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May 12, 2023

California Department of Public Health
Office of Regulations
1415 L Street, Suite 500
Sacramento, CA 95814
Re: P-22-001 CSPI Synthetic Dye Petition

The Consumer Healthcare Products Association (CHPA)¹ appreciates this opportunity to comment on the Synthetic Dye Petition² submitted to the California Department of Public Health requesting that a warning be placed on food and dietary supplement products related to adverse neurobehavioral effects purportedly associated with ingestion of synthetic food dyes (i.e., FD&C Colors). CHPA member companies marketing over-the-counter (OTC) medicines and dietary supplements containing approved, batch-certified FD&C colors have an interest and expertise in this area.

The CSPI Petition notes the review undertaken by the California Office of Environmental Health Hazard Assessment (OEHHA) as supportive evidence for inclusion of the warning. As we have expressed in previous comments³ to OEHHA, CHPA believes that the available evidence does not demonstrate an association between the intake of synthetic food dyes and adverse neurobehavioral outcomes. As such, if California were to mandate the inclusion of additional information on dietary supplement product labels warning of potential adverse neurobehavioral effects, it would not only be misleading to consumers, it would also be bad public policy.

Adoption of this policy would increase administrative burdens and reduce the efficiency of food and dietary supplement manufacturers by forcing them to comply with separate regulations federally and in California and create confusion and complexity for businesses operating across state lines. Consumers would also likely be confused by state-specific labeling requirements given the well-established role of FDA in regulating these color additives. As current FDA labeling requires that all color additives added to foods (including dietary supplements) and medicines be specifically listed on the product's ingredient label, consumers can easily identify color additives on product labels and thus avoid exposure should they choose.

¹ The Consumer Healthcare Products Association (CHPA), founded in 1881, is the national trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines, dietary supplements, and consumer medical devices. Every dollar spent by consumers on OTC medicines saves the U.S. healthcare system more than \$7, contributing a total of \$146 billion in savings each year. CHPA is committed to empowering consumer self-care by preserving and expanding choice and availability of consumer healthcare products.

² Petition for Rulemaking to Implement Warning Labels on Food Products and Dietary Supplements that Include Certain Synthetic Food Dyes; Center for Science in the Public Interest et al., submitted December 8, 2022.

³ Comments submitted to the California Office of Environmental Health Hazard Assessment (OEHHA) Public Review Draft report entitled "Health Effects Assessment: Potential Neurobehavioral Effects of Synthetic Food Dyes in Children." November 12, 2020.

Further, there is no supportive evidence that a warning label will benefit consumers. In fact, in Europe and the U.K., there is no documented evidence that the warning label for 6 synthetic (azo) colors has impacted neurobehavioral effects in children, including any decrease in the prevalence of ADHD.

Prior to their use in food, drugs, or cosmetics, the Food and Drug Administration (FDA) must review color additives to ensure they are safe for their intended purposes. FDA also maintains and regularly monitors postmarket surveillance databases to which consumers, health professionals and industry can submit adverse events believed to be related to color additives (as well as other products).⁴ Color additives have been safely used in a wide variety of consumer products for decades.

Multiple expert bodies have reviewed the available evidence assessing a possible association between intake of synthetic food dyes and behavior and have concluded that the available evidence does not demonstrate a consistent association between intake and adverse behavioral effects. This includes the FDA, the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Studies used to support an association between intake of color additives and adverse neurobehavioral effects suffer from a series of limitations including examination of mixtures of colors, unverified validity of behavior scores, small sample size and lack of a dose-response relationship.

FDA has reviewed the available information on color additives and behavioral effects in children and convened a Food Advisory Committee Meeting (March 2011) to consider the possible association between consumption of certified color additives and hyperactivity. The committee found that “...*relevant scientific data did not support a causal link between consumption of certified color additives in food and hyperactivity and other problematic behaviors in children.*” and voted against additional information being added to product labeling.

This topic was also discussed in a 2019 Advisory Committee Meeting of the Science Board to the FDA.⁵ FDA noted during this meeting that “...*findings did not support the use of artificial food color exclusions as an efficacious dietary intervention in the nonpharmacological treatment of children with ADHD and related problem behaviors.*”⁶ A recent review also notes that “[t]here is no clear evidence that supports dietary interventions for the treatment of ADHD”⁷

⁴ The CFSAN Adverse Event Reporting System (CAERS) database collects reports submitted by consumers, health professionals, industry, and others about adverse health events and product complaints related to CFSAN-regulated products. It includes voluntary reports involving conventional foods, including food additives and color additives, and cosmetics, and both mandatory and voluntary reports with respect to adverse events involving dietary supplements. The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products.

⁵ Color Additives and Behavioral Effects in Children, October 7, 2019

⁶ Quote from Dr. T. Scott Thurmond, Ph.D.. Science Board to the Food and Drug Administration Advisory Committee Meeting, October 7, 2019

⁷ Cagigal C, Silva T, Jesus M and Silva C 2019 Does Diet Affect the Symptoms of ADHD? *Curr Pharm Biotechnol* 20(2):130-136.

Subsequent to the 2011 meeting FDA published an exposure assessment for FD&C colors in 600 representative foods, finding that the estimated daily intake of food colors were well below acceptable daily intake values.⁸ Similar results have been obtained in more recent studies,⁹ including one supported by OEHHA.¹⁰

Since the 2011 Advisory Committee meeting there have been a number of reports published examining a possible relationship between ingestion of color additives and ADHD, including two meta analyses,^{11,12} a double-blind placebo-controlled trial¹³ and a systematic review.¹⁴ While FDA recently noted¹⁵ that they are aware of these studies, no update of their previous position has been issued based on these findings.

Robust reviews of the available scientific evidence by regulatory bodies outside the US have also found that a causal relationship between color additive intake and adverse neurobehavioral effects does not exist. In 2008, the EFSA Panel on Food Additives, Flavourings, Processing Aids, and Food Contact Materials reviewed a study¹⁶ examining a possible association between intake of food colors and a preservative (sodium benzoate) on hyperactivity in children. EFSA concluded that there was limited evidence that the colors studied had a statistically significant effect on behavior; the reported effects were not consistent for the two mixtures of color additives; the study findings could not be extrapolated to the general population; and it was not possible to determine sensitivity to individual color additives.¹⁷ Limitations identified by EFSA included investigation of color mixtures (not individual colors); unverified validity of the behavioral score; lack of information on a dose-response relationship; the absence of a possible

⁸ Doell DL, Folmer DE, Lee HS, Butts KM and Carberry SE 2016 Exposure estimate for FD&C colour additives for the US population *Food Addit. Contam Part A Chem Anal Control Expo Risk Assess* 33(5):782-797.

⁹ Bastaki M, Farrell T, Bhusari S, Bi X and Scrafford C 2017 Estimated daily intake and safety of FD&C food-colour additives in the US population *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 34(6):891-904.

¹⁰ Thilakarathne R, Castorina R, Gillan M, Han D, Pattabhiraman T, Nirula A, Miller MD, Marty M, Lehmkuhler A, Mitchell A, and Bradman A, 2022. Exposures to FD&C synthetic color additives from over-the-counter medications and vitamins in United States children and pregnant women *J Exp Sci Environ Epidemiol* DOI: [10.1038/s41370-022-00418-9](https://doi.org/10.1038/s41370-022-00418-9)

¹¹ Nigg JT, Lewis K, Edinger T and Falk M 2012 Meta-analysis of attention-deficit/hyperactivity disorder or attention-deficit/hyperactivity disorder symptoms, restriction diet, and synthetic food color additives, *J Am Acad Child Adolesc Psych* 51(1):86-97.

¹² Sonuga-Barke EJ *et al.*, 2013 Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *Am J Psych* 170(3):275-289.

¹³ Lok KYW, Chan RS, Lee VW, Leung PW, Leung C, Leung J and Woo J 2013 Food Additives and Behavior in 8- to 9-Year-Old Children in Hong Kong: A Randomized, Double-blind, Placebo-Controlled Trial, *J Dev Behav Pediatr* 34(9):642-650.

¹⁴ Pelsler LM, Frankena K, Toorman J, Rodrigues RP 2017 Diet and ADHD, Reviewing the Evidence: A Systematic Review of Meta-Analyses of Double-Blind Placebo-Controlled Trials Evaluating the Efficacy of Diet Interventions on the Behavior of Children with ADHD *PLoS One* 12(1): e0169277.

¹⁵ In an October 7, 2019 Advisory Committee Meeting of the Science Board to the FDA, Dr. Scott Thurmond, Ph.D., Review Toxicologist, (CFSAN FDA) noted that FDA performed a literature search in “early or mid-2019”

¹⁶ McCann D, Barrett A, Cooper A, Crumpler D, Dalen L, Grimshaw K, Kitchin E, Lok K, Porteous L, Prince E, Sonuga-Barke E, Warner JO and 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* 370(9598):1560-1567.

¹⁷ EFSA AFC (European Food Safety Authority and Additives, Flavourings, Processing Aids and Contact Material). (2008). Assessment of the results of the study by McCann *et al.* (2007) on the effect of some colours and sodium benzoate on children’s behavior. *EFSA Journal*. 660:1-54. <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2008.660>

biological mechanism underlying the behavioral changes; and use of an unconventional/inadequately justified statistical model. Between 2009 and 2016 EFSA conducted additional reviews of food colors (including Red No. 40)^{18,19} and found no evidence to support a causal link between intake of these colors and adverse neurobehavioral effects.²⁰

The Joint FAO/WHO Expert Panel on Food Additives (JECFA) has also reviewed the safety of food colors, including all noted in the OEHHA report, and confirmed their safety for all users.^{21,22} These reviews considered available data on possible adverse neurobehavioral effects of certain dyes and found that results were not consistent.

Conclusion

When viewed in its entirety, the available evidence informing a possible link between synthetic color additive intake from a number of different sources (*e.g.* foods, drugs, cosmetics) and adverse neurobehavioral effects does not demonstrate a causal effect. Although some results suggest that certain sensitive populations may exist, color additives are required to be listed on product labels and as such, consumers can easily avoid products containing them if they so choose.

Thank you again for the opportunity to submit these comments.

Sincerely,



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¹⁸ EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) Scientific Opinion on the re-evaluation of Allura Red AC (E 129) as a food additive, 2009 EFSA J 7(11):1327.

¹⁹ EFSA 2015 Refined exposure assessment for Allura Red AC (E 129) EFSA J 13(2):4007.

²⁰ <https://www.efsa.europa.eu/en/topics/topic/food-colours>

²¹ Joint FAO/WHO Expert Committee on Food Additives, 2016 Evaluation of certain food additives WHO Technical Report Series, 1000.

²² Joint FAO/WHO Expert Committee on Food Additives, 2017 Safety evaluation of certain food additives