



March 15, 2016

The Honorable Robert Califf, M.D., Commissioner  
Dr. Susan Mayne, Director, Center for Food Safety and Applied Nutrition  
Food and Drug Administration (FDA)  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

**Re: The Urgent Need for Warning Label on Synthetically Dyed Foods to Highlight Risks to Children's Health** (Docket No. 2008-P-0349)

Dear Commissioner Califf and Dr. Mayne,

The FDA has acknowledged that synthetic food dyes<sup>1</sup> may trigger adverse behavioral reactions in children.<sup>2</sup> CSPI estimates that more than half a million children in the United States suffer adverse behavioral reactions after ingesting food dyes, with an estimated cost for just those children with attention-deficit/hyperactivity disorder of between \$3.5 billion and more than \$5 billion dollars.<sup>3</sup> Despite FDA's acknowledgement and the high costs associated with behavioral problems induced by food dyes, the FDA has failed to ban the dyes or even require labeling that informs consumers about the problem.

We previously filed a letter and report to this docket urging the withdrawal of current approvals for synthetic dyes given the serious deficiencies in FDA's safety analysis.<sup>4</sup> This letter is a further comment to our petition to ban synthetic dyes and demonstrates that prior agency precedent demands that it take action in the present case to provide consumers with, at the very least, a warning label describing the link between food dyes

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<sup>1</sup> Hereinafter referred to solely as "food dyes," and including FD&C Blue 1, FD&C Blue 2, FD&C Green 3, FD&C Red 3, FD&C Red 40, FD&C Yellow 5, and FD&C Yellow 6.

<sup>2</sup> FDA Background Document for the Food Advisory Committee: Certified Color Additives in Food and Possible Association with Attention Deficit Hyperactivity Disorder in Children, March 30-31, 2011. "For certain susceptible children with Attention Deficit/Hyperactivity Disorder and other problem behaviors, however, the data suggest that their condition may be exacerbated by exposure to a number of substances in food, including, but not limited to, synthetic color additives."

<sup>3</sup> See the analysis of costs and prevalence in *Seeing Red* (citing ADHD data from CDC as of July 8, 2015. <http://www.cdc.gov/ncbddd/adhd/data.html>); and Pelham WE, Foster EM, Robb JA. The economic impact of attention-deficit/hyperactivity disorder in children and adolescents. *Ambul Pediatr.* 2007; 7 (1 Suppl):121-31); and Nigg JT, Lewis K, Edinger T, et al. 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 Psychiatry.* 2012; 51 (1): 86-97.e8. doi: 10.1016/j.jaac.2011.10.015.

<sup>4</sup> Letter from CSPI to Dr. Ostroff. Docket No. 2008-P-0349: A new report regarding the evidence on the failure of current color additive approvals to meet the legal standard for safety. Jan. 19, 2016.

and behavioral problems in children. Based on the history of agency practice and the risks to the consumers, including children, FDA should require warning labels on dyed foods stating: "WARNING: This food contains synthetic food colorings that may impair the behavior of some children."

In addition to the analysis below, we are submitting as enclosures for the docket with this letter the 2,007 complaints that parents have shared with us concerning the negative impact that dyes have had upon their children and families from August 2008 until today.<sup>5</sup> Their moving stories motivate our work, and demonstrate the needless suffering of families from dyes.

In one testimonial that CSPI received, Erica Stewart from Chicago, Illinois, indicated that she took her son to several doctors in an attempt to ameliorate his severe emotional and behavioral problems. Several doctors diagnosed him with ADHD and autism; one doctor hospitalized him and prescribed to him heavy dosages of Zoloft. Only after her son stopped eating foods and beverages containing Red No. 40 did she see any meaningful improvement.<sup>6</sup> The costs associated with the needless doctor visits, medications, and hospitalization could have been entirely avoided had she read warning labels on foods that associated dyes with adverse behavioral issues in children.

As long as dyes are permitted, only a warning label will provide consumers with the appropriate information to enable them to make the association between foods containing these dyes and their children's behavioral symptoms. The FDA has mandated such labeling in the past on several occasions. For the same reason, labeling is necessary in the context of food dyes.

#### *FDA's Current Failure to Require a Warning Label is Contrary to Prior Agency Precedent*

The FDA has previously determined in several key instances that warning labels should be provided when consumers lack the information to associate a food ingredient or food product with a negative symptom that may result from consumption of that food. This rationale was the motivating factor behind the FDA's decision to require a warning label on products containing olestra<sup>7</sup> and unpasteurized juice products,<sup>8</sup> for example.

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<sup>5</sup> We note that these comments were shared with CSPI following only incidental promotion of the issues through normal media channels, and therefore that these comments likely represent only a tiny fraction of similar consumer experiences.

<sup>6</sup> See Appendix C: The Human Toll: Parents' First-hand Accounts in *Seeing Red: Time for Action on Food Dyes*. CSPI. Jan. 2016, available at <http://cspinet.org/reports/seeing-red-report.pdf>.

<sup>7</sup> "Food additives permitted for direct addition to food for human consumption; olestra," 61 Fed. Reg. 3118. (January 30, 1996).

<sup>8</sup> "Food labeling: warning and notice statement; labeling of juice products," 63 Fed. Reg. 37030 (July 8, 1998).

In regards to olestra, the FDA's principal concern in requiring a warning label was not related to the severity of the symptoms caused by its ingestion. In fact, the FDA repeatedly stated that it found "no safety concerns with respect to the effect of olestra on the gastrointestinal (GI) tract."<sup>9</sup> FDA stated:

[T]he agency believes that consumers should be provided with information to enable them to associate olestra with the GI symptoms it may cause. The agency believes that providing this information to consumers would preclude unnecessary concerns about the origin of GI effects, were they to be observed, and may also prevent unnecessary or inappropriate medical treatment of those symptoms.<sup>10</sup>

In other words, FDA wanted consumers to have the appropriate information to associate a given symptom *with* a particular food.

FDA's decision to remove the olestra warning label in 2003 further reinforces the FDA's approach to warning labels. The agency removed the requirement for a warning label on snacks containing olestra because "postapproval consumer perception studies and tracking surveys show that there is currently a *high degree of awareness* about olestra and its ability to cause GI effects."<sup>11</sup> The agency believed evidence demonstrated insufficient awareness by consumers of the symptoms of olestra consumption in 1996, yet felt comfortable enough with the high degree of consumer awareness by 2003 to remove the labeling requirement.

This same rationale was the impetus behind the agency's decision to require labeling on unpasteurized juices in 1998. It found that the risks associated with unpasteurized juices were a "new phenomenon."<sup>12</sup> Because consumers were not aware of this new phenomenon, the FDA noted that consumers "do not associate such pathogens, and the risk that they present, with the consumption of untreated juice."<sup>13</sup> In response to a comment claiming that the agency's decision to require unpasteurized juice labeling was discriminatory because other foods cause similar foodborne illnesses as unpasteurized juice (*i.e.*, fruits, berries, eggs, melons, poultry, hamburgers, meat products, seafood, etc.), the agency stated that consumers already have "some awareness" of the risks associated with these foods and, in the seafood context, there are other regulatory approaches to

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<sup>9</sup> 61 F.R. 3118, 3159.

<sup>10</sup> *Id.* at 3161.

<sup>11</sup> "Final Rule; Procter and Gamble Co.; Olestra: Removal of label statement prescribed for savory snack products," 68 Fed. Reg. 46364, 46387 (Aug. 5, 2003) (*Emphasis added*). The agency also found compelling Procter & Gambles' post-approval studies that showed that "customary or usual consumption of olestra in savory snacks causes only minor GI effects...." *Id.* at 46388. It is likely, however, that the high degree of awareness by 2003 was more central to the agency's reasoning to remove labeling because the agency, in 1996, had already determined that "olestra's GI effects were not adverse health effects." *See* 61 F.R. 3118, 3159. FDA's knowledge of the minor GI effects remained constant from 1996 to 2003; consumer awareness of olestra's ability to cause GI effects did not.

<sup>12</sup> 63 F.R. 37030, 37033.

<sup>13</sup> *Id.*

ensure [sic] food safety.<sup>14</sup> Again FDA was primarily concerned about the lack of awareness consumers had regarding their ability to associate unpasteurized juice *with* the negative symptoms it may cause in some consumers.

In the case of food dyes, many if not most parents are completely unaware of the risks to their children from the consumption of these dyes. CSPI has collected almost 2,000 testimonials from parents who struggled to identify food dyes as a contributing source of their children's behavior problems.<sup>15</sup> The sheer volume of responses CSPI has received moves these testimonials beyond the realm of merely anecdotal evidence (and, of course, numerous clinical studies have demonstrated that dyes affect children's behavior). There is clearly widespread confusion and unawareness among consumers about the adverse symptoms that many children face after consuming dyes. In addition, many of the testimonials CSPI received from parents reflect the widespread, and unhelpful, lack of awareness of the link between dyes and behavior among medical professionals, including pediatricians.

The lack of public awareness is unsurprising given that FDA's own materials currently mislead the public. Currently, the FDA/IFIC brochure/website includes the question, "Do additives cause childhood hyperactivity?" FDA/IFIC firmly and quickly dismiss any possible link, describing the results from studies as being "inconclusive, inconsistent, or difficult to interpret." With false reassurances, it states:

*Food and color additives are strictly studied, regulated and monitored. Federal regulations require evidence that each substance is safe at its intended level of use before it may be added to foods. Furthermore, all additives are subject to ongoing safety review as scientific understanding and methods of testing continue to improve. Consumers should feel safe about the foods they eat.*<sup>16</sup>

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<sup>14</sup> *Id.*

<sup>15</sup> See, e.g., Appendix C: The Human Toll: Parents' First-hand Accounts in *Seeing Red: Time for Action on Food Dyes*. CSPI. Jan. 2016, available at <http://cspinet.org/reports/seeing-red-report.pdf>; see also testimonials from Change.org petition "M&M's Candies: Stop Using Artificial Dyes Linked to Hyperactivity" (including almost 200,000 signatures), available at <https://www.change.org/p/m-m-s-candies-stop-using-artificial-dyes-linked-to-hyperactivity>; testimonials in response to "How Food Dye Almost Ruined Our Lives" from Momma Lew blog, available at [http://www.mommalew.com/2015/08/how-food-dye-almost-ruined-our-lives/?utm\\_content=buffer5aa07&utm\\_medium=social&utm\\_source=twitter.com&utm\\_campaign=buffer](http://www.mommalew.com/2015/08/how-food-dye-almost-ruined-our-lives/?utm_content=buffer5aa07&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer). Parents also movingly describe their struggles in videos on this CSPI site: <http://cspinet.org/fooddyes/>.

<sup>16</sup> IFIC Foundation and FDA. Overview of food ingredients, additives & colors. See <http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm094211.htm>. Brochure available at: <http://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/ucm094249.pdf>.

A 2014 blog by a Chief Medical Officer for the Agency reiterates the conclusion that the studies linking color additives and ADHD have been “inconclusive, inconsistent, or difficult to interpret.”<sup>17</sup>

Yet another FDA consumer information site and brochure called “How safe are color additives” promises that dyes are not just safe, but “very safe:”

“Color additives are very safe when used properly,” says Linda Katz, M.D., M.P.H., Director of the Office of Cosmetics and Colors in FDA’s Center for Food Safety and Applied Nutrition (CFSAN).<sup>18</sup>

Glaringly absent from FDA’s website are the facts that many experts (as detailed in our *Seeing Red* report and in the letter from scientists to FDA<sup>19</sup>), as well as FDA’s report to the FAC,<sup>20</sup> agree upon: that dyes can trigger adverse behaviors in sensitive children.

As FDA did in the olestra and juice pasteurization regulations, the agency should require foods that contain these dyes to bear a warning statement. The association between consumption of food dyes and behavioral issues in children is a phenomenon about which most parents are completely unaware. The agency must act to provide consumers with this important information so that those parents who do notice adverse behavioral effects in their children can attempt to take remedial action (such as keeping dyes out of their children’s diets) and thereby avoid unnecessary or inappropriate medical treatment of those symptoms.<sup>21</sup>

*The Severity of Harm Associated with Food Dyes Far Exceeds That Associated with Other Products that Require Labeling*

As stated above, the agency’s stance is to require warning statements when doing so would inform consumers of the association between consumption of a food and the symptoms it

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<sup>17</sup> Katz, Linda M. How safe are color additives? Aug. 6, 2014. See [http://www.foodsafety.gov/blog/color\\_additives.html](http://www.foodsafety.gov/blog/color_additives.html).

<sup>18</sup> FDA Consumer Health Information. How safe are color additives? Dec. 10, 2007. See <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048951.htm>.

<sup>19</sup> Letter from 13 scientists to Dr. Ostroff. Docket No. 2008-P-0349. Jan. 19, 2016. See <http://cspinet.org/new/pdf/dyes-letter-from-scientists-final-signed.pdf>.

<sup>20</sup> FDA. Background document for the FAC: Certified color additives in food and possible association with attention deficit hyperactivity disorder in children. Mar. 30–1, 2011. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/FoodAdvisoryCommittee/UCM248549.pdf>.

<sup>21</sup> See FDA’s approval of a warning label on snack products containing olestra. 61 F.R. 3118, 3161 (“[T]he agency believes that consumers should be provided with information to enable them to associate olestra with the GI symptoms it may cause. The agency believes that providing this information to consumers would preclude unnecessary concerns about the origin of GI effects, were they to be observed, and may also prevent unnecessary or inappropriate medical treatment of those symptoms.”).

might cause. Clearly, some threshold level for harm must be exceeded before the association between a product and a symptom should be communicated to the public. In the case of food dyes, that threshold has been far surpassed.

When the FDA required warning statements on foods containing olestra, the symptoms involved were determined by FDA not to be “adverse health effects.”<sup>22</sup> Furthermore, the FDA found “no safety concerns with respect to the effect of olestra on the GI tract.”<sup>23</sup>

Similarly, FDA requires a warning label on food products containing sorbitol if reasonable consumption of said food might result in daily consumption of more than 50 grams of sorbitol.<sup>24</sup> Such products are required to bear the warning: “Excess consumption may have a laxative effect.”<sup>25</sup> FDA requires such a label even though the Select Committee on GRAS Substances determined that: “[t]here is no evidence that consumption of sorbitol as a food ingredient has had adverse effects on man in the many years it has been so used.”<sup>26</sup>

The harms associated with consumption of food dyes far exceed the no “adverse health effects” associated with products that may cause laxative effects. Consumption of dyes has been shown to produce adverse behavioral reactions in certain children, as FDA acknowledges, and is not limited to hyperactivity but can include sleep disturbances, irritability, and other physical responses. Given the near-daily exposure of many children to significant amounts of synthetic dyes, those reactions directly threaten the ability of susceptible children to grow, thrive, and learn. In addition, they are major impediments to positive relationships within families, between teachers and affected children, and in the community at large.

Some children have been responsive to the amount of food dyes in a single cupcake or glass of Kool-Aid.<sup>27</sup> Furthermore, two studies have shown that children in the general population—not just children with behavior disorders that might be associated with special sensitivities to dyes—sometimes suffer behavior reactions to artificial colorings.<sup>28</sup>

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<sup>22</sup> 61 F.R. 3118, 3159.

<sup>23</sup> *Id.*

<sup>24</sup> 21 C.F.R. § 184.1835.

<sup>25</sup> *Id.* The FDA requires a similar warning label on food products containing mannitol and polydextrose, among others. See 21 C.F.R. § 180.25 (e) (“The label and labeling of food whose reasonably foreseeable consumption may result in a daily ingestion of 20 grams of mannitol shall bear the statement ‘Excess consumption may have a laxative effect.’”); 21 C.F.R. § 172.841 (e) (“The label and labeling of food a single serving of which would be expected to exceed 15 grams of [polydextrose] shall bear the statement: ‘Sensitive individuals may experience a laxative effect from excessive consumption of this product.’”).

<sup>26</sup> Select Committee on GRAS Substances (SCOGS) Opinion: Sorbitol. Updated 2015. See <http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260079.htm>. Studies have since persuaded the FDA and others that SCOGS was not correct. Regardless, the FDA required a warning label on products containing sorbitol in spite of SCOGS’s findings that sorbitol does not cause any adverse effects.

<sup>27</sup> *Seeing Red: Time for Action on Food Dyes*, at 5. CSPI. Jan. 2016.

<sup>28</sup> *Seeing Red: Time for Action on Food Dyes*, at 9-11. CSPI. Jan. 2016.

A 2012 review by prominent researchers concluded that food dyes “may contribute significantly to some cases [of ADHD], and in some cases may additively push a youngster over the diagnostic threshold.”<sup>29</sup>

The symptoms associated with consumption of food dyes *do* represent an adverse health effect. Look no further than the thousands of parents who try to cope with their child’s uncontrolled fits of agitation, inattentiveness, mood-swings, anger, and rage.<sup>30</sup> Those adverse behaviors negatively impact thousands of families across the country and countless schoolrooms where teachers are faced with preventable disruption and inattentiveness from their students.

They also cause, conservatively, billions of dollars in avoidable medical costs for families and may lead to the needless treatment with medication, and over-medication, of children, as described above. The harm children face from consumption of food dyes dwarfs an occasional episode of loose stool, and FDA’s response should be proportional to the harm, particularly where a vulnerable population and the health of the next generation is at stake.

#### *FDA Has Required Labeling to Protect Vulnerable Subpopulations of Consumers*

On products containing the artificial sweetener aspartame, the FDA requires the following statement: “PHENYLKETONURICS: CONTAINS PHENYLALANINE.”<sup>31</sup> The purpose of this labeling statement is to enable phenylketonuric children, as well as pregnant women known to have hyperphenylalaninemia, to avoid consumption of aspartame<sup>32</sup> which, due to its phenylalanine content, causes abnormal brain development in these populations.<sup>33</sup> Phenylketonuria (PKU) occurs in 1 in every 10,000 to 15,000 newborns,<sup>34</sup> which means that there are between roughly 262 and 393 new cases of PKU each year.<sup>35</sup> The number of women of child-bearing age with hyperphenylalaninemia is also quite small. There were an estimated 1,750 women affected in 1980 when the FDA first considered the issue,<sup>36</sup> which corresponds to an estimated 2,494 women in 2016.<sup>37</sup>

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<sup>29</sup> *Seeing Red: Time for Action on Food Dyes*, at 11. CSPI. Jan. 2016.

<sup>30</sup> *See, e.g.*, Appendix C: The Human Toll: Parents’ First-hand Accounts in *Seeing Red: Time for Action on Food Dyes*. CSPI. Jan. 2016, available at <http://cspinet.org/reports/seeing-red-report.pdf>.

<sup>31</sup> 21 C.F.R. § 172.804.

<sup>32</sup> “Aspartame; Commissioner’s final decision,” 46 F.R. 38283, 38290.

<sup>33</sup> Decision of the Public Board of Inquiry on Aspartame, Docket No. 75F-0355, 11-12, 19, available at <http://www.sweetpoison.com/articles/pdfs/fdapetition.pdf>.

<sup>34</sup> NIH Genetics Home Reference. Phenylketonuria. Feb. 2012. *See* <http://ghr.nlm.nih.gov/condition/phenylketonuria>.

<sup>35</sup> CDC. Births and Natality. July 20, 2015. *See* <http://www.cdc.gov/nchs/fastats/births.htm>. The CDC estimates that there were 3,932,181 births in 2013.

<sup>36</sup> Decision of the Public Board of Inquiry on Aspartame at 19.

<sup>37</sup> This figure is based on the U.S.’s population as of February 9, 2016 (322,968,100 people). The current U.S. population is estimated by the Census Bureau, found at: <http://www.census.gov/popclock/>. To calculate the estimated number of women of child-bearing age with hyperphenylalaninemia in 2016, we utilized the

In contrast to the small number of children and pregnant women affected by phenylalanine, about eight percent of children with ADHD are estimated to have symptoms caused by food dyes,<sup>38</sup> and the U.S. Centers for Disease Control and Prevention (CDC) estimates that 6.4 million children have been diagnosed with ADHD in the United States as of 2011.<sup>39</sup> Thus, roughly 500,000 American children who have been diagnosed with ADHD may be affected by dyes.

In addition, the studies funded by the British government and other analyses suggest that children without hyperactivity or ADHD may suffer adverse reactions to dyes. If just one-half of one percent of all children were sensitive to dyes, that would be an *additional* 250,000 U.S. children.

If the FDA is willing to place a label on products containing aspartame to protect (from a malady that we recognize may be far more severe than symptoms of ADHD) a vulnerable subpopulation of less than 10,000, the agency should also require a label on products containing food dyes that affect over half a million children.

Even without the warning label for aspartame, children with PKU already have some protection against consuming phenylalanine because they are tested and their parents are put on notice of their disorder at birth. All 50 states and the District of Columbia require newborns to be screened for PKU and the testing identifies almost all cases of it.<sup>40</sup> Unfortunately, without any sort of warning label, parents of children that are affected by food dyes have no notice that the dyes will cause adverse behavioral reactions in their children.

The FDA must no longer sit idly by as parents across the country struggle to find meaningful solutions to their children's behavioral problems. To do so is an abdication of FDA's role as protector of the public health. Instead, the FDA should take immediate action to require warning labels on all foods that contain synthetic food dyes in order to educate parents about the association between food dyes and adverse behavior issues in children.

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following equation, solving for "X": (Estimated number of women of child-bearing age with hyperphenylalaninemia in 1980) ÷ (U.S. population in 1980) = X ÷ (Estimated U.S. population in 2016).

<sup>38</sup> Nigg JT, Lewis K, Edinger T, *et al.* 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 Psychiatry.* 2012; 51(1): 86-97.e8. doi: 10.1016/j.jaac.2011.10.015. The study was funded by the North American Branch of the International Life Sciences Institute, which "receives support primarily from its industry membership," and from the National Confectioners Association.

<sup>39</sup> CDC. Attention Deficit/Hyperactivity Disorder. July 8, 2015. *See* <http://www.cdc.gov/ncbddd/adhd/data.html>.

<sup>40</sup> Mayo Clinic. Phenylketonuria. Nov. 26, 2014. *See* <http://www.mayoclinic.org/diseases-conditions/phenylketonuria/basics/tests-diagnosis/con-20026275>; D.C. Code Ann. § 7-833, available at <http://dccode.org/simple/Title-7/Chapter-8A/>.



Sincerely,

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