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**Time for Action on Food Dyes**



CENTER FOR  
Science IN THE  
Public Interest



# SEEING RED

Time for Action on Food Dyes

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## Executive Summary

In the early 1970s, an allergist, based on observation of his patients, first proposed that food dyes and other chemicals in food can trigger symptoms of inattention and hyperactivity. That hypothesis generated enormous interest among parents and researchers.

The first controlled studies of behavioral effects of dyes on children with suspected sensitivities were conducted in the late 1970s. More than 30 studies were conducted over the following several decades. Two large studies done in the United Kingdom found that dyes appear to affect the behavior of children in the general population.

Since FDA last examined the issue in 2011, eight major independent analyses, including two meta-analyses, concluded that excluding food dyes, or a diet that eliminates dyed foods and certain other foods and ingredients, reduces adverse behavior in some children.

The mounting evidence has led to a growing consensus among researchers, physicians, psychologists, and others who treat patients with such behavioral disorders as attention deficit hyperactivity disorder (ADHD) that avoidance of food dyes benefits some children.

Recent analyses of the dye content of foods and beverages indicate that many American children are consuming amounts of dyes far higher than the levels demonstrated in some clinical trials to impair the behavior of susceptible children. The amount of dyes contained in just a single cupcake or glass of Kool-Aid can be enough to prompt adverse behavioral reactions in certain children.

We estimate that over half a million children in the United States suffer adverse behavioral reactions after ingesting food dyes, with an estimated cost exceeding \$5 billion per year, using information cited by the US Centers for Disease Control and Prevention and a recent meta-analysis sponsored by an arm of the food industry. The harm to children and the costs to society from dyes are needless and preventable.

A study of food labels in one supermarket found that more than 90 percent of child-oriented candies, fruit-flavored snacks, and drink mixes and powders are artificially colored. A majority of child-oriented foods made by such companies as Kraft, PepsiCo, and General Mills are dyed.

Dyes confer no health or nutritional benefit. They are completely unnecessary, but are sometimes used to spare companies the expense of using actual fruit or other “real” ingredients, and to trick consumers into thinking the colors in blueberry muffins, breakfast cereals, or fruit-flavored beverages derive from real fruits and vegetables, rather than synthetic chemicals.

In response to the accumulating evidence, the British government and the European Union took actions to inform and protect the public from the risks of dyes. Warnings are now required on most dyed foods sold in the EU. The British government encouraged companies to find alternatives and issued public advisories

to inform families that eliminating certain food dyes might benefit children with hyperactivity or ADHD.

Most companies reformulated their products sold in Europe, eliminating dyes to avoid having to include a warning label on their packages. But some of the same companies continue to sell the same foods in the United States with artificial food dyes in them.

In contrast to the European actions, the U.S. Food and Drug Administration (FDA) has failed to protect or even inform consumers of the risks of dyes to children. The FDA last examined the issue in 2011 when it convened an advisory committee to review the evidence on associations between food dyes and children's behavior, in response to a Citizen Petition filed by the Center for Science in the Public Interest (CSPI).

**At the meeting, FDA acknowledged that “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.”**

Yet rather than asking the committee whether dyes therefore violate the federal safety standard for color additives, FDA asked whether there was a *causal link* between dye consumption in the general population and adverse behavior—a difficult scientific question to answer, and one that is unnecessary, given the requirement that dyes meet the federal safety standard for color additives.

**If they can do it there...why not here?**

**McDonalds: STRAWBERRY SUNDAE Topping**

**US:** Strawberries, Sugar, Water, High Fructose Corn Syrup, Natural Strawberry Flavor with other Natural Flavors (Fruit Source) Citric Acid, Pectin, Sodium Benzoate (Preservative), Carob Bean Gum, **Red 40**, Calcium Chloride.

**UK:** Strawberries (38%), Sugar, Glucose Syrup, Water, Gelling Agent (Pectin), Acidlant (Citric Acid).



Committee members raised serious questions about the FDA's general dismissal of the neurobehavioral toxicity of dyes, the agency's poorly done estimates of children's exposure to dyes, and its estimation of safe levels for dyes. The committee recommended that FDA require additional safety testing of dyes and develop a robust intake estimate. In a closely divided vote, the committee did not recommend that the FDA require a warning notice on the labels of foods containing dyes.

Meanwhile, independent analyses published since FDA's 2011 meeting confirm the link between food dyes and adverse behavior and demonstrate that dyes fail to meet the federal safety standard for color additives, which requires convincing evidence that dyes are safe under the law.

First-hand testimonials included in this report illustrate the difficulties parents and children face in dealing with the adverse reactions triggered by dyes. Parents recount troubling episodes of hyperactivity, inattention, repetitive motions, aggression, and even violence. When their children avoided artificial colorings, they saw dramatic improvements in their child's behavior.

Despite government inaction, adverse publicity about dyes has prompted several major companies to pledge to stop using them in at least some of their products. Those companies include Kraft, Campbell Soup, Frito-Lay, General Mills, Kellogg, Chick-fil-A, Panera, Subway, and Taco Bell.

Even with those welcome voluntary commitments, foods made with dyes are still commonplace in supermarkets, schools, and restaurants, which puts the burden on families to learn of dyes' effects and try to keep their children from eating dyed foods. To protect children's health, FDA should revoke approvals for all food dyes. Until it takes that action, the FDA should follow the lead of European authorities and encourage companies to reformulate foods without dyes and require dyed foods to bear a label warning consumers that dyes can trigger behavioral problems in children.

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SEEING RED

## Introduction

More than 40 years ago, Benjamin Feingold, Chief of Allergy at Kaiser-Permanente Hospital in California, startled the nation by contending that commonplace foods consumed by practically every child in America could cause hyperactivity and inattention. He believed that the culprits were artificial colorings, artificial flavors, preservatives (BHT), and natural sources of substances called salicylates, like apples and tomatoes, to which some people are sensitive. His contention was based on years of observations of patients, rather than controlled studies, and generated a firestorm of controversy and excitement.

Many parents were desperately searching for a solution to their children's behavior problems. They knew how debilitating hyperactivity (now called attention deficit hyperactivity disorder, or ADHD) was to their children and their family. Ritalin or other drugs helped to address some children's problems, but many parents, concerned about possible risks of medicating their children, instead sought to identify and eliminate the cause of their problems.

Following Feingold's suggestions, parents put their children on special diets. Some of the children found quick and remarkable relief from their long-standing problems. This restrictive diet (then called the "Kaiser Permanente diet" or "K-P" diet), became known as the Feingold diet and is still used by some parents today.

Feingold and his hypothesis generated so much attention that the U.S. Food and Drug Administration (FDA) and others in the United States and abroad sponsored research into the issue. The studies are hard to do and expensive, but several dozen have been conducted. Once the results came in, other scientists and organizations convened workshops to review the findings and conducted meta-analyses and reviews of the evidence.

Ultimately, government regulatory agencies in the United States and United Kingdom and the European Parliament were drawn into the controversy. This report reviews the use of dyes in the food supply, the research on dyes and behavior, and policy responses.

## Artificial Food Colorings

Artificial colorings, also sometimes called dyes,\* are used in thousands of foods, especially those intended for children who are drawn to the eye-popping colors of foods like Cheetos and M&Ms.\*\* (Some foods are artificially colored with naturally-derived colorings, from fruits, vegetables, microbes, or even insects. Those are not associated with behavioral problems.) (FDA appropriately treats all added colors, including natural colors, as "artificial" for labeling purposes. In this report, "artificial" refers to the more narrow category of synthetic dyes.)

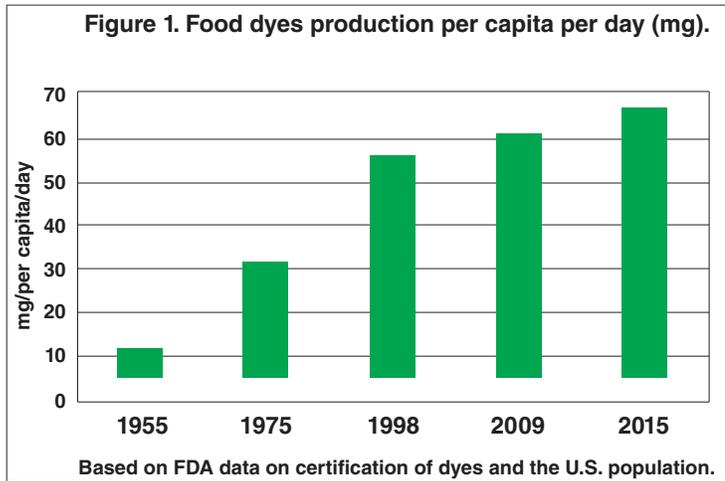
Since the 1950s, the variety of dyed foods has exploded. Everything from candies and ice cream to pickles and salad dressing may be dyed. Even Pedialyte, a product intended for sick infants and children to replace fluids and electrolytes lost during diarrhea and vomiting, contains dyes. The per capita production of artificial colorings approved for use in food

\* Dyes dissolve in water. The term "lake" is the technical term used for the water-insoluble form of a dye (used in fatty foods and low-moisture foods).

\*\* FDA approved dyes include FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, Orange B, FD&C Red. No. 3, FD&C Red. No. 40, FD&C Yellow No. 5, FD&C Yellow No. 6. Citrus Red 2, only to color the peels of some Florida oranges, is rarely used. Orange B, approved only for coloring sausage casings, is no longer used.

increased more than five-fold since 1955, with Red 40, Yellow 5, and Yellow 6 comprising about 90 percent of all dyes used today.<sup>1</sup> In 1955, 1.6 million pounds of dyes, or 12 mg per person per day, were certified for use in foods. By 2015 that figure jumped to over 17 million pounds, or 67 mg per person per day.<sup>2</sup> That more than five-fold increase reflects the increasing number of soft drinks, breakfast cereals, candies, baked goods, snacks, desserts, and other foods and drinks made with dyes.

(Figure 1)



A recent study conducted by a researcher at the University of North Carolina, Chapel Hill, and by the Center for Science in the Public Interest (CSPI) found that more than 90 percent of child-oriented candies, fruit-flavored snacks, and drink mixes and powders are artificially colored.<sup>3</sup> It also showed that a majority of child-oriented foods made by such companies as Kraft, PepsiCo, and General Mills are dyed.

Dyes lack nutritional value and are often used as cheap replacements for healthful ingredients. For example, most of the color in the “carrot-flavored pieces” in Betty Crocker’s Super Moist Carrot Cake Mix comes not from the smidgen of carrot powder, but from the Yellow 6 and Red 40 dyes.<sup>4</sup> Similarly, there are no cherries or berries in Tropicana Twister Cherry Berry Blast. The color comes primarily from Red 40.<sup>5</sup> (Figure 2).

**Figure 2. Dyes help replace healthful ingredients in food.**

**Where are the Cherries & Berries in Tropicana Twister Cherry Berry Blast?\***

Ingredients: Filtered Water, High Fructose Corn Syrup, Apple and Grape Juice Concentrates, Citric Acid, Natural and Artificial Flavors, Ascorbic Acid (Vitamin C) and **Red 40**.

Contains 10% Juice.

**\*Answer: on the label (not in the bottle)**

### Behavioral Problems in Children

ADHD is one of the most common neurodevelopmental disorders of childhood. In 2011, about 11 percent of U.S. children 4–17 years of age—6.4 million children—had been diagnosed with ADHD, and the percentage of children who have ADHD has increased over time.<sup>6</sup> The causes of ADHD are not well understood. Genetics plays an important role, but many other factors can cause or trigger ADHD symptoms.<sup>7</sup>

ADHD can be debilitating. While all children have trouble focusing and behaving at times, children with ADHD experience that routinely, and the behavior can cause problems at school, at home, or with friends.<sup>8</sup> Many children do not grow out of ADHD, but experience its symptoms throughout their lives. By adulthood, it can lead to substance abuse, criminal behavior, depression, and suicide.<sup>9</sup> Treatments for ADHD include amphetamines, other medications, behavioral therapy, and dietary changes.

## Children's Growing Exposure to Food Dyes

### Exposure to Dyes is Widespread and Higher Than Many Researchers Realized

Many early studies examining the relationship between food dyes and behavior challenged children with foods or beverages containing 26–30 mg of a mixture of dyes. That amount was chosen because it was thought to approximate the amount of dyes consumed by the average person in a day. It was calculated by dividing the total amount of food dyes certified by the population of the United States.<sup>10</sup> Since that was an estimate of the amount of food coloring consumed by each person in a whole day, many studies gave children half that amount, twice per day. A blend of colors was normally used, with the proportion of each individual color based on the amount of each color certified.

At least in hindsight, studies that used dosages of only 26–30 mg of dyes were clearly inadequate. About half the population consumes more than the average, and some people, especially children, consume much more. Children consume more food per pound of body weight than adults and are also more likely to consume dyed foods. As far back as 1985, FDA estimated that high-end (90th percentile) consumers who were 5 to 12 years old ingested 150 mg of dyes per day<sup>11</sup>—five times higher than the amount used in many early studies. While that estimate was probably overstated, it indicates that FDA realized that doses of 26–30 mg were inadequate.

The flawed advice on how much dye to test came from an organization called the Nutrition Foundation.<sup>12</sup> While the Nutrition Foundation described itself as a “public, non-profit institution...dedicated to the advancement of nutrition knowledge,” it was established and funded by the food industry.<sup>13</sup>

Moreover, the amount of food dyes certified per person has more than doubled over the past four decades. To take Red 40 as an example, the typical daily challenge dose of Red 40 used in many studies was about 10 mg. According to a preliminary exposure assessment by FDA in 2014,<sup>14</sup> people may consume as much as 52 mg of a single dye—Red 40—in a day, and some children between the ages of 2 and 5 consume 38 mg of Red 40 in a day. Thus, the amount of dye used in those early studies was far too low to reflect the amounts of dyes that many people consume.

A third deficiency is that those researchers failed to consider exposures from drugs and cosmetics, although FDA is directed by law to consider those sources of exposure.<sup>15</sup> Most of the dyes used in food are also permitted to be used in other products such as cosmetics, personal-care products like mouthwash, shampoo, and toothpaste; over-the-counter medications; dietary supplements; and prescription drugs. Ironically, two forms of the drug Ritalin, which is often used to treat children with ADHD, contain dyes as the first inactive ingredient.<sup>16</sup>

Laura Stevens and her colleagues at Purdue University published the first studies of the dye content of brand-name beverages<sup>17</sup> and foods,<sup>18</sup> such as cookies and candies, consumed by children. Because of criticisms of their methods, the researchers reanalyzed the data on beverages, using a method adapted from FDA.<sup>19</sup> The Purdue researchers found that in some cases a single serving of a beverage contained more dyes than the doses used in the early studies—and an amount that other research shows is sufficient to produce behavioral responses in some children.

For example, the reanalysis showed that a cup of Kool-Aid Burst Cherry contains 50 mg of dyes—almost twice as much as the dose that caused behavioral reactions in some children. Similarly, 16 ounces of Sunny D Strawberry Orange contains nearly 40 mg of dyes.

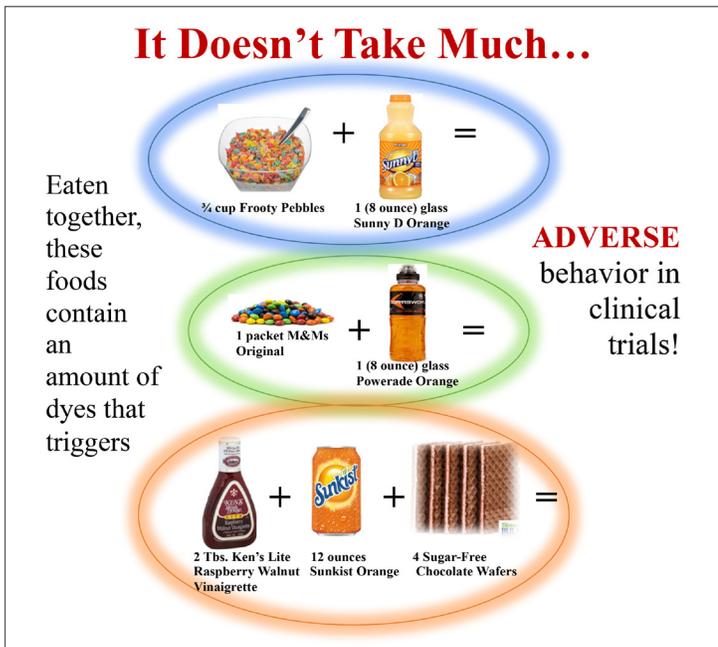
The Purdue reanalysis and other test results we obtained from FDA (Appendix A) show how easily a child can consume large doses of dyes. For example, two tablespoons of Pillsbury Confetti Funfetti Chocolate Fudge Frosting contains 41.5 mg of dyes, more than the amount of dyes that triggered adverse reactions in some children. Similarly, a child who drinks a cup of Crush Orange (14.7 mg) or

Hawaiian Punch (14.1 mg) and has a treat such as 4 pieces of Twizzlers (15.4 mg) or a Red, White and Blue Popsicle (21.6 mg) would consume more than the amount of dyes that were used in the early studies—amounts that triggered behavioral reactions in some children. (Figure 3)

These recent data show how important it is to administer a realistic dose in studies that assess the risks from food dyes. C.K. Connors, a prominent researcher who used a dose of 26 mg in several studies, later regretted using so little:

*Unfortunately, we accepted the recommendations of the interagency collaborative group of the National Institute of Mental Health to employ a double-blind challenge material supplied by the Nutrition Foundation. The figure of 15 mg of artificial colors recommended by that group as half the average daily intake of colors by adults may, in retrospect, be a considerable underestimation.<sup>20</sup>*

**Figure 3. Small amounts of dyes in foods trigger adverse reactions in sensitive children.**



## Food Dyes' Effects on Behavior

The highly publicized debate over the “Feingold diet” stimulated a wave of scientific studies. The first controlled study suggesting a link between artificial food colorings and adverse behavior was published in 1976.<sup>21</sup> Since then, researchers from around the world have published studies and examined the role that dyes play in hyperactivity and other behavioral disorders in children.<sup>22</sup>

The studies are of two general types: those that gave children food dyes and measured how they responded, and others that eliminated certain foods from the diet (such as foods containing food dyes as well as other foods and food components) and measured if symptoms abated.

Within this body of research, a number of studies produced startling findings. Some studies showed that even small amounts of artificial dyes—smaller than might be contained in a single cupcake or glass of Kool-Aid—can prompt adverse behavioral reactions in certain children. Other studies showed that children in the general population—not just those with behavioral disorders that might make them sensitive to food dyes—sometimes suffer behavioral reactions to artificial colorings.

Moreover, several recent reviews of the evidence, including those with a systematic approach, in some cases pooling data from multiple studies, concluded that eliminating food dyes or adopting a broader elimination diet produces behavioral improvements for some children.

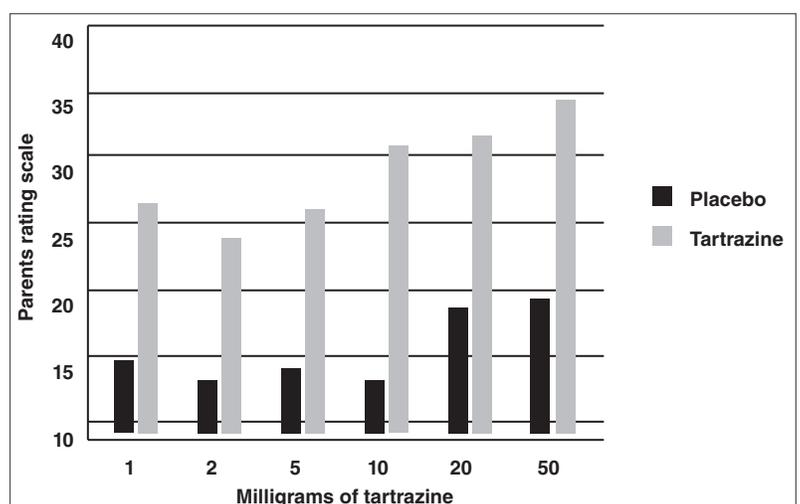
### Most Double-blind Studies Concluded Dyes Affect Behavior

The best medical studies are “double-blind,” meaning that neither the subjects nor the researchers know which group is receiving the treatment. Because these studies are especially stringent, this report focuses on studies with a double-blind design.

About 30 double-blind studies have investigated the effect that artificial colorings and other suspect additives and foods have on children’s behavior.<sup>23</sup> Many focused only on dyes, and some tested the effect of one dye alone—Yellow 5, also called tartrazine, the second most commonly used dye in the United States.

Many of the early studies used relatively small doses of artificial colorings, as explained above. The amount of dyes

**Figure 4. Dose-response study using Yellow 5 dye; parent rating scale.**



Source: Stevens *et al.*, 2011, adapted from Rowe and Rowe.

to which children are exposed appears to matter. In a double-blind study that tested multiple doses of a single dye (Yellow 5 in this case), the more dye that was consumed, the worse the children scored on a behavioral test.<sup>24</sup> (Figure 4) Such a “dose-response” relationship is strong evidence of a true effect, rather than a random or spurious finding.

Some studies examined the effect of a diet that eliminates dyes as well as other additives and certain foods. For example, the diet proposed by Feingold eliminated synthetic dyes as well as other artificial ingredients and certain natural foods. Thus, the results of some studies examining the Feingold diet apply to more than colorings. Those studies sometimes find greater effects than just dye-free diets. Still, because it is much harder to keep children on such diets, and to make it easier to identify the particular causes of behavioral effects, many studies have focused exclusively on mixtures of dyes.

In 1980, two notable studies were published in the same issue of the journal *Science*. One, funded by the FDA, tested 22 children, ages 2 to 7—not as a group, but as 22 separate experiments—suspected of reacting to artificial colorings and flavors.<sup>25</sup> The subjects were kept on a dye-free diet. For 77 consecutive days, each child drank a beverage that on eight randomly selected days concealed a 35.3 mg mixture of dyes. Two of the children showed clear reactions, according to their parents. A 34-month-old girl reacted “dramatically” on the days she received the dyes and a 3-year-old boy displayed convincing evidence of a reaction that his mother considered typical of his outbursts. The researchers stated: “[t]hese data further strengthen the accumulating

evidence from controlled trials, supplemented by laboratory experiments, that modest doses of synthetic colors, and perhaps other agents excluded by elimination diets, can provoke disturbed behavior in children.”

A sensible guide would surely be to reduce exposure to hazard whenever possible, to accept substantial hazard only for great benefit, minor hazard for modest benefit, and no hazard at all when the benefit seems relatively trivial.

*Philip Handler, former president of the National Academy of Sciences*<sup>27</sup>

The second study used higher doses of dyes, as well as laboratory tests, rather than assessments by parents or teachers.<sup>26</sup> Researchers challenged 40 children, 20 of whom were considered hyperactive, with doses up to 150 mg, thought to represent the 90th percentile intake of artificial colors. For three days the children, ages 5 to 12, were put on a Feingold diet. The researchers then administered either placebos or a mixture of either 100 or 150 mg of dyes. Compared to the placebo, the dyes decreased the attention span of the hyperactive children, and 17 of the 20 hyperactive children suffered impaired performance on a learning test. The authors suggest that the negative results in some previous studies of dyes might have been a result of testing too low of a dose.

In 1982, the National Institutes of Health (NIH) organized a conference on “Defined Diets and Childhood Hyperactivity” to evaluate the few early studies on dyes and behavior. The NIH panel concluded that the studies indicated “a limited positive association between ‘the defined diets’ and a decrease in hyperactivity.” It highlighted the need for further research.<sup>28</sup>

## Meta-analyses Assessing Clinical Studies

Despite the strength of the double-blind study design, these clinical studies, many of them conducted decades ago, have limitations. They studied small groups of children and were not as statistically powerful as larger studies would have been. Also, measuring adverse behavior is not as simple as measuring other types of effects, such as changes in body weight. Some authors reported the amounts of dyes used without reporting the weights of the children, and some did not adequately “blind” subjects or researchers.

To compensate for limitations in studies and indicate where the weight of the evidence lies, researchers use a powerful technique called a meta-analysis. Meta-analyses can develop conclusions with greater statistical power, because they typically identify all available studies, use specific criteria to determine which data to include, consider the quality and other aspects of the studies, and pool the results. The results are weighted by sample size.

In 1983, a meta-analysis of the evidence concluded that the Feingold diet was not effective for treating hyperactivity.<sup>29</sup> That review understandably fed the skepticism about the links between diet—including food dyes—and ADHD or other behavioral symptoms. However, some clinicians, parents, and groups (such as the Feingold Association) with direct experience with the effects of dyes continued to advocate for eliminating dyes from the diet as an effective way to treat ADHD in some children. Over the next two decades, numerous higher-quality studies were done, leading to new meta-analyses.

Three different groups of researchers selecting slightly different studies conducted meta-analyses over the past dozen years. They drew upon the more than 30 double-blind studies. Each concluded that excluding dyes from the diet has beneficial effects on the symptoms of ADHD for some children.

The first meta-analysis was conducted in 2004 and analyzed 15 double-blind, placebo-controlled studies. It concluded that the “results strongly suggest an association between ingestion of [synthetic food dyes] and hyperactivity.”<sup>30</sup> The analysis found that dyes had a detrimental effect on behavior estimated at one-third to one-half of the deterioration that would occur if medications were withdrawn from children being treated for ADHD.

Two other meta-analyses were published after FDA convened a meeting of its Food Advisory Committee in 2011 (discussed below). A 2012 meta-analysis, which was funded by an arm of the food industry, found that adopting a diet free of food dyes and certain other foods and ingredients improved ADHD symptoms for approximately 33 percent of children with the disorder.<sup>31</sup>

The same authors separately analyzed studies according to whether adverse behavior was assessed by parents (20 studies, 794 children), teachers or another observer (10 studies, 323 children), or by attention tests (6 studies, 154 children). They found that synthetic colorings were associated with a slight statistically significant increase

Until safety can be better determined, we suggest minimizing children's exposure to [artificial food colorings].

*Arnold, et al., 2012.  
Neurotherapeutics.<sup>32</sup>*

in ADHD symptoms when assessed by parents or by attention tests. The results regarding assessments by teachers/observers fell just short of statistical significance.

After restricting its conclusions only to FDA-approved dyes and objective measures of attention, the study concluded that FDA-approved colorings had significant effects on attention. That meta-analysis was the first to examine the data based on testing for attention, which may be important since those results are not susceptible to a rater's beliefs about whether or not a child experienced a reaction to food dyes.

The same study estimated that as many as eight percent of children with ADHD may suffer symptoms directly related to synthetic food colorings and concluded that the benefits of dietary intervention "could be quite substantial from the perspective of population-wide prevention efforts." The authors deemed the findings "too substantial to dismiss."

A 2013 meta-analysis differed from the earlier two by analyzing only studies of children who had been formally diagnosed with ADHD. It examined six forms of non-drug treatment for ADHD, three dietary and three psychological approaches (cognitive training, neurofeedback, and behavioral).<sup>33</sup> It reviewed 54 studies from the past 40 years, finding that all of the treatments produced statistically significant effects when based on assessments made by raters, such as parents or teachers.

Because some studies had been criticized for ineffectual blinding, this meta-analysis also separately analyzed the studies in which the raters were highly likely to be blinded as to which subjects received the treatment. When limited to only the "best probably blinded assessments," the effects remained statistically significant for only two treatments: diets that excluded artificial colors and diets supplemented with free fatty acids. (A third dietary treatment, a restricted elimination diet, was just shy of statistical significance.) The researchers concluded that excluding artificial food colors from the diet "appears[s] to have beneficial effects on ADHD symptoms," but noted that the effect may be limited to ADHD patients with food sensitivities.

The effect of excluding food dyes from children's diets was greater in the 2013 meta-analysis than in the 2012 meta-analysis, perhaps because this study was limited to children diagnosed with ADHD. In contrast, the 2004 meta-analysis found that effects of dyes on children whose diagnosis of hyperactivity was rigorously evaluated were no greater for those children than for children whose diagnosis was more informal or who were not hyperactive at all.

## **Other Critical Reviews Confirm That Dyes Affect Behavior**

Some reviews of a body of research are not as quantitative as meta-analyses, but also can help decipher the varied results from a large body of research. For instance, a 2011 review (published after the meeting of the FDA's Food Advisory Committee) of the research over a 35-year period considered the impacts on children with ADHD, as well as children in the general population. It concluded that:

## While FDA Fiddles, Europe Acts

Almost all studies on dyes and behavior tested children with hyperactivity, ADHD, or other behavioral problems. But two large, groundbreaking studies commissioned and funded by the British government and published in 2004 and 2007 tested children in the general population.<sup>46,47</sup>

The first British study, published in 2004, was a double-blind, placebo-controlled study that tested a mixture of four dyes (20 mg total, including Yellow 5 and Yellow 6, plus the preservative sodium benzoate\*) on 277 3-year-olds living on the Isle of Wight. The children had been screened for hyperactivity and tested with a skin-prick test to see if they were atopic (prone to allergies). The researchers found a general adverse effect of the dye mixture on the behavior of the children that was not influenced by the presence or absence of hyperactivity or the presence or absence of certain allergies. In other words, “normal” children were affected, just as were children in other studies who were hyperactive or had allergies.

The researchers followed up with a second double-blind, placebo-controlled trial—called the Southampton study because it was conducted by researchers at the University of Southampton.<sup>48</sup> Even the food-dyes industry admitted that it was the “most robust and extensive study” on the issue that had been done.<sup>49</sup>

This study tested 153 3-year-olds and 144 children aged 8 to 9. The children were screened for hyperactivity. Over a six-week period, a placebo and two mixtures of chemically-related azo dyes were administered to the children.\*\*

- At least half of the mixtures of dyes tested in the two studies consisted of two of the three dyes (Red 40, Yellow 5, Yellow 6) most widely used in the United States. The rest was made up of three dyes not permitted in food in the United States.<sup>50</sup> Mix A used four dyes, including Yellow 5 and Yellow 6, for a total of 20 mg of dyes for the 3-year olds and 25 mg for the 8- to 9-year-olds. (The same mixture was used in the first study.)
- Mix B also used four dyes, including Yellow 6 and Red 40, for a total of 30 mg for the 3-year-olds and 62 mg for the 8 to 9-year-olds.

Compared to the placebo, Mix A affected the group of younger children, and both mixtures caused adverse reactions in the older group (including only those children who consumed at least 85 percent of the mixtures). The researchers concluded that “[a]rtificial colours...in the diet result in increased hyperactivity in 3-year-old and 8/9-year-old children in the general population.” Had the researchers used higher, more realistic doses, it is likely that more children would have reacted, and that the children who did react would have reacted more strongly.

An independent scientific committee that reviewed the Southampton study “conclude[d] that the results of this study are consistent with, and add weight to, previous published reports of behavioral changes occurring in children following consumption of particular food additives.”<sup>51</sup> The Editor of a journal published by the American Academy of Pediatrics wrote:

*...the overall findings of the study are clear and require that even we skeptics, who have long doubted parental claims of the effects of various foods on the behavior of their children, admit we might have been wrong.*<sup>52</sup>

\* Benzoate was included in the study since some of the early challenge studies included it as part of the challenge and there was concern that it might also affect behavior.

\*\* The mixtures also included sodium benzoate, and one dye in mix B was not an azo dye (Quinoline Yellow is approved in the United States as D&C Yellow 10 only for drugs and cosmetics).

In Europe, the British research led to governmental action to protect the public. The Food Standards Agency (the counterpart of the FDA) informed parents that “[i]f a child shows signs of hyperactivity or Attention Deficit Hyperactivity Disorder (ADHD) then eliminating the colours used in the Southampton study from their diet might have some beneficial effects.”<sup>53</sup> The FSA’s Chair, Dame Deirdre Hutton, noted that:

*These additives give colour to foods but nothing else. It would therefore be sensible, in the light of the findings of the Southampton Study, to remove them from food and drink products.*<sup>54</sup>

Notably, the FSA based its advice on the effects of the mixtures of dyes rather than insisting that each dye be tested separately. Hutton maintained that the best approach to food dyes would be to eliminate them from all foods:

*[T]he evidence suggests it would be sensible for these colours to be taken out of the food that children eat, and by definition, out of all foods as you cannot separate the food that adults and children eat.*<sup>55</sup>

The FSA urged food makers to discontinue the use of dyes, but initially, only a few companies complied. In response, Hutton publicly criticized the food industry: “The board expresses its astonishment that industry has not moved more quickly to remove these artificial colors from their products, in the light of serious concerns raised by consumers.”<sup>56</sup>

Health Canada noted that its “scientists reviewed the results of the U.K. study and agreed with the conclusions of the U.K. Committee on Toxicology that the results of this study are consistent with, and add weight to, previous published reports of behavioral changes occurring in children following consumption of particular food additives which included a number of azo food colours.”<sup>57</sup>

Unfortunately, Health Canada has done nothing to protect Canadian children.

The European Food Safety Authority (EFSA) also reviewed the Southampton study, but downplayed the “limited evidence” that the mixture of dyes had a statistically significant effect on the activity and attention of children selected from the general population.<sup>58</sup> (EFSA’s panels have been criticized for their industry-oriented opinions and for including members with conflicts of interest.<sup>59</sup>)

Nevertheless, because of FSA’s pressure, many companies began dropping artificial colors from their products. The FSA now maintains a helpful list of dye-free foods.<sup>60</sup>

**Figure 5. Warning label required on most dyed foods in the European Union.**



Cadbury's Mighty Perky Nana Chocolate Bar

Following the British actions, the European Parliament passed a law requiring a warning label on products containing any of the six artificial colorings tested in the Southampton study. The warning states: “[name colorings] may have an adverse effect on activity and attention in children.” (Figure 5) The Parliament also prohibited the use of food dyes in foods for infants and young children.<sup>61</sup> That law helped rid the European food supply (which never had as many dyed foods as the American food supply) of most dyed foods, so the warning appears on only a few products.

*There is a subpopulation of children with ADHD who improve significantly on an AFC-[artificial food color-]free diet and reacts with ADHD-type symptoms on challenge with AFCs. The size of this subpopulation is not known. The [U.K.-commissioned studies] suggest that sensitivity to AFCs ... is not confined to the ADHD population but is instead a general public health problem and probably accounts for a small proportion of ADHD symptoms.<sup>34</sup>*

A 2012 review by prominent researchers concluded that artificial dyes can have “a small but significant deleterious effect...on children’s behavior that is not confined to those with diagnosable ADHD.” It further 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>35</sup>

In 2013, the same authors rated the quality (*i.e.*, the level of certainty) of evidence for elimination diets (diets that eliminated many foods and ingredients in addition to dyes) as “good” for treating ADHD symptoms in both typically developing children and children diagnosed with ADHD.<sup>36</sup> Their recommendation for diets that eliminated many foods and ingredients in addition to dyes, however, was limited to those children with ADHD who were “documented reactors” (*i.e.*, they responded to food dyes or other ingredients in food with irritability, restlessness, sleep disturbance, or other adverse behaviors).

A 2014 review by an international team of researchers critically appraised the meta-analyses investigating dietary interventions for ADHD.<sup>37</sup> The researchers concluded that “food colour elimination is a potentially valuable treatment approach for ADHD” and that “[a]rtificial food colours exclusion may be beneficial for children thought to be adverse responders to food colour exposure.”

Another 2014 review approached the issue by using guidelines developed by the Oxford Center for Evidence-Based Medicine to examine different non-drug treatments for ADHD.<sup>38</sup> Those guidelines are used to assess the degree to which different treatments are supported by scientific studies. The review gave both exclusion of food dyes and restricted elimination diets its second-highest rating (4 out of 5), much stronger than psychotherapy (which earned a 1 out of 5) and just slightly behind FDA-approved medications (5 out of 5).<sup>39</sup> (Figure 6)

In addition, they were rated as far more effective than such ADHD treatments as behavioral parent training or supplementation with omega-3 fatty acids, although less effective than drugs.

**Figure 6. Strength of the Evidence for Dietary Treatments for ADHD.**

The Strength of the Evidence for Different ADHD Treatments Using Oxford Center for Evidence-Based Medicine Guidelines <sup>1</sup>	
RATING	TREATMENT
5 out of 5	FDA-approved medications, Omega-3 fatty acids, Elementary school-based interventions
4 out of 5	Artificial Food Color Exclusions, Restricted Elimination Diets, Neurofeedback, Family Therapy
3 out of 5	Exercise, Pycnogenol, Ningdong Herb, Iron, Zinc, Cognitive Behavioral Therapy (Adolescents)
2 out of 5	Magnesium
1 out of 5	Computer Cognitive Training, Psychotherapy, Clinic Based Social Skills Training

<sup>1</sup> Faraone S, Antshel K. Towards an evidence-based taxonomy of nonpharmacologic treatments for ADHD. *Child Adolesc Psychiatr Clin N Am* 2014; 23(4):965-972.

## An Emerging Consensus on the Hazards of Dyes

The recent meta-analyses and other reviews of the evidence, some not available until after FDA's review of the issue in 2011, reveal an emerging consensus on the risks posed by dyes, and the benefits from excluding them from the diet, both as a treatment for ADHD and for public health generally.

The authors of a 2012 review highlight the impacts on children regardless of diagnosis:

*AFCs appear to be more of a public health problem than an ADHD problem. AFCs are not a major cause of ADHD per se, but seem to affect children regardless of whether or not they have ADHD, and they may have an aggregated effect on classroom climate if most children in the class suffer a small behavioral decrement with additive or synergistic effects.*<sup>40</sup>

The magnitude of the effect on dyes on behavior has also been compared to the behavioral effects from low doses of lead, an effect that prompted the banning of lead in gasoline.<sup>41</sup>

A 2014 review on dietary treatments for ADHD stated:

*A small but extensively discussed literature yields an emerging consensus that dietary intervention to remove food additives (color and perhaps preservatives) likely yields a small aggregate benefit.*<sup>42</sup>

Similarly, an editorial published in 2015 by the editor-in-chief of the *Journal of Child Psychology and Psychiatry*, who co-authored one of the meta-analyses, referred to the “growing literature” with regard to the effects of diet on children’s behavior:

*Studies suggest a statistically significant but clinically limited role for dietary treatments (both supplements and exclusions)—far less than envisaged by some of the promoters of the diet-behavior narrative but greater than expected by their sceptics.*<sup>43</sup>

The authoritative *Diagnostic and Statistical Manual of Mental Disorders*, published by the American Psychiatric Association, cites two of the recent reviews, stating: “A minority of cases [of Attention-Deficit/Hyperactivity Disorder] may be related to reactions to aspects of diet (Nigg *et al.*, 2012; Stevens *et al.*, 2011).”<sup>44</sup>

The American Academy of Family Physicians (AAFP) has also been persuaded by the accumulating data. Its website states that: “[s]tudies have shown that certain food colorings and preservatives may cause or worsen hyperactive behavior in some children. Talk to your doctor about whether you need to make any changes to your child’s diet.”<sup>45</sup>

In summary, studies conducted over the past 40 years demonstrate that dyes clearly affect the behavior of some children, including both children with ADHD or other behavior problems, children with food allergies, and children without these conditions. Later in this report we discuss our conservative estimate that food dyes likely affect the behavior of over half a million children in the United States.

## The Preventable Costs of Food Dyes

Parents whose children are sensitive to dyes are stuck with the burden of determining the cause of their children's problem behaviors. Linking dyes to those behaviors is especially difficult because any child's behavior can be erratic. Even most physicians and teachers are not aware that dyes can affect behavior, and federal health agencies have not provided timely and accurate information. Figuring out that dyes can be part of the problem is further complicated because adverse behaviors can have many causes.

Even once a link is made, dyes are difficult to avoid. They are ubiquitous not just in packaged foods, but in restaurant foods and bakery products as well. They are encountered at birthday parties, in school meals, and at the homes of friends. Parents may be able (with effort) to control what products a child consumes at home, but have little ability to restrict a child's diet in other environments, especially as the child becomes more independent.

### How Many Children Are Sensitive to Dyes?

According to one estimate, eight percent of children with ADHD have symptoms caused by food dyes,<sup>62</sup> and the U.S. Center for Disease Control and Prevention (CDC) estimates<sup>63</sup> that 6.4 million children have been diagnosed with ADHD in the United States as of 2011. 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.

As the family testimonials included in the appendix illustrate, behavioral disorders triggered by dyes can cripple a child's family life, interpersonal relationships, and performance in school. Dyes affect the child as well as the child's family, friends, and classmates.

### The Economic Costs

In economic terms, the impact of ADHD to society is enormous. One analysis estimated the annual societal cost of ADHD in children and adolescents as between \$36 billion and \$52.4 billion in 2005 dollars<sup>64</sup> (\$44 billion to \$64 billion in 2015 dollars). That estimate assumed that five percent of children and adolescents have ADHD.

If eight percent of children with ADHD have symptoms caused by dyes, then the annual cost to society from dyes is between \$2.9 billion and \$4.2 billion in 2005 dollars, or from \$3.5 billion to more than \$5 billion in 2015 dollars—a cost to children, parents, teachers, and society that is entirely preventable.

That cost estimate may be low because:

- It omits the costs related to children without ADHD whose behavior is affected by dyes.
- It assumes that only five percent of children have ADHD, far lower than the CDC's estimate of 11 percent.
- It does not include costs due to allergic reactions or cancer risks related to dyes.
- It is based on a conservative estimate of the costs to society from ADHD, cited by the CDC.

A recent prospective study of three-year-old children living in England found that preschoolers with high levels of hyperactivity had a 17-fold increase in mental health, educational, social service, and criminal justice system costs compared to their non-hyperactive peers after taking into account other preschool characteristics and factors.<sup>65</sup> The study considered costs across childhood, adolescence, and early adulthood associated with pre-school hyperactivity.

The numbers are shocking, and the costs of continued use of artificial dyes are far too high, both in economic terms and in the needless suffering of families and children.

## FDA's Failure to Regulate Food Dyes

In 2008, CSPI petitioned the FDA to take four actions: 1) ban eight of the nine approved food dyes; 2) until a ban could be fully implemented, require that products containing dyes bear a warning label; 3) revise statements on the agency's website denying a link between food dyes and adverse reactions; and 4) require neurotoxicity testing of new food additives and colors.<sup>66</sup>

In support of that petition, 20 physicians and researchers cosigned a letter to the FDA about the adverse effects of dyes on children's behavior. They noted the "substantial body of scientific evidence," and called on the agency to adopt "measures that would help protect children from unnecessary harm," including ending use of food dyes.<sup>67</sup>

In partial response to CSPI's petition, in 2011 FDA convened a meeting of its Food Advisory Committee (FAC) to examine the link between dyes and adverse behaviors. FAC Members included scientists, food industry representatives, and consumer representatives (including the author of this report prior to her employment with CSPI).

In preparation for the meeting, the FDA prepared a memorandum and a background document to familiarize committee members with the scientific evidence on dyes and behavior. The agency's unpublished review found a host of reasons to downplay or dismiss the reliability of the numerous double-blind studies that found a link between dyes and impaired behavior, rather than properly analyzing them to determine how each study contributes to the evidence as a whole.

The agency emphasized flaws in studies that diminished the reliability of positive findings, but did not highlight flaws that reduced the ability of studies to find impacts on behavior. For example, many studies on dyes had small numbers of subjects and used small doses of dyes—weaknesses that could prevent the studies from detecting a true effect. When such studies detect behavioral effects, it is all the more compelling that the effects are real.

Bernard Weiss, a prominent neurotoxicologist from the University of Rochester who made a presentation to the FAC, questioned FDA's approach:

*The FDA responses puzzle me. It's as though they were saying, you have to conduct a GLP [good laboratory practice, a system used for animal and test-tube studies] study in humans in order to verify this hypothesis.... Well, you can't do a GLP study in humans unless you're an Arab dictator. It's absurd. You can't hold those studies captive to that criterion. What the studies have shown is that a challenge of food colors (two cases, a single food color) can provoke responses that generally we would consider adverse.<sup>68</sup>*

FDA also failed to conduct a meta-analysis, which is the best approach for judging the strength of a body of research. Three recent meta-analyses (two done after the FAC meeting) all concluded that dyes can trigger adverse behavior in some children. But notwithstanding its criticisms of the research, FDA's background paper

ultimately did acknowledge the evidence linking artificial colorings and adverse behavior:

*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>69</sup>*

Jason Aungst, a toxicology reviewer for the agency who gave a presentation to the FAC, echoed that conclusion.<sup>70</sup> It was also later cited by FDA official Mitchell Cheeseman in an article defending the agency's position on food dyes.<sup>71</sup>

Exposure to food and food components, including artificial food colors and preservatives, may be associated with adverse behaviors, not necessarily related to hyperactivity, in certain susceptible children with ADHD and other problem behaviors, and possibly in susceptible children from the general population.

*FDA. Interim Toxicology Review Memorandum. September 1, 2010.*

FDA, then, clearly acknowledged that dyes may exacerbate problem behaviors for susceptible children. That should have prompted FDA to ask the FAC for its opinion on a question fundamental to the agency's responsibilities: does the use of dyes satisfy the legal standard for the safety of colorings, when the evidence on behavioral impacts in sensitive children is considered?

The legal standard for the safety of colorings requires "convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive."<sup>72</sup> FDA should have charged the FAC with weighing the evidence on dyes against that standard to determine whether the demonstrated impacts of dyes on susceptible children meet it.

Instead, FDA directed the FAC to focus on a different question: whether a "causal" relationship had been established between the consumption of dyes and hyperactivity or other adverse effects on behavior in children. Establishing a cause-effect relationship between food dyes and hyperactivity is far more difficult than establishing whether dyes meet the legal definition for safety. As a committee member stated:

... the cumulative evidence is sufficient for society to demand adherence to the precautionary principle and begin to restrict the use of artificial dyes, at least in foods that target children.

*Bonnie J. Kaplan,  
University of Calgary<sup>73</sup>*

*This charge question, to me, asks a very hard question when it asks for us to decide whether there is a causal relationship. It's very different, in fact, even than the legal standard .... Reasonable certainty of no harm is different than believing that there is a causal relationship.<sup>74</sup>*

Similarly, another committee member, Francisco Xavier Castellanos, research director at the NYU Child Study Center, New York University Langone School of Medicine, appointed just for this meeting because of his expertise, clearly stated his concern about the safety of food dyes, as distinct from scientifically establishing a cause-effect relationship:

*As I've mentioned, causality is a distant aspiration, but certainly these data don't give us any confidence that we can say there's nothing to worry about here, this problem is taken care of, this shouldn't be looked at.<sup>75</sup>*

Had FDA asked the committee to vote on whether food dyes were safe under the law—*i.e.*, if there were “convincing evidence that establishes, with reasonable certainty, that no harm will result” from food dyes—it seems likely that the FAC would have voted no, as these and other quotes suggest. But FDA did not ask the FCA that question.

Importantly, the FDA also asked the FAC to assess whether dyes certified in the United States affect children in the general population, but did not ask whether dyes affect sensitive subpopulations of children, such as those with behavioral problems or dietary sensitivities, which has been the focus of almost all of the research. Just two good studies have been conducted on the effects of dyes in the general population, and both were done in the United Kingdom. (The mixtures of dyes tested in those two studies included the three dyes most widely used in food in the United States, but also three approved for use in food in Europe but not in America.)

Therefore, it is impossible to know whether the effects seen in the British studies were due in whole or in part to colorings used in the United States. Still, given that most of the dyes tested were chemically similar\* and that many other studies on dyes used in America linked dyes to hyperactivity or other adverse behaviors, it certainly is plausible that the dyes used in America were responsible for some or all of the British results.

In fact, the law directs FDA to consider the “cumulative effect” of color additives in the diet, taking into account “chemically or pharmacologically related” substances.<sup>76</sup> If this part of the law had been brought to the committee’s attention, and had the legal standard of a “reasonable certainty of no harm” had been applied by the committee, the committee may well have concluded that current evidence demonstrates that dyes are not “safe.”

## FDA Blames Sensitive Individuals, not Dyes

It is not well understood why some children are sensitive to food dyes and others are not, although scientists have made some progress in understanding genetic differences that may play a role.<sup>77</sup> Those differences are part of the natural variability and diversity that exists among individuals. For example, some people are much more sensitive to caffeine than others; while some experience an adverse reaction to a drug, others tolerate it well. Similarly, some children are highly sensitive to food dyes, while others are not sensitive at all, and some fall in between.

Differences in sensitivity are routinely taken into consideration by regulatory agencies. For example, the U.S. Environmental Protection Agency (EPA) revised its air quality standards in 1997 to better protect children with asthma from pollutants like ozone and particulates.

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\* All but one of the dyes tested in the British studies were members of the azo chemical class. (The exception is Quinoline Yellow, approved in the United States as D&C Yellow 10 only for drugs and cosmetics.) In the United States, the azo dyes Red 40, Yellow 5, and Yellow 6 represent 90 percent of all food dye usage.

Yet rather than recognize the variability in behavioral responses to dyes and protect children who are sensitive, FDA saw in that variability a reason not to take action. FDA said the behavioral effects from dyes were not because the dyes were toxic to children's developing bodies, but because some children have "a unique intolerance" to dyes.<sup>78</sup> An FDA document made available at the FAC meeting argued that instead of conducting reliable neurobehavioral testing, that this unique intolerance:

*can best be addressed by continuing efforts to understand the biomolecular factors that may predispose an organism to this type of unique disruptive behavioral response to otherwise non-neurotoxic chemical substances.*<sup>79</sup>

In other words, FDA indicated it should focus on better understanding what makes some people sensitive—not on protecting them from dyes. That line of thinking is also embraced by the manufacturers of food dyes.<sup>80</sup>

But several members of the committee disputed FDA's hypothesis that dyes may not be toxic to children's developing nervous system. For example, Charles Vorhees, professor of neuroscience at the Cincinnati Children's Hospital Medical Center, one of two FAC members appointed for this meeting because of his specialized expertise, noted:

*you don't have data that speaks directly to the issue of whether or not there's developmental neurotoxicity... that's not an adequate basis to make a determination that the preclinical studies have ruled out the possibility that these might have developmental neurotoxicity.*

In the end, the FAC voted that additional testing was needed, though in the years since the 2011 meeting we are not aware of any new tests that FDA has required or commissioned. The FAC recommended that FDA conduct a rigorous exposure assessment of color additives and additional safety studies, specifically developmental neurotoxicity (DNT) studies. Notably, FDA's website has been revised to omit mention of the recommendation for conducting DNT studies and is currently vaguer than it once was regarding the FAC's conclusions.<sup>81</sup>

Many scientists have emphasized the importance of testing chemicals for DNT since it is such a sensitive endpoint. Development of the brain is incredibly complex and known to be sensitive to a wide variety of chemicals.<sup>82</sup> In fact, testing beyond standard DNT testing is likely needed, considering the different types of human behaviors that appear to be affected by dyes, as noted by one expert FAC member.<sup>83</sup> Other government agencies, such as the EPA, routinely require DNT testing and use the results in risk assessments. In light of the evidence on adverse behavior in children, it is clear that setting an ADI using animal data, without DNT or other relevant neurobehavioral information, is inadequate. Moreover, FDA's own methodological guides call for application of the most sensitive endpoint for determining acceptable exposures.<sup>84</sup>

Two members of the FAC also urged that the FDA pay special attention to Blue 1, the fourth-most widely used dye (about five percent of dyes used), because it crosses the blood-brain barrier. Castellanos emphasized that "that Blue Number

1 should be put at the top of somebody's list" for better testing.<sup>85</sup> Jeanne Freeland-Graves, a professor at the University of Texas, said, "The only [dye] that would make me uncomfortable really would be the Blue Number 1, which crossed the blood-brain barrier. That would be my concern as a grandmother."<sup>86</sup>

## FDA's "Acceptable Daily Intakes" Are Too High to Protect Children

FDA's background document for the FAC<sup>87</sup> explains that part of the agency's safety determination involves comparing the estimated intake of the dye with an "acceptable daily intake," or ADI, for that dye.\* (Table 1) If the estimated actual intake is less than the ADI, that supports a conclusion that the use of a dye at the current levels in food is safe.

In fact, while ADIs based on standard toxicity tests and using standard safety factors may be appropriate for ordinary types of long-term toxicity (liver damage, inhibition of growth, etc.), they are not appropriate for neurobehavioral, allergic, and certain other effects, including short-term effects, and may not provide sufficient protection for children. Dyes have provoked behavioral symptoms at doses far below FDA's "acceptable" daily intakes. The ADIs that FDA developed, taken together, add up to an amount for a 35-pound child that is more than 15 times greater than the amount that in a 1980, FDA-funded study triggered adverse reactions in some children. (Table 1)

Several members of the FAC told FDA that the studies FDA used to establish ADIs for dyes were not appropriate and that the ADIs it established do not ensure safety with regard to behavioral effects. For example, neurobiology expert Vorhees had this exchange with FDA's Jason Aungst:

*Vorhees: Did any of those studies [used to establish the ADIs] include neurobehavioral outcomes?*

*Aungst: Not specific neurobehavioral testing, but clinical observations of... behaviors in the normal cage setting.*

*Vorhees: Which are known to be completely insensitive.<sup>88</sup>*

Vorhees concluded:

*I do not believe that the tests done, including the two-year rodent bioassays, provide a sufficient basis for determining a NOAEL [no observed adverse effect level, the first step in estimating an ADI].... Since the FDA bases ADIs on NOAELs from two-year rodent bioassays, there is a significant risk that the ADIs are set too high... there could be significant risk that the ADIs are erroneous, [that] they're incorrect.<sup>89</sup>*

\* ADIs were derived from conventional animal toxicology studies. They apply an uncertainty factor, or safety margin, of 100 to the highest level at which adverse effects were not observed (the "No Observed Adverse Effect Level," or NOAEL).

Another FAC member, Penny Fenner-Crisp, a retired EPA toxicologist, stated:

*[T]he value of the chronic bioassays that were the basis of the ADIs would have no value in assessing any kind of neurological responses. As you point out, the kinds of cage-side observations that are done as a quick screen in those studies don't tell you anything.<sup>90</sup>*

The ADIs that FDA set, and the safety factors that the agency applied, fail to explicitly take the health risks of infants and children into account—something EPA has done since the 1990s—and do not include adequate safety margins in line with current scientific knowledge on the vulnerability of children and current practice at other federal agencies.<sup>91</sup> They fail to reflect consideration of the most sensitive end-point—as evidenced by the data in children—and as required by the agency's own methodological standards.<sup>92</sup>

### “Children Are Not Little Adults”

Since at least the 1990s, scientists have recognized that “children are not little adults” when it comes to chemical exposures and that the developing child and fetus are often more vulnerable. As such, they deserve special protection. That recognition is reflected in several laws, such as the Food Quality Protection Act, as well as the 1997 Presidential Executive Order 13045, “Protection of Children from Environmental Health Risks and Safety Risks.” That measure directs all federal agencies, including FDA, to make it a high priority to identify and assess health and safety risks that may disproportionately affect children and to ensure that their policies, programs, activities, and standards address those risks.<sup>97</sup>

In contrast, EPA routinely uses an additional 10-fold uncertainty factor whenever its database is incomplete, in particular to account for potential toxicity to infants and children. EPA specifically asks, “What are the resulting uncertainties in the database with regard to children's risk?” and “Have any uncertainties in developmental exposure been identified?”<sup>93</sup>

Vorhees noted that the safety margin FDA used in establishing the ADIs “may not be adequate for the protections of infants and children.”<sup>94</sup>

In reviewing the adequacy of its ADIs, the FDA should have been guided by the recommendations of the National Academy of Sciences (NAS) in its 2009 report on modernizing methods for risk assessment. A key recommendation was for risk assessments to better identify and address both uncertainty and variability in human exposure and vulnerability so that all people are better protected.<sup>95</sup>

The NAS emphasized that special attention should be paid to vulnerable individuals and populations that may be particularly susceptible or more highly exposed. It recommended that science-based default assumptions that protect health should be used.<sup>96</sup> Finally, NAS recommended the need for cumulative risk assessments—assessments that take into account the combined risks posed by the total exposure to multiple agents, from all routes and sources of exposure.<sup>98</sup> For dyes, that would include the risks posed by closely related dyes and exposure to dyes from drugs and cosmetics, as well as foods.

Applying these recommendations, FDA should have:

- Based its “acceptable” exposure to dyes on clinical behavioral studies involving children sensitive to food dyes;
- Used adequate safety factors to take into account uncertainty and ensure protection of the most sensitive individuals;

- Moved beyond a single-chemical assessment approach and conducted a risk assessment based, for example, on the total dye intake of children or on intake of the chemically related azo dyes (Red 40, Yellow 5, and Yellow 6) that currently represent about 90 percent of dyes certified in the United States for use in food, as required by the law.

## FDA's Recent Exposure Assessment Is Seriously Flawed

FDA has taken some steps in response to the FAC's request that it conduct an updated exposure assessment. In 2014, FDA released its initial assessment and in 2015 an updated assessment (as posters at the American Chemical Society's annual meetings).<sup>100</sup> Unfortunately, the agency's assessment is flawed.

First, FDA's exposure assessment did not consider exposures to dyes in drugs and cosmetics, although it is directed by law to consider those sources of exposure, too.<sup>99</sup> Most of the dyes used in food are also permitted to be used in cosmetics and personal-care products, as well as over-the-counter medications, dietary supplements, and prescription drugs. And other dyes used in these medical and personal-care products may be chemically similar to food dyes.

Second, FDA estimated the exposure to consumers of each dye separately, even though the law requires FDA to consider the cumulative effects of exposure to chemically or pharmacologically related substances in the diet.<sup>101</sup> FDA should have measured the total amount of certified dyes that children or adults consume, or at least the total amount of the chemically related azo dyes, which comprise 90 percent of the food dyes certified in the United States.

Third, FDA's assessment also estimates exposure to dyes over 10 to 14 days, but it is short-term exposures that cause adverse behavioral reactions at home or in clinical trials. Exposures averaged out over the long-term are lower than the amount a child might consume in the short-term, at, say, a birthday party.

## FDA's Website Provides Misleading Information about Dyes and Behavior

Totally separate from the FDA's mishandling of the FAC's inquiry, FDA's public information about dyes has long been incomplete and misleading. Since 1992, FDA's information for the public on dyes has been prepared in partnership with the International Food Information Council (IFIC). IFIC is sponsored by major food companies, many of which use food dyes and some of which are members of the food-dye trade association.<sup>102</sup>

The FDA brochure issued in 1992 stated: “[a]lthough [the link between artificial dyes and adverse behavior] was popularized in the 1970's, well-controlled studies conducted since then have produced no evidence that food color additives cause hyperactivity or learning disabilities in children.”<sup>103</sup> By 1992, numerous double-

blind studies provided evidence that food dyes could trigger hyperactivity or other adverse behavior in some children, including an FDA-funded study published in *Science* a decade earlier.

Similarly, the same brochure on the Agency's website stated that the "Consensus Development Panel of the National Institutes of Health concluded in 1982 that there was no scientific evidence to support the claim that colorings or other food additives cause hyperactivity." In fact, that committee actually acknowledged that "[s]tudies also indicated that some hyperactive children on a defined diet experience an increase in hyperactivity when given moderate doses of artificial food dyes, and did not experience similar increases after receiving a placebo."<sup>104</sup>

The website went on to state that "[t]he [NIH] panel said that elimination diets should not be used universally to treat childhood hyperactivity, since there is no scientific evidence to predict which children may benefit." In fact, the NIH panel stated: "[h]owever, the panel recognizes that initiation of a trial of dietary treatment or continuation of a diet in patients whose families and physicians perceive benefits, may be warranted."

In 2000, five members of Congress<sup>105</sup> urged the FDA to revise the brochure to reflect "that some ADHD children may benefit from dietary changes," but the brochure remained unchanged on FDA's website for at least eight years.

Currently, the FDA/IFIC brochure/website includes the question, "Do additives cause childhood hyperactivity?" FDA/IFIC firmly dismiss any possible link, describing the results from studies as being "inconclusive, inconsistent, or difficult to interpret." (Figure 7) With false reassurance, it also 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>106</sup>

**Figure 7. Excerpt from a brochure prepared by the International Food Information Council and the FDA.**

## **Q** Do additives cause childhood hyperactivity?

**A** Although this hypothesis was popularized in the 1970's, results from studies on this issue either have been inconclusive, inconsistent, or difficult to interpret due to inadequacies in study design.

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>107</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>108</sup>

Glaringly absent from FDA’s website is the fact that many experts, as well as FDA’s report to the FAC, agree upon: that dyes can trigger adverse behaviors in sensitive children. FDA also does not tell Americans that most dyed foods in Europe must bear warning labels that state that the dyes “[m]ay have an adverse effect on activity and attention in children.”

The FDA misleads the public, even though a federal law, the Data Quality Act, requires federal agencies to meet guidelines to maximize the objectivity, utility, and integrity of information provided to the public.<sup>109</sup> CSPI is filing a petition under the Act to request corrections in the agency’s public communications. The FDA is legally required to provide truthful and factual information. It clearly isn’t doing so now.

**Table 1. FDA’s “Acceptable Daily Intakes” (ADIs) for Food Dyes**

<b>Certified Color</b>	<b>ADI (mg/kg-bw/day)</b>	<b>Acceptable Intake for a 35 lb. (~16 kg) child</b>	<b>Typical Dose Used in Studies that Triggered Reactions*</b>
FD&C Blue 1	12.0	190 mg	0.80 mg
FD&C Blue 2	2.5	40 mg	0.15 mg
FD&C Green 3	2.5	40 mg	0.11 mg
FD&C Red 3	2.5	40 mg	0.57 mg
FD&C Red 40	7.0	111 mg	13.80 mg
FD&C Yellow 5	5.0	79 mg	9.07 mg
FD&C Yellow 6	3.75	60 mg	10.70 mg
<b>Totals</b>		<b>560 mg</b>	<b>35.26 mg</b>

Of note:

The ADIs are based on long-term animal toxicology studies that don’t adequately assess a chemical’s effects on behavior.

FDA’s acceptable daily intake for a 35-pound child is more than 15 times the dose that triggered behavioral reactions in an FDA-funded study that used 35.3 mg of dyes per day.

\* Typical dose based on FDA-funded study that used a 35.26 mg blend of dyes: Weiss B. *J Am Acad Child Psychiatry*. 1982; 21(2):144–52. Many other double-blind studies linking dyes to adverse behavior used a 26 mg/day (or lower) dose.

## Progress in Eliminating Dyes

The studies conducted over the past 35 years have not yet spurred the FDA to protect children from the harm caused by food dyes, as they have European authorities. But pressure from Europe and from parents and the media in the United States is waking up the public and the food industry.

### Double Standard: Companies Reformulate in Europe, not America

**Figure 8. Many companies reformulate popular foods in Europe, but not America, to avoid having to use the warning label.**



	Starburst Fruit Chews Ingredients:		Starburst Fruit Chews Ingredients:
CORN SYRUP, SUGAR, HYDROGENATED PALM KERNEL OIL AND/OR PALM OIL, FRUIT JUICE FROM CONCENTRATE (APPLE, STRAWBERRY, LEMON, ORANGE, CHERRY), LESS THAN 2% - CITRIC ACID, DEXTRIN, GELATIN, FOOD STARCH-MODIFIED, NATURAL AND ARTIFICIAL FLAVORS, ASCORBIC ACID, <b>COLORS RED 40, YELLOW 6, YELLOW 5, BLUE 1.</b>	GLUCOSE SYRUP, SUGAR, VEGETABLE FAT, CITRIC ACID, CONCENTRATED FRUIT JUICES 1.4%* (APPLE, ORANGE, BLACKCURRANT, STRAWBERRY, LIME, LEMON), MODIFIED STARCH, MALIC ACID, DEXTRIN, FLAVOURINGS, MALTODEXTRIN, ANTIOXIDANT ASCORBIC ACID, EMULSIFIER SOYBEAN LECITHIN, <b>COLOURS ANTHOCYANINS, CAROTENES, CHLOROPHYLLS AND CHLOROPHYLLINS.</b>		

In Europe, where governing bodies have targeted artificial colorings, many retailers, manufacturers, caterers, and restaurants have agreed not to use the six dyes tested in the Southampton studies and reformulated their products to avoid having to use the required warning label. (Figure 8)

Some of Britain’s biggest supermarket chains—Tesco, Sainsbury’s, Asda, Marks & Spencer, and the Co-op—dropped artificial dyes from their house-brand products.<sup>110</sup> Far fewer foods with dyes remain on the market in Britain today than before these actions, and the same is true throughout the EU.

However, the FDA has made no effort to address concerns over artificial colorings,

and only a few companies have begun eliminating dyes in the United States. In fact, some products that are sold dye-free in Europe are sold in the United States laden with dyes. (Table 2) For example, Mars, Inc., promised to eliminate the Southampton additives from its candies in Britain by the end of 2008, but not in the United States.<sup>111</sup>

### Public Outcry Results in Positive Steps, but Fails to Solve the Problem

Public concern in America over artificial colorings is growing. Internet activist Vani Hari (aka “Food Babe”) garnered over 350,000 signatures on her petition on the online site Change.org.<sup>112</sup> The petition, and attendant publicity (such as the “Dr. Oz” show), called on Kraft to remove artificial colorings from its macaroni and cheese, and Kraft responded.

Another petition on Change.org, sponsored by Renee Shuttters, whose son Trenton is highly sensitive to dyes, asked candy-maker Mars, Inc., to remove artificial dyes from

its M&M's.<sup>112</sup> The petition collected almost 200,000 signatures. Mars has not responded. Shuttters previously traveled to the FAC meeting at her own expense to provide oral testimony on how dyes affected Trenton.<sup>113</sup>

A third petition was started by CSPI member Julie Rossi, whose daughter Alessandra has hyperactive reactions to food dyes. Her Change.org petition aimed at getting Crayola, the famous crayon maker, to stop marketing "Color Your Mouth" candies to children. The amounts of dyes in these candies are so high that they stain children's mouths and fingers bright red, yellow, green, orange, and blue.

Some state legislators have introduced bills targeting artificial food colorings. In October 2007, following a New York Times article about the Southampton studies, a committee of the New York State Assembly held a hearing on food additives and behavioral disorders.<sup>114</sup> The chair of the committee, Peter Rivera, subsequently called for warning labels on foods containing certain dyes and sodium benzoate.

In 2009, state senator Norman Stone Jr., of Baltimore County, Maryland, introduced two bills to phase out dyes from foods in schools and in all foods in the state of Maryland.<sup>115</sup> Facing intense opposition, the bills were killed before making it to a full vote.<sup>116</sup> In 2015, the Chemical-Free Schools Act in Maryland sought to prohibit public schools from purchasing, selling, or serving foods containing artificial colors and some other additives. And several school districts, including Fairfax County in Virginia and Montgomery County in Maryland, have eliminated some dyes from foods sold in schools.<sup>117</sup>

Due to consumer pressure, some food manufacturers, restaurants, and grocery chains are removing dyes from at least some of their products. (Food Dyes: Honorable Mentions)

These voluntary changes by several large companies are a welcome sign of progress. These efforts, and the efforts in Europe, show that the food industry is fully capable of removing dyes from its products. Natural colorings such as beta-carotene, paprika, beet juice, and turmeric provide safe alternatives to artificial dyes. (Cochineal extract and carmine are not good substitutes because they cause allergic reactions.) And of course, there is also the option of not adding colorings to products at all and instead relying on more nutritious and naturally colorful fruits, vegetables, and other ingredients for color. Natural colorings are usually not as bright, stable, or cheap as dyes.



**M&M's Candies: Trenton Shuttters is trying to get dyes out of M&M's.**



**Crayola: Stop Telling Kids to "Color Their Mouth" with Fake Dyed Candies.**

But voluntary efforts are far from an adequate solution. In the absence of a ban or, at the least, a requirement for a warning label from FDA, dyes will continue to be used in a plethora of children's foods, and children will continue to suffer as a result.

### **Food Dyes: Honorable Mentions**

*These companies have begun eliminating dyes from some or all of their products.*

Aldi  
Campbell Soup Co.  
Chick-fil-A  
Chipotle  
Frito-Lay (PepsiCo)  
General Mills  
Kellogg  
Nestle  
Noodles & Co.  
Panera  
Papa John's  
Pizza Hut  
Schwan Food Co.  
Subway  
Taco Bell  
Trader Joe's  
Whole Foods

Table 2. Dyes in American and European Foods, a Double Standard

Product*	U.S. Version		European Version	
	Synthetic Dyes	Other Colorings	Synthetic Dyes	Other Colorings
Froot Loops (Kellogg)	Red 40, Yellow 6, Blue 1	Turmeric extract, annatto extract	None	Paprika extract
McDonald's Strawberry Sundae	Red 40	None	None	None added
Original Starburst (Wrigley)	Red 40, Yellow 5	None	None	Anthocyanins, carotenes, chlorophylls, chlorophyllins
Milk Chocolate M&Ms (Mars)	Blue 1 Lake, Yellow 6, Red 40, Yellow 5, Blue 1, Red 40 Lake, Blue 2 Lake, Yellow 6 Lake, Blue 2	None	Blue 2	Curcumin, carmine, carotenes, apocarotenal, titanium dioxide
Nutri-Grain Bars (Kellogg)	Strawberry		Strawberry	
	Red 40	Caramel coloring	None	Anthocyanins, paprika extract
	Apple Cinnamon		Apple	
	None	Caramel coloring	None	None added
	Blueberry		Blueberry	
	Red 40, Blue 1	None	None	Anthocyanins
	Blackberry		Blackberry and Apple	
	Red 40, Blue 1	Caramel coloring	None	None added
Pop Tarts (Kellogg)	Frosted Wild Berry		Frosted Bustin' Berry	
	Blue 2 lake, Red 40, Red 40 Lake, Blue 1 Lake, Blue 2, Yellow 5 lake, Yellow 6	Caramel coloring, carmine	None	Anthocyanins, caramel coloring
Pop Tarts (Kellogg)	Frosted Wild Berry		Frosted Bustin' Berry	
	Blue 2 lake, Red 40, Red 40 Lake, Blue 1 Lake, Blue 2, Yellow 5 lake, Yellow 6	Caramel coloring, carmine	None	Anthocyanins, caramel coloring
	Frosted Strawberry		Frosted Strawberry Sensation	
	Red 40, Yellow 6, Blue 1	Caramel coloring	None	Beetroot red, annatto, paprika extract
Special K Toaster Pastries (Kellogg)	Strawberry Pastry Crisps		Strawberry Biscuit Moments	
	Red 40	Unspecified natural colorings ("color added"), caramel coloring	None	Anthocyanin, paprika
	Blueberry Pastry Crisps		Blueberry Biscuit Moments	
	Red 40, Blue 1	Unspecified natural colorings ("color added")	None	None added

**Table 2. Dyes in American and European Foods, a Double Standard, cont.**

Product*	U.S. Version		European Version	
	Synthetic Dyes	Other Colorings	Synthetic Dyes	Other Colorings
Betty Crocker Cake Mix (General Mills)	Red Velvet		Red Velvet	
	Red 40	None	None	Paprika extract, carmine
	Carrot Cake		Carrot Cake	
Special K Cereals (Kellogg)	Yellow 6, Red 40	None	None	Caramel coloring
	Special K Blueberry		Special K Red Berries	
Skittles Original (Mars)	Red 40, Blue 2, Green 3, Blue 1, Red 40 Lake, Blue 2 Lake	None	None	None added
	Red 40 Lake, Red 40, Yellow 5 Lake, Yellow 5, Yellow 6 Lake, Yellow 6, Blue 2 Lake, Blue 1, Blue 1 Lake	Titanium dioxide	Blue 1	Beetroot red, titanium dioxide, curcumin, alpha carotene, indigo carmine, anthocyanins, apocarotenal
Nestle Ice Cream Bars	Strawberry Shortcake Bar		Strawberry and Chocolate Nobbly Bobbly	
	Red 40, Red 3	None	None	Beetroot red, curcumin, chlorophyllin
Fanta Orange (Coca-Cola)	Yellow 6, Red 40	None	None	Vegetable concentrates
Gatorade Orange (PepsiCo)	Yellow 5, Red 40	None	None	Beta carotene
Sunny D Strawberry (Sunny Delight Beverages Co. (US)/Suntory (Europe))				
	Yellow 5, Yellow 6	None	None	Fruit juices from concentrate
Gatorade (PepsiCo)	Gatorade Fruit Punch		Gatorade Tropical Punch	
	Red 40	None	None	Black carrot juice concentrate

## Recommendations

For nearly 40 years, scientific studies have investigated dyes, most commonly testing them as mixtures. Three recent meta-analyses as well as other reviews of the evidence convincingly link dyes to adverse behavioral reactions in sensitive children.

Under the law, FDA has the responsibility for ensuring that dyes are safe for consumption. FDA is also legally responsible for ensuring that the information it provides to the public about dyes is accurate. Parents, in particular, deserve such information as they seek ways to help children suffering from behavioral problems such as ADHD. FDA's assertions that dyes are "very safe" and denials of their effects on children's behavior are both grossly inconsistent with the scientific evidence and irresponsible as a matter of public health and safety.

To protect children, FDA should:

- Ban synthetic dyes in foods and beverages since they do not meet the legal safety standard. Companies that wish to use a synthetic dye in food must submit convincing evidence showing that the dye is safe and does not cause adverse behavior, using sensitive studies. FDA must have adequate data on these endpoints, and take sensitive subpopulations, such as children, into account when determining whether a dye is safe.
- As an interim measure, require warning labels on dyed foods stating: "WARNING: This food contains synthetic food colorings that may impair the behavior of some children."
- Update information on its website and in other materials to accurately inform the public that food dyes can impair the behavior of some children.

## Appendix A: Dye Content of Common Foods and Beverages<sup>118</sup>

Product (Brand)	Serving Size (Weight)	Amount of Dyes (mg)
Pillsbury Confetti Funfetti Chocolate Fudge Frosting (JM Smucker)	2 tbsp. (34 g)	41.5
Red, White and Blue Popsicle (Foodhold USA)	1 pop (55 g)	21.6
Twizzlers (Licorice) (Hershey)	4 pieces (45 g)	15.4
Skittles (Original) (Mars)	1 packet (61.5 g)	14.7
Hawaiian Punch (Dr Pepper/Seven Up, Inc.)	8 fl. oz. (237 g)	14.1
Fruity Pebbles (Post)	¾ cup (27 g)	13.9
M&Ms (plain) (Mars)	1 packet (47.9 g)	13.4
Sunkist Orange Soda (Dr Pepper/Seven Up, Inc.)	12 fl. oz. (355 g)	12.6
Ken's Light Raspberry Walnut Vinaigrette (Ken's Foods)	2 tbsp. (32 g)	10.2
Sugar Free Chocolate Wafers (Voortman Cookies)	3 cookies (27 g)	10.0
Utz Baked Cheese Curls (Utz)	1 oz. (28.35 g)	8.6
Fruit by the Foot (Strawberry) (General Mills)	1 roll (21 g)	6.5
Open Pit Barbecue Sauce (Original) (Pinnacle Foods)	2 tbsp. (34 g)	6.5

## Appendix B: Food Dyes and Behavior 2010–2015

- 2010** FDA concludes “for certain susceptible children with ADHD and other problem behaviors, the data suggest that their condition may be exacerbated by exposure to a number of substances in food, including, but not limited to, artificial food colors,” a conclusion it reiterates in 2011 and 2012.
- 2011** *The Lancet* publishes a study by Pelsser *et al.* that shows considerable effects of a restricted elimination diet in unselected children with ADHD on ADHD and oppositional defiant disorder; it recommends that dietary intervention be considered in all children with ADHD.
- 2011** FDA convenes a Food Advisory Committee to consider available data on the possible association between consumption of food dyes and hyperactivity in children. The committee is asked whether a *causal* relationship between “certified color additives” and hyperactivity/adverse behavior in the *general population* has been established, and it concludes it has not. It votes 8 to 6 against recommending that warnings or other information be disclosed on labels of foods containing dyes to ensure their safe use. The committee is not asked to comment on the relationship between food dyes and adverse behavior in *susceptible children*, or whether food dyes are safe as defined by law (*i.e.*, whether there is “convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive”).
- 2011** CSPI petitions FDA to require front-of-label disclosure of colorings in foods.
- 2012** Nigg *et al.* publish a meta-analysis funded by an arm of the food industry that concludes that a restriction diet reduces ADHD in one-third percent of children with ADHD and estimates that 8% of children with ADHD have symptoms related to food dyes. In objective, computerized measures of attention, a significant effect was associated with food dyes. The authors deemed the findings “too substantial to dismiss.”
- 2012** Doshi *et al.* report that the overall national annual costs of ADHD ranged from \$143 billion to \$266 billion, including costs incurred by adults, children, and spillover costs borne by family members of individuals with ADHD.
- 2013** Sonuga-Barke *et al.* publish a meta-analysis of six non-drug treatments for ADHD that found that excluding food dyes from the diet produced the largest effects of the treatments analyzed, often in individuals selected for food sensitivities.
- 2014** An international team led by Stevenson reviews available meta-analyses and concludes “food colour elimination is a potentially valuable treatment approach for ADHD.”

- 2014** Faraone and Antshel summarize the quality and strength of the evidence for ADHD treatments, ranking the effectiveness of food-dye exclusions and restricted elimination diets at level 4 of 5 levels.
- 2015** An editorial by the editor-in-chief of the *Journal of Psychology and Psychiatry* notes that the “pendulum has swung” away from the mainstream view that diet did not trigger symptoms of ADHD, concluding that “studies suggest a statistically significant but clinically limited role for dietary treatments” of ADHD, a role that is “far less than envisaged by some promoters of the diet-behavior narrative but greater than expected by their sceptics.”
- 2015** Chorozoglou's prospective study of three-year old children living in England found that those with high levels of hyperactivity had 17-fold higher mental health, educational, social service, and criminal justice system costs compared to non-hyperactive peers after taking into account other available pre-school characteristics and factors.

## Appendix C: The Human Toll: Parents' First-hand Accounts

Since 2008, CSPI has collected by means of a website first-hand accounts of parents' struggles with food dyes.<sup>119</sup> Those emails, while only anecdotal, illustrate the real-world harm that dyes inflict on children and their families. The following are excerpts from parents. (See three videos to learn directly from parents of children who have been helped by avoiding food dyes: (<https://www.cspinet.org/diet.html>).

### **Erica Stewart, Chicago, Illinois**

We spent years battling my middle son's severe emotional and behavioral problems. He was non-verbal, violent to the point of hurting himself and others. He was utterly out of control and would require up to four adults to restrain him. We took him to several doctors who diagnosed ADHD and autism. One doctor wanted him hospitalized and others prescribed heavy dosages of medications such as Zoloft. He was 4 years old at the time, and we decided to log his diet and behavior before resorting to medications. We found that the common link between his behavioral episodes was consumption of Red No. 40.

Two weeks after he stopped eating any food with red dye, he began talking, stopped hurting people, and was a whole new child. The transformation was miraculous considering what we had gone through. For the first four years of his life, we did not know our son. After the food dye was eliminated, we finally got our real child!

To this day he has to be careful about what he eats. Although the behavior isn't as severe, he will still get nervous and agitated if he ingests too much red dye. Red No. 40 affects all three of my sons, but it affects my middle son most dramatically. Although we have had several different doctors over the last 15 years, whenever I list Red No. 40 as an allergy, they always look at me like I'm crazy. This includes school personnel as well, but it only took one class party for the teachers to really believe us.

### **Shannon Corley, Eldridge, Iowa**

For several years, my son was angry. He ate candy (Skittles and Starburst were his favorites) often and he was always agitated. He would become frustrated over the smallest things. This happened on a daily basis. A friend suggested we eliminate food dyes from his diet and I convinced him to try this for two weeks. We eliminated all foods with artificial dyes and saw AMAZING results. He was relaxed and calm. He was not frustrated or angry AT ALL. I was so excited, and he felt so much better. When we let him have Skittles after the two weeks were over, he became agitated and angry once again. He no longer wants these substances in his body because he feels so much better without them. He does miss the candies he loved so much, but he will not eat them no matter what. I was able to find dye-free candies at our local grocer, but they cost over \$8 for six small bags of fruit snacks. There are no regulations and companies making dye-free foods are charging a fortune. I wish we had affordable options available to us in the U.S. I beg you to listen to our story and hopefully we can have a positive impact on children that are diagnosed with ADHD and other behavioral disorders, because in reality, they may just be eating too many dyes. When we talked to our physician, she had never even heard of such a thing, and she seemed surprised of our findings. This was very concerning to me.

**Krztena Brooks, Kingsport, Tennessee**

My daughter is typically very laid-back and happy. She is well-mannered and behaves wonderfully—most people think she is 5 instead of 3. But if she ingests Red No. 40 she is a totally different child. She becomes agitated, has mood swings and difficulties concentrating. She is unable to calm down physically or emotionally and can't go to sleep at night.

When she was younger, we realized that after she was given children's medications with red dye she would get very hyper and irritable. Then we noticed the same effect with certain foods. Our sweet and very smart daughter with no ADHD or behavioral problems became a very out-of-control and agitated little girl who couldn't calm down or be calmed down. Her normal bedtime is 8:30–9:00 p.m., but if she has consumed Red No. 40, she is unable to calm down and can't go to sleep until 11:30 or later, and it is not a restful sleep. Physically, red dye makes her cheeks flush and she also usually gets a stomach ache and diarrhea. After consuming it, the next day it is like she has crashed and doesn't feel well or have any energy.

**Courtney Sucato, Phoenix, Arizona**

Two days in a row I gave my son Cheez-Its and within five minutes he melted down. He became mean, irritable, and uncontrollable. I never gave him Cheez-Its again. Soon after, my father-in-law gave him an orange soda. He reacted the same way. I gave him Keebler cheese and peanut butter crackers and within five minutes he had the same reaction. With a little research, I found that all three contained Yellow No. 6. When I googled it, looking at the effects the dye can have, it all made sense. Since then we've avoided Yellow No. 6 and my son is like a new kid! A well-behaved kid! He is happy and he listens and our home life is so much better! In the past he's also had horrible gas pains that have been so bad that I've taken him to the ER. Since we've cut out Yellow No. 6, he doesn't have the gas pains anymore.

**Christine Blake, Columbia, South Carolina**

We noticed when our child was 2 years old that within 20 minutes of consuming food gummies he was a different person. He couldn't maintain eye contact. He would engage in self-stimulating behaviors like moving his hand really fast in front of his eyes. The effects would wear off within a few hours and by the next day he was back to normal. Also, we consume a very natural diet most of the time, so we really noticed the difference when we added in a food with dyes. Sugar was not the issue, because he would eat other foods made with sugar and no issues. Chocolate caused no problems either. To this day we still see the impact. Today he got a box of organic candies with Yellow No. 6 and we let him eat them. All day he has had a hard time concentrating. We talk and it's like he can't hear us. He keeps asking us to repeat things. He stares off into space and we have a hard time getting his attention. He says his brain feels all scrambled and static-y. Every doctor we have ever told about this has treated us like fanatics.

**Lori Schonhorst, Huxley, Iowa**

We have almost completely avoided food dyes for the past week as an experiment after noticing that our son's hyperactive and rather bizarre sensory seeking behaviors became more apparent after eating them. We tried this upon recommendation of a chiropractor. I cannot begin to tell you the changes we have noticed in this short period of time. In fact, my five-year-old son told me just this morning that he "feels like a normal kid" now. When someone put chips that contained Red No. 40 on his plate today at a potluck, I mentioned to him that they had Red No. 40 in them. I gave him the option as to whether he wanted to eat them or not to see how he would respond. He didn't touch them. He knows how those foods make him feel and he doesn't want them anymore. That speaks volumes to me.

**Bobbi Cunningham, Durham, New York**

My normally outgoing and responsive 4-year-old daughter turns aggressive and non-verbal within 10 to 20 minutes of ingesting Red No. 40, Yellow No. 5, or Yellow No. 6. Her tantrum will last 15 to 25 minutes until she seems to burn it off. She is then remorseful and sad about the way she acted, saying, “I’m sorry Mommy, I don’t know why I can’t stop it.” This is not a parenting or discipline issue. She will take discipline or redirection easily unless she has these dyes in her system. I am thankful I figured this out early and have the ability to advocate for my child. I feel for the children whose parents and schools have no idea why they are acting the way they are and are mislabeled as “problem children.” THIS HAS TO STOP.

**Laurie Hoff, Fairborn, Ohio**

My son shows extreme irritability, defiance and tantrums on-and-off for three days after eating food dyes. His entire demeanor is so different that I wish I had a brain scan to see what is really happening. We only see these reactions when he accidentally eats something at school or day care. He is otherwise a calm, helpful, well-behaved child who excels in school and reads two grade levels ahead of his class.

He has mostly been off dyes for a year, and now he is consistently calm and well-behaved. He can practice piano and finish homework daily without argument or difficulty. He completes household chores without being told to and is a positive big brother to his brother and sister. He is honest and chooses not to eat things with food dye because he is tired of how awful he feels after eating the stuff.

**Becky Hall, Atlanta, Georgia**

When our daughter consumed artificial dyes, she had uncontrollable fits of rage. Afterwards, she was very apologetic and upset at her behavior, but while she was in the middle of it, there was no stopping her. She yelled, tossed herself on the ground and threw things. She made comments like she hates everyone and hates herself. We’ve noticed these fits last about 30 minutes—it’s almost like you can time it out to know when they will end. (Knowing this helps me get through them.) Since we removed artificial dyes from her diet, she no longer has these fits. Don’t get me wrong, she does have temper tantrums every once in a while. However, they are brief and we are able to talk through them. We have found that food dyes are the main problem, especially Yellow No. 5.

**Cynthia Ogea, Lake Charles, Louisiana**

My child has been out of control since he was 2 years old. We tried every ADHD medication available with little success. After changing his diet to dye-free foods, he’s been a completely different person. I want to cry knowing that all we had to do was avoid dyes. The last four years have been full of stress and uncertainty, to the point where I was making myself sick with worry. I breathe easier knowing I figured this out.

**Rochelle Tafoya, Aurora, Colorado**

Each time my daughter ate foods with artificial dyes in them, she would have meltdowns and tantrums. When I asked her what the problem was, she just stared at me like she didn’t know what I was asking. Then she would start crying and go into a full-on scream-fest. She would not listen to what I asked her to do and instead would run to her room and hide while throwing a tantrum. When I learned about the dyes, I changed what she was eating, and now she is a NEW person. She does not have crying fits anymore and she is a much happier child who follows directions without the crying and tantrums like before. Please FDA, take these dyes out of our foods. It DOES make a big difference.

## Appendix D: Allergy and Cancer Concerns about Food Dyes

### Allergic/Hypersensitivity Reactions

Food dyes can cause allergic or hypersensitivity reactions, such as hives, itching, and swelling in sensitive individuals.<sup>120</sup> Red 40, for instance, caused reactions in 15 percent of patients with a history of hives and other allergic reactions.<sup>121</sup> The researchers used relatively low doses compared to the amounts many people consume.<sup>122</sup> In the 1970s, Yellow 5 was found to cause hives and asthma.<sup>123</sup> A double-blind study that used a low dose (much less than what is used in most dyed foods) of Yellow 5 found hypersensitivity reactions in 8 percent of patients with chronic hives and 20 percent of patients with aspirin intolerance.<sup>124</sup> Yellow 6 was first found to cause hypersensitivity in 1949.<sup>125</sup> Since that time, multiple studies and reports reached similar findings.<sup>126</sup>

### Cancer, Genotoxicity, and Long-Term Testing Concerns

Genotoxicity, or a chemical's ability to cause mutations or damage chromosomes, is another concern associated with some food dyes. All of the most-used dyes have tested positive in some studies. For example, Yellow 5, the second-most widely used dye, tested positive for in 6 out of 13 studies.

Genotoxicity suggests that a chemical might cause cancer or, when the genetic damage occurs in an egg or sperm cell, affect offspring (*e.g.*, cause birth defects). Genotoxicity is evaluated in brief tests using bacteria, mice, or tissue cultures. But to better determine whether genotoxic chemicals actually cause cancer, long-term studies in animals must be conducted.

Unfortunately, most long-term animal studies on food dyes suffered from serious limitations that reduce their ability to detect cancer.

Most studies were not optimally sensitive because they were too brief, included too few animals, and/or lacked *in utero* exposure data.

- Almost all of the studies tested dyes individually, even though most consumers ingest several dyes at the same time or over a day.
- Almost all studies (as for most food additives) were sponsored by the manufacturers. Such tests might be designed, or the results interpreted, to downplay signs of problems.

Nevertheless, numerous food dyes, including Green 1, Red 1, Red 2, and Violet 1, were banned in the United States due to cancer concerns. More food dyes have been banned than any other class of food additive.\*

In 1990, FDA concluded that Red 3 caused thyroid cancer in rats, and terminated a “provisional” listing of it for use in cosmetics and externally applied drugs, as well as a provisional listing of an

\* Sudan 1 was banned for toxicity reasons and later found to be carcinogenic. Other food dyes banned due to health concerns include Orange 1, Orange 2, Yellow 1, Yellow 2, Yellow 3, and Yellow 4. Red 4 was banned from food but is still allowed in some drugs and cosmetics. Red 32, also called Citrus Red 2, was banned from some uses but is still legally permitted to color oranges.

insoluble form (called Red 3 lake) for use in food, drugs, and cosmetics.<sup>127</sup> However, in 1969 FDA had permanently approved the soluble form of Red 3 in foods and ingested drugs, and that listing remains on the books today. In 1985, FDA's Acting Commissioner, Mark Novitch, told The New York Times that Red 3 was "of greatest public health concern...."<sup>128</sup> Red 3 currently represents about 1.5 percent of dyes used.

## Carcinogenic Contaminants

In addition to concerns about inherent carcinogenicity, dyes may also contain more than 10 percent impurities from the manufacturing process. Some of those impurities, such as benzidine that contaminates Yellow 5 and Yellow 6, are known to cause cancer in humans. Though FDA ostensibly limits their presence, its method is flawed.

The FDA's restrictions on benzidine in Yellow 5 and Yellow 6 are still based on usage-level estimates from 1990,<sup>129</sup> even though per capita dye exposure has more than doubled since then.

FDA also does not take into account the higher vulnerability of children, who are more sensitive to carcinogens and consume more dyes per unit of body weight than adults. Most importantly, in the 1990s, the FDA and Health Canada discovered that benzidine was bound to other molecules and released from foods once consumed. That "bound" fraction greatly exceeded the unbound ("free") amount in dyes.<sup>130</sup> However, FDA's limit for benzidine does not consider "bound" benzidine and thus may greatly underestimate consumer exposure to these contaminants. No tests have been done since the 1990s, so it is not known whether Yellow 5 and Yellow 6 are still contaminated.

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