OEHHA Public Review Draft:

Health Effects Assessment: Potential Neurobehavioral Effects of Synthetic Food Dyes in Children

November 2020

The undersigned health-based organizations and physicians and researchers applaud California's Office of Environmental Health Hazard Assessment (OEHHA) for producing the most comprehensive and rigorous assessment of the neurobehavioral effects of synthetic dyes ever conducted.

OEHHA's draft report was informed by expert scientists attending a public scientific symposium organized by OEHHA, and by the public who were invited to submit information. The process was and is transparent, inclusive and resulted in a well-written draft report with clear, robust conclusions.

Overall, the draft assessment concludes that:

> "The scientific literature indicates that food dyes may cause or exacerbate neurobehavioral problems in some children."

We therefore strongly agree, as the draft assessment notes, that:

> "At a minimum, in the short-term, the neurobehavioral effects of synthetic food dyes in children should be acknowledged and steps taken to reduce exposure to these dyes in children."

The OEHHA draft assessment breaks new ground in **seven important ways:**

First: The draft health effects assessment uses a state-of-the-art structured approach of systematic review and evidence integration that has never been undertaken on the neurobehavioral effects of synthetic food dyes. Systematic review and evidence integration methodology and structured frameworks are increasingly recommended by a wide range of agencies and institutions to address environmental health questions, to ensure collection of the most complete and reliable evidence, allowing them to be integrated to form the basis for conclusions.[1]

OEHHA's approach involved a rigorous, well-designed literature search strategy, systematic evaluation of study methods and quality to ensure an emphasis on studies of high quality, a thorough and exacting evaluation of the human, animal, and mechanistic evidence, and the development of conclusions both within and across evidence streams. Confidence in the analysis is supported by the fact that three evidence streams (human,

animal, mechanistic) support the important conclusions reached: that synthetic food dyes can cause or exacerbate neurobehavioral effects in children.

Second: OEHHA's evaluation of human evidence is very stringent; we note that the amount and quality of human evidence on synthetic food dyes is arguably among the greatest of the thousands of substances intentionally added to food. It is worth underscoring that for the human evidence, the OEHHA assessment relies exclusively on controlled clinical trials, considered the "gold standard" of study design for evaluating causality. Rarely, if ever, are clinical trials available for additives or other substances added to food. In fact, 27 clinical trials in children met OEHHA's inclusion criteria. We thus agree that "high confidence" is warranted for conclusions from the results of these human studies, and that there is "a substantial amount of evidence that consumption of synthetic food dyes is associated with adverse neurobehavioral outcomes in children."

Our confidence in the conclusions is further bolstered by the fact that OEHHA was unable to identify, after extensive analyses, any clear set of biases or other factors, such as inadequate blinding or randomization, that may have invalidated positive associations reported in the epidemiological literature.

Since excellent meta-analyses of the human evidence on behavioral effects of synthetic food dyes had been published recently, OEHHA sensibly did not perform a full meta-analysis, and instead undertook an unprecedented evaluation to examine strengths and weaknesses and trends in the evidence, considering many important factors including blinding, dose levels, and wash-out periods, as they may have compromised study results. OEHHA conducted its own statistical analyses to verify or add to reported associations and effect sizes. We fully support this approach.

Third: Prior to this review, no such structured and robust systematic reviews of the animal and mechanistic evidence have ever been conducted on the neurobehavioral effects of synthetic food dyes. The assessment contracted by the U.S. Food and Drug Administration (FDA) for its Food Advisory Committee meeting in 2011 included only a two-page overview of animal studies, and the animal evidence was not discussed by the committee.

OEHHA's assessment of animal studies was far more extensive and rigorous. In addition, it includes studies published since 2011 not available to FDA that are relevant to an assessment of neurobehavioral effects. OEHHA's assessments of the animal evidence on specific food dyes, as well as on mixtures of dyes, support the conclusions from the human evidence that dyes can cause neurobehavioral effects in children. They also bridge some of the gaps in understanding from the human evidence, which is largely focused on the effects of mixtures of food dyes resulting from exposures in children. Overall, the animal literature indicates that synthetic dyes can affect activity, memory and learning, and effect changes in neurotransmitter systems in the brain and microscopic changes in brain structure in animals.

Similarly, FDA's contractor included only a two-page discussion of possible biological processes/mechanisms. In contrast, OEHHA undertook an extensive evaluation of dyes tested in high-throughput assay systems, finding that there is evidence for a number of ways that neurobehavioral effects of synthetic dyes might occur, including interaction of food dyes with neurotransmitter systems.

The only other such review of the mechanistic data was funded by the American Beverage Association and was far less comprehensive, using fewer assays and using data on cytotoxicity to exclude potentially important information (i.e., considering certain results to be false positives that might not be) rather than flagging it for further consideration.[2]

Fourth: The report includes the most up-to-date and comprehensive exposure assessment ever conducted on synthetic food dyes in the United States, building on that conducted by the FDA. The OEHHA analysis is the only assessment to evaluate U.S. exposures to synthetic food dyes in pregnant women, women of child-bearing age, and in as many different age groups of children (0-<2 years, 2-<5 years, 5-<9 years, 9-<16 years, 16-18 years). This is noteworthy since these populations are suspected of being at greater risk from synthetic food dyes, compared to the general population.

In comparison with FDA's exposure assessment,[3] OEHHA's assessment also looked at more population/age groups, used more recent NHANES food consumption data, covered a broader distribution of estimates (mean, median, 75th and 95th percentiles), and incorporated food dye concentration measurements from University of California, Davis (UC-Davis) as well as from the FDA. Because it was assessing neurobehavioral effects that result from short-term exposures, as documented by numerous clinical trials, it was appropriate that the assessment used single day and 2-day averages of food consumption, rather than the 2-day and 10-14-day data previously used by FDA.

We took note that the highest 95th percentile single-day exposure estimate was for FD&C Red No. 3 in children under 2, an age group that FDA did not evaluate in its exposure assessment.

OEHHA's analysis found that beverages were the dominant sources of exposure for children to the dyes that contributed most to exposure to synthetic food dyes: FD&C Red No. 40, Yellow No. 5, and Yellow No. 6. Specifically, fruit juice drinks and soft drinks were the primary sources of exposure for FD&C Red No. 40 and Yellow No. 6, and powdered fruit flavored drinks and fruit juice drinks for FD&C Yellow No. 5 in children.

In addition, white foods, brown foods, and other foods that many do not associate with food dyes were found to be major contributors to food dye intake, including chocolate pudding and fruit muffins— important sources of FD&C Blue No. 2 for children under 2—and white icing, the largest contributor to Blue No. 1 exposure for children under 5, and a primary source of exposure to FD&C Red No. 3. These findings illustrate some of the challenges that consumers face in identifying foods containing synthetic dyes, as consumers are unlikely to expect that such foods contain dyes.

Beverages, including juice drinks, fruit-flavored drinks from powders that get reconstituted, and soft drinks should be a priority for exposure reduction efforts, since they are among the products most commonly associated with food dye exposure.

Fifth: The report provides the first substantial data on socioeconomic differences, such as poverty level and race, that have long been suspected to impact levels of exposure to synthetic dyes. It is concerning that Non-Hispanic Black children (0-18) and women of childbearing age (18-49) had significantly higher intake of synthetic food dyes compared to their non-Hispanic White or Asian counterparts; and total food dye exposures were significantly higher among women of childbearing age with lower income, when compared to women with higher income.

Lower income consumers may face greater challenges in avoiding synthetic food dyes than do higher income consumers. They are more likely to lack or have limited access to grocery stores or other stores that carry the same range of products available in more affluent communities.[4,5] In addition, more affluent neighborhoods are more likely to include supermarket chains such as Whole Foods or Trader Joes that have explicit policies barring dyed foods, or others that carry "free-from" brands that prohibit food dyes.[6]

This is just one reason why putting the burden on consumers to avoid synthetic food dyes is unlikely to be fully effective and raises real equity issues. It is also important in that lower income communities experience higher rates of neurodevelopmental disorders like ADHD, as well as a concentration of other risk factors.[7,8] The accumulation of such risk factors likely contributes to the increased incidence of diagnosable ADHD in these socially disadvantaged groups. Therefore, to better protect these and indeed all populations at risk, risk factors that can be addressed, should be, to reduce cumulative population risk and cost and aggravating social/racial inequities. The fact that synthetic food dyes are a risk factor whose only function is cosmetic makes it all the more compelling.

Sixth: The assessment is the first to conduct a risk characterization comparing the basis for current "safe" levels established by the FDA between 35 and 70 years ago, called acceptable daily intakes (ADIs), with the results from studies relevant to the neurobehavioral effects of synthetic food dyes. We agree with OEHHA's conclusion that: "[t]he animal studies that form the basis of the FDA ADIs are many decades old and were not capable of detecting the types of neurobehavioral outcomes measured in later studies, or for which there is concern in children consuming synthetic food dyes." This critical fact was pointed out as well by members of FDA's Food Advisory Committee back in 2011.[9]

The OEHHA analysis makes a further contribution by providing quantitative estimates showing how far off the mark the FDA's current "safe" levels are. Remarkably, according to the report, the ADIs that FDA set for FD&C Red No. 3, Red No. 40, Yellow No. 5, and Yellow No. 6, are 10 to 100 times higher than they would be if they were

based on the results of more recent studies that are appropriate for evaluating neurobehavioral effects. OEHHA notes that in the case of FD&C Red No. 40 and Yellow No. 5, they could be 1,000 times lower, depending on the method used to estimate the ADI.

Seventh: OEHHA's efforts also resulted in the first publicly available data on the amounts of food dyes in over-the-counter (OTC) medications and supplements marketed to children and pregnant women in the United States. FDA never has meaningfully considered the contribution of non-food sources of food dyes to overall exposure, although federal law requires the agency to consider "the probable consumption of, and/or other relevant exposure from the additive and of any substances formed in or on food, drugs, or cosmetics because of such additive; and the cumulative effect, if any, of such additive in the diet of man or animals…."[10]

Researchers from UC-Davis tested national brands of OTC medications and supplements sold in well-known retailers (Target, CVS, WalMart, and RiteAid) in three states, testing samples from three different lots for each brand. The results reveal, as noted in the report, that some brands, and in particular some grape-flavored pain-relief syrups and cough/cold/allergy syrups marketed to children, can contain high levels of dyes, particularly FD&C Red 40, but also Blue 1. Following the label instructions can result in intakes that exceed FDA's outdated ADIs (even without accounting for any intake of synthetic dyes from foods).

OEHHA found that OTC medications can produce 10 to 40 times higher exposures to FD&C Red 40 on a given day than does typical consumption from food. Although consumption of most OTC medications may be infrequent, some (e.g., those for allergies) may be used more frequently, almost daily in certain seasons. Even for OTC medications given infrequently to sick children, it is unacceptable to include (for cosmetic purposes only) high amounts of agents that may cause or exacerbate neurobehavioral symptoms.

Additional Important Points

We also wish to underscore a few other findings from the report that have important public health ramifications:

It is not possible to predict which children will react negatively to dyes. OEHHA considered multiple factors that might influence susceptibility to synthetic food dyes, but concluded that "while it seems likely that sensitive populations exist, we did not find evidence that there is a simple and accurate way to identify these particularly sensitive children." For example, OEHHA's assessment considered children in the general population, with or without a diagnosis of ADHD or hyperactivity, and found that studies including only such children with such a diagnosis were not more likely to report an association with adverse impacts of food dyes.

For this and other reasons, efforts to reduce exposure to synthetic food dyes should be directed at the population at large. Indeed, the entire concept of isolating a susceptible

group is suspect. All environmental exposures affect people variably, whether the exposure be smoking, lead exposure, or COVID-19. That some people are more susceptible than others should not be a consideration in determining whether protective measures are needed for the population. Only population-wide measures can protect the community's sensitive members at this point.

The effects of food dyes go beyond short-term effects on activity and attention and can have long-term, serious consequences. In addition to hyperactivity, inattentiveness, and restlessness, studies in children report other neurobehavioral effects of synthetic food dyes, including sleeplessness, irritability, and aggression.

While the effects of dyes may be short-term, and resolve after discontinuation of exposure, given the prevalence of synthetic food dyes in foods, supplements, and drugs, it is likely that exposures and, therefore, the related effects will occur repeatedly, impacting the ability of children to learn, succeed at school, and get along with peers on an on-going basis, with serious long-term consequences. The symptoms of synthetic food dye exposure overlap with ADHD-type symptoms, and ADHD itself is associated with lifelong impairment in functioning and long-term outcomes that can include academic achievement (e.g., failure to complete high school), serious substance abuse, criminality, and depression.[11,12]

Evidence on effects from in utero exposure in animals raises concerns about pregnant women's exposure to synthetic dyes. While clinical trials have focused on adverse behavioral impacts from short-term exposure to synthetic food dyes in children, animal studies indicate that food dyes can also cause effects from in utero exposure, including for levels of food dyes found to have no effects in the (outdated and insensitive) studies used by FDA.

Furthermore, these effects can be long-term, including effects on activity in the animals as adults. As the report notes, "the finding of behavioral and tissue marker effects of in utero- only exposure detected long after discontinuation of treatment speaks to an interference with developmental processes. More research would be needed to define a mechanism pathway from the tissue assays."

Animal studies provide some evidence of impacts due to adult exposures. Animal studies find neurobehavioral effects resulting from exposures in adults at levels much lower than those reported to cause toxic effects in studies used as the basis of FDA's ADIs. These results suggest that an approach limiting exposure to synthetic food dyes to populations *in addition* to children may be prudent.

There is no convincing rationale to exempt any of the dyes examined from efforts to reduce exposure. Much of the focus on synthetic dyes and neurobehavioral effects has centered around azo dyes, a chemical class of synthetic dyes which includes FD&C Red 40, Yellow 5, and Yellow 6, which together comprise over 90% of the dyes certified for use in foods in the U.S. This is primarily for two reasons: they were the subject of the largest and best-conducted clinical trials on neurobehavioral effects of dyes in children

(i.e., the Isle of Wight and Southampton studies funded by the U.K. government), and because they constitute the largest fraction of mixtures of dyes typically used in clinical trials of dyes used in the United States. Azo dyes also trigger a requirement in Europe for a warning label when present in food.

However, we note OEHHA's conclusion that FD&C Red No. 3 has at least as much evidence as FD&C Red No. 40 and Yellow 5 (these three have been the subject of more studies). Furthermore, while the mechanism by which synthetic food dyes cause or exacerbate neurobehavioral symptoms is not known, OEHHA has characterized the evidence for a serotonergic pathway for FD&C Red No. 3 to be "both convincing and plausible."

In addition, according to the draft report, "Red 3 and Green 3 had hits for all the neuro-relevant molecular targets that they were tested in" in the high throughput screening evaluation. Similarly, the OEHHA report finds that "[a]ll the FD&C synthetic food dyes (except for yellow dyes) are active for antagonistic effects with the thyroid hormone," which, it explains, may be linked to developmental neurotoxicity. It also found that all dyes were active in assays targeting dopaminergic and opioid receptors.

OEHHA acknowledges that these are several pertinent associations between dyes and certain molecular targets of interest. OEHHA's intent was "to provide initial information on whether the in vitro HTS [high throughput screening] assays could be linked with the ability of the FD&C synthetic food dyes to promote a biological response in the nervous system." However, it cautions that these assays "are limited in predicting long term or indirect adverse effects in biological systems, in part due to the complexity of the mechanistic processes that underlie detrimental neurotoxic or neurobehavioral outcomes compared to the current limited spectrum of the ToxCast assays."

In sum, there does not seem to be a sound basis for concluding that any of the seven dyes examined should be singled out as lacking evidence of neurobehavioral effects.

Recommendations:

Overall, we urge that OEHHA move expeditiously to finalize its excellent draft report. OEHHA's conclusion that "[a][t a minimum, the neurobehavioral effects of synthetic food in children should be acknowledged and steps taken to reduce exposure to these dyes in children" is fully justified. At this point, the burden of proof should be shifted to those who believe food dyes are safe. It should no longer rest on those concerned with their harm in view of the range of evidence assembled by OEHHA. The stakes for children and for human welfare are simply too high.

In addition, we offer the following recommendations to further strengthen this excellent report as you move to finalize it.

We urge that OEHHA expand on its conclusion that steps be taken to reduce exposure to these dyes in children by investigating effective ways to reduce exposure

to synthetic food dyes, both in foods and in OTC medications and supplements. This is needed to ensure that its important findings are translated into measures that effectively reduce exposures and provide meaningful public health protection for children.

For example, a recent meta-analysis found that health warning labels were effective in reducing consumer selection of targeted food and alcohol products when compared to those without a health warning label.[13] Further, a recent randomized, controlled experiment found that warning labels on high-sugar products informed consumers of health risks more effectively than the ingredient list or nutrition facts panel alone.[14]

In addition, synthetic food dyes should not be given to children in schools or daycare, as they contribute to inattention and problematic behavior.

It is important to recognize that many consumers may be unaware that synthetic food dyes may cause or exacerbate neurobehavioral effects in children, and thus, simply telling consumers who are concerned to read ingredient labels, as FDA advises on its website, is unlikely to be effective at reaching a majority of affected consumers—particularly when other products are not easily obtained.

A warning label requirement has been shown to influence manufacturers so that companies reformulate their food products to remove dyes. In 2008, the European Food Safety Authority (EFSA) passed a law requiring food products containing any of six artificial food dyes of concern to include a health disclosure that reads: "name or E number of the color(s): may have an adverse effect on activity and attention in children."[15] In response, food manufacturers removed many synthetic dyes from their products sold in Europe.[16]

As a result, food products sold in the U.S. and E.U. may differ in their formulations. For example, Betty Crocker Red Velvet Cake Mix contains Red 40 in the U.S. version[17] and paprika extract and carmine in the E.U. version.[18] It is reasonable to anticipate that food manufacturers would reformulate U.S. versions of food products to avoid a warning label, as they have in the E.U.

We recommend that OEHHA further clarify that efforts to reduce synthetic food dyes should not wait for additional research. We wish to emphasize, as OEHHA states, that additional research is "a long-term proposition," and add that at this juncture, waiting, perhaps indefinitely, for even more evidence is inappropriate. Additional research is always generally desirable, including in the five areas that OEHHA describes.

But a laudable desire for better data does not justify indefinite delay in using the data we have available. It is clear that there is more than sufficient evidence, from the 27 clinical trials as well as the animal and mechanistic evidence streams, to conclude that synthetic food dyes can affect children, as OEHHA has concluded. Efforts should be made "in the short-term," to reduce exposure to synthetic food dyes, as recommended by OEHHA. Indeed, the burden of proof should be shifted—food dyes should be reduced in the

population until further research can provide evidence of their safety sufficiently strong to over-ride the extensive evidence assembled to-date.

We recommend that OEHHA include more information on exposure to mixtures of dyes, though not at the expense of delaying the current final report. Children and other consumers of synthetic food dyes do not consume food dyes one at a time; they consume mixtures of synthetic food dyes, over the course of a day, over the course of a meal, and even in a single product. Furthermore, clinical trials typically test mixtures of food dyes. However, OEHHA focuses mostly on exposure estimates of individual dyes. The information that is presented on total dye exposure is presented for children over a large range of ages, which has limitations since children vary so much in body weight over different ages. It would be helpful to know how the exposures of children of different age groupings to mixtures of dyes compares to clinical trials testing mixtures of dyes for certain age groups.

We recommend that OEHHA characterize risk by comparing estimated exposures to short-term reference levels based on appropriate studies relevant for assessing neurobehavioral effects of food dyes. Currently, OEHHA compares estimated exposures to Acceptable Daily Intakes established by FDA and the Joint Expert Committee on Food Additives (JECFA). However, as OEHHA acknowledges, these do not characterize the risk of neurobehavioral changes. OEHHA should therefore develop more appropriate reference levels to use in characterizing risk.

Thank you for considering our comments, and for your important efforts.

Sincerely,

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[1] U.S. National Toxicology Program Office of Health Assessment and Translation (OHAT). Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. 2019.
[2] Chappell GA et al. Systematic assessment of mechanistic data for FDA-certified colors and neurodevelopmental processes. *Food Chem Toxicol* 2020;140: 111310.
[3] Doell D et al. Exposure estimate for FD&C colour additives for the US population. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 2016;33(5):782-97.
[4] Hilmers A et al. Neighborhood disparities in access to healthy foods and their effects on environmental justice. Am J Public Health 2012;102(9):1644-1654.
[5] Larson NI et al. Neighborhood environments: disparities in access to healthy foods in the U.S. Am J Prev Med 2009;36(1):74-81,
[6] Powell LM et al. Food store availability and neighborhood characteristics in the United States. Prev Med. 2007;44(3):189-95.
[7] Zablosky B et al. Racial and ethnic differences in the prevalence of Attention-deficit/Hyperactivity Disorder and learning disabilities among U.S. children aged 3-17 years. NCHS Data Brief No. 358, March 2020. https://www.cdc.gov/nchs/products/databriefs/db358.htm
[8] Miller L et al. Is the association of ADHD with socio-economic disadvantage explained by child comorbid externalizing problems or parent ADHD? *J Abnorm Child Psychol* 2018;46(5):951-963.
[9] Statements by C. Vorhees and P. Fenner-Crisp , March 31, 2011, Food Advisory Committee transcript, pp. 142-143, 214-216. Cited in Lefferts LY. Seeing Red: Time for Action on Food Dyes. Center for Science in the Public Interest, 2016.
[10] 21 CFR 71.1(c)E.
[11] Erskine HE et al. Long-term outcomes of Attention-Deficit/Hyperactivity Disorder and Conduct Disorder: A systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry 216;55(10):841-50.
[12] Chronis-Tuscano A. Attention-Deficit/Hyperactivity Disorder (ADHD). Presentation to the FDA Food Advisory Committee, March 30, 2011. https://wayback.archive-it.org/org-1137/20170406211701/https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/FoodAdvisoryCommittee/ucm271532.htm.
[13] Clarke N et al. Impact of health warning labels on selection and consumption of food and alcohol products: systematic review with meta-analysis [published online ahead of print, 2020 Jul 2]. *Health Psychol Rev*. 2020;1-24.
[14] Khandpur N et al. Choosing a front-of-package warning label for Brazil: A randomized, controlled comparison of three different label designs. *Food Res Int*. 2019;121:854-861.
[15] European Union, Regulation 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. *Off J Eur Union* L345:16–33 (2008).
[16] Saltmarsh M. Recent trends in the use of food additives in the United Kingdom. *J Sci Food Agric*. 2015;95(4):649-652.
[17] Betty Crocker. *Betty Crocker Super Moist Delights Red Velvet Cake Mix.* n.d. https://www.bettycrocker.com/products/betty-crocker-baking-and-cake-mixes/red-velvet. Accessed September 8, 2020.
[18] Tesco. *Betty Crocker Red Velvet Cake Mix 425G.* n.d. https://www.tesco.com/groceries/en-GB/products/289584856. Accessed September 8, 2020.