento, CA 95814

May 12, 2023

To Whom It May Concern:

On behalf of the undersigned associations and entities (hereafter "coalition"), thank you for the opportunity to provide comments in response to the CSPI et al. petition to the California Department of Public Health (CDPH) requesting rulemaking to implement warning labels on food products and dietary supplements that include certain synthetic food colors. The coalition additionally incorporates by reference the comment letter from the International Association of Color Manufacturers (IACM). The coalition and IACM have been working collaboratively to review and respond to the CSPI et al. petition to the CDPH.

Executive Summary

The Office of Environmental Health Hazard Assessment (OEHHA) assessment for which the CSPI petition is predicated, does not establish a causal relationship between synthetic colors and negative health or behavioral effects. Therefore, due to insufficient scientific evidence, this assessment should not form the basis for regulatory action.

Colors are safely used in a wide variety of consumer products and are among the most widely studied food ingredients subject to strict global regulatory requirements. The U.S. Food and Drug Administration (FDA) and international regulatory bodies have all concluded that synthetic dyes are safe for children and have acknowledged there is no compelling evidence that these colors cause adverse behaviors.

Any risk management actions such as a warning label would be scientifically unfounded and unnecessary. U.S. regulations already require that every color be clearly listed on the label. A warning statement based on inconclusive science would not provide meaningful impact to Californians but would mislead consumers and undermine consumer confidence in a safe food supply. Parents of children who may be sensitive to food ingredients, including colors, can avoid such foods in consultation with their doctor based on existing ingredient declarations and labeling requirements.

OEHHA's Assessment Cannot Be Used as Basis for Regulatory Action

OEHHA published a final hazard assessment on April 16, 2021, after being tasked to conduct "a risk assessment of the potential impacts of synthetic food dyes on children, particularly for neurobehavioral and other neurologic effects." OEHHA concluded that the scientific literature provides evidence in humans, animals, as well as mechanistic information, that synthetic food dyes may cause or exacerbate neurobehavioral problems in some children. However, international expert bodies have consistently drawn different conclusions than that of OEHHA

regarding the potential causal link. Authoritative bodies like the European Food Safety Authority (EFSA) in 2008, the FDA in 2011 and 2019, and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 2011 and 2016, have evaluated the evidence suggesting associations between exposure to FD&C colors and adverse behavior in children with ADHD and the general population. These assessments have all concluded that no causal relationship has been established, and no additional risk management is warranted. The difference between OEHHA's outcome and those of other expert bodies raises serious questions about the validity of OEHHA's investigation, assessment, conclusions, and report.

While OEHHA was tasked with preparing a risk assessment, the report issued by the agency is instead a hazard assessment. This distinction is important, as a hazard assessment identifies *potential* sources of harm or danger, while a risk assessment assesses the possibility or likelihood that danger will occur from quantifiable exposures. So, while the OEHHA assessment concludes that there is potential for synthetic colors to cause adverse behavioral outcomes, it failed to assess the likelihood of those outcomes to occur. Additionally, OEHHA's analysis included reported neurobehavioral impacts in human trials, but limitations in the methodologies employed in these studies significantly reduce the certainty and value of their results in this application.

Notably, these limitations were also highlighted in the independent peer review process; the reviewers pointed out the need for further evaluation of study quality and pointed out publication bias. Two critical points raised during peer review included:

- Randomized control trials (RCTs) were conducted on a “convenience” sample of children and thus these trials have limitations related to selection bias and external validity. Thus, these RCTs may not be representative of what happens in the general population (Taioli, 2020).
- Most studies utilized various mixtures of synthetic dyes to assess and define their effects on the nervous system and behavior. Such study designs yield results that can be very difficult, if not impossible, to interpret (Spencer, 2020).

Additionally, the results of the review of integrated evidence found a lack of evidence of consistent or sustained adverse changes within studies, or across studies with individual colors (Gentry et al., 2021). This provides a strong indication that the consideration of study design is critical, which the OEHHA assessment critically lacks. A weight-of-evidence analysis considering multiple streams of scientific evidence, including structural, mechanistic, animal behavioral data and human clinical studies, do not support a causal association between exposure to synthetic dyes and behavioral effects in children. Significant study limitations and weaknesses exist in the studies OEHHA relied upon to formulate their conclusions, including the infrequent reporting of the source and/or purity of the colors tested, bringing into question the quality of the color preparation and relevance of any effects observed being attributed exclusively to the test material.

Any study used in a weigh of evidence for regulatory decision-making should meet minimum quality and reliability criteria, and many of the studies considered within the OEHHA analysis did not. For studies considered adequate for quantitative risk assessment, evidence of effects following doses higher than the JECFA or U.S. FDA no-observed-adverse-effect levels

(NOAELs) were inconclusive. In some cases, isolated changes were not sustained over time, despite chronic exposure to the test color, and are limited to a small number of endpoints intended to evaluate neurobehavioral domains.

FD&C Colors are Structurally Distinct

While OEHHA concludes that effects may exist for all FD&C colors, the studies evaluated in the OEHHA assessment do not support a causal relationship between exposure to any food dyes and hyperactivity or neurologic effects in children. Additionally, OEHHA inappropriately treats all synthetic colors similarly when each has different chemical attributes and effects.

As noted by both IACM comments and by a peer reviewer to the draft report (Spencer, 2020), the synthetic dyes that are approved for use in the United States belong to distinct chemical classes and include azo dyes, a triarylmethane derivative, an indigotine derivative, and an iodofluorescein derivative. Given the lack of chemical similarity, the color additives in different classes would be expected to be distinct in any biological activity displayed, and it would be remarkable if substances of such different structures were to each trigger the same behavioral changes. To ascribe effects to and suggest risk management generally for all synthetic colors that would structurally different is inappropriate. Collectively, there is a lack of sufficient evidence to warrant any risk management decisions.

Limitations of Warning Labels

Although the EU instituted a warning statement for the colors included in the Southampton studies (McCann et al., 2007), its scientific experts at EFSA did not find a safety concern. In fact, European authorities concluded that the data from these studies provide only limited evidence that food additives, including colors, cause even very small effects on a child's activity and attention levels. Therefore, experts in Europe join experts in the U.S. in considering the results of the Southampton Studies to be 'inconsistent' and 'mixed' resulting in no recommended mitigation action for the use of colors in foods. Although the EU ultimately instituted warning labels for colors, it did so for political reasons, contrary to the evidence provided by its own scientific body, EFSA. Notably, only three FD&C colors are included in the warning label requirement, rather than all nine that were the subject of OEHHA's assessment.

Warning statements for synthetic colors are not used in geographies that consider the weight of scientific evidence for policy development. There is no evidence that supports the claim that a warning label will result in any benefits to consumers. In fact, in Europe and the U.K., there is no documented evidence that the warning label for added azo colors have impacted neurobehavioral effects in children, including any decrease in the prevalence of ADHD. Given the scientific and regulatory consensus that synthetic colors in foods are safe, a warning label for food products and dietary supplements in the state of California containing FD&C colors would be misleading and incorrectly imply that parents can improve their child's behavior by avoiding one specific ingredient.

Sincerely,

American Bakers Association

California Chamber of Commerce

California League of Food Producers

California Restaurant Association

Chemical Industry Council of California

Consumer Brands Association

Consumer Healthcare Products Association

International Association of Color Manufacturers

National Confectioners Association

SNAC International

References

European Food Safety Authority. (2008). Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC). *The EFSA Journal*, 660, 1-54. https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2008.660

Gentry, R., Greene, T., Chappell, G., Lea, I., Borghoff, S., Yang, C., Rathman, J., Ribeiro, J. V., Hobocienski, B., Mostrag, A., Rodricks, J., & Clewell, H. (2021). Integration of evidence to evaluate the potential for neurobehavioral effects following exposure to USFDA-approved food colors. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, 151, 112097. https://doi.org/10.1016/j.fct.2021.112097

International Association of Color Manufacturers. (2020). Comments in Response to Public Review Draft of "Health Effects Assessment: Potential Neurobehavioral Effects of Synthetic Food Dyes in Children" (August 28, 2020). https://oehha.ca.gov/media/dockets/19884/19962-international_association_of_color_manufacturers/11-12-2020_oehha_final_report_comments_inc_appendices.pdf

Joint FAO/WHO Expert Committee on Food Additives. (2011). Evaluation of certain food additives and contaminants. *Seventy-fourth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO technical report series; no. 966).* https://apps.who.int/iris/bitstream/handle/10665/44788/WHO_TRS_966_eng.pdf?sequence=1

Joint FAO/WHO Expert Committee on Food Additives. (2016). Evaluation of certain food additives. *Eighty-second report of the Joint FAO/WHO Expert Committee on Food Additives (WHO technical report series; no. 1000).* *https://apps.who.int/iris/bitstream/handle/10665/250277/9789241210003-eng.pdf?sequence=1*

McCann, D., Barrett, A., Cooper, A., Crumpler, D., Dalen, L., Grimshaw, K., Kitchin, E., Lok, K., Porteous, L., Prince, E., Sonuga-Barke, E., Warner, J. O., & Stevenson, J. (2007). Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. *Lancet (London, England),* 370(9598), 1560–1567. https://doi.org/10.1016/S0140-6736(07)61306-3

Office of Environmental Health Hazard Assessment. (2021). Potential Neurobehavioral Effects of Synthetic Food Dyes in Children. https://oehha.ca.gov/media/downloads/risk-assessment/report/healthefftsassess041621.pdf

Spencer, P. (2020). Review of "Health Effects Assessment: Potential Neurobehavioral Effects of Synthetic Food Dyes in Children". *OEHHA*. https://oehha.ca.gov/media/downloads/risk-assessment/peer/peterspencerfooddyepeerreview.pdf

Taioli, E. (2020). Review of "Health Effects Assessment: Potential Neurobehavioral Effects of Synthetic Food Dyes in Children". *OEHHA*. https://oehha.ca.gov/media/downloads/risk-assessment/peer/emanuelataiolifooddyepeerreview.pdf

U.S. Food and Drug Administration. (2011). Food Advisory Committee March 31, 2011, Meeting Transcript. https://wayback.archive-it.org/org-1137/20170406211705/https:/www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/FoodAdvisoryCommittee/UCM255119.pdf

U.S. Food and Drug Administration. (2019). Science Board to the Food and Drug Administration Advisory Committee October 7, 2019 Meeting Transcript. https://www.fda.gov/media/135001/download