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UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Petition to Ban the Use of Yellow 5 and
Other Food Dyes, in the Interim to
Require a Warning on Foods Containing These
Dyes, to Correct the Information the
Food and Drug Administration Gives to Consumers
On the Impact of These Dyes on the Behavior of
Some Children, and to Require Neurotoxicity
Testing of New Food Additives and Food Colors.

Docket No. FDA-2008-P-0347

submitted by the

CENTER FOR SCIENCE IN THE PUBLIC INTEREST

June 3, 2008

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This petition is dedicated to the late Dr. Ben Feingold, whose astute clinical observations and relentless advocacy helped thousands of parents protect their children from the neurotoxic effects of food dyes and other food ingredients.

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Dockets Management Division
Food and Drug Administration
Room 1061 (HFA-305)
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CITIZEN PETITION

I. Preliminary Statement

About 3 to 10 percent of school-age children in the United States suffer from hyperactivity, attention-deficit/hyperactivity disorder (“ADHD”), or related behavioral problems.¹ In the early 1970s, Dr. Ben Feingold popularized a dietary treatment that appeared to reduce symptoms of hyperactivity in many children.² The prescribed diet lacked synthetic food dyes, artificial flavorings, and foods believed to contain salicylates (it also excluded aspirin). As discussed below, numerous scientific studies have provided at least partial substantiation of what became known as the “Feingold Diet.” Those studies show that in some children behavioral problems³ are exacerbated by Yellow 5 and other synthetic food dyes.^{4,5}

It is medically and ethically unwise to burden hyperactive children and their parents with concerns about foods with synthetic dyes. After all, parents (and pediatricians) first would have to know about the potential risk and then figure out if their children were adversely affected by dyes. Then they would have to protect their children from packaged and restaurant foods with dyes and from dyed foods served at friends’ parties, school events, picnics, and elsewhere. Parents (and children) should not be burdened with having to fend off the almost ubiquitous risks (see Appendix 1). The appropriate public health approach is to remove those dangerous and unnecessary substances from the food supply. Food manufacturers voluntarily could substitute safe natural colors or other ingredients (such as fruit or fruit juices) for dyes, but that’s unlikely to happen throughout the food supply without the level playing field provided by government regulation.⁶ Accordingly, the Food and Drug Administration (“FDA”) should ban the use of dyes in all foods; until such action takes effect, the FDA should require a prominent warning notice on product labels.⁷

¹ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr.* 2004;25:423-34 at 423.

² See web site of the Feingold Association of the United States: www.feingold.org/aboutFAUS.html (accessed April 27, 2008).

³ We use the term “behavioral problems” to include ADHD, hyperactivity, Attention-Deficit disorder (ADD), impulsivity, irritability, interference with learning, and various other behavior disorders, as assessed in the studies. Food colorings are not the sole cause of ADHD and hyperactivity.

⁴ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr.* 2004;25:423-34 at 431.

⁵ We generally use the terms food dyes and artificial colorings interchangeably to refer to synthetic dyes.

⁶ In the 30 years since the diet-behavior link was first hypothesized, major companies have not voluntarily removed dyes from their products.

⁷ Artificial colorings have not been tested for behavioral effects in adults, and natural colorings have not been tested

II. Action Requested

The FDA divides 40 approved food colors into two categories: nine synthetic dyes that are subject to FDA certification and 31 colorings that are not (the latter are derived from minerals, plants, or insects).⁸ It is only the certified food dyes that are suspected of adversely affecting children's behavior and that are the subject of this petition.

The Center for Science in the Public Interest⁹ ("CSPI") requests¹⁰ that the FDA immediately initiate a rulemaking to revoke the approvals of the following eight synthetic food dyes: FD&C Blue No. 1, 21 C.F.R. 74.101; FD&C Blue No. 2, 21 C.F.R. 102; FD&C Green No. 3, 21 C.F.R. 203; Orange B, 21 C.F.R. 74.250; FD&C Red. No. 3, 21 C.F.R. 74.303; FD&C Red. No. 40, 21 C.F.R. 74.340; FD&C Yellow No. 5, 21 C.F.R. 74.705; FD&C Yellow No. 6, 21 C.F.R. 74.406.¹¹ Considering the onerous, time-consuming steps that the color additives law (section 721 of the Federal Food, Drug, and Cosmetics Act ["FFDCA"]) stipulates, it is clear that banning all those dyes would take a very long time. Hence, as an interim measure, we ask that foods containing synthetic food dyes be required to bear a warning notice, such as: "WARNING: The artificial colorings in this food cause hyperactivity and behavioral problems in some children," on the principal display panels.

In addition, we ask that the FDA correct statements made in its public information about dyes and behavior. The FDA now tells visitors to its web site that there is "no evidence that food color additives cause hyperactivity or learning disabilities in children."¹² We request that the FDA correct that guidance.¹³

for behavioral effects in children or adults.

⁸ CSPI has long been concerned about the safety of food colorings. In the 1970s, we communicated with the FDA regarding Red No. 40 and the now-banned Violet No. 1. With regard to a natural coloring, in response to a petition submitted by CSPI in August 1998, the FDA proposed in 2006 to require that food and cosmetic products containing cochineal extract or carmine declare that fact on their labels because they cause an allergic reaction in some people. 71 Fed. Reg. 4839 (January 30, 2006). Those colors come from insects.

⁹ CSPI, based in Washington, D.C., is supported largely by 900,000 members in the United States and Canada who subscribe to its Nutrition Action Healthletter. CSPI has been working to improve the nation's health through better nutrition and safer food since 1971.

¹⁰ This petition is submitted pursuant to section 4(e) of the Administrative Procedure Act, 5 U.S.C. 553(e), and 21 C.F.R. 10.25 and 10.30.

¹¹ Another dye, Citrus Red 2, is used in only small amounts on the peels of oranges and poses a negligible risk to children.

¹² Food Color Facts (Center for Food Safety and Applied Nutrition 1993) www.cfsan.fda.gov/~lrd/colorfac.html (accessed January 18, 2008).

¹³ Commenting on a similar FDA statement, University of Rochester School of Medicine and Dentistry researcher Bernard Weiss states, "This is a rather baffling statement. In fact, my own study (Weiss 1982) was funded by the FDA, and its results, along with a number of others from that period, definitively demonstrated adverse behavioral effects of synthetic food colors. During the intervening years, with a plethora of confirmations, the FDA has remained blindly obstinate. It continues to shield food additives from testing for neurotoxicity and apparently believes that adverse behavioral responses are not an expression of toxicity." Weiss B. Food additives and hyperactivity. *Environ Health Perspect.* 2008;116(6)June.

Elsewhere on its web site, the FDA states: "A 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."¹⁴ In fact, that panel acknowledged that "Studies 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."¹⁵ The FDA's web site also states: "The [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: "However, 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." We ask that the relevant sections of FDA's web site be removed or revised to reflect the evidence from many studies that diet *can* affect behavior.

Finally, in recognition of the ability of food dyes, and possibly other ingredients, to have neurotoxic effects, we ask the FDA to add to its recommended protocols for testing new food ingredients¹⁶ tests for neurotoxicity, as some have urged for more than a quarter-century.¹⁷ We note that such common additives as aspartame¹⁸ and monosodium glutamate¹⁹ may have neurotoxic effects in some individuals.

III. Numerous Scientific Studies Show that Yellow 5 and Other Food Dyes Can Adversely Affect the Behavior of Some Children.

The publicity that Feingold generated in the mid-1970s on the basis of his clinical practice spurred scientific research on diet, including dyes, and behavior. As early as 1982, behavioral toxicologist Bernard Weiss concluded that "The total evidence, although not wholly consistent, nevertheless suggests that [the Feingold] hypothesis is, in principle, correct."²⁰ In

¹⁴ Color additives. Do color additives in food cause hyperactivity? www.cfsan.fda.gov/~dms/qa-topad.html (accessed March 18, 2008).

¹⁵ National Institutes of Health Consensus Development Conference Summary. Defined Diets and Childhood Hyperactivity. Vol 4, No. 3. (Government Printing Office 890-228). NIH held a broader consensus conference on November 16-18, 1998, on the diagnosis and treatment of ADHD. The treatment portion of that conference focused almost entirely on pharmaceuticals, with dietary treatment only an afterthought. The report noted that "Some of the dietary elimination strategies showed intriguing results suggesting the need for future research." However, reflecting the conferees' apparent limited interest in the topic, the lengthy list of recommended research topics did not mention diet at all. (NIH Consensus Statement. Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder (ADHD). Nov. 18, 1998. Vol. 16, No. 2.)

¹⁶ Agency Review of Toxicology Information in Petitions for Direct Food Additives and Color Additives Used in Food, www.cfsan.fda.gov/~acrobot/rediiabc.pdf (accessed March 18, 2008).

¹⁷ Weiss B. Food additives and environmental chemicals as sources of childhood behavior disorders. *J Am Acad Child Psychiatry*. 1982;21:144-52.

¹⁸ Lipton RB, Newman LC, Cohen JS, Solomon S. Aspartame as a dietary trigger of headache. *Headache*. 1989;29(2):90-2.

¹⁹ See review in: Fernstrom JD. "Health issues relating to monosodium glutamate use in the diet" in Kilcast D, Angus F. *Reducing Salt in Foods: practical strategies* (Boca Raton: CRC Press, 2007).

²⁰ Weiss B. Food additives and environmental chemicals as sources of childhood behavior disorders. *J Am Acad Child Psychiatry*. 1982;21(2):144-52.

1999, CSPI published a critical review on “Diet, ADHD, and Behavior: a quarter-century review” (see Attachment 1). That review discusses more than 20 controlled studies on diet and behavior, including research involving food dyes, and concludes that the weight of the evidence demonstrates that modest doses of dyes, or mixtures of dyes, adversely affect the behavior of some children.²¹ Some of the studies that found effects of food dyes include the following (additional studies, both positive and negative, are discussed in CSPI’s review):

- Conners, one of the leading, early researchers on food ingredients and behavior, and his colleagues conducted several studies in which children were challenged with food dyes. One study placed 16 children between four and 11 years old and diagnosed with hyperactivity on a “modified Feingold diet” from which only dyes were eliminated.”²² That diet, introduced openly, appeared to reduce behavior problems by 34 percent (as rated by teachers) or 57 percent (as rated by parents). The researchers then challenged, in a double-blind fashion, the children with cookies that contained or lacked a mixture of food dyes (26 milligrams [mg] per day). Parents and teachers did not identify any effect, but three of the children (six and seven years old) showed “a marked deterioration of performance” in an objective visual-motor attention task. The three children were affected only at about one hour after eating a cookie. The parents’ and teachers’ failure to discern when children were consuming the dye, the authors conjectured, might have been because they rated the children not at the one-hour point, but only at the end of the day. Also, Conners suggested that several subjects dropped out of the study because of severe reactions to the dyes.
- Another study by Conners and colleagues tested 13 children between the ages of three and nine, including eight children who were diagnosed as hyperactive and five who were considered borderline hyperactive.^{23,24} When put on a dye-free diet (not double-blind) for several weeks, the subjects demonstrated a 41-percent reduction in behavior problems, with 77 percent of the children appearing to respond. The children then, in a double-blind study, ate two cookies made with or without dyes (13 mg each, one after breakfast, the other after dinner) for one week each. Parents rated their children’s behavior for a three-hour period after dinner. For the group as a whole, the children exhibited significantly more behavioral problems after they ate the dye-containing cookies. Four children (31 percent) displayed marked reactions. One girl was retested twice and showed repeated reactions to colors. The authors concluded, “These data firmly establish that artificial colors may be particularly disruptive to younger children and that it will be important to ... examine the possible mechanisms whereby these chemicals act on the CNS [central nervous system].”

²¹ Following receipt of CSPI’s report, the FDA told CSPI that the FDA was “not aware of any definitive research establishing a causal relationship between diet or food ingredients, including color additives, and ADHD.” (Letter from Commissioner Jane Henney, Dec. 23, 1999.)

²² Conners CK. *Food Additives and Hyperactive Children*. (New York: Plenum Press, 1980), pp. 45-54.

²³ Conners CK. *Food Additives and Hyperactive Children*. (New York: Plenum Press, 1980), pp.55-68.

²⁴ Goyette CH, Conners CK, Petti TA, Curtis LE. Effects of Artificial Colors on Hyperkinetic Children: A Double-Blind Challenge Study. *Psychopharmacol Bull.* 1978;14:39-40.

- In a study sponsored by the FDA, 22 children were kept on a diet free of artificial colors, flavors, and certain other additives and foods and then covertly challenged with dyes on certain days.²⁵ (The subjects had not been diagnosed as hyperactive, but were suspected by their parents of having behavioral reactions to artificial colorings or flavorings and had been kept on some sort of restricted diet). For 77 consecutive days, each child drank a specially prepared beverage. On eight randomly selected days, the drink concealed a mixture of seven dyes (35.3 mg). Two subjects showed clear reactions, according to their parents. A 34-month-old girl “reacted dramatically” on the days she received the dyes. A three-year-old boy displayed convincing evidence of sensitivity to the color challenge for behaviors his mother considered typical of his outbursts. “These 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,” the researchers stated.
- In one of the few studies using relatively high doses of dyes, researchers challenged 40 children, half of whom were considered hyperactive based on their responsiveness to stimulant medications.²⁶ The other children responded adversely to those drugs and were presumed not to be hyperactive. After being put on a “Feingold Diet”—free of dyes, artificial flavors, BHT, BHA, and natural sources of salicylates (such as apples and tomatoes)—for three days, the children were challenged on one day with a mixture of dyes and on another day with a placebo. Using a double-blind protocol, the researchers tested doses of 100 mg and 150 mg (the latter estimated by the FDA to be the 90th-percentile intake). Compared to the placebo, the dyes decreased the attention span of the hyperactive children, but not the other children. Seventeen of the 20 hyperactive subjects suffered impaired performance in a learning test. The authors suggested that negative results in some of the previous studies were due to the use of doses of dyes that were too low.
- Another study using a large dose of a mixture of dyes, tested 19 children between three and 15 years old.²⁷ According to their parents, the children exhibited poor concentration, excessive fidgeting, and other behavioral problems after consuming foods that contained dyes. For that reason the children were put on restricted diets. During the (double-blind) study, the children were kept on their restricted diets. Every day for seven weeks, the children consumed a gelatin capsule with their breakfast. During two of those weeks the capsules contained 125 mg of a mixture of four food colors, including tartrazine (Yellow 5), sunset yellow (Yellow 6), carmoisine (not used in the United States), and amaranth

²⁵ Weiss B, Williams JH, Margen S, et al. Behavioral responses to artificial food colors. *Science*. 1980;207:1487-8.

²⁶ Swanson JM, Kinsbourne M. Food dyes impair performance of hyperactive children on a laboratory learning test. *Science*. 1980;207:1485-7.

²⁷ Pollock I, Warner JO. Effect of artificial food colours on childhood behaviour. *Archives of Disease in Childhood*. 1990;65:74-7.

(Red 2, now banned in the United States).²⁸ During the other weeks the capsules contained a lactose placebo. Seventeen of 19 sets of parents rated their children's behavior as worse—in several cases sharply worse—when their children consumed the food colors.

- A 1978 study tested 26 schoolchildren who had been diagnosed with ADHD and had been taking stimulant drugs.²⁹ The children were put on a diet free of artificial colors and flavors, though at least seven of the children “cheated.” Then, in a double-blind study using a 2 x 2 factorial design, the children were challenged on separate days with chocolate cookies containing or lacking a mixture of food dyes (26 mg per day) in the presence or absence of their medications. The children's teachers observed “clearly significant reductions [in hyperactive behavior] related to diet for approximately one-fourth [3 to 8] of the children.” A detailed reanalysis by Weiss found that one child responded “sharply and consistently.”³⁰

In 2004, Schab and Trinh published a meta-analysis of studies on dyes and behavior.³¹ Their study identified 427 non-duplicative studies on the link between diet and behavior. From that body of literature, they identified 21 double-blind, placebo-controlled studies on the impact of artificial food colorings. Fifteen of those studies included children clinically diagnosed with hyperactivity. Four of the 15 studies focused on Yellow 5, one evaluated both Yellow 5 and Yellow 6 individually, and the other ten used various mixtures of artificial colors.³² Yellow 5 and Yellow 6 are the second- and third-most-widely used dyes in the United States.³³ After examining such factors as sample size,³⁴ Schab and Trinh concluded that the effect of dyes on children was statistically significant, particularly with regard to parents' ratings.

Schab and Trinh also analyzed eight studies, or subsets of studies, that included non-hyperactive children or heterogeneous groups of children that were primarily non-hyperactive. Two of those studies used Yellow 5, one tested both Yellow 5 and carmoisine, and five used mixtures of dyes. The investigators found that the dyes impaired the behavior of children who were suspected of being responsive to such colors prior to entering the blinded trial. Figures 1–4

²⁸ Studies done abroad did not use dyes certified by the FDA. Nonetheless, we use the FD&C nomenclature interchangeably with the generic names of the dyes.

²⁹ Williams JJ, Cram DM, Tausig FT, et al. Relative effects of drugs and diet on hyperactive behaviors: an experimental study. *Pediatrics*. 1978;61:811-7.

³⁰ Weiss B. Food additives and environmental chemicals as sources of childhood behavioral disorders. *J Am Acad Child Psychiatry*. 1982;21:144-52.

³¹ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr*. 2004;25:423-34 at 425.

³² For example, one study that found diet could reduce symptoms in some children used a mixture of nine artificial colors (Red 2, 3, and 4; Blue 1 and 2, Yellow 5 and 6; Green 3; and Orange B). Williams J, Cram D, et al. Relative Effects of Drugs and Diet on Hyperactive Behaviors: An Experimental Study. *Pediatrics* 1978;6:811-7.

³³ Color Certification Reports. Center for Food Safety and Applied Nutrition. www.cfsan.fda.gov/~dms/col-cert.html (accessed March 13, 2008).

³⁴ For example, one study that found no impact involved a single child. Mattes J, Gittelman-Klein R, A Crossover Study of Artificial Food Colors in a Hyperkinetic Child. *Am J Psychiatry* 1978;135:987-8.

of their paper show that several studies showed statistically significant adverse effects of dyes on behavior, and none showed a statistically significant benefit.³⁵ The authors provided several reasons why their results might have been different from that of a 1982 meta-analysis,³⁶ which found no impact of dyes on behavior. Among them, the 1982 meta-analysis considered the effect of the “Feingold Diet” and not just food dyes, did not include two large trials that were published subsequently, overlooked two studies included in the 2004 review, and used less-sophisticated statistical methods.³⁷ Schab and Trinh concluded that dyes “promote hyperactivity in hyperactive children, as measured on behavioral rating scales” and that “society should engage in a broader discussion about whether the aesthetic and commercial rationale for the use of [artificial food colorings] is justified.”³⁸

Weiss’s trenchant 1982 review highlighted weaknesses of design (such as dosage, assessments done at inappropriate times, etc.) and analysis in previous studies.³⁹ For instance, he reanalyzed the original data of several studies and discovered that group averages that did not indicate behavior change sometimes obscured the fact that individual children reacted significantly to dyes:

Conventional statistical tests are inappropriate here....If only a proportion of [subjects] are potential responders, their data may be buried by group statistics....If only 30% of a sample are responders, and they shift by an average of one standard deviation, the total sample average shifts only minutely. Investigators need to be sensitive to these problems.

Subsequent to the Schab–Trinh meta-analysis, the British Food Standards Agency (“FSA”) funded two randomized, double-blind, placebo-controlled trials by Southampton University researchers to test whether food dyes (and a preservative) affect childhood behavior. Importantly, unlike most previous studies, these studies involved children from the general British population, rather than children who were diagnosed as hyperactive or suspected of being affected by dyes and other food ingredients.

- The first study tested the effects of 20 mg of a mixture of four dyes (two of which are used in the United States)⁴⁰ and 25 mg of sodium benzoate (a widely used preservative) on 277 three-year-old children. Parents, but not clinical testing, detected statistically significant benefits during weeks in which children were not exposed to the chemicals

³⁵ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr.* 2004;25:423-34 at 427-8.

³⁶ Kavale KA, Forness SR. Hyperactivity and diet treatment: a metaanalysis of the Feingold hypothesis. *J Learn Disabil.* 1983;16:324–30.

³⁷ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr.* 2004;25:423-34 at 428.

³⁸ Schab D, Trinh N. Do Artificial Food Colors Promote Hyperactivity in Children with Hyperactive Syndromes? A Meta-Analysis of Double-Blind Placebo-Controlled Trials. *J Dev Behav Pediatr.* 2004;25:423-34 at 428 and 431.

³⁹ Weiss B. Food additives and environmental chemicals as sources of childhood behavior disorders. *J Am Acad Child Psychiatry.* 1982;21:144-52 at 147, 150.

⁴⁰ Sunset yellow (used in the United States as Yellow 6), tartrazine (used in the United States as Yellow 5), carmoisine, ponceau 4R.

and deterioration during weeks in which children were exposed.⁴¹

- In the second study, the authors tested two mixtures of four food dyes (20 mg in Mixture A and 30 mg in Mixture B) and sodium benzoate (45 mg in both mixtures)⁴² on 3-year-olds and 8- and 9-year-olds. In the younger children, Mixture A had an adverse effect, but Mixture B only showed a trend that was not statistically significant. In the older children who adhered well to the protocol, both mixtures had adverse effects. The authors concluded that “artificial colors or a sodium benzoate preservative (or both) in the diet result in increased hyperactivity in 3-year old and 8/9 year-old children in the general population....The implications of these results for the regulation of food additive use could be substantial.”⁴³

A European Food Safety Authority (“EFSA”) review concluded that the two British studies provided “limited evidence that the two different mixtures of synthetic colours and sodium benzoate tested had a small and statistically significant effect on activity and attention in children selected from the general population.”⁴⁴ However, EFSA downplayed the significance of the findings. The authors of the Southampton studies wrote a detailed rebuttal of EFSA’s review.⁴⁵ (See Appendix 2 for CSPI’s assessment of the Southampton studies.) We note again that, in contrast to most previous studies, the subjects in this study represented a cross-section of the population and not children who had ADHD or were thought by their parents to be sensitive to dyes. Also, the British researchers averaged the ratings of all the children, rather than considering each child as an individual experiment. Thus, the non-responders (probably a majority of the children) may have largely obscured sharp reactions to dyes in a subgroup of children.

Some of the studies that have been conducted used doses of dyes lower than what the average child is likely to consume and far lower than what heavy consumers of dyes are likely to consume. Several of the studies used doses of 26 mg or less per day, which was thought several decades ago to be about the average amount consumed by children. Obviously, many individuals consumed far more dye than the average. Furthermore, in 1976 an FDA scientist estimated that 10 percent of children between one and five years old consumed more than 121 mg of dyes per

⁴¹ Bateman B, Warner JO, Hutchinson E, et al. The effects of a double blind, placebo controlled, artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of preschool children. *Archives of Disease in Childhood*. 2004;89:506-11.

⁴² Mixture A contained sunset yellow, carmoisine, tartrazine, and ponceau 4R; Mixture B replaced the last two colors with quinoline yellow and allura red. Carmoisine, ponceau 4R, and quinoline yellow are not approved for use in food in the United States although their use is permitted in the United Kingdom; the other three colors are approved by the FDA as Yellow 6, Yellow 5, and Red 40.

⁴³ McCann D, Barrett A, Cooper A et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomized, double-blinded, placebo-controlled trial. *Lancet*. 2007(Nov 3);370:1560-7.

⁴⁴ The EFSA Journal. 2008;660:1-54.

⁴⁵ See Annex 3 of FSA’s statement on Food Additives and Hyperactivity, April 10, 2008. www.food.gov.uk/multimedia/pdfs/board/fsa080404a.pdf (accessed April 10, 2008).

day, and 10 percent of children between six and 11 years old consume 146 mg or more.⁴⁶ The average level might have been as high as 76 mg—not 26 mg—and the maximum as high as 315 mg per day. Those figures suggest that many studies used dosages of dyes inadequate to elicit the behavioral effects that some children's ordinary diets triggered. Indeed, Conners, who used a challenge dose of 26 mg in one study, 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."⁴⁷ In contrast, two of the studies that challenged children with 100 mg or more of dye per day found effects in comparatively large percentages of children.⁴⁸ That amount is not unreasonable given the large amounts of food dyes in commonly eaten products (see table below).

In considering the dosages of dyes used in various studies, it is noteworthy that the quantities of dyes being certified for use have been increasing steadily. The average per capita amounts rose from 12 mg per day in 1955 to 32 mg per day in 1975, 47 mg per day in 1998, and 59 mg per day (or about 22 grams per year) in 2007, a five-fold increase over five decades (see graph below).⁴⁹ While true consumption figures are not known, current amounts of dyes certified for use in the United States suggest that the amounts now being consumed are greater than what was used in most studies. The increased exposure to dyes may be causing higher rates of behavioral disturbances.⁵⁰ (It is noteworthy that while dye certification increased by 84 percent between 1975 and 2007, calorie availability increased by only 26 percent between 1975 and 2005.⁵¹ Thus, dye availability has been increasing at more than three times the rate of calorie availability.)

⁴⁶ Memorandum from a nutritionist, Department of Health, Education, and Welfare, Division of Consumer Studies, to T. J. Sobotka, Biochemical Toxicology Branch, Food and Drug Administration, July 30, 1976. Cited in Swanson JM, Kinsbourne M. Food dyes impair performance of hyperactive children on a laboratory learning test. *Science*. 1980;207:1485-7.

⁴⁷ Conners CK, Goyette CH, Newman EB. Dose-time effect of artificial colors on hyperactive children. *J Learning Disabilities*. 1980;13(9):48-52.

⁴⁸ Pollock I, Warner JO. Effect of artificial food colours on childhood behaviour. *Archives of Disease in Childhood*. 1990;65:74-7. Swanson JM, Kinsbourne M. Food dyes impair performance of hyperactive children on a laboratory learning test. *Science*. 1980;207:1485-7.

⁴⁹ Calculations by CSPI based on FDA data on certification of straight dyes and lakes (adjusted for weight of dyes) and current U.S. population. Color Certification Reports. Center for Food Safety and Applied Nutrition. www.cfsan.fda.gov/~dms/col-cert.html (accessed March 13, 2008). Consumers are also exposed to about another 4 percent of dyes approved only for use in drugs and cosmetics (D&C colors).

⁵⁰ The National Institute of Mental Health estimates that between 3 and 5 percent of children have ADHD, or approximately 2 million children in the United States. www.nimh.nih.gov/health/publications/adhd/complete-publication.shtml (accessed May 30, 2008). The annual production quota for Ritalin soared from 2,000 kg in 1990 to 15,000kg in 2000. www.usdoj.gov/dea/pubs/cngrtest/ct051600.htm#fig1 (accessed, May 30, 2008). In recent years, other stimulant drugs and non-stimulant drugs have become popular in treatment of behavioral disorders.

⁵¹ Economic Research Service, U.S. Department of Agriculture. Average daily per capita availability of calories, adjusted for spoilage and other waste. www.ers.usda.gov/Data/FoodConsumption/spreadsheets/foodloss/Calories.xls#Totals!a1 (accessed May 17, 2008).

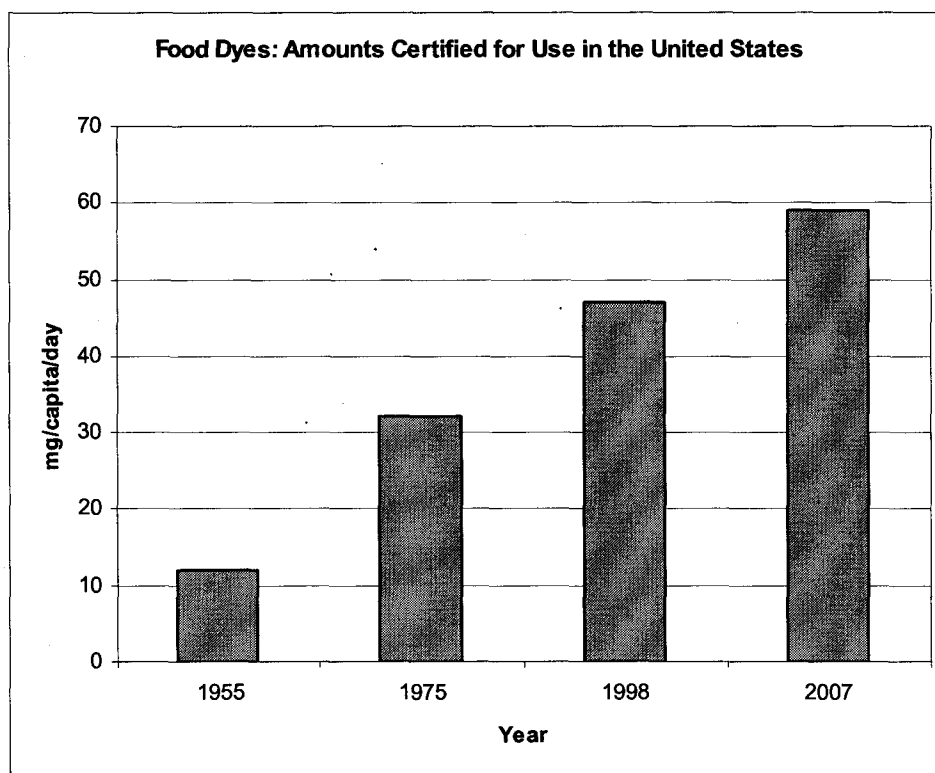
Amounts of Food Dyes in Typical Foods

	RACC*	Range of Dye Content (mg per RACC)
Candy and confections		
Mini hard candy	5g	0.05 – 2.00
Other hard candies, baking candies	15g	0.15 – 6.00
Beverages	240ml	1.20 – 48.0
Dessert powders	21.4g	0.11 – 12.9
Cereals	30g	6.00 – 15.0
Bakery goods		
heavy cakes, pies, fruit crisps	125g	1.25 – 62.5
coffee cakes, donuts, sweet rolls, muffins	55g	0.55 – 27.5
granola bars, breakfast bars	40g	0.40 – 20.0
cookies	30g	0.30 – 15.0
Ice creams	66g	0.66 – 13.2
Snack foods	30g	0.75 – 15.0
<p>* Reference amounts customarily consumed per eating occasion, as defined by FDA.</p> <p>CSPI calculations based on coloring levels reported in Marmion D. <i>Handbook of U.S. Colorants</i> (New Jersey: Wiley InterScience, 1991). The levels Marmion cites were apparently originally published in Certified Color Industry Committee. Food Technol. 1968;22(8):14.</p>		

We also note that the FDA normally requires acceptable daily intakes of food additives to be based on the highest no-observed-effect level in animal or human studies, divided by an appropriate safety factor.⁵² The tests of dyes on children did not include exaggerated amounts of dyes to help compensate for the small numbers of subjects and the fact that some children could be more sensitive than any of the subjects participating in the small studies. Also, almost all

⁵² See, for example, Agency Review of Toxicology Information in Petitions for Direct Food Additives and Color Additives Used in Food, www.cfsan.fda.gov/~acrobat/rediiabc.pdf (accessed March 18, 2008).

studies used smaller doses of dyes than appear to be consumed by Americans today. Studies have not identified a no-effect level, and on that basis alone dyes should be banned. Applying a 10-fold safety factor to the lowest-effect levels would indicate even more strongly the appropriateness of a ban.



Most of the studies of dyes and behavior used mixtures of up to nine dyes. The advantages of that approach are (a) that most artificially colored foods contain two or more dyes (see Appendix 1) and (b) colorings might have synergistic effects with one another or with other additives, as has been demonstrated in one *in vitro* study.⁵³ However, for regulatory agency action, it is most useful to test dyes individually.

Only Yellow 5 was tested alone in multiple studies. Three of four studies of hyperactive children indicated an adverse effect on behavior. (Three tests of *non-hyperactive* children did not find significant adverse effects from Yellow 5, though several individuals did react sharply to that dye.) Perhaps the best study, because it used several doses, tested 34 children whose parents thought they were likely or possible reactors to dyes. All 34 were suspected of having ADHD, but only two were diagnosed as such. An additional 20 children were not thought to be

⁵³ Lau K, McLean WG, Williams DP, et al. Synergistic interactions between commonly used food additives in a developmental neurotoxicity test. *Toxicol Sci.* 2006;90:178–87.

hyperactive or have ADHD. Doses of Yellow 5 ranged from 1 mg to 50 mg per day. All six dosage levels produced reactions. On the days they consumed the dye, 19 of 23 (83 percent) likely reactors, three of 11 (27 percent) possible reactors, and two of the 20 (10 percent) non-hyperactive children became more irritable, restless, and sleep-disturbed, according to their parents. The researchers stated that the “amplitude and duration of effect increased with increasing dosage levels.”⁵⁴ Yellow 6 was tested alone in just one small study (with 2 of 13 children reacting).⁵⁵

The absence of tests on most individual dyes should not deter the FDA from revoking the approvals of the dyes, because of several considerations. As a practical matter, multiple high-quality tests of each individual dye on various populations of children (such as children of different ages with and without previously identified behavioral problems) will not be conducted without a requirement by the FDA, and such tests almost certainly would take many years to fund, design, conduct, analyze, and replicate.⁵⁶ Meanwhile, children would be suffering harm. Furthermore, with countless combinations of dyes being used in foods (see Appendix 1), it would be impossible to test every combination of dyes. To protect the public’s health, the FDA needs to accept the strong evidence that mixtures of dyes, as well as Yellow 5 on its own, affect behavior and initiate proceedings to revoke the approval of all the dyes addressed here. The burden of proof should shift to industry to prove that dyes, individually or in combination with one another, do not affect children’s behavior—but responsible companies could voluntarily and immediately switch to safer natural colorings or simply use nutritious ingredients, such as fruit or fruit juice, that the dyes are used to simulate.

IV. Calls for Eliminating the Use of Food Dyes

Based on the results of the two studies it sponsored, as well as the earlier body of research, the FSA has strongly urged companies to eliminate use of the dyes. FSA Chair Dame Deirdre Hutton stated in April 2008:

It is the Agency's duty to put consumers first. 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. UK industry has already taken great strides to remove these colours from food; this decision

⁵⁴ Rowe KS, Rowe KJ. Synthetic food coloring and behavior: a dose response effect in a double-blind, placebo-controlled, repeated-measures study. *J Pediatr.* 1994;125:691-8.

⁵⁵ Sarantinos J, Rowe KS, Briggs DR. Synthetic food colouring and behavioural change in children with attention deficit disorder: a double-blind, placebo-controlled, repeated measures study. *Proceeding of the Nutrition Society of Australia.* 1990;15:233.

⁵⁶ Not enough is known about dyes and behavior to base decisions on their chemical structures, though some of the dyes have related structures. Yellow 5, the one dye tested on its own in several tests is an azo dye, as are Red 40, Yellow 6, Orange B, and Citrus Red 2. Blue 1, Blue 2, Green 3, and Red 3 are not azo dyes, but they, like most of the azo dyes, are complex, sulfonated (not Red 3 or Citrus Red 2), multi-ringed, organic chemicals. All three dyes used in the British “Southampton” study, but not allowed in the United States, are multi-ringed and sulfonated, and two of the three have the azo structure.

builds on the work already done and will encourage industry to continue down this path.⁵⁷

The FSA also stated: “The FSA is recommending to UK Ministers that industry takes voluntary action to remove these colours by 2009 and is pressing for action at EU level.” According to a news account, Dame Hutton added: “If one puts consumers first, then the 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.”⁵⁸

In May 2008, the European Union’s Environment Committee voted to ban artificial colors in foods for babies and small children.⁵⁹ That measure also included a warning label on other children’s foods: “Azo dyes may provoke allergenic effects and hyperactivity in children.” If the European Parliament approves the measure, member governments would have to approve it for the regulatory actions to take effect.

Similarly, in recognition of the risk posed by food dyes, researchers and physicians in the United States now have renewed their call for eliminating dyes from the food supply (see Appendix 3). They note that “the artificial colorings provide no health benefit whatsoever to consumers....On the other hand, the colorings clearly have a significant adverse effect on some children.” Therefore, they are urging the FDA “to implement measures that would help protect children from unnecessary harm....[and] to begin proceedings to end the use of food dyes and other unnecessary ingredients that might adversely affect children’s behavior.”

Those recent calls for action to protect children from food dyes came almost a decade after CSPI’s 1999 report and recommendation to the Department of Health and Human Services (“HHS”) that it should inform medical professionals and the public that some children are affected by diet and that dietary therapy should be considered as a first course of treatment.⁶⁰ CSPI also recommended new research on foods and behavior, more routine testing for behavioral effects of food additives, consideration of a ban on dyes in foods widely consumed by children, and revising HHS’s literature and web sites that deny that diet affects behavior.

At the same time, a group of doctors and researchers urged HHS and the FDA to require

⁵⁷ Food Standards Authority. Board discusses colours advice. April 11, 2008.

www.food.gov.uk/news/newsarchive/2008/apr/coloursadvice (accessed April 12, 2008).

⁵⁸ Crowley L. Southampton colours should be phased out, says FSA. Food Navigator.com—Europe. April 10, 2008. www.foodnavigator.com/news/printNewsBis.asp?id=84575 (accessed April 10, 2008). Perhaps because of the limited research identifying sodium benzoate as a promoter of behavior problems, the British government’s advice focuses on colors. See, for example, www.food.gov.uk/safereating/chemsafe/additivesbranch/colours/hyper/ (accessed April 27, 2008).

⁵⁹ Crowley L. MEPs vote for ban on unnecessary colours for kids. Food Navigator.com—Europe. May 7, 2008. www.foodnavigator.com/news/ng.asp?n=85135&c=4ad7aAzQZOnmdHoqSmGJwQ%3D%3D (accessed May 9, 2008).

⁶⁰ Letter to Secretary Donna Shalala, sent on Oct. 25, 1999.

new, as well as certain existing, food additives to be tested for behavioral effects and to consider banning the use of dyes in foods and other products widely consumed by children.⁶¹

V. The Food Industry Can Eliminate Food Dyes.

As a result of the 2007 study that it sponsored, the FSA asked food manufacturers to voluntarily stop using the six dyes that were tested. Some of Britain's biggest supermarket chains—Tesco,⁶² Sainsbury's,⁶³ ASDA,⁶⁴ Marks & Spencer,⁶⁵ and the Co-op⁶⁶—have pledged to drop those colors or all dyes from 99 percent or all of their house-brand products.⁶⁷ Some multinational companies sell foods without dyes in the United Kingdom (UK), but with dyes in the United States. For instance:

- Kraft has eliminated artificial colors and flavors from its Lunchables line in Britain,⁶⁸ but not in the United States.⁶⁹
- Mars has eliminated some or all of the dyes from its Starburst Chews, Skittles, and M&M'S candies in Britain,⁷⁰ but not in the United States.⁷¹

⁶¹ Letter to Secretary Donna Shalala, Oct. 25, 1999, signed by Sidney MacDonald Baker, M.D., research director, Children's Development Database; former faculty member, Yale Medical School; former director, Gesell Institute of New Haven; Joseph Bellanti, M.D., professor of pediatrics and microbiology-immunology, Georgetown University Medical Center, Washington, DC; Marvin Boris, M.D. pediatrics, allergy, and immunology, Woodbury, NY; William G. Crook, M.D., director, International Health Foundation, Jackson, TN; Donald R. Davis, Ph.D., Biochemical Institute, University of Texas Austin; Leo Galland, M.D., director, Foundation for Integrated Medicine, New York, NY; William T. Kniker, M.D., clinical professor of pediatrics and internal medicine, University of Texas Health Science Center at San Antonio, TX; Sheldon Margen, M.D., professor emeritus, Public Health Nutrition, University of California, Berkeley; Chairman, editorial board, U.C. Berkeley Wellness Letter; Sidney Walker III, M.D., founder, Behavioral Neurology International, La Jolla, CA. www.cspinet.org/new/adhdletters.html (accessed April 22, 2008).

⁶² Tesco. Healthier Food For Kids. https://secure.tesco.com/health/food/healthy_kids/healthier_foods.html (accessed April 30, 2008).

⁶³ Sainsbury's. Safety & Quality. (May 2007).

www.sainsburys.co.uk/food/foodandfeatures/safety_quality/articles/artificial_colours_flavours.htm (accessed April 30, 2008).

⁶⁴ ASDA. ASDA gives artificial flavourings and colours the elbow (Dec, 21, 2007). www.asda-press.co.uk/pressrelease/148 (accessed April 30, 2008).

⁶⁵ Marks & Spencer. Additives Update (September 2007) www.marksandspencer.com/gp/node/n/63635031/026-3931778-8158034?ie (accessed April 30, 2008).

⁶⁶ The Co-operative Food. Responsible Retailing. www.co-operative.coop/food/Responsibleretailing/righttoknow/righttoknowourachievements/ (accessed April 30, 2008).

⁶⁷ The proof food additives are as bad as we feared. Daily Mail (Sept. 8, 2007).

www.dailymail.co.uk/pages/live/articles/health/womenfamily.html?in_article_id=453431&in_page_id=1799 (accessed March 11, 2008).

⁶⁸ Kraft Cuts Dairy Fat and Salt. BBC News. (Feb. 9, 2007). <http://news.bbc.co.uk/1/hi/business/6345205.stm> (accessed May 6, 2008).

⁶⁹ Oscar Mayer Lunchables. Kraft Foods Inc. 2007.

www.kraftfoods.com/kf/Products/ProductInfoSearchResults.htm?CatalogType=1&BrandId=128&SearchText=Oscar%20Mayer%20Lunchables&PageNo=1 (accessed May 5, 2008).

⁷⁰ Mars. Statement on Artificial Colours. <http://marsconsumercare.co.uk/additives.asp> (accessed May 1, 2008).

⁷¹ Mars. Product Nutrition Information. 2007. www.marshealthyliving.com/nutrition_info.jsp?brandId=8# (accessed

- Kellogg's cereals, Pop-Tarts and Fruit Winders in the UK do not have dyes,⁷² while similar Kellogg products in the United States do have them.⁷³
- In the UK, McDonald's vanilla syrup for milk shakes, strawberry syrup for milk shakes, and strawberry sauce for sundaes are colored with caramelized sugar and caramel coloring, beetroot juice concentrate, and actual strawberries, respectively; however in the United States, the same foods are colored with Yellows 5 and 6, Red 40, and Red 40, respectively.⁷⁴
- Coca-Cola's Orange and Lemon Fanta soft drinks contain dyes in the United States, but not in the UK.⁷⁵
- Haribo's Gold-Bears (gummi candies) contain dyes in the United States, but not in the UK.⁷⁶

Finally, it's worth noting that the Whole Foods Markets and Trader Joe's supermarket chains in the United States do not market any foods that contain dyes (or other artificial ingredients).^{77,78}

VI. The FDA Has Ample Legal Authority to Ban the Use of Yellow 5 and Other Dyes in Food.

Section 721(b)(4) of the Federal Food, Drug, and Cosmetic Act ("FFDCA"), 21 U.S.C. 379e(b)(4), bars the use of any color additive in food⁷⁹ unless the FDA has found that "the data...establish that such use, under the conditions of use specified in the regulations, will be safe." Section 721(b)(5)(C)(i) authorizes the "amendment or repeal" of any food color regulation.⁸⁰ Section 201(u) of the FFDCA, 21 U.S.C. 321(u), says that "the term 'safe,' as used in... section 721, has reference to the health of man or animal."

The FDA's regulations say that "safe means that there is *convincing evidence* that

May 1, 2008)

⁷² Kellogg's. Products. 2008. www.kelloggs.co.uk/products/ (accessed April 30, 2008).

⁷³ Kellogg's. Products. 2008. www2.kelloggs.com/Product/Product.aspx (accessed April 30, 2008).

⁷⁴ McDonald's web sites. www.mcdonalds.com (accessed April 30, 2008).

⁷⁵ Coca-Cola web site. www.coca-cola.co.uk/yourhealth/whats_in_our_drinks/; telephone with Coca-Cola Co., Atlanta, GA, May 30, 2008.

⁷⁶ Product purchased in London on March 15, 2008, and in the District of Columbia on Feb. 12, 2008.

⁷⁷ www.wholefoodsmarket.com/products/ (accessed April 10, 2008).

⁷⁸ www.traderjoes.com/labels_and_lists.html (accessed May 10, 2008).

⁷⁹ The statute also applies to the safety of color additives in drugs, devices, and cosmetics.

⁸⁰ Section 721(d) of the FFDCA permits the manufacturer (or anyone else adversely affected by a proposed repeal or amendment of a color regulation) to ask for a hearing before an Administrative Law Judge ("ALJ") if the FDA proposes to repeal or amend a color regulation. Following the ALJ's decision, the FDA can repeal or amend the regulation. That final order is then subject to review by the federal courts. If the FDA were considering amending a color regulation because of a concern about cancer (which we are not asserting in this petition), then the manufacturer could ask for a review of the evidence by the National Academy of Sciences prior to the ALJ hearing. A legal commentator attributed this complex process "to the foresight and effective lobbying of the cosmetics industry in the 1960s." James T. O'Reilly, *Food and Drug Administration*, 3rd ed. (July 2007) volume 1 at 12-13.

establishes with *reasonable certainty* that *no harm* will result from the intended use of the color additive.” [emphasis added] 21 C.F.R. 70.3(i).

Congress has directed a federal court to sustain the FDA’s repeal or amendment of a food color regulation if the FDA’s decision is “based upon a fair evaluation of the entire record...” Sections 721(d)(4) and 409(g)(2) of the FFDCA, 21 U.S.C. 379e(d)(4) and 21 U.S.C. 348(g)(2).

A fair evaluation of all the scientific evidence discussed above makes it clear that Yellow 5 and mixtures of various dyes in food are *unsafe* within the meaning of the FFDCA and the FDA’s own regulations. Instead of there being “convincing evidence” that the dyes cause “no harm,” there is “convincing evidence” that the dyes *do cause* harm to many children.

Moreover, section 721(b)(8) of the FFDCA further provides that in deciding whether to approve a color for all uses the FDA should “take into account...(subject to the paramount criterion of safety)...the availability, if any, of other color additives suitable and safe for one or more of the uses proposed.” As discussed above, dyes can easily be replaced by natural food colors or other ingredients.

VII. The FDA Has the Legal Authority to Require, as an Interim Measure, a Warning on Foods Containing Yellow 5 and Other Dyes that these Colorings Can Adversely Affect the Behavior of Some Children.

The FDA’s labeling regulations for Yellow 5 and other food dyes merely require that their presence in a food be disclosed on the food’s ingredient list.⁸¹ The FDA could amend those regulations to require—as an interim measure before the approvals are revoked—a warning, such as: “WARNING: The artificial colorings in this food cause hyperactivity and behavioral problems in some children.” Such a notice should be provided on the principal display panel of products to help ensure that shoppers see it. A warning label is not nearly as protective of the public health as a ban, because (a) it would continue to put the burden on parents to recognize that their child may be sensitive to dyes and then preventing their child from consuming such products and (b) it would be difficult to warn consumers about dyed foods sold at restaurants, cafeterias, and vending machines. Still, a warning notice would impose less of a burden on the food industry than a ban, and some companies would prefer to remove dyes from their products than to put a warning notice on the labels.

Section 721(b)(3) of the FFDCA provides that in order “to assure the safety of the use” of a color additive the FDA “shall...prescribe the conditions under which such additive may be safely employed for such use or uses (including, but not limited to...labeling...for such additive).”⁸²

⁸¹ See, for example, the general ingredient-labeling requirement, Section 403(i)(2) of the FFDCA, 21 U.S.C. 343(i)(2), and the requirement for Yellow 5, 21 C.F.R. 74.705(d).

⁸² The FDA relied on this statutory provision when it proposed a regulation requiring that food and cosmetic products containing cochineal extract or carmine declare that fact on their label. 71 Fed. Reg. 4839 (January 30,

Moreover, section 721(b)(6) of the FFDCA goes on to say that “the Secretary shall not list a color additive ... for a proposed use if the data before him show that such proposed use would promote deception of the consumer in violation of this Act or would otherwise result in misbranding ...within the meaning of this Act.” Section 201(n) of the FFDCA, 21 USC 321(n), provides, in pertinent part, that “in determining whether the labeling...is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling...fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling...relates under the conditions of use prescribed in the labeling...thereof or under such conditions of use as are customary or usual.” The omitted fact that dyes cause behavioral problems in some children is certainly a “material” fact for parents of affected children. Therefore, FDA should announce that beginning in 2009 it will consider as misbranded any food containing Yellow 5 or other dyes unless the food’s label warns that the food may adversely affect children’s behavior.⁸³

VIII. Conclusion

For the reasons stated above, the FDA should: (1) ban the use of Yellow 5 and seven other synthetic food dyes and, while revocation proceedings are in progress, require a warning notice on the principal display panels of foods, (2) immediately correct its 1993 advice (updated in 2004) to consumers about research on the risks of food dyes to children with behavioral problems, and (3) add neurotoxicity tests to the standard tests industry is asked to conduct when seeking approval for any new color additives and food additives.^{84,85} Eliminating dyes from the food supply should yield a direct health benefit without any health risk, and companies that wish to voluntarily stop using dyes would benefit from the “even playing field” that regulation would provide.

IX. Environmental Impact

The action requested is subject to a categorical exclusion under 21 C.F.R. 25.30 and

2006) at 4845.

⁸³ Misbranded food cannot, of course, be sold in interstate commerce. Section 301(a) of the FFDCA, 21 USC 331(a).

⁸⁴ For at least 25 years, behavioral toxicologists have urged the FDA to require neurotoxicity testing of proposed food additives. For example, Bernard Weiss wrote in 1982: “Behavioral toxicity is not yet a component of standard food additive safety testing, but the absence of behavioral criteria from food additive test protocols is beginning to seem a curious anomaly....And the Toxic Substances Control Act of 1976, which mandates premarket toxicity evaluation of all new chemicals introduced into commerce, specifies behavior as one of the criteria of toxicity.” (Weiss B. Food additives and environmental chemicals as sources of childhood behavior disorders. *J Am Acad Child Psychiatry*. 1982;21(2):144-52 at 151.)

⁸⁵ See, for example, Environmental Protection Agency. Health Effects Test Guidelines: OPPTS 870.6200 Neurotoxicity Screening Battery. August 1998. www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/870_Health_Effects_Test_Guidelines/Series/870-6200.pdf (accessed May 9, 2008).

25.32 and therefore does not require the preparation of an environmental assessment.

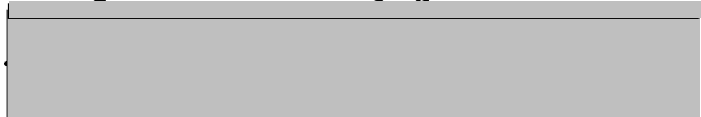
X. Economic Impact

No statement of the economic impact of the requested action is presented because none has been requested by the Commissioner.⁸⁶

XI. Certification

The undersigned certify that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and it includes representative data and information known to the petitioner that are unfavorable to the petition.

Respectfully submitted,



Michael F. Jacobson, Ph.D., Executive Director



Benjamin Cohen, Senior Staff Attorney



Stephen Gardner, Director of Litigation

Attachments:

Attachment 1: Diet, ADHD & Behavior – A Quarter-Century Review (updated June 2008)

Appendices:

Appendix 1: Examples of Food Dyes in Processed and Restaurant Foods

Appendix 2: Comment on European Food Safety Authority Review of Dyes and Hyperactivity by
Center for Science in the Public Interest

Appendix 3: Letter sent to FDA by physicians and researchers concerned about dyes and
children's behavior

⁸⁶ 21 C.F.R. 10.30(b).

Examples of Food Dyes in Processed and Restaurant Foods⁸⁷

Key: B = Blue, R = Red, Y = Yellow, L = Lake⁸⁸

I. PACKAGED FOODS

Chips, Crackers and Dips		
Nabisco	Cheese Nips Four Cheese	Y6, Y5
PepsiCo	Frito-Lay Cheetos Twisted Puffs	Y6
PepsiCo	Frito-Lay Cheetos Flamin' Hot Crunchy	R40L, Y6L, Y6, Y5
PepsiCo	Frito-Lay Doritos Blazin' Buffalo & Ranch	R40L, Y6, Y5, R40, B1, Y5L
PepsiCo	Frito-Lay Doritos Fiery Habanero	Y6L, R40L, Y6, Y5
PepsiCo	Frito-Lay Doritos Cool Ranch	R40, B1, Y5
PepsiCo	Frito-Lay Sun Chips French Onion	R40, B1
PepsiCo	Frito-Lay Sun Chips Harvest Cheddar	Y6, Y5
PepsiCo	Frito-Lay Tostitos Salsa con Queso	Y5, Y6
Sunshine	Cheez-It Crisps Four Cheese	Y6, Y5
Snacks		
ConAgra	Hunt's Snack Pack Pudding Vanilla, ConAgra	Y5, Y6
ConAgra	Hunt's Snack Pack Pudding Butterscotch, ConAgra	Y6, Y5
Dole	Pineapple in Lime Gel, All Natural Fruit	Y5, B1
Dole	Mandarins in Orange Gel	Y6
General Mills	Betty Crocker Fruit by the Foot Fruit Flavored Snacks Berry Tie-Dye	Y5, R40, B1
General Mills	Betty Crocker Fruit by the Foot Fruit Flavored Snacks Strawberry	Y5, R40, B1
General Mills	Betty Crocker Fruit Roll-ups, Crazy Pix, Cool Chix Berry Wave	R40, Y5, Y6, B1, B3
General Mills	Betty Crocker Fruit Roll-ups, Fruit Stackerz Tropical Berry	R40, B1, Y5, Y6
General Mills	Betty Crocker Sour Fruit Gushers Tropical Berry Shock	R40, B1
General Mills	Betty Crocker Scooby-Doo! Fruit Flavored Snacks	R40, Y5, Y6, B1
General Mills	Yoplait Trix Wildberry Blue	B1, R40
General Mills	Yoplait Trix Triple Cherry	R40
General Mills	Yoplait Whips Light & Fluffy	Y5, B1
General Mills	Yoplait Spongebob Squarepants GoGurt Portable Lowfat Yogurt, Strawberry Riptide	R40, B1
Kellogg	Spongebob's Atlantis Squarepants Fruit Flavored Snacks	Y5, R40, B1

⁸⁷ Sources of information: CSPI survey of Washington-area grocery stores and chain-restaurant web sites (May 2008).

⁸⁸ Lakes are the water insoluble forms of dyes and are used in coated tablets, cake and donut mixes, hard candies, chewing gums, and other products.

Kellogg	Barbie Fruit Flavored Snacks	Y5, R40, B1
Kellogg	Yogos Bits Yogurty Covered Fruit Flavored Bits Strawberry Slam	R40L, R40, Y5L
Kellogg	Yogos Bits Yogurty Covered Fruit Flavored Bits Island Explosion	Y5L, Y6L Y6, B2L, B1L
Kraft	Handi-Snacks Vanilla Pudding	Y5, Y6
Kraft	Kraft Handi-Snacks Sugar-Free Creamy Caramel Pudding	Y6
Kraft	JELL-O Gelatin Dessert, Lemon	Y5, Y6
Kraft	JELL-O Gelatin Dessert, Strawberry	R40,
Kraft	JELL-O Gelatin Dessert, Black Cherry	R40, B1
Kraft	JELL-O Instant Pudding & Pie Filling, Pistachio	Y5, B1, Y6
Kraft	JELL-O Instant Pudding & Pie Filling, Chocolate	R40, Y5, B1
Mott's	Strawberry Flavored Apple Sauce	R40
PepsiCo	Quaker Oatmeal to Go, Raspberry Streusel	R40, Y6
PepsiCo	Quaker Oatmeal to Go, Apples & Cinnamon	Y6
Cereal		
General Mills	Reeses Puffs	R40, Y5, Y6, B1
General Mills	Fruity Cheerios	R40, Y6, B1
General Mills	Lucky Charms	Y5, Y6, B1, R40
General Mills	Trix	R40, Y6, B1
Kellogg	Froot-Loops	R40, B2, Y6, B1
Kellogg	Apple Jacks	Y6, R40, B1
Kellogg	Pops, Chocolate Peanut Butter	R40, Y5, B1
Kraft	Post Fruity Pebbles	R40, Y6, Y5, B1, B2
Kraft	Post Honeycomb	Y5
PepsiCo	Quaker Cap'N Crunch's Crunch Berries	Y5, R40, Y6, B1
PepsiCo	Quaker Oatmeal Squares Crunchy Oatmeal Cereal	Y5, Y6
PepsiCo	Quaker Instant Oatmeal, Dinosaur Eggs	R40L, Y6L, Y5L, B1L
Other Breakfast Foods		
Kellogg	Pop-Tarts one serving of whole grain Strawberry	R40, Y6
Kellogg	Pop-Tarts Frosted Cherry	R40L, R40, Y6, B1
Kellogg	Pop-Tarts Hot Fudge Sundae	Y6L, B2L, R40L, Y5L, Y5, R40, Y6, B1, B2
Kellogg	Eggo Homestyle Waffles	Y5, Y6
Kellogg	Eggo Whole Grain Blueberry Waffles	B2L, R40L
Kellogg	Eggo Blueberry Waffles	B2L, R40L
Kellogg	Eggo Cinnamon Toast Waffles	Y5, Y6
Kellogg	Eggo Lego Homestyle Waffles	Y5, Y6
Kellogg	Eggo Strawberry Waffles	B2L, R40L
Kellogg	Eggo Mini Muffin Tops Blueberry	B2L, R40L
Kellogg	Eggo Cinnamon French Toaster Sticks	Y5, Y6
Meals, Entrees, and Sides		
ConAgra	Kid Cuisine Cheese Blaster Mac & Cheese	Y5, Y6, R40
ConAgra	Kid Cuisine Kung Fu Panda Mac & Cheese	Y5, Y6, R40, Y5, B1

ConAgra	Kid Cuisine Kung Fu Panda Chicken Breast Nuggets	Y5, Y6, R40, Y5, Y6, B1, Y5L
ConAgra	Kid Cuisine Magical Cheese Stuffed Crust Pizza	R40, Y6, B1, B2L, Y5
ConAgra	Kid Cuisine Bug Safari Chicken Breast Nuggets	Y5, Y6, R40, Y5, B1
ConAgra	Kid Cuisine Cheeseburger Builder	R40, Y6, B1, R3
General Mills	Betty Crocker Hamburger Helper Microwave Singles Cheeseburger Macaroni	Y5L, Y6L, Y5, Y6
General Mills	Betty Crocker Cheesy Lasagna with Beef	Y5L, Y6L, Y5, Y6
General Mills	Betty Crocker Beef Taco	Y5L, Y6L, Y6, Y5
General Mills	Betty Crocker Sweet Potato Mashed Potatoes	Y6L, Y5L
General Mills	Betty Crocker Au Gratin 100% Real Potatoes	Y5L, Y6L
General Mills	Betty Crocker Four Cheese Mashed Potatoes	Y5L, Y6L
Kraft	Macaroni & Cheese Three Cheese with Mini-Shell Pasta	Y5, Y6
Kraft	Macaroni & Cheese Thick 'n Creamy	Y5, Y6
Kraft	Spongebob Macaroni And Cheese Dinner	Y5, Y6
Kraft	Scooby Doo Macaroni And Cheese Dinner	Y5, Y6
Kraft	Spiderman Macaroni And Cheese Dinner	Y5, Y6
Kraft	Whole Grain Macaroni And Cheese Dinner	Y5, Y6
Kraft	Pokemon Macaroni And Cheese Dinner	Y5, Y6
Kraft	Shrek Macaroni And Cheese	Y5, Y6
Kraft	Oscar Mayer Lunchables Stackers Ham & Cheddar	Y5
Kraft	Oscar Mayer Lunchables Chicken Dunks	B1
Kraft	Oscar Mayer Lunchables Pizza & Treatza	B1L, Y5L, Y6, Y6L, R40L
Kraft	Oscar Mayer Lunchables Mini Burgers	Y6, Y5, Y5L, R40, R40L
Kraft	Oscar Mayer Lunchables Mini Hot Dogs	Y6, Y5, Y5L, R40, R40L
Kraft	Oscar Mayer Lunchables Mini Tacos	R40L
Kraft	Oscar Mayer Lunchables Pizza Extra Cheesy	R40, Y5, Y6, B1
Kraft	Oscar Mayer Lunchables Pizza Pepperoni Flavored Sausage	R40, Y5, Y6, B1
Kraft	Oscar Mayer Lunchables Cracker Stackers Ham & American	B1
Kraft	Oscar Mayer Lunchables Nachos Cheese Dip & Salsa	B1
Kraft	Oscar Mayer Lunchables Maxed Out Cracker Combo Ham & Cheddar	R40, B1
Kraft	Oscar Mayer Lunchables Maxed Out Ultimate Nachos, Nacho Dip & Salsa	Y5L, Y6L, Y5
Kraft	Oscar Mayer Lunchables Maxed Deep Dish Pizza Pepperoni Flavored Sausage	R40, B1
Nestlé S.A.	Lean Pockets Whole Grain Turkey Broccoli & Cheese	Y5, Y6, Y5L, Y5, Y6, Y6L
Nestlé S.A.	Lean Pockets Turkey Broccoli & Cheese	Y5L, Y5, Y6, Y6L
Nestlé S.A.	Lean Pockets Ham & Cheddar	Y5, Y6
Nestlé S.A.	Hot Pockets Croissant Crust Ham & Cheese	Y6L, Y5L, Y5, Y6
Nestlé S.A.	Hot Pockets Ham & Cheese	Y6L, Y5L, Y5, Y6
Nestlé S.A.	Hot Pockets Croissant Crust Philly Steak & Cheese	Y5L, Y6L

Baked Goods		
Archway	Home Style Cookies, Buttery Vanilla	Y5L
Interstate Bakeries Corporation	Hostess 100 Calorie Packs Golden Cake with Creamy Filling	Y5, R40
Interstate Bakeries Corporation	Hostess Blueberry Streusel Muffins	B2L, R40L
Interstate Bakeries Corporation	Hostess Twinkies	Y5, R40
Interstate Bakeries Corporation	Hostess Orange Cup Cakes	Y5L, Y6L, Y5, R40
Baking Dough and Mixes		
Pinnacle Foods Group Inc.	Duncan Hines Moist Deluxe Butter Recipe Golden Premium Cake Mix	Y5L, R40L
Pinnacle Foods Group Inc.	Duncan Hines Moist Deluxe Strawberry Supreme Premium Cake Mix	R40L, R40, B2
General Mills	Betty Crocker Sunkist Lemon-Poppy Seed Premium Muffin & Quick Bread Mix	Y5, Y6
General Mills	Pillsbury Flaky Cinnamon Twists with Glaze	Y5, R40
General Mills	Pillsbury Reduced Fat Cinnamon Rolls	Y5, R40
General Mills	Pillsbury Crescent Big & Flaky	Y5, R40
Frostings		
General Mills	Betty Crocker Ready To Spread Rainbow Chip Frosting	Y5L, Y6L, R40L, B1L, B2L, Y5, Y6
General Mills	Betty Crocker Frosting Rich And Creamy Cherry	R40, B2
General Mills	Betty Crocker Ready To Serve Creamy Vanilla Frosting	Y5, Y6
General Mills	Betty Crocker Rich And Creamy Coconut Pecan Frosting	Y5, Y6, R40, B1
General Mills	Betty Crocker Ready To Spread Cream Cheese Frosting	Y5, Y6
General Mills	Pillsbury Ready To Serve Vanilla Funfetti Frosting	Y5, R40, Y6, B1
General Mills	Pillsbury Whipped Supreme Strawberry Frosting	R40
Pinnacle Foods Group Inc.	Duncan Hines Whipped Frosting Vanilla	Y5, R40
Pinnacle Foods Group Inc.	Duncan Hines Whipped Frosting Chocolate	R40, Y5, B1
Frozen Desserts		
Nestlé S.A.	Edy's Grand Cherry Chocolate Chip Ice Cream	R40
Nestlé S.A.	Edy's Classic Real Strawberry Ice Cream	B1, R40
Nestlé S.A.	Edy's Grand Neapolitan Ice Cream	R40, B1
Nestlé S.A.	Edy's Loaded Nestle Butterfinger Ice Cream	Y5, R40
Nestlé S.A.	Edy's Dibs Mint Bite Size Ice Cream With Chocolate Coating	Y5, B1
Nestlé S.A.	Edy's Dibs Strawberry Ice Cream	R40
Mars, Inc.	M&M'S Cookie Ice Cream Sandwich	Y5L, B1L, R40L, Y6L, B2L
Schwan's Bakery, Inc.	Edwards Butterfinger Creme Pie Slices	Y5, R40
Unilever	Popsicle Sugar-Free Life Savers	Y5, Y6, R40, B1
Unilever	Popsicle Ice Pops Dora the Explorer Fruit Flavors Snack-Size	Y5, R40, B1
Unilever	Popsicle Firecracker Pops	R40, B1

Unilever	Popsicle Pops Firecracker Super Heroes	R40, R3, B1, Y5, Y6
Unilever	Popsicle Scribblers Pops	R40, B1, Y5, Y6
Unilever	Popsicle Spongebob Squarepants Pop Ups	R40, Y6
Unilever	Popsicle Variety Mighty Magic Minis	R40, B1, Y5, Y6
Unilever	Popsicle Orange Cherry Grape Pops	Y6, R40, R3, B1
Candies		
Mars, Inc.	M&M'S Milk Chocolate Candies	R40L, Y6, Y5, B2L, R40, B1, B2, Y5L, Y6L
Mars, Inc.	M&M'S Milk Chocolate Peanut Candies	R40L, B2L, B1L, Y6, Y5, R40, B1, B2, Y5L, Y6L
Mars, Inc.	Skittles Original Candy	Y6L, R40L, Y5L, B2L, B1L, Y5, R40, Y6, B1
Mars, Inc.	Skittles Sour Candy	Y6L, R40L, B1L, Y5L, B2L, R40, Y5, Y6, B1
Mars, Inc.	Starburst Original Fruit Chews Candy	R40, Y5, Y6, B1
Nestlé S.A.	Wonka Nerds Grape/Strawberry	B1, B1K, B2, B2L, R40, R40L, Y5, Y5L, Y6, Y6L
Nestlé S.A.	Wonka Sweetarts Candy	B1L, B2L, R40L, Y5L, Y6L
Nestlé S.A.	Nestle's Butterfinger	Y5, R40
The Hershey Company	Hershey's Kissables	R40L, B2L, Y5L, Y6L, B1L
The Hershey Company	Reeses Whipples Light And Fluffy Peanut Butter Bar	Y5L, Y6L, B2L, R40L
The Hershey Company	Hersheys Rainbow Twizzler Twist Candy	R40, B1, Y6, Y5
The Hershey Company	Twizzlers Strawberry Candy	R40
The Hershey Company	Jolly Ranchers Screaming Sours Soft & Chewy Candy	Y5, R40, B1
The Hershey Company	Reeses Pieces	B1L, R40L, Y5L, Y6L
The Jelly Belly Company	Jelly Belly 20 Flavors	R40L, Y5L, Y6L, B1L, B2L, Y5, Y6, R40, B1
Drinks		
Dr. Pepper/Seven-Up Inc.	Canada Dry Caffeine Free Cranberry Ginger Ale	R40, B1
Dr. Pepper/Seven-Up Inc.	Sunkist Orange Soda	Y6, R40
Dr. Pepper/Seven-Up Inc.	Diet Dr. Pepper Cherry Chocolate	R40
Dr. Pepper/Seven-Up Inc.	Hawaiian Punch Fruit Juicy Red	R40, B1
PepsiCo	Propel Invigorating Water, Berry	R40
PepsiCo	Propel Invigorating Water, Citrus	Y6, R40
PepsiCo	Gatorade A.M. Orange-Strawberry Thirst Quencher	R40, Y6, Y5
PepsiCo	Gatorade Lemon-Lime Thirst Quencher	Y5
PepsiCo	Gatorade Orange Thirst Quencher	Y6, R40
The Coca-Cola Company	Minute Maid Lemonade	Y5
The Coca-Cola Company	Fanta Orange	Y6, R40
The Coca-Cola Company	Fanta Grape	R40, B1

II. RESTAURANT FOODS		
McDonald's	Tangy Honey Mustard Sauce	Y5, Y6
	Spicy Buffalo Sauce	R40
	Orange Glaze	R40
	Strawberry Sundae	R40
	McFlurry with M&M'S Candies	Y5, R40, B1L, Y6L, B2L, R40, Y5, Y6
	Strawberry Triple Thick Shake	R40
	Vanilla Triple Thick Shake	Y5, Y6
	Hi-C Orange Lavaburst	Y6, R40
	POWERade Mountain Blast	B1
Burger King	Mott's Strawberry Flavored Applesauce	R40
	Sweet and Sour Dipping Sauce	R40
Wendy's	Cheddar Cheese Sauce	Y5, Y6
	Chili	R40
	Dill Pickles	Y5, B1
	Fat Free French Style Dressing	Y6
	Frosty Shake, Strawberry	R40, B1
	Honey Mustard Dressing	Y5
	Honey Mustard Nugget Sauce	Y5
	Low Fat Honey Mustard Dressing	Y5
	Maraschino Cherries	R40
	Mayonnaise Dressing	Y5, Y6
	M&M'S Candy Crumbles	R40L, B1L, Y6, Y5, R40, B1, B2L, Y6L, Y5L, B2
	Seasoned Tortilla Chips	R40, Y5, B1
	Sweet & Sour Nugget Sauce	R40
KFC	HBBQ Sauce	R40
	Chicken Pot Pie	Y5, R40
	Sweet and Spicy Wings	R40
	Sweet and Spicy Boneless Wings	R40
	Mac and Cheese (<i>depends upon regional supplier</i>)	Y5, Y6
	Potato Salad	B1
	Baked! Cheetos	Y6
	Quaker Chewy S'mores Granola Bar	B1
	Apple Pie Mini's	Y5, Y6
	Lil' Bucket Fudge Brownie	R40
	Lil' Bucket Lemon Crème	Y5L
	Lil' Bucket Strawberry Short Cake	R40
	Mountain Dew	Y5

Subway	Banana Peppers	Y5
	Pickles	Y5
	Red Wine Vinaigrette	R40, B1
	Berry Lishus Fruizle Express	R40
	Peach Pizazz Fruizle Express	Y5, B1, Y6, R40
	Pineapple Delight Fruizle Express	Y5, Y6
	Sunrise Energizer	Y5, Y6
	M&M Cookie	R40L, Y5, Y6, B2L, R40, B1L, B1, B2, Y5L, Y6L
Jack in the Box	Blueberry French Toast Sticks	R40, B2, B1, B2L
	Cheddar Cheese Sauce	Y5, Y6
	Egg Nog Syrup	Y5, Y6
	Fanta Orange	Y6, R40
	Fanta Strawberry	R40
	Honey Mustard Dipping Sauce	Y5, Y6
	Maraschino Cherry	R40
	Minute Maid Lemonade	Y5
	Mozzarella Cheese Sticks	Y5, Y6
	Dill Pickle Slices	Y5, B1
	Strawberry Syrup	R40
	Warm Cinnamon Roll	Y5, Y6

**Comment on European Food Safety Authority Review of Dyes and Hyperactivity
by
Center for Science in the Public Interest**

The European Food Safety Authority (EFSA) review acknowledges that the Southampton study found “limited evidence that the two different mixtures of synthetic colours and sodium benzoate tested had a small and statistically significant effect on activity and attention in children selected from the general population.”⁸⁹ However, EFSA took great pains to highlight qualifications, such as (a) whether the effects were clinically significant, (b) that dose-response effects were not tested, (c) that each of the chemicals were not tested alone to ascertain which affected behavior, (d) that there were inconsistencies between the two mixtures, and (e) that a novel metric was used.⁹⁰

EFSA’s focus on limitations blinded it from the key result: the Southampton studies found effects of dyes on behavior even though the subjects were children in the general population, not children who had been diagnosed with behavior problems or whose parents thought they were sensitive to dyes and/or other food ingredients. In fact, the studies *excluded* children being treated for ADHD, the children likeliest to be sensitive to dyes, but they *still* found a statistically significant effect of dyes on behavior.

Another factor greatly reduced the chances of finding an effect: the researchers averaged in the results of all the subjects, the vast majority of whom likely were not affected by dyes. Ideally, the study would have presented the results for each individual child (as, for instance, the 1980 Weiss/Williams/Margen study did) to see what percent of the children were affected.

Several other factors reduced the chances of detecting an effect of the dyes on behavior. For instance, though not noted by EFSA, the subjects may have been consuming other food dyes or ingredients that affected behavior, and the subjects may not have adhered as carefully to the diet during the washout periods as they had claimed. In addition, though toxicology studies normally give exaggerated doses of the test chemicals, many children actually consume much more dye than was used in the study.

Still, EFSA is correct in saying that it is impossible to know if all the dyes tested and benzoate affected behavior, because they were not tested individually (or in other combinations). As a practical matter, most of the studies on dyes and behavior used a mixture of dyes, reflecting the real-life situation, not the needs of a regulatory agency. Testing dyes individually would multiply the costs considerably.

⁸⁹ The EFSA Journal. 2008;660:1-54.

⁹⁰ The authors of the Southampton study provide a more detailed analysis of EFSA’s review in a comment to the FSA. See Annex 3 of FSA’s statement on Food Additives and Hyperactivity, April 10, 2008. www.food.gov.uk/multimedia/pdfs/board/fsa080404a.pdf (accessed April 10, 2008).

**Letter sent to FDA by physicians and researchers concerned
about dyes and children's behavior**

June 3, 2008

Dr. Andrew von Eschenbach, Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. von Eschenbach:

The undersigned physicians and researchers are concerned about the adverse effects of food ingredients, especially food dyes, on children's behavior, and are troubled by federal inaction on this important issue.

The first hints that food ingredients could impair children's behavior came in the early-1970s, when Kaiser-Permanente allergist Dr. Ben Feingold publicized his clinical findings. His contentions not only generated great public concern, but also spurred scientific research. Many of the studies done over the years, in the United States and abroad, have confirmed that some children are affected by foods or food ingredients, with food dyes being the most frequently identified problem. One of the early studies was actually funded by the U.S. Food and Drug Administration (FDA),⁹¹ and two recent studies were funded by the Food Standards Agency of the British government.⁹²

A 2004 meta-analysis of controlled studies concluded that "our results strongly suggest an association between ingestion of [artificial food colorings] and hyperactivity."⁹³ The researchers stated that "society should engage in a broader discussion about whether the aesthetic and commercial rationale for the use of [artificial food colorings] is justified."

Despite all the evidence from clinical trials, the FDA publishes (jointly with the food industry's

⁹¹ Weiss B, Williams JH, Margen S, et al. Behavioral responses to artificial food colors. *Science*. 1980;207:1487-8.

⁹² McCann D, Barrett A, Cooper A, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomized, double-blinded, placebo-controlled trial. *Lancet*. 2007 Nov 3;370:1560-7. Published online Sept. 6, 2007. The same research group published a study of 3-year-olds that also found an effect of a mixture of four dyes and sodium benzoate on hyperactivity. Bateman B, Warner JO, Hutchinson E, et al. The effects of a double blind, placebo controlled, artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of preschool children. *Arch Dis Child*. 2004;89:506-11. The authors stated: "We believe that this suggests that benefit would accrue for all children if artificial food colours and benzoate preservatives were removed from their diet."

⁹³ Schab DW, Trinh N-H T. Do artificial food colorings promote hyperactivity in children with hyperactive syndromes? A meta-analysis of double-blind placebo-controlled trials. *J Dev Behav Pediatr*. 2004;25:423-34.

International Food Information Council) a pamphlet on “Food Ingredients and Colors” that asserts that there is “no evidence” of a link between dyes and hyperactivity.⁹⁴ In contrast, the British government is vigorously urging the food industry to stop using the food dyes that were used in the research that it sponsored.⁹⁵ In addition, a committee of the European Parliament recently voted to ban dyes from foods consumed by babies and small children and also required a warning notice on foods consumed by older children.⁹⁶

It is important to weigh the risks and benefits of any federal action—or inaction—considering health, economic, and other issues. In the present case, food dyes pose a health risk to many consumers, but no health benefit whatsoever to any consumers. Moreover, the economic benefit to industry appears to be negligible; indeed, some food processors may feel obliged to use dyes only because their competitors use them, but if no one used them, that wouldn’t be an issue.

Considering the substantial body of scientific evidence, we urge you to press for measures that would help protect children from unnecessary harm. We suggest the following:

- Begin proceedings to end the use of food dyes that might adversely affect children’s behavior.
- Revise or withdraw the FDA’s inaccurate brochure “Food Ingredients and Colors.”
- Establish testing protocols based on neurobehavioral endpoints for new food additives.⁹⁷

- continued -

⁹⁴ www.cfsan.fda.gov/~dms/foodic.html (accessed March 9, 2008). A previous version, “Food Color Facts,” is also on FDA’s web site.

⁹⁵ www.foodstandards.gov.uk/news/newsarchive/2007/sep/additivesboard (accessed March 9, 2008). The British government is focusing on food dyes and the preservative sodium benzoate, which were mixed together in the studies it sponsored.

⁹⁶ Crowley L. MEPs vote for ban on unnecessary colours for kids. Food Navigator.com—Europe. May 7, 2008. www.foodnavigator.com/news/ng.asp?n=85135&c=4ad7aAzQZOnmdHoqSmGJwQ%3D%3D (accessed May 9, 2008).

⁹⁷ See, for example, Environmental Protection Agency. Health Effects Test Guidelines: OPPTS 870.6200 Neurotoxicity Screening Battery. August 1998. www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/870_Health_Effects_Test_Guidelines/Series/870-6200.pdf (accessed May 9, 2008).

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Diet, ADHD & Behavior

A QUARTER-CENTURY REVIEW



Center for Science in the Public Interest

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Diet, ADHD & Behavior

A QUARTER-CENTURY REVIEW

Michael F. Jacobson, Ph.D., and David Schardt, M.S.



Center for Science in the Public Interest
Washington, D.C.

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The contents of this pamphlet are not intended to provide personal medical advice, which should be obtained from a qualified health professional.

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2008 Update on Food Dyes and Behavior

Since "Diet, ADHD, and Behavior" was published in 1999, several new studies have been published that shed light on diet's adverse effects on behavior and on possible problems with methylphenidate (Ritalin), the drug frequently used to treat Attention Deficit Hyperactivity Disorder (ADHD). In addition, public officials, at least in the United Kingdom, have begun to take action.

Research and policy action on diet and behavior

Following two more than two decades of research on food dyes and hyperactivity, an important 2004 meta-analysis concluded that "our results strongly suggest an association between ingestion of [artificial food colorings] and hyperactivity."¹

The most important new research funded by the British government. That study, unlike previous ones, involved a cross-section of young children instead of children selected because their parents suspected their behavior was impaired by food ingredients.

The University of Southampton researchers studied the preservative sodium benzoate along with one of two mixtures of several food dyes (some of which are used in the United States), as well as children given a placebo.² The study involved 153 3-year-olds and 144 children 8 to 9. One of the two mixtures had a significantly affected the younger children. Both mixtures had an adverse effect on older children who consumed the additives as directed. The researchers' concluded that "Artificial colours or a sodium benzoate preservative (or both) in the diet result in increased hyperactivity in 3-year-old and 8/9-year-old children in the general population."

The editors of the American Academy of Pediatrics' journal, AAP Grand Rounds, stated: "Thus, 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."³

The British Food Standards Agency (FSA) offered this advice to parents: "If 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."⁴ As a preventive measure, the FSA is urging food manufacturers to stop using the colorings studied. When few companies responded promptly, the chair of the FSA board said, "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."⁵ Some of Britain's biggest supermarket chains—Tesco, Sainsbury's, ASDA, Marks & Spencer, and the Co-op—have pledged to drop the dyes from their house-brand products.⁶ Kraft has eliminated artificial colors and flavors from its Lunchables line in Britain, but not in the United States. Haribo has done the same for its Gold-Bears (gummi candies), as have McDonald's, Mars, and Kellogg for the dyes in some of their foods.

In 2008, the European Food Safety Authority (EFSA) reviewed the Southampton study and concluded that it "provides limited evidence that the two different mixtures of synthetic colours and sodium benzoate tested had a small and statistically significant effect on activity and attention in some children..."⁷ However, EFSA cited several uncertainties regarding clinical relevance, small effect size, and that the study could not identify the effects of individual additives.

Following a *New York Times* article about the British study, a committee of the New York State Assembly held a hearing in October 2007 on food additives and behavioral disorders.⁸ The chair of the committee, Peter Rivera, subsequently called for warning labels on foods containing certain artificial colorings and sodium benzoate.

More importantly, in May 2008, the European Union's Environment Committee voted to ban artificial colors in foods for babies and small children.⁹ That measure also included a warning label on other children's foods: "Azo dyes may provoke allergenic effects and hyperactivity in children." If the European Parliament approves the measure, member governments would have to approve it for the regulatory actions to take effect.

The U.S. Food and Drug Administration (FDA) has done nothing to protect children from food additives that affect children's behavior. Instead, a 1993 pamphlet stated: "Although this theory 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."¹⁰ In 2000, five Members of Congress urged the FDA to revise the brochure to reflect "that some ADHD children may benefit from dietary changes," but the brochure remained on the FDA's web site in 2008.¹¹ An FDA official said the agency would review the Southampton study, but stated: "However, we have no reason at this time to change our conclusions that the ingredients that were tested in this study that currently are permitted for food use in the United States are safe for the general population."¹²

The National Institute of Mental Health (NIMH) should be America's leading advocate of research into causes of and treatments for ADHD. In 2000, NIMH director Steven Hyman stated: "research on dietary interventions is considered an integral part of the overall effort to develop safe and effective treatments for children with ADHD."¹³ However, NIMH apparently has not funded any such research in recent years.

Research on the safety of drugs used to treat ADHD

With methylphenidate (Ritalin) having long been the drug of choice for treating millions of children, safety is an important issue. As discussed in this report, a 1995 National Toxicology Program (NTP) study

found that methylphenidate causes cancer in mice. The FDA acknowledged¹⁴ that the study found "a weak signal of carcinogenic potential and said it would "initiate additional follow-up studies, including both animal tests and epidemiological studies in humans using Ritalin." The agency, however, appears not to have done anything beyond including drug companies to revise the "label," which is not provided to patients and parents, by briefly summarizing the results of the NTP study. A letter from seven cancer experts urging the Department of Health and Human Services to inform the public of possible risks from methylphenidate was ignored.¹⁵

To get direct evidence on risks to children of stimulant drugs, researchers at the University of Texas Medical Branch at Galveston administered methylphenidate to children and then examined blood lymphocyte cells. They found roughly three-fold increases in chromosome aberrations, sister chromatid exchanges, and micronuclei frequencies. They concluded that their study was "a cautionary sign" and urged further research, because of the "well-documented relationship between elevated frequencies of chromosome aberrations and increased cancer risk."¹⁶ That study appears to have spurred the National Institute of Child Health and Human Development to commission a larger genetic toxicity study in children and research on monkeys.¹⁷

Sensitive epidemiology studies of the carcinogenicity of methylphenidate are difficult to conduct because of the need to include large numbers of subjects who had consumed the drug for long periods. Lifelong follow-up periods are needed, but most people who consumed the drug as children are still rather young. Nevertheless, one 2007 epidemiology study done by the Kaiser Permanente Medical Care Program linked the drug's usage with a significantly higher incidence of lymphocytic leukemia.¹⁸ The researchers emphasized, though, that the apparent association might be due to chance.

Summary and recommendations

In a letter to Congress in 2000, Ohio State University professor emeritus of psychiatry L. Eugene Arnold questioned the continued use of food dyes.¹⁹ If such dyes were eliminated from the food supply, this expert stated:

The only economic segment to suffer would be the dye manufacturers; that cost should be weighed against the possibility of solving 5–15% of the ADHD problem. Would subsidizing the dye industry's loss be cheaper than the medical and educational costs of that proportion of ADHD?

Likewise, the authors of the 2004 meta-analysis noted earlier urged that “society should engage in a broader discussion about whether the aesthetic and commercial rationale for the use of [artificial food colorings] is justified.”²⁰ Such a discussion is particularly appropriate considering that the per capita production of food dyes has increased five-fold between 1955 and 2007.²¹

Currently, ingredients in children's foods are impairing children's behavior, and then the symptoms are treated with a possible carcinogen. The Center for Science in the Public Interest recommends the following actions:

- ◆ Congress should fund the Institute of Medicine to evaluate the studies on diet and behavior and on the safety of pharmaceuticals used to treat ADHD, keeping in mind the benefits and risks of food ingredients and of pharmaceuticals. The IOM should suggest research and regulatory options and more thorough protocols for testing new food additives.
- ◆ Congress should hold hearings on the effects of diet on behavior, including possible risks associated with drugs used to treat ADHD, and on the FDA's response to the body of research. Congress then should consider legislation to ban the synthetic dyes.
- ◆ The FDA should revoke the approval of food and color additives that may provoke adverse behaviors. If the FDA fails to do that,

Congress should pass a law to protect children from the unsafe ingredients. The FDA should also require neurobehavioral testing of new food additives.

In June 2008, the Center for Science in the Public Interest, with support from two dozen physicians and researchers, formally petitioned the FDA to ban the use of food dyes. Because a ban would take several years to implement, the petition recommended an immediate requirement that foods with synthetic dyes bear a warning notice. The petition noted that some food companies have already switched to safer, natural colorings and that two large grocery chains, Trader Joe's and Whole Foods Markets, do not carry any foods that contain dyes.

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Executive Summary

This report reviews 23 controlled studies of the effect of food dyes and other dietary constituents on the behavior of children with Attention-Deficit/Hyperactivity Disorder (ADHD) or other behavioral problems. Though the studies are limited due to the number of subjects, extent of dietary changes tested, assessment techniques, and other factors, 17 of the 23 studies found evidence that some children's behavior significantly worsens after they consume artificial colors or certain foods, such as milk or wheat. Limited research with such tools as electroencephalography (EEG) indicates that certain foods trigger physiological changes in sensitive individuals.

Notwithstanding the evidence from numerous studies, many health organizations and medical experts deny that diet can provoke adverse behaviors and that modified diets may benefit patients. The National Institute of Mental Health (NIMH) largely dismisses diet as a treatment approach, and the U.S. Food and Drug Administration (FDA) has cosponsored with an industry trade association a misleading pamphlet that denies the effect of diet on behavior.

Ignoring or denying (or exaggerating) the effect of diet on behavior is not helpful to children and their families. The federal government, the food industry, organizations concerned about children with behavioral problems, and psychiatrists, psychologists, and social workers should recognize that diet sometimes can help children who have behavioral problems. Parents should consider modifying their children's diets for several weeks to ascertain any benefit before resorting to medications. That is particularly the case because the stimulant drugs routinely used to treat ADHD may cause side effects, and the most commonly used drug, methylphenidate (Ritalin), increased the incidence of liver cancer in a study on mice. Of course, modifying a child's diet can be difficult in a society in which problem foods are ubiquitous, though perhaps no more difficult than adhering to a kosher or vegetarian diet.

This report recommends:

- Government, private agencies, and health practitioners concerned about children with ADHD and other behavioral problems should acknowledge the potential for diet to affect behavior and should advise parents to consider modifying their child's diet as a first means of treatment. Those organizations should update their publications to describe accurately the effect of diet on behavior and the evidence that methylphenidate caused cancer in mice and may pose a risk in humans.
 - Parents should consider dietary changes (along with behavioral therapy) as the first course of treatment for children with behavioral problems before turning to stimulant drugs.
 - The National Institutes of Health should sponsor research to determine which (and to what extent) foods and food additives affect behavior, develop methods for identifying children most sensitive to foods, investigate the underlying biological bases for sensitivity to dietary constituents, develop techniques to reduce the impact of foods on children's behavior, develop techniques for increasing the ease and effectiveness of dietary treatment, conduct animal studies to investigate possible long-term effects (carcinogenic, behavioral, reproductive, teratogenic, and other) of stimulant drugs, conduct long-term studies on large numbers of users of stimulant drugs to identify any adverse effects (such as behavioral disorders, social problems, cancer, reproductive problems, or other health problems), and study the efficacy of nutritional supplements (including fatty acids, minerals, and vitamins) in treating behavioral disorders. Also, NIH should sponsor a new consensus conference
-

on diet and ADHD/behavior to supersede a previous inadequate conference.

- The FDA should require certain new and existing additives to be tested for behavioral effects. It should consider banning from foods consumed widely by children any dyes and other additives that affect behavior. The FDA should stop endorsing literature that denies that diet can affect behavior. Also, it should advise the public that because methylphenidate caused liver

cancer in mice that drug should not be the primary choice for treating ADHD.

- Fast-food chains and manufacturers of foods, drugs, and vitamin supplements popular with children should minimize the use of dyes and other unnecessary additives.
 - Pediatric hospitals and psychiatric clinics, as well as schools and camps, should minimize the use of food additives that may contribute to behavioral disorders.
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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a syndrome diagnosed in millions of American children and adults.* The main symptoms of ADHD are reduced attentiveness and concentration, excessive levels of activity, distractibility, and impulsiveness. Additional children are affected by other behavioral problems. For the past quarter-century, controversy has swirled around the hypothesis that diet can trigger symptoms of ADHD and other behavioral problems.

The exact percentage of children with ADHD is not known. The usual estimates are 3 percent to 5 percent of school-age children.²² Using broader diagnostic definitions, some surveys find that the percentage is as high as 17 percent.²³ School-age boys with the disorder outnumber girls by a margin of roughly two or three to one. On average, at least one child in every classroom in the United States needs help for ADHD. Indeed, one recent study found that in 1995 18 percent to 20 percent of fifth-grade white boys in two Virginia cities had been diagnosed with ADHD and were being treated with stimulant drugs.²⁴

Children often outgrow or learn how to control their symptoms. But symptoms sometimes persist into adulthood, making it more difficult to succeed in careers, to start and maintain families, and to become involved in community activities. Adults with ADHD have higher rates of alcoholism, drug use, and imprisonment.²⁵

ADHD takes an enormous toll on affected children and their families. The child falls behind in school, does not learn what his or her peers are learning, loses self-esteem, and needs extra help. A family must cope daily with the need to focus the child's attention on essential activities or restrain his or her impulsive behavior. A family must also deal

with the fact that its child is not always welcome in other people's homes, in play groups, or on teams. Siblings may suffer because their own needs are not met, and many marriages suffer from the constant stress of dealing with ADHD.

ADHD is most often diagnosed with the use of a checklist of typical behaviors, such as the one published in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders-IV* (see box on page 2), and by considering other factors, such as age of onset and degree of impairment. Many of the studies on diet and behavior discussed in this report evaluated children's behavior by means of the 10-item Conners' Parent-Teacher Questionnaire, an earlier, widely used means of identifying hyperactivity.²⁶ That questionnaire rated ten behaviors, such as failure to finish tasks, fidgeting, excitable/impulsive, restless or overactive, and disturbs other children, on a scale of 0 to 3. Scores of 15 or greater indicate hyperactivity.

Researchers generally agree that ADHD has genetic roots. Thus, if one child has the syndrome, his or her siblings have a greater risk of developing it.²⁷ Doctors cannot yet diagnose ADHD by using blood analyses, brain scans, or other laboratory tests, but researchers are working hard to develop such methods. Recently, researchers have found subtle differences in brain structure and metabolism between children with and without ADHD.²⁸

The Feingold diet

In the mid-1970s, Benjamin Feingold, a California allergist, generated a firestorm of excitement and controversy by maintaining that artificial colorings and flavorings and certain natural chemicals (salicylates in apricots, berries, tomatoes, and other foods)

*ADHD was formerly called hyperactivity or attention-deficit disorder (ADD). The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* identifies three types of AD/HD: predominantly inattentive (ADD), predominantly hyperactive (ADHD), and combined subtype (the most common).

could trigger ADHD.²⁹ Feingold, who was Chief Emeritus of the Department of Allergy at the Kaiser Foundation Hospital and Permanente Medical Group in San Francisco, stated that 30 percent to 50 percent of the hyperactive children that he had treated benefited from diets free of those substances.³⁰ He discovered that when he prescribed a restricted diet (but not other treatments) for hives, asthma, or other allergic reactions, his patients' behavioral problems (if present) sometimes also would diminish.

Thousands of beleaguered families, eager for drug-free relief for their hyperactive children, tried Feingold's diet. Many reported marked improvement in their children's behavior. Those parents launched Feingold-diet support groups throughout the country to share information and provide encouragement

and help to other families.

But not everyone agreed that diet might affect children's behavior. The processed-foods industry and many child-behavior experts and researchers were skeptical of Feingold's claim, noting that it was based solely on his and parents' observations and was not supported by any controlled studies. The reported successes of his diet could be due to something else the families were doing, they said, and not to the absence of chemicals in the food. Until the relationship between diet and behavior was demonstrated in well-conducted research, they insisted, Feingold's claim should be considered an unproven hypothesis. Nevertheless, in 1975 a committee of the U.S. Department of Health, Education and Welfare concluded that "the evidence taken as a whole is sufficient to merit further

DSM-IV Checklist for Diagnosing ADHD

The *Diagnostic and Statistical Manual of Mental Disorders IV*, published by the American Psychiatric Association, describes three patterns of behavior that indicate ADHD. People with ADHD may show several signs of being consistently inattentive. They may have a pattern of being hyperactive and impulsive. Or they may show all three types of behavior.

Signs of inattention include:

- becoming easily distracted by irrelevant sights and sounds
- failing to pay attention to details and making careless mistakes
- rarely following instructions carefully and completely
- losing or forgetting things like toys, or pencils, books, and tools needed for a task
- avoiding tasks that require sustained mental effort

Signs of hyperactivity and impulsivity include:

- feeling restless, often fidgeting with hands or feet, or squirming
- running, climbing, or leaving a seat in situations where sitting or quiet behavior is expected
- acting as if driven by a motor
- blurting out answers before hearing the whole question
- having difficulty waiting in line or for a turn

Because everyone shows some of those behaviors at times, the DSM contains specific guidelines for determining when they indicate ADHD. The behaviors must appear early in life, before age seven, and continue for at least six months. In children, they must be more frequent or severe than in others the same age. Above all, the behaviors must create a real handicap in at least two areas of a person's life, such as school, home, work, or social settings. So someone whose work or friendships are not impaired by those behaviors would not be diagnosed with ADHD. Nor would a child who seems overly active at school but functions well elsewhere.

(Adapted from *Attention Deficit Hyperactivity Disorder*, National Institute of Mental Health, 1994.)

investigation into the relationship of diet and the hyperkinetic syndrome.”³¹

Slowly, university researchers began testing Feingold’s claim. The first study, conducted by C. Keith Conners and his colleagues at the University of Pittsburgh and published in 1976, found that at least four of 15 children diagnosed with ADHD improved on a diet free of artificial colors and flavors, according to evaluations by parents, teachers, and the researcher.³²

Within the next five years, about a dozen controlled trials of varying quality were conducted. In those studies, children with ADHD (most of whose parents believed their behavior was affected by diet) were either put on a reduced-additive diet and then challenged with specific additives or provided with diets containing (placebo) or not containing (test diet) those substances. Most of those studies found some evidence of a dietary effect on behavior. (The hypothesis that foods containing salicylates affect behavior remains essentially untested.³³)

In 1982, the National Institutes of Health (NIH) convened a “consensus development conference” on “Defined Diets and Childhood Hyperactivity.”³⁴ That NIH panel concluded that food additives and certain foods affect a small proportion of children with behavioral problems. The panel stated that controlled studies “did indicate a limited positive association between defined [Feingold-type] diets and a decrease in hyperactivity.” It noted that a major limitation of the research was that most studies tested only food dyes and not flavors and preservatives that also might promote hyperactivity. It recognized “that initiation of a trial of dietary treatment . . . may be warranted” for hyperactive children. Also, it recommended that more animal and human research be conducted to determine

which foods and additives cause problems, how those ingredients affect the brain and behavior, and which children may be most likely to respond to dietary treatment.

During the 17 years since that NIH meeting, the NIH has sponsored little of the research recommended by its consensus panel. Nevertheless, a number of studies conducted by researchers in the United States, Canada, Europe, and Australia provided new evidence that synthetic colors and possibly other additives and foods, such as milk and corn, adversely affect some children with behavioral problems.

The issue of diet and ADHD needs to be considered in the context of current treatment practices. Pediatricians, though they often have reservations about treating ADHD with medications, typically prescribe stimulant drugs for children along with behavioral counseling for parents and children. The drug most frequently prescribed is methylphenidate (Ritalin and other brands). The use of methylphenidate increased by 2.5-fold between 1990 and 1995, according to one study, with an estimated 1.5 million youths aged five to 18 taking the drug in 1995.³⁵ The U.S. Drug Enforcement Administration (DEA) of the U.S. Department of Justice, which treats methylphenidate as a controlled substance, reports that manufacturers’ sales increased nearly five-fold between 1990 and 1998³⁶ and that the U.S. now consumes 90 percent of the methylphenidate produced throughout the world.³⁷ While prescriptions for methylphenidate began leveling off between 1995 and 1997, prescriptions for amphetamines, which are also used to treat ADHD, tripled, so overall use of stimulant drugs has continued to rise.³⁸ One reason for the increase is that more elementary-school children are remaining on those drugs into their teens.³⁹ Later in this report, we consider safety concerns about methylphenidate.

“[Controlled studies] did indicate a limited positive association between defined [Feingold-type] diets and a decrease in hyperactivity.”

NIH 1982 Consensus Conference

Studies on Diet and Behavior

We review in this report 23 double-blind (plus several other) studies* that investigated the effect of food additives and/or foods on children's behavior. We do not include studies that tested the effect of minimal amounts (1-5 mg) of food coloring,⁴⁰ nor do we address research on dietary deficiencies of, or supplementation with, vitamins, minerals, or fatty acids. Because some people contend that sugars can affect children's behavior, we review the limited research on sugars and behavior in Appendix 1.

The children studied had been diagnosed with ADHD or suffered from other behavioral problems, such as irritability and sleeplessness. However, for several reasons, those children generally were not representative of all children with ADHD or behavioral problems. In some of the studies the subjects were thought by their parents to behave worse when they ate certain foods or additives and had been kept on restricted diets. In several studies, many of the children suffered from asthma, hives, eczema, and other allergies or sensitivities. And in several studies, the children had severe behavioral disorders.

The double-blind studies compared the behavior of the subjects when they were consuming suspect additives or foods to their behavior when consuming presumably inactive placebos. For instance, in some studies children were given cookies or capsules containing food colors, and their behavior was compared to when they were given similar cookies or capsules free of food colors. (As discussed later, the "placebo" sometimes contained chocolate, wheat, or other ingredients to which children might be sensitive.) Many studies focused only on dyes and, in some cases, on only one dye, tartrazine (Yellow 5), the second most widely used dye in the United States. In several studies, after being placed on restricted diets, children were challenged not with individual dyes or foods,

but with whole different diets that contained additives or foods suspected of affecting behavior. Some of the double-blind studies included preliminary non-blind phases, such as when baseline diets were replaced with experimental diets.

The effects of the ingredients or diets on behavior usually were rated by parents, teachers, and/or researchers using standardized checklists (most often the Conners' scale), inventories based on the children's previous behavior, or open-ended questionnaires. In some cases, laboratory tests of attention, distractibility, locomotor activity, or neurophysiologic activity were employed.

Let us turn now to the studies themselves and review the results of some of the more significant ones. Additional details are provided in Appendix 2.

Studies that found some effect of diet on behavior

The early controlled studies of diet and behavior focused on possible effects of artificial colorings and, sometimes, flavorings and salicylate-containing foods. In the first study, published in 1976, Conners *et al.* compared the Feingold diet, which was free of certain foods, including those with artificial colors and flavors, to a diet that included those substances.⁴¹ The researchers sought to make both diets appear to be experimental diets so that participants couldn't guess which was the "elimination" diet. In a group of 15 children diagnosed with hyperkinesis (the older term for ADHD), four or five children improved on the Feingold diet, two showing "dramatic results." (See Table 1 on page 5.) The average improvement was about 15 percent, though there was an "order effect" (improvement on the Feingold was seen primarily in the subjects who ate the control diet before the Feingold diet; see Appendix 2 for further discussion). A possible flaw in this study is that, according to the researchers, some mothers might have been able to figure out which diet their

*In double-blind studies, neither the researchers/observers nor the subjects know when the subjects are consuming the treatment or placebo. Non-blind studies are not as reliable, because the participants' knowledge of the subjects treatment can affect the results.

Table 1 **Studies (Double-blind) of Diet on Behavior**

These double-blind studies compared the behavior of children who had ADHD or other behavioral problems when they consumed certain foods or additives (usually dyes) to when they did not. The duration of the test diets varied from one exposure to several weeks. The percentage of responders is shown below. The degree of response varied from slight to dramatic. Some subjects (not shown) appeared to respond adversely more to the restricted diet than the diet containing provoking ingredients. See text and Appendix 2 for further information and citations.

Double-blind study	Number of Subjects	Percent of subjects improving on diet
Wilson and Scott (1989)	4	0%
Conners et al. (1980)	9	0%
David (1987)	24	0%
Conners (1980)	30	0%
Harley et al. (1978)	7	0%-11%
Goyette et al. (1978)	16	0% (parents), 19% (lab test)
Weiss et al. (1980)	22	9%
Williams et al. (1978)	26	13%-31%
Schmidt et al. (1997)	49	24%
Rowe (1988)	8	25%
Conners et al. (1976)	15	27%-33%
Goyette et al. (1978)	13	31%
Harley et al. (1978—school-age)	36	36% (mothers' ratings); 47% (fathers'); 17% (teachers'); 11% (both parents and teachers')
Kaplan et al. (1989)	24	42% (strong response); 58% (any response)
Egger et al. (1985)	28	54% to 71%
Rowe and Rowe (1994)	34	65%
Boris and Mandel (1994)	16	69%
Carter et al. (1993)	19	74%
Swanson and Kinsbourne (1980)	20	85%
Pollock and Warner (1990)	19	89%
Harley et al. (1978—pre-school)	10	100% (mothers' ratings); 57% (fathers')

children were on, potentially influencing their judgments. Future studies sought to overcome that problem by providing special foods that hid the ingredients being tested.

In several follow-up studies, Conners' research team put children on a "modified Feingold diet" from which dyes were excluded. In two studies, when the children were switched from their normal diet to a dye-free diet (not in a double-blind manner), the behavior of up to 88 percent of the children improved significantly.^{42,43} (That high percentage of responders is typical in the non-double-blind phases of studies when children switch from their conventional diet to one that lacks certain foods that might provoke

symptoms [see Table 2 on page 6]. Part of that apparent improvement is undoubtedly due to the Hawthorne effect [any change in the environment might affect behavior] and wishful thinking on the part of the parents or researchers.) When the children consumed cookies with the dyes, some children showed markedly worse behavior. In one double-blind study, performance of three out of 16 children worsened as judged by a lab test, but parents did not notice a difference. In the other study, parents of four of 13 children observed significantly worse behavior during periods their children were consuming dyes. (See below for negative studies by Conners' team.)

In the late 1970s another research group,

All ten mothers and four of seven fathers rated their children's behavior better on the reduced-additive diet.

this at the University of Wisconsin, compared the effect on ten hyperactive preschool boys of diets containing or lacking "ordinary" levels of dyes and salicylate-containing

foods.⁴⁴ Those researchers controlled the diets by replacing all foods at home (and at parties) with specially coded foods. All ten mothers and four of seven fathers rated their children's behavior as being better on the reduced-additive diet than on the ordinary diet.

Harley *et al.* also studied a group of 36 hyperactive school-age boys using the same kinds of diets.⁴⁵ The results were mixed. Laboratory tests and teacher ratings did not indicate improvements, but "improved behavior [was] found on the experimental diet" according to the fathers' and mothers' ratings. As in Conners *et al.*'s first study, an order effect was seen.

Much of the next wave of studies concentrated on possible effects of dyes, even though many more substances also might affect behavior. One such study was conducted by Weiss *et al.* and used an experimental design different from that of most other studies.⁴⁶ Instead of having children consume diets with and without certain foods for several weeks each, the children were kept on a diet free of artificial colors, flavors, and certain other additives and foods and then covertly challenged with dyes on certain days. (The 22 subjects, though not diagnosed as hyperactive, were suspected by their parents of having behavioral reactions to artificial colorings or flavorings and had been kept on some sort of restricted diet). For 77 consecutive days, each child drank a specially prepared beverage. On eight randomly selected days, the drink concealed a mixture of seven dyes (35.3 mg). Two subjects showed clear reactions according to their parents. A 34-month-old girl "reacted dramatically" on the days she received the dyes. A three-year-old boy displayed convincing evidence of

Table 2 Studies (not Double-blind) of Diet on Behavior

These studies (some of which were part of studies that also included double-blind phases) compared the behavior of subjects (who had ADHD or other behavioral problems) on a restricted diet to their behavior on an ordinary diet or to a test diet (when they ate provoking foods or additives.) The duration of the test diets varied from one exposure to several weeks. The percentage of responders is shown below, though some of the reported response likely was due to the Hawthorne effect. The behavior of some subjects (not shown) appeared to worsen on the restricted diet as compared to the diet containing provoking foods. See text and Appendix 2 for further information and citations.

Non-blind study (or phase)	Number of subjects	Percentage of subjects improving on restricted diet
Egger <i>et al.</i> (1992)	185	63%
Uhlig <i>et al.</i> (1997)	45	71%
Conners (1980)	30	73%
Carter <i>et al.</i> (1993)	78	73%
Rowe (1988)	55	73%
Boris and Mandel (1994)	26	73%
Rowe and Rowe (1994)	200	75%
Goyette <i>et al.</i> (1978)	13	77%
Breakey <i>et al.</i> (1991)	516	80%
Egger <i>et al.</i> (1985)	76	82%
Goyette <i>et al.</i> (1978)	16	88%

This experiment not only demonstrated unequivocal individual susceptibility, but also disclosed that even relatively normal children may be sensitive to the behavioral toxicity of food dyes.

Bernard Weiss

sensitivity to the color challenge for behaviors his mother considered typical of his outbursts: throwing things inappropriately, and biting, kicking, and hitting.

"These 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," the researchers stated.

One limitation of most of the studies using dyes is that they tested only 26 to 33 mg per day, a level of consumption considered average at the time, but much less than many children actually consumed. In a 1980 study, Swanson and Kinsbourne tested 100 mg and 150 mg doses of dyes.⁴⁷ They put 20 hyperactive children and 20 children who were probably not hyperactive on a Feingold diet for three days, then gave them dyes or a placebo for one day each and assessed their behavior. Compared to the placebo, the dyes decreased the attention span of the hyperactive children, but not the others. Seventeen of the 20 hyperactive subjects suffered impaired performance in a learning test. The authors suggested that negative results in some of the previous studies were due to the use of too low a dose of dyes.

Similarly, I. Pollock and J.O. Warner put 19 fidgety, inattentive children (two diagnosed with ADHD) on a diet that eliminated food additives and challenged them with 125 mg per day of four dyes or a placebo.⁴⁸ Seventeen of 19 sets of parents rated their children's behavior as worse—sometimes sharply worse—while their children were consuming the dyes.

Rowe and Rowe extended the research on dyes by testing six different doses—ranging from 1 mg to 50 mg—of tartrazine on children

who suffered from irritability, sleep disturbances, and restlessness (two out of 34 were diagnosed as having ADHD). The researchers found that the greater the dosage of dye, the greater the effect on behavior.

Beginning in 1985, researchers began to broaden their focus beyond dyes and conducted studies that tested the effects of other additives and ordinary foods. The underlying rationale was that children might have allergies or sensitivities to numerous substances.

Using a highly restricted diet, Egger *et al.* studied 76 children suffering from severe hyperactivity, often accompanied by neurological disorders, allergies, and other symptoms.⁴⁹ Thus, the children were not representative of all children with ADHD and other behavioral problems. They placed the children on a severely restricted "few food" ("oligoantigenic") diet that consisted of two meats, two carbohydrate sources (for example, potatoes and rice), two fruits (banana and apple), a variety of vegetables, and vitamin-and-mineral supplements. That diet excluded dyes, milk, chocolate, citrus fruit, and other foods suspected of affecting behavior. Sixty-two subjects (82 percent) responded favorably to dietary modification, though that phase was not double-blind.

Subsequent dietary challenges (also not double-blind) led the researchers to conclude that all of those 62 children were affected adversely by tartrazine, benzoic acid (a food preservative), milk, wheat, oranges, eggs, chocolate, or other ingredients, but because of the open testing protocol, those results are unreliable.

Next, 28 of the children who were considered to be diet-sensitive participated in a double-blind study. Depending on which researcher was doing the rating, 54 percent or 71 percent of the children behaved better on the restricted diet than they did during the one to two weeks they each were covertly fed one

"[A modified diet] did seem to make a remarkable difference to the lives of many of these families."

Joseph Egger et al.

food to which they were thought to be sensitive. Irritability and unreasonableness were more affected than hyperactivity and poor concentration. Eighteen percent of the children did worse on the restricted diet.

Carter *et al.*, who studied 78 children with ADHD, reported that 73 percent improved on a few-food (oligoantigenic) diet, though that phase of the study was not double-blind.⁵⁰ In a follow-up double-blind, placebo-controlled trial of 19 responders, ratings by parents of 14 children indicated that dyes, chocolate, milk, and other foods affected behavior.

Another study that used a highly restricted diet was conducted by Boris and Mandel on 26 children with ADHD, most of whom also suffered from asthma, eczema, or hives.⁵¹ In a non-blinded phase, 15 out of 17 children who had those allergies appeared to respond to that diet, compared to only five of nine children lacking those allergies. Then, in a placebo-controlled, double-blind phase, the researchers challenged 16 children with dyes (100 mg per day) or foods to which the children appeared to be sensitive. The behavior of 11 (69%) of the children deteriorated when they consumed the foods or dyes.

In a double-blind trial of a restricted diet, Kaplan *et al.* tested 24 preschool boys diagnosed with ADHD.⁵² During a seven-week period, each boy's family ate only the foods the researchers provided them. During four of those weeks, the meals were free of artificial colors, flavors, and other substances, such as chocolate, MSG, preservatives, and caffeine, that families thought might be affecting their children. During the other weeks, the foods included those substances. On the restricted diet, according to their parents, ten boys improved an average of 50 percent, while four more averaged a 12-percent improvement.

A study by Uhlig *et al.* went a step further than previous studies by using electroencephalograms (EEG) to monitor brain electrical activity when children with ADHD were eating a diet that did or did not include provoking foods.⁵³ In a first phase that was not double-blind, the behavior of 71 percent of 45 children appeared to improve on an oligoantigenic diet. The children were then

challenged (again, not in a double-blind protocol) with various foods, and some appeared to be sensitive to beet sugar, artificial colorings, wheat, milk, and other foods. In a third phase, the researchers used EEG and found a significant increase in beta-1 activity in certain areas of the brain after the children ate provoking foods but not other foods. One of the researchers examining the EEGs did not know which diet the children were on. The import of that finding needs to be further

investigated. (Another study using EEG and other methods found that when food-sensitive hyperactive children avoided provoking foods they experienced increased beneficial REM sleep and decreases in the number of arousals when sleeping.⁵⁴)

"These data support the hypothesis that in a subgroup of children with attention deficit hyperactivity disorder certain foods may not only influence clinical symptoms but may also alter brain electrical activity."

T. Uhlig *et al.*

Studies that found little or no effect of diet on behavior

Several studies found little or no effect of food ingredients on children's behavior.

Conners and his colleagues put 30 children, 22 of whom were diagnosed as hyperkinetic, on an elimination diet.⁵⁵ In that non-blind phase, the behavior of 73 percent of the children improved. However, in the more important double-blind phase, the researchers found "no effect whatsoever" when the children ate cookies containing dyes or placebo cookies alternately for four one-week periods.

In a small study, Conners *et al.* tested nine hyperactive schoolchildren who had previously appeared to improve on the Feingold diet.⁵⁶ While on that diet, the children were challenged, double-blind, on just one day each with cookies containing 0 or 26 mg of artificial colors. Consumption of the dyes was not associated with significantly more errors

"[W]e must surely conclude that the artificial color hypothesis of hyperactive behavior is unproven."

C. Keith Conners

hyperactive behavior is unproven." (Of course, Feingold had not proposed an "artificial color hypothesis," but claimed that many different additives and foods cause symptoms of hyperactivity.)

A study by T. J. David, of the University of Manchester in the United Kingdom, tested 24 children (six with ADHD), all of whom were on restricted diets because their parents said they

on a learning task, and no differences were seen with regard to physical activity. Though he later concluded that diet can affect behavior, on the basis of this study Conners stated that the "artificial color hypothesis of

suffered behavioral reactions after consuming tartrazine and sometimes benzoic acid and other additives. In a double-blind, placebo-controlled study, the children consumed tartrazine or benzoic acid for just one day each.⁵⁷ None of the children reacted after consuming a huge amount (300 mg) of the dye or benzoic acid.

Mattes and Gittelman tested 11 children, most of whom were thought to have ADHD.⁵⁸ Parents claimed that each child was sensitive to additives and was on the Feingold diet. With the children remaining on the Feingold diet, their behavior did not appear to be affected in a placebo-controlled, double-blind study by consuming up to 78 mg of dyes. Whether the children might have reacted to substances excluded from their diets other than dyes was not tested.

Discussion

The possibility that food additives and natural food constituents could affect children's behavior, particularly those with ADHD, was first raised by Feingold in the mid-1970s. In 1982, an NIH consensus conference reviewed the early research and concluded that dyes and other dietary components do, indeed, contribute to ADHD in a small fraction of children. However, the panel did not agree with Feingold's claim that diet is responsible for as many as half of all cases of hyperactivity.

Subsequent to the NIH conference, additional studies found that synthetic dyes and certain foods affect the behavior of some children. In all, 17 of 23 double-blind studies found that the behavior of some children significantly worsened after they consumed dyes and certain foods. Six studies did not find an effect. Diet, with dyes being the component most frequently studied, appears to affect some children dramatically, others slightly, and many others not at all. In uncontrolled portions of eleven studies, the behavior of about three-fourths of the children appeared to improve when they switched from their conventional diet to a diet restricted in

numerous foods and additives. Those observations need to be investigated further.

Conners, who conducted several of the early studies and was skeptical that diet affected behavior, in 1990 reviewed the research on diet and behavior and concluded:

I have to admit that I have changed my mind about the Feingold idea since the 1970s.... my judgment is that the evidence is strong enough, at least for preschoolers, and especially those with confirmed allergic symptoms, that one should eliminate a broad range of unnecessary and possibly harmful ingredients from these children's diets.... Taken with the caveat that diets do not cure, there seems good reason to try them as part of a total therapeutic effort including medical, educational, and behavioral treatments.⁵⁹

Boris and Mandel found that children with behavioral problems who also suffered from asthma, eczema, or hives might be particularly helped by dietary changes. That suggests that children with those symptoms are good candidates for dietary therapy. Other studies (Weiss, *et al.* (1980), Harley, Ray, Tomasi, *et al.*) indicated that younger children

might be likelier to respond to dietary restrictions than older children, though that

"Through a simple elimination diet symptoms can be controlled.... Elimination of the causes of ADHD is preferable to the pharmacologic therapy of this condition."

Marvin Boris and Francine S. Mandel

was not always the case (Carter *et al.*). It was the two youngest children in the Weiss *et al.* study who reacted, and Harley, Ray, Tomasi, *et al.* found a greater effect in preschool than in school-age children. However, the greater apparent sensitivity of younger children might be due to the fact that in studies

that tested sensitivity to dyes all subjects consumed a fixed amount of dye regardless of their weight. Thus, lighter children were exposed to a significantly higher dosage per kilogram of body weight.

Weiss *et al.*'s 1980 study offers several important lessons concerning the conduct and interpretation of studies. First, if the two children who reacted to dyes had not been included among the 22 subjects, the study would have been interpreted as "proving" that dyes do not affect behavior. Negative results from studies involving small numbers of subjects might, simply by chance, not include any of a sensitive subgroup. Second, the study demonstrates the importance of examining each subject's behavior individually, rather than averaging together the effects on all the children. Had Weiss and his colleagues done that averaging, they would not have observed any effect. Finally, the researchers individualized their questionnaires so that the parents' ratings were based on the problems their children usually experienced. In contrast, most other studies used a standardized questionnaire, even if it did not include the behaviors that the children actually had problems with. For instance, the Conners' questionnaire "places little emphasis on irritability and contains no measure of sleep disturbance," which behaviors are not part of ADHD but appear to be caused by dyes in some research.⁶⁰

How many children with ADHD are affected by diet?

The exact percentage of children with behavioral problems who are sensitive to food ingredients is not known, because most of the studies tested children who were suspected by their parents of being sensitive to certain foods. NIMH estimates that "5 percent of children with ADHD, mostly either young children or children with food allergies" are food-sensitive, but does not provide a basis for that estimate. That figure is consistent with several of the studies (such as Weiss *et al.*'s [9 percent]) using food dyes. Greater percentages of children responded in double-blind studies when they were challenged not just with dyes but also with foods to which they were suspected of being sensitive. Thus, in several studies that eliminated a wide variety of foods and then added one or more of them back, half or more of the subjects appeared to be affected by foods or dyes: Kaplan *et al.* (42 percent-58 percent), Carter *et al.* (74 percent), and Boris and Mandel (69 percent); (see Table 1).

One of the few studies that did not test subjects preselected for food sensitivities was Schmidt *et al.*'s. That study found that 24 percent of the children studied improved on a diet that eliminated tartrazine, cereal proteins, and citrus fruit. However, those children were severely hyperactive and disruptive inpatients and not representative of the average child with behavioral problems. (Only 44 percent of the subjects improved when given methylphenidate, suggesting that many had problems other than ADHD.) Similarly, Carter *et al.* found that the behavior of 14 out of 19 children (74 percent), who had not been selected for being sensitive to foods, reacted to dyes or foods.

Of course, the overall percentage of children affected by foods does not matter when it comes down to *your* child.

"This trial indicates that diet can contribute to behaviour disorders in children."

Christine Carter et al.

Commenting on the inconsistencies of studies and the fact that some children respond to the Feingold diet, Conners observed, "If there are any children whose behavior is reliably worsened by food additives, then the problem is significant."⁶¹ The obvious public-health response would be to remove the irritants, if possible, from the foods that children eat.

How much dye do children consume?

The interpretation of studies in which children were challenged with dyes is clouded by the lack of information on how much dye children actually consume in their everyday lives.⁶² Several of the studies used a dose of 26 mg per day, the presumed average daily consumption of six to nine dyes. However, children may well consume more dye than adults, because so many child-oriented candies, beverages, cakes, frozen desserts, breakfast cereals, and other foods are artificially colored (and also contain a multitude of preservatives, artificial flavorings, artificial sweeteners, and other additives).

In 1976 an FDA scientist estimated that 10 percent of children between one and five years old consume more than 121 mg of dyes per day and 10 percent of children between six and 11 consume 146 mg or more.⁶³ The average level might have been as high as 76 mg—not 26 mg—and the maximum as high as 315 mg per day. Those figures suggest that many studies used dosages of dyes inadequate to elicit the behavioral reactions that some children's ordinary diets may produce. Indeed, Conners, who used a challenge dose of 26 mg in one study, later regretted using so little.⁶⁴ In contrast, two of the studies (Pollock and Warner; Swanson and Kinsbourne) that challenged children with 100 mg or more of dye per day found effects in comparatively large percentages of children.

It is noteworthy that, according to FDA data, dye production has been increasing steadily. Production per capita amounted to 12 mg in 1955, 32 mg in 1975, and 47 mg in 1998, a fourfold increase over four decades.⁶⁵ While true consumption figures are not known, current production levels are greater than the

amounts used in most studies. The increased exposure to dyes may be causing higher rates of behavioral disturbances.

Limitations in study designs

The designs of many of the studies might have limited their power to detect effects of diet.⁶⁶ One limitation is that most double-blind studies tested only the effects of food dyes, and not anything else in the diet. If children are sensitive to several foods or additives, their behavior might not change much if they avoid just dyes. As the old saying goes, if a child is limping because he has five nails in his shoe, removing one nail won't help him much.⁶⁷ Studies might have yielded more dramatic effects if additives in addition to dyes, as well as potentially reactive foods, had been eliminated from the diets and then added back as challenges.

Some researchers used chocolate cookies as the vehicle for administering dyes and placebo. Some children might have reacted to the chocolate, thereby making it more difficult to detect effects of the dyes. Egger *et al.* (1985) concluded that chocolate caused symptoms in 59 percent of the subjects tested, though that observation was not based on a controlled study. Breakey *et al.*, whose uncontrolled study found that 31 percent of 516 children were sensitive to chocolate, commented: "With hindsight, it is probable that the results of early research were confounded by the usage of chocolate bars and cookies as the vehicle for test doses of colours..."⁶⁸

Another limitation concerns the assessment tools. The laboratory tests or Conners' scale used in many studies did not assess certain behaviors, such as irritability or sleep disturbances, that might be caused by foods or additives. To overcome that problem, Rowe and Rowe developed a 30-item checklist based on children's past behavior. Similarly, Weiss *et al.* (1980) worked with parents to identify ten problem behaviors specific to each child and then to rate their children on those behaviors.

Also, some studies might underestimate the effect of diet if sensitive children selectively

refused to participate or dropped out. Conners acknowledged that problem in his own research, observing, "If these children dropped out because they experienced severe reactions to the artificial colors, then we would have inadvertently screened out some of our most promising subjects."⁶⁹

On the other hand, some of the research might imply that the effect of diet is greater than it really is. For instance, some of the effects seen in laboratory tests might not be meaningful in the child's real world.

Experts' denials of effects of diet

In spite of the substantial evidence to the contrary, several prominent public and private health organizations—and researchers themselves—have ignored, downplayed, or dismissed any relationship between diet and children's behavior (see Appendix 3 for a more detailed discussion). It is not surprising that organizations funded by the food industry, such as the International Food Information Council (IFIC) and the American Council on Science and Health (ACSH), would dismiss the evidence for such a relationship. It is surprising that some of those who conducted studies finding an effect would seek to dismiss their own findings. For instance, Harley *et al.* concluded that "the overall results [of the study on preschool children] do not provide convincing support for the efficacy of the experimental (Feingold) diet" because the teachers' evaluations and the laboratory tests did not corroborate the parents' reports.⁷⁰ Noting that all ten mothers rated their child's behavior as improved, neurotoxicologist Weiss subsequently observed: "[Harley *et al.*'s] astonishing claim, offered after results embarrassing to the sponsors of the study, is a salient example of the extra-scientific barriers posed to the Feingold hypothesis."⁷¹ (The sponsors Weiss alluded to were the Nutrition Foundation and Wisconsin Food Research Institute, both funded by industry.)

Even a 1998 NIH Consensus Panel on the treatment of ADHD virtually ignored the studies on diet—despite the fact that the

expert invited to describe non-drug treatments summarized the research showing that dietary treatment is beneficial to some children.⁷²

L. Eugene Arnold, a psychiatrist at the Ohio State University College of Medicine, wrote in his published review, "The oligoantigenic or few-foods diet has convincing double-blind evidence of efficacy in multiple trials for a properly selected subgroup [of patients]."⁷³ The NIH conference report noted only in passing, "Some of the dietary elimination strategies showed intriguing results suggesting future research." The committee then failed to include dietary research in its recommendations for future research.

Likewise, the FDA, which funded an important study (Weiss, Williams, Margen, *et al.*) demonstrating that food dyes can trigger adverse behavior, nevertheless endorsed a pamphlet published by IFIC, an industry group, stating that studies have produced no evidence that food additives cause hyperactivity.

Some of the leading authorities on ADHD appear to be unaware of, or dismiss, the research showing that foods can affect behavior. Russell A. Barkley, a professor at the University of Massachusetts Medical Center and a widely respected expert on hyperactivity, wrote: "many studies have discredited the [diet-behavior] hypothesis."⁷⁴ While they may believe, correctly, that drugs offer much more reliable relief, researchers should recognize that diet contributes to some children's behavioral problems and dietary changes might provide partial or sufficient relief.

Denying that food ingredients can exacerbate ADHD or other behavioral effects reflects ignorance of the scientific research, and ignoring that research jeopardizes children's well-being. Millions of young children have been prescribed stimulant drugs that may have unpleasant or serious side effects, as discussed below. Parents, physicians, teachers, and school officials need to know that some children benefit from avoiding certain additives and foods, and it makes sense to remove from children's diets unnecessary contributors to behavioral problems.

Choosing a treatment: medication or diet?

In contrast to the ease of use of stimulant drugs, controlling the diets of children is difficult, particularly once the children go to school. Problem foods are advertised aggressively and are available everywhere, and children who do not eat whatever their friends are eating may feel left out or stigmatized. However, some of the dietary changes involved in the Feingold diet, or simply avoiding dyes, may be manageable in many families. (Adhering to the highly restricted oligoantigenic diet is complicated and might best be reserved for severely affected children and institutionalized or hospitalized patients.) Breakey, an Australian dietitian, observed: "Compliance was surprisingly high considering the effort involved in monitoring all meals, including food eaten at school and socially."⁷⁵ Some parents consider the Feingold diet to be no more troublesome than a kosher or vegetarian diet: perhaps difficult at the beginning or a nuisance at times, but relatively easy once one becomes accustomed to it.

Each family will need to consider for itself whether even a several-week test of a restricted diet is feasible. To facilitate the dietary changes that may benefit children suffering from ADHD or other behavioral disturbances, the entire family should seek to modify its diet. Change may be easier in certain situations. For instance, hospitals and psychiatric facilities, as well as overnight camps and boarding schools, should be able to exercise substantial control over children's diets.

Parents need to recognize that most children will not respond strongly or at all to dietary changes.

Pediatricians and other practitioners might consider dietary modifications worth trying, particularly in younger children."

Bonnie Kaplan et al.

In contrast, 70 percent to 90 percent of children respond to stimulant drugs. The most effective option might be to use a restricted diet and a stimulant drug in

combination (and might allow a reduced dosage of the drug).⁷⁶

Ideally, considering the difficulty of avoiding provocative foods and the adverse side effects of drugs, ways would be developed to reduce or neutralize an individual's sensitivities. Much more research needs to be conducted, possibly along the lines of a desensitization technique tested by Egger *et al.* (1992).⁷⁷

Until some preventive method or cure is developed, parents of a child with ADHD need to determine, based on their own personal considerations and in consultation with open-minded professionals, whether to attempt to keep their child on a restricted diet or to use stimulant-drug therapy. In either case, experts routinely recommend that parents should use behavior-modification techniques to supplement the drug or diet in improving behavior.

Concerns about stimulant drugs

Parents need to consider the potential adverse effects and cost (several dollars a day) of drugs used to control attention and hyperactivity disorders. Methylphenidate (Ritalin) and other drugs, such as amphetamines (Adderall is a popular brand), provide relief to many children (and their parents, teachers, and classmates), but may cause reduced appetite and weight loss, stomachaches, and insomnia. And, rarely, methylphenidate has been reported to cause tics or Tourette's syndrome. Pemoline (Cylert) has been associated with fatal liver failure and is strongly discouraged as a treatment for ADHD.⁷⁸ Furthermore, long-term studies have not been done to determine whether treatment in childhood (or adulthood) with stimulant drugs has adverse effects on the nervous system (or on reproduction, aging, etc.) later in life.⁷⁹ As Richard Bromfield, a psychologist at Harvard Medical School, noted in an article about the overprescription of Ritalin, "But the brain, the neurological seat of the soul and the self, must be treated with the utmost respect."⁸⁰

One cause for concern is that in 1995 the federal government's National Toxicology Program (NTP) found that methylphenidate

caused liver tumors in mice (but not rats).⁸¹ Females developed benign liver tumors (hepatocellular adenomas), while males developed both benign and malignant (hepatoblastomas) liver tumors. Unlike many animal studies that have been criticized because of the extraordinarily high dosages that were used, the dosage of methylphenidate that caused cancer in the NTP study was as little as 2.5 times higher than the maximum recommended dose in humans.⁸² In another NTP study, amphetamine did not cause tumors in animals.⁸³

Samuel Epstein, professor of occupational and environmental health at the School of Public Health at the University of Illinois, is particularly concerned about the

"The NTP study sends a powerful warning that Ritalin may cause cancer ... in humans."

Samuel Epstein

hepatoblastomas, which are normally extremely rare. Epstein says, "The NTP study sends a strong warning that Ritalin may cause cancer—in the liver or other organs—in humans. Millions of young

children take Ritalin for years on end, and children may be especially vulnerable. It would be prudent for the FDA to discourage doctors from prescribing Ritalin as the first choice of treatment for ADHD."⁸⁴

The FDA acknowledges that the NTP findings constitute "a weak signal of carcinogenic potential," but still considers methylphenidate to be safe.⁸⁵ The FDA notes that the drug did not cause cancer in rats and questioned whether the mice used in the study were good predictors of human risk.⁸⁶

There is no evidence that methylphenidate has caused cancer in humans, but that simply may be because no good studies have been conducted.⁸⁷ Studies are expensive and difficult to conduct, because if the drug does cause cancer those tumors might not occur for several decades. What is needed, in addition to more animal studies, is studies that follow for as many as 50 years thousands of children who took methylphenidate for long periods of time.

Clearly, parents face troubling choices. First, should they consent to treating their child with a drug to make him or her behave more appropriately at home and in school? And if they decide to go the drug route, should they use the most popular drug, methylphenidate, which is simple to use and often effective, but may have side effects, possibly including a slightly increased risk of cancer? It would be a tragedy if a small percentage of children developed cancer later in life because of a drug they took in childhood. One escape from that dilemma is to try, as a first course of treatment, changing the child's diet for several weeks to see if his or her behavior improves significantly. (See Appendix 4.) In some cases, diet may help enough to eliminate the need for medication; in other cases, diet may make it possible to reduce the dosage. If the dietary approach proves inadequate or is considered inappropriate for a particular child, amphetamines (or other drug) could be tried. In any case, parents who want to try helping their child by modifying his or her diet deserve sympathetic and knowledgeable assistance from physicians and dietitians, as well as by government agencies and health organizations concerned with children's welfare. Parents may obtain information and assistance (and perhaps the names of local health professionals) from the Feingold Association of the United States (Box 6550; Alexandria, VA 22306; 703-768-3287 or 800-321-3287; www.feingold.org).

The need for research

Numerous studies of varying quality have shown that dietary constituents affect some children's behavior, but many of the studies involved just a handful of children, involved children who were not representative of most children with ADHD, or tested inadequate dietary changes.

Despite the 1982 NIH consensus conference's call for more research on diet and ADHD, the

High-quality research is critically needed to determine how best dietary changes and supplements could be used to treat ADHD.

government has sponsored precious few studies. High-quality research is critically needed to determine how best dietary changes could be used to treat ADHD in childhood and beyond. NIH should fund research to:

- study large numbers of randomly chosen children with ADHD and other behavioral problems to determine how many are affected by various dietary constituents (food dyes; benzoate; conventional foods such as wheat, egg, milk, soy, chocolate; salicylates; etc.);
- identify subgroups of children (type of behavioral problem, age, gender, race/ethnicity, types of allergies or other health problems, *in utero* exposure to nicotine or alcohol, etc.) who are most responsive to dietary changes;
- develop ways to promote adherence to modified diets;
- compare long-term efficacy and effects of diet and drug therapies;
- develop means of minimizing children's reactions to foods, such as through desensitization techniques.
- study the efficacy of nutritional supplements (including fatty acids, minerals, and vitamins) in treating behavioral problems.

In addition, because large numbers of children are taking stimulant drugs for increasing periods of time, more animal and human research, conducted by the government or drug manufacturers, is needed on the long-term effects of those drugs.

- The NTP's studies need to be extended by testing methylphenidate and other drugs on other strains of rodents over their lifetime (beginning *in utero*) for carcinogenicity and effects on reproduction and behavior.
- A large cohort of children who take stimulants (and a matched control group) should be followed over their lifetimes to investigate the drugs' long-

term effects on behavior, academic performance, and physical health (including allergies, resistance to disease, cancer, reproduction, etc.).

The role of regulation

As long ago as 1977, an FDA-sponsored committee of toxicologists indicated the need to test additives for "psychotoxicology."⁸⁸ In 1993, the FDA itself, in a draft protocol for the testing of food additives, recognized the importance of behavioral measures:

Because of the impact that nervous system toxicity can have on human health, assessing the neurotoxic potential of a chemical proposed for use as a food or color additive should be an essential element in that chemical's toxicological profile.⁸⁹

However, currently the FDA only requires neurotoxicity testing if a chemical is closely related to known toxins or if other toxicological tests or medical reports suggest a problem. Despite the evidence that food colorings can affect children's behavior, the FDA has not proposed any limitations on their use.

To better protect the public's health, greater regulatory activity is needed. The FDA should require that all proposed new additives be tested for behavioral effects, unless there was good reason not to. Following approval, that agency should require further research if consumers or physicians identify possible problems.

Furthermore, the FDA should consider banning the use of synthetic dyes in foods (for example, cupcakes, candies, sugary breakfast cereals, and children's vitamin pills, drugs, and toothpaste) widely consumed by children, because dyes adversely affect some children and do not offer any essential benefits. Safe naturally occurring colorants (such as beet juice or beta-carotene) or real food (orange juice could provide the color and flavor in orange drinks) could be used instead. The FDA also could encourage parents who believe their children are adversely affected by certain additives to avoid buying foods that contain those additives.

Recommendations

1. NIH should sponsor research to:

- (a) determine which foods and food additives provoke behavioral problems and what fraction of children are susceptible;
- (b) develop methods for identifying children who are sensitive to foods and additives;
- (c) investigate the underlying biological mechanisms for how food affects behavior;
- (d) develop techniques (such as desensitization) to reduce adverse effects of dietary constituents on children's behavior;
- (e) develop means of increasing the ease and effectiveness of dietary treatment;
- (f) conduct animal studies to investigate the possible carcinogenic, behavioral, reproductive, teratogenic and other effects of stimulant drugs;
- (g) conduct long-term studies on large numbers of users of stimulant drugs to identify any adverse effects, such as behavioral disorders, social problems, cancer, reproductive problems, or other health problem;
- (h) investigate the potential efficacy of nutritional supplements (including fatty acids, minerals, and vitamins) in treating ADHD.

2. NIH should sponsor a new consensus conference of experts on diet and behavior to provide a full and fair review of studies on diet and ADHD.

3. Public and private health organizations, such as NIMH, the FDA, American Academy of Pediatrics, American Academy of Family Physicians, and Children and Adults with Attention Deficit/Hyperactivity Disorder (CHADD) should inform parents, school

officials, and health-care providers that studies show that certain foods and additives provoke symptoms of ADHD or other behavioral problems in some children. They should suggest that dietary therapy, which is benign and inexpensive, be considered as the first course of treatment (along with psychological counseling, skills training for parents, and other behavioral strategies). Young children and children who have asthma, hives, and other allergies may be the most helped by dietary changes. They should revise and reissue publications that dismiss diet as a contributor to ADHD. They also should emphasize that stimulant drugs may have side effects, including possibly cancer in the case of methylphenidate.

4. The FDA should:

- (a) require new, as well as certain existing, food additives to be tested for behavioral effects;
- (b) consider banning the use of synthetic dyes in foods and other products (such as cupcakes, candies, sugary breakfast cereals, and children's vitamin pills, drugs, and toothpaste) widely consumed by children;
- (c) cease sponsorship of any literature that denies that food additives contribute to ADHD/hyperactivity;
- (d) advise the public that methylphenidate caused cancer in animals and is a poor first choice for treating ADHD.

5. Fast-food chains and manufacturers of foods, drugs, and vitamin supplements popular with children should minimize the use of dyes and other unnecessary additives.

6. Pediatric hospitals and psychiatric clinics, summer camps, and schools should make their standard meals and snacks as free as possible from dyes and other additives that may contribute to behavioral disorders.

Appendix I: Sugar and ADHD

Some parents and health professionals have believed firmly that refined sugars trigger hyperactivity. Assessing the effect of “sugars” on behavior is complicated by the fact that several different types of sugar are added to foods: sucrose obtained from sugar cane and sugar beets, and the corn-derived glucose (corn sugar), corn syrup, and high-fructose corn syrup (HFCS). Currently, about half of the refined sugars Americans consume comes from sugar cane and sugar beets, the other half from corn. Of course, sugars are natural constituents of fruits and vegetables, and so, intuitively, it seems unlikely that they would cause problems. However, children typically consume huge quantities of refined sugars at a time, and those sugars might contain contaminants from corn, beets, and cane. Also, dyes, caffeine, and artificial flavors are often present in sugary foods, so even if a soft drink or high-sugar breakfast cereal appeared to affect behavior, identifying the actual culprit would not be easy.

In the best study, 23 supposedly sugar-sensitive children (five with ADHD) and their families were provided with foods for nine weeks, with artificial colors, flavors, preservatives, and other ingredients suspected of affecting behavior being kept to a minimum.⁹⁰ The foods were sweetened for three weeks each by sucrose, aspartame, or saccharin. None of the children reacted to sucrose. (The authors note in passing that “behavior ratings and test scores generally improved during the dietary periods, as compared with the base-line values,” suggesting that the restricted diet benefited numerous children.)

Three smaller and briefer studies involving a total of 35 “sugar-sensitive” children, including some with ADHD, also found no effect.^{91,92,93}

Several other studies attributed some

changes in motor activity and attentiveness to consumption of sugars. In a study of 12 psychiatric inpatients with a variety of disorders, Conners and his colleagues found that sucrose or fructose caused a significant increase in total motor activity.⁹⁴ Wender and Salient found that sucrose reduced attention to tasks in children with ADHD, but not in other children.⁹⁵ Both of those studies were funded by the sugar industry.

In four other studies, a total of 93 children who had ADHD or a supposed “sugar sensitivity” was challenged up to three times with sucrose, glucose, or a placebo.^{96,97,98,99} The behavior of one child in each of those studies appeared to be affected repeatedly by sucrose or glucose as compared to the placebo. Those responses might have been due to chance or could have reflected a true sensitivity to sugars.

The bottom line on sugars is that few good studies—of sufficient duration, with sizable numbers of subjects, and employing child-by-child analyses—have been conducted.¹⁰⁰ The studies that have been done indicate that sugars may affect a small number of children, but not nearly as many or as dramatically as some people believe.

Parents could test their child by putting him or her on a low-sugar (and low-additive) diet for two weeks. They could then “challenge” their child on several different days with a sugar-sweetened (usually corn sugar) beverage or table sugar and on other days with an artificially sweetened drink and carefully monitor his or her behavior.

Of course, whether or not refined sugars affect behavior, most children should, on purely nutritional grounds, eat fewer sugary foods. Children (and many adults) are consuming an average of twice as much sugar as the U.S. Department of Agriculture recommends.¹⁰¹

Appendix 2: Studies of Diet and Behavior

Studies showing some effect of diet on behavior

◆ In the first controlled study (1976), C. Keith Conners and his colleagues at the University of Pittsburgh tested the Feingold diet (free of artificial colors, flavors, and certain foods) on 15 children (average age was eight years) diagnosed with hyperkinesis (the earlier term for ADHD).¹⁰² The response over four weeks to that diet was compared to the children's response over an additional four weeks to a diet that was presented to them as another experimental diet, but that allowed foods with artificial colors and flavors. The average improvement on the special diet was about 15 percent. According to parents and teachers, four or five (27 to 33 percent) children improved on the diet. Two showed "dramatic results."

The study was criticized because the restricted diet appeared to have a greater effect in children who consumed it after, as compared to before, the unrestricted diet, though that difference, called an "order effect," was not statistically significant. The authors suggested that the placebo-first group, by chance, might have had more diet-responsive children.

◆ Conners and his colleagues subsequently conducted several studies in which children were challenged with food dyes only. One study started with placing 16 children between four and 11 years old and diagnosed with hyperactivity on a "modified Feingold diet" from which only dyes were eliminated."¹⁰³ That diet, introduced openly rather than in a double-blind fashion, appeared to reduce behavior problems by 34 percent (as rated by teachers) or 57 percent (as rated by parents). The researchers then challenged the children with chocolate cookies that contained (or lacked) a mixture of food dyes (26 mg per day). Parents and teachers did not identify any effect, but three of the children (six and seven years old) showed "a marked deterioration of performance" in an objective

visual-motor attention task. The three children were affected only at about one hour after eating one cookie. The parents and teachers' failure to discern when children were consuming the dye, the authors conjectured, might have been because they rated the children not at the one-hour point, but only at the end of the day. Also, Conners has raised the possibility that several subjects dropped out of the study because of severe reactions to the dyes.

◆ In another study, Conners' team tested 13 children between the ages of three and nine.¹⁰⁴ Eight of the children were diagnosed as hyperactive, and five were considered borderline hyperactive. When put on a dye-free diet (not double-blind) for several weeks, the subjects demonstrated a 45-percent reduction in behavior problems, with 77 percent of the children appearing to respond. The children then ate two cookies made with or without dyes (13 mg each, one after breakfast, the other after dinner) for one week each. Parents rated their children's behavior for a three-hour period after dinner. For the group as a whole, children exhibited significantly more behavioral problems after they ate the dye-containing cookies. Four children (31 percent) displayed marked reactions. One girl was retested twice and showed repeated reactions to colors.

The authors conclude, "these data firmly establish that artificial colors may be particularly disruptive to younger children and that it will be important to ... examine the possible mechanisms whereby these chemicals act on the CNS [central nervous system]."

◆ Several studies were conducted at the University of Wisconsin and published in 1978. In one study, J. Preston Harley and his colleagues tested a diet free of artificial colors, flavors, and foods containing salicylates on ten hyperactive preschool boys.¹⁰⁵ Those researchers controlled the children's diets by replacing all foods at home (and at parties and special family get-togethers) with specially coded foods. For several weeks, those diets

either contained or lacked "ordinary" levels of dyes, flavorings, and salicylates. The families did not know when they were getting which diet. All ten mothers and four of seven fathers rated their children's behavior as improved when they were eating the additive-free diet.

◆ Harley's group also tested 36 school-age boys with the same kinds of diets as were provided to participants in their study on preschoolers.¹⁰⁶ The results were mixed: Laboratory tests and teachers' ratings did not find improvements when the children were on the Feingold diet, but "improved behavior [was] found on the experimental diet for the father [47 percent] and mother [36 percent] ratings ..." The parents especially noted improvement in the children who consumed the placebo diet before the Feingold diet. The same "order effect" seen in Conners *et al.*'s first study was also seen in this study. Regarding the order effect, Swanson speculated, "The fact that behavior remained improved when children were switched from the additive-free to the placebo phase of the experiment may simply reflect a carryover effect of the 4 weeks on the Feingold diet."¹⁰⁷

◆ In a 1978 study, Jeffrey Mattes of the Long Island Jewish-Hillside Medical Center in Glen Oaks, New York, and Rachel Gittelman-Klein of the New York State Psychiatric Institute in New York City conducted a double-blind trial on a 10-year-old boy who had been diagnosed with hyperactivity.¹⁰⁸ His parents said that he responded well to a Feingold diet. In an 11-week study, the boy was given cookies with or without a mixture of food dyes (a baseline test used 5 mg or 10 mg daily for three days; the study phase used 10 mg on two days per week).¹⁰⁹ His overall diet was not described. In nine of the 11 weeks, the boy's mother correctly guessed whether or not he was eating the cookies with dye. That was statistically significant. However, the researchers concluded that their findings did not support the Feingold hypothesis because, while the dyes made the boy irritable and fidgety, the boy never exhibited true hyperactivity as judged by the Conners' scale. A larger, but negative, study by the same authors is discussed below.

◆ J. Ivan Williams and his colleagues at the University of Toronto tested 26 schoolchildren who had been diagnosed with ADHD and had been taking stimulant drugs.¹¹⁰ In this 1978 study, the children were kept on a diet free of artificial colors and flavors, though at least seven of the children "cheated." The children were challenged with chocolate cookies containing or lacking a mixture of food dyes (26 mg per day) in the presence or absence of their medications. The children's teachers observed "clearly significant reductions [in hyperactive behavior] related to diet for approximately one-fourth [3 to 8] of the children." A detailed reanalysis by Weiss found that one child responded "sharply and consistently."¹¹¹ The authors concluded that while diet was sometimes effective, the stimulant drug was more effective, but that "drugs and diet provide the best treatment effect."

◆ In a 1980 study funded by the FDA and other agencies, Bernard Weiss of the University of Rochester School of Medicine and Dentistry and his colleagues tested 22 children between the ages of two and seven.¹¹² None of the subjects had been diagnosed as hyperkinetic, but their parents complained of their short attention span, habit of throwing and breaking things, whining, and acting as if driven by a motor. The parents believed that those problems were relieved when artificial colors and flavors were excluded from their children's diets.

The children were put on a diet free of artificial colors, flavors, and certain other additives and foods. For 77 consecutive days, each child drank a specially prepared beverage at a specified time. On eight randomly selected days, the drink concealed a mixture of seven dyes (35.3 mg). That amount represented the average consumption by children, as judged by dietary histories of 80 children who resembled the study population. One child, a 34-month-old girl, reacted "dramatically" on the days she received the colors. A three-year-old boy also displayed convincing evidence of sensitivity to the color challenge for two behaviors his mother considered typical of his outbursts: throwing things inappropriately, and biting, kicking, and hitting.

◆ In 1980, James Swanson of the Hospital for Sick Children in Toronto and Marcel Kinsbourne of the University of Toronto conducted a study using larger amounts of dyes.¹³ They challenged 40 children, half of whom were considered hyperactive based on their responsiveness to stimulant medications. The other half responded adversely to those drugs and were presumed not to be hyperactive. After being put on a diet free of dyes, artificial flavors, BHT, BHA, and natural sources of salicylates (such as apples and tomatoes) for three days, the children were challenged on one day each with a mixture of dyes or a placebo. The researchers tested larger doses of dyes, 100 mg and 150 mg (the latter estimated by the FDA to be the 90th-percentile intake) than had been used in previous studies. Compared to the placebo, the dyes decreased the attention span of the hyperactive children but not the other children. Seventeen of the 20 hyperactive subjects suffered impaired performance in a learning test.

◆ In 1985, Joseph Egger and his colleagues at the Institute of Child Health and the Hospital for Sick Children in London, England, studied 76 children (two to 15 years old) suffering from severe hyperactivity, neurological disorders, allergies, and other problems (those children were not typical of children with ADHD).¹⁴ The researchers placed the children on a severely restricted "few food" ("oligoantigenic") diet that consisted of two meats, two carbohydrate sources (for example, potatoes and rice), two fruits (banana and apple), and variety of vegetables, as well as vitamins and minerals. That diet excluded dyes, milk, chocolate, citrus fruit, and other foods suspected of affecting behavior. Sixty-two of the subjects (82 percent) appeared to behave better on the modified diet, though because that part of the study was not double-blind some of that improvement may not have been due to diet. The researchers then challenged, not in a double-blind manner, those 62 children with various foods or additives and associated adverse reactions in every child with at least one, and usually to more than one, substance. The most common reactions were attributed to tartrazine, benzoic acid (a food preservative), milk, wheat,

oranges, eggs, and chocolate. However, because of the non-blinded testing protocol, those observations are not reliable. Contrary to Feingold's hypothesis, few subjects appeared to react to cucumbers, peaches, and other salicylate-containing foods.

The next step was a double-blind trial of 28 of the children presumed to be diet-sensitive. Parents, a psychologist, and a neurologist all rated the children, as a group, as better behaved while eating the limited diet than when, for one to two weeks, each subject was covertly fed one substance to which he or she was thought to be sensitive. When the children were rated individually, depending on which researcher was doing the rating, 54 percent or 71 percent of the children behaved worse when exposed to the provocative food as compared to a placebo. However, 18 percent of the children behaved better when fed the food to which they were thought to be sensitive.

◆ In 1988, Katherine Rowe of the Royal Children's Hospital in Victoria, Australia, tested 55 preschool and school-age children who were hyperactive (15 children) or whose parents thought their behavior was affected by diet.¹⁵ When those children were placed on a "Feingold diet" (largely free of synthetic additives, but not necessarily of salicylate-containing foods), 40 showed improved behavior. Fourteen of those children reacted adversely when they returned to a diet containing dyes, preservatives, and other synthetic additives. That first phase of Rowe's research was not double-blind.

In a second phase, eight of the children whose behavior improved on a Feingold diet were kept on that diet and challenged, double-blind, for two one-week periods with 50 mg per day of tartrazine (and another two weeks with carmoisine, a dye not used in the United States) or lactose (placebo). Two (25 percent) of the children reacted sharply to both dyes, as judged by daily behavioral checklists compiled from parents' reports. A seven-year-old girl responded with increased activity, irritability, sleeplessness, and other symptoms. Her symptoms disappeared within several days after she stopped consuming the dyes. Also, a 12-year-old boy reacted with increased activity,

irritability, short attention span, aggression, and other symptoms, which persisted for several weeks after he stopped consuming the dyes. Both responders suffered from asthma and other allergies. As in other studies that tested only dyes, additional children might have reacted if challenged with a wider range of food ingredients and additives.

◆ In 1989, Bonnie Kaplan and her colleagues at the University of Calgary enrolled into a total-diet study the entire families of 24 preschool boys diagnosed with ADHD.¹¹⁶ Each family agreed to eat only the foods the researchers provided them during a seven-week period. During four of those weeks, the meals were free of artificial colors, flavors, and other substances, such as chocolate, MSG, preservatives, and caffeine, that parents thought might be affecting their children. During the other three weeks, the meals provided to the families were unrestricted but designed to resemble the experimental meals as closely as possible.

To keep the families in the dark about which diets they were getting, Kaplan and her colleagues misled the participants with false clues, such as designating some days as "corn" days or by limiting beverage consumption to no more than one cup per meal for three days.

Ten (42 percent) of the 24 boys improved an average of about 50 percent on the restricted diet, according to their parents' ratings, while four (17 percent) additional families reported a more modest 12-percent average improvement. The other ten boys did not respond.

◆ In 1990, I. Pollock and J.O. Warner of St. George's Hospital in London, England, studied 19 children between three and 15 years old.¹¹⁷ The children, according to their parents, exhibited poor concentration, excessive fidgeting, and other behavioral problems after consuming foods that contained dyes, so they had been put on restricted diets.

During the study, the children were kept on their food-additive elimination diet. Every day for seven weeks, the children consumed a gelatin capsule with their breakfast. During two of those weeks the capsules contained 125 mg of a mixture of four food colors, including

tartrazine. The other weeks the capsules contained a lactose (milk sugar) placebo. Seventeen of 19 sets of parents rated their children's behavior as worse—in several cases sharply worse—when their children were consuming the food colors.

◆ In 1993, Christine Carter and her colleagues at the Institute of Child Health in London, England, studied 78 children, three to 12 years old, who had been diagnosed with ADHD.¹¹⁸ Though some were on special diets, they were not chosen for being food-sensitive. In an open (non-blinded) trial, the children were placed on a severely restricted "few-food" diet free of additives and certain foods. The parents of 59 children (73 percent) felt there had been worthwhile improvement in behavior. Two children became worse, and the remainder did not respond. When foods were reintroduced at a rate of one a week in a non-blind manner, half or more of the children who ate "additive-containing foods," chocolate, milk, and oranges were said to react.

The researchers then conducted a double-blind, placebo-controlled trial on 19 of the children who seemed to have improved in the open trial. For one-week periods, each child received either a placebo or a test food (like chocolate or milk disguised in other foods, or a mixture of food colors [six to 26 mg] in a capsule). During the weeks they were getting the test foods or food colors, the behavior of 14 (74 percent) of the children worsened, according to their parents' ratings. Parents reported that their children were more likely to be restless, to disturb others, to cry often, and to suffer temper outbursts. A psychologist also rated the children's hyperactive behavior as worse during the challenge weeks, especially for fidgetiness. The researchers stated that when the children avoided problem foods, "Many parents commented ... that their children had become more manageable and more amenable to reasoning rather than less active or better able to concentrate."

◆ In 1994, Katherine S. Rowe and Kenneth J. Rowe, of the Royal Children's Hospital in Victoria, Australia, followed up on the former's 1988 study by testing 200 children whose parents believed they were affected by diet.¹¹⁹

The parents of 150 children reported improvement in behavior with a diet free of dyes, but deterioration after exposure to dyes, in a non-blind test. On the basis of that research they developed a system that they felt was better for rating the behavior of children in their study than the Conners' scale.

The Rowes then studied 54 other children between two and 14 years old. The parents of 34 of those children said they were likely or possible reactors to dyes. Those children suffered irritability, sleep disturbances, and restlessness. All 34 had been suspected of having ADHD, but only two were so diagnosed using the Conners' scale. The other 20 subjects served as controls. The children were put on a dye-free diet and then each morning for three weeks given a capsule or orange juice containing either a placebo or one of six dosages (1 mg to 50 mg) of tartrazine. Each day, the parents evaluated their children's behavior using a 30-item checklist that was based on their children's past behavior.

On the days they consumed the dye, 24 of the children (including 19 of 23 [83 percent] likely reactors, three of 11 [27 percent] possible reactors, and two of the 20 [10 percent] control children) became more irritable, restless, and sleep-disturbed, according to their parents. All six dosage levels produced reactions, which increased in severity with dosage. The researchers concluded, "Behavioral changes in irritability, restlessness, and sleep disturbance are associated with the ingestion of tartrazine in some children." All of the children who reacted to the dye also had asthma, eczema, or other signs of allergy, although none of those symptoms was caused by tartrazine.

◆ Also in 1994, Marvin Boris and Francine S. Mandel of the North Shore Hospital-Cornell Medical Center in Manhasset, New York, studied 26 children, ages three to 11, who had been diagnosed with ADHD and most of whom also suffered from allergies (asthma, hives, eczema, or other symptom). In a preliminary non-blinded phase, 19 (73 percent) of those children showed marked improvement when placed on a severely restricted diet that excluded artificial colors, preservatives, and foods such as dairy products, wheat, corn, yeast, soybeans, citrus

fruit, eggs, chocolate, and peanuts.¹²⁰ In open (non-blind) challenges, all of the children appeared to react to three or more items.

Those 19 children then participated in a double-blind, placebo-controlled study, which 16 children completed. Each day for seven days, the children ate lentil soup or apple-cranberry sauce. On one to three days, concealed in the soup or sauce were small amounts of the one food or mixture of dyes (100 mg of six dyes) thought to provoke the strongest reaction. The parents rated their children's behavior on each day. Eleven of the 16 children (69 percent) had much worse behavior (Conners-scale scores were doubled) during the challenge period than when consuming the placebo.

◆ A whole-diet study was conducted in 1997 by M.H. Schmidt and his colleagues on inpatients at the Central Institute of Mental Health in Mannheim, Germany.¹²¹ They studied in a double-blind manner the effects of diet on 49 schoolchildren who suffered from severe hyperactivity and disruptive behavior. Unlike the subjects in most other studies, the children had not previously been suspected of being diet-sensitive. The children were fed special diets for nine days each. When they ate a diet free of potentially provoking additives and foods, including tartrazine, cereal proteins, and citrus fruit, 12 (24 percent) children showed a clear improvement in behavior, while two children's behavior deteriorated.

The researchers then tested methylphenidate on 36 of the same children. Sixteen children (44 percent) showed improvement when eating a typical diet, while the behavior of four children worsened. Interestingly, three children who responded to diet did not improve with the drug. The degree of improvement was about the same with diet and drug. The limited response to methylphenidate suggests that many of the subjects did not have ADHD, but suffered from other problems unaffected by the drug.

"Although only effective in a minority of children," concluded the authors, "dietary treatment cannot be neglected as a possible access to treating hyperactive/disruptive children and merits further investigation."

Studies showing limited or no effect on behavior

■ Conners' team tested 30 children, 22 of whom were diagnosed as hyperkinetic.¹²² The children were between three and 12 years old. Children on a dye-free diet consumed 26 mg of dyes hidden in two chocolate cookies per day. Conners concludes: "It is obvious from the data that there was no effect whatsoever of the challenge..." (Conners notes that when initially put on the special diet, not in a double-blinded manner, half of the children showed a reduction of symptoms by 50 percent or more, with another seven children showing 25 percent to 50 percent improvements.)

■ Conners and his colleagues tested nine hyperactive schoolchildren who had previously appeared to improve on the Feingold diet.¹²³ The children were put on a Feingold diet and then challenged on one day each with either 0 or 26 mg of artificial colors. When eating the dyes incorporated into cookies, they did not make significantly more errors on a learning task, and no differences were seen with regard to physical activity. Conners later regretted not using more subjects, larger amounts of dyes, and a visual-motor tracking task.

■ Harley and his colleagues tested seven boys who in previous research behaved better on a diet free of artificial colors and flavors.¹²⁴ (Two other boys were put back on medication for part of the study.) Inexplicably, the researchers tested school-age boys even though they had found that preschool boys had responded better to a modified diet. The boys were put on a diet free of artificial colors, flavors, and foods high in salicylates and then challenged for two- or three-week periods over the next nine weeks with snacks that provided 0 mg or 27 mg per day of a mixture of food dyes. The researchers found that, on average, the children did not respond to diet. But they acknowledge: "[O]ne subject displayed a behavioral profile . . . that even approximated the predicted on-off effect of the challenge and placebo materials." Weiss has questioned this study on the basis of diagnostic and measurement criteria.¹²⁵ (Interestingly, the mothers, but not the fathers or teachers, of all nine boys reported improved behavior when

the boys were initially put on the restricted diet.¹²⁶ Presumably, at least part of that improvement was due to the Hawthorne effect.)

■ In 1981, Mattes and Gittelman, whose study of one hyperactive boy was discussed above, tested the effect of up to 52 mg to 78 mg of a mixture of food dyes on 11 children between four and 12 years old.¹²⁷ Most of the children were considered as having ADD or ADHD. Parents claimed that each child was sensitive to food additives and adhered to the Feingold diet. In this study, with the children remaining on their ordinary (Feingold) diet, eating cookies containing increasing amounts of dyes each day for one week did not appear to affect the children's behavior. Parents reported that three children reacted to cookies with dyes and three to cookies without dyes. Whether the children might have been sensitive to substances excluded by the Feingold diet other than dyes was not tested.

■ In 1987, T.J. David of the University of Manchester in England, tested only tartrazine and benzoic acid on 24 children, six of whom had ADHD.¹²⁸ Parents said that all of the children suffered behavioral reactions within two hours of consuming tartrazine, six were said to be sensitive to benzoic acid, and all were on restricted diets. In a hospital setting, the children were challenged in this double-blind, placebo-controlled study on one day with tartrazine and on one other day with benzoic acid. None reacted after consuming a large dose of tartrazine (50 mg) followed several hours later by a huge dose (250 mg). Similar amounts of benzoic acid also had no effect. The author conceded that the negative result might be attributable to the unfamiliarity of the ward environment. One girl, for instance, had "gross, prolonged, and frequent temper tantrums," making it difficult to detect any effect of the additives. Five other children displayed abnormal behavior, such as aggressive behavior or pronounced overactivity.

■ Nicola Wilson and Alex Scott of the Hammersmith Hospital in London, England, tested four children whose parents had put them on additive-free diets to avoid behavioral effects.¹²⁹ (An additional five children refused

to follow the study's guidelines or dropped out early.) The children were challenged at home for 12 days each with a placebo, 17 mg of dyes (tartrazine and sunset yellow [Yellow 6]), or preservatives (sulfites, benzoic acid). Parents of the four children whose behavior was thought to be affected by diet did not see any effects. This study is limited by the many dropouts. (Fifteen other children with various allergies also were tested. One two-year-old boy, whose eczema was suspected of being caused by dyes, displayed "extremely abnormal behavior" after consuming preservatives.)

Non-blind studies

Several studies were not double-blind, so they cannot be considered reliable indicators of sensitivity to diet. Following are summaries of several such studies.

- Over a five-year period, Joan Breakey and colleagues tested 516 children.¹³⁰ The percentage of children who had ADHD was not indicated. A positive response to a low-additive, low-salicylate diet was observed in a total of 80 percent of the children, with 55 percent of children considered "good responders." Some children also were reported to have benefited from avoiding milk, grains, or chocolate.

- In 1992, Egger, whose 1985 study was described above, conducted another study that began with placing 185 hyperactive patients on

the same "few food" diet without additives for four weeks.¹³¹ One hundred sixteen (63 percent) patients improved enough that they would no longer be diagnosed as hyperactive, according to the Conners' scale. (Some of the responders then participated in a double-blind study that tested the effectiveness of a desensitization technique.)

- In 1997, T. Uhlig and his colleagues in Australia and Germany reported an association in children with ADHD between the consumption of provoking foods and electrical activity in the brain.¹³² Forty-five school-children were placed on a "few-food" diet, and 71 percent improved significantly, with their Conners scores falling below the cutoff level for ADHD. Various foods were then reintroduced (again, not in a double-blinded manner) into the children's diets. If a food caused symptoms during three separate attempts, a child was considered to be affected by it. Those foods included beet sugar, artificial colorings, wheat, milk, and others. In a third phase, the researchers used EEG to study 12 children who showed marked improvements in behavior when they did not eat provoking foods, though it is unclear if the children knew when they were eating such foods. The researchers found a significant increase in beta-1 activity in the frontotemporal areas of the brain after the children ate sensitizing foods but not other foods. The EEG recordings were interpreted by two researchers, one of whom was blind to the order of treatment.

Appendix 3: The Conventional Wisdom on Diet and ADHD

Many public and private health and professional organizations, as well as some prominent experts, largely dismiss the notion that diet can affect children's behavior.

U.S. Food and Drug Administration (FDA)— International Food Information Council (IFIC)

The FDA is the federal agency responsible for ensuring that synthetic food colors and other additives are properly tested for safety. In 1993, the FDA published "in cooperation" with IFIC a pamphlet entitled "Food Color Facts." Actually, the pamphlet was written by IFIC and only edited by the FDA.¹³³ IFIC is an organization directed by officials of, and funded by, many makers of food additives and processed foods, such as General Mills, Kraft, Procter and Gamble, Pepsi-Cola, Coca-Cola, Monsanto (maker of aspartame), and Ajinomoto (maker of monosodium glutamate).¹³⁴

The pamphlet states:

Q. Do food color additives cause hyperactivity?

A. Although this theory was popularized in the 1970s, well-controlled studies conducted since then have produced no evidence that food color additives cause hyperactivity or learning disabilities in children. A 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. The 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.

The pamphlet has rewritten history. As noted earlier, the NIH panel concluded that controlled studies "did indicate a limited positive association" between diet and hyperactivity and that dietary treatment may be worth trying. Moreover, the one study (by Weiss, Williams, Margen, *et al.*) funded by the FDA found an effect of diet on behavior.

Endorsement by the FDA—its name and logo are on the back cover—confers great credibility on a pamphlet that, from beginning to end, is a one-sided argument in favor of color additives. (Not mentioned is that colors usually are used in foods with little nutritional value; that artificial colors and flavors often replace more valuable ingredients, such as fruit; and that numerous colors have been banned because they caused cancer, liver damage, or other problem in laboratory animals.¹³⁵)

National Institute of Mental Health (NIMH)

NIMH, a division of NIH, supports research on the brain, mental illness, and mental health. In 1994, the NIMH published a pamphlet titled "Attention Deficit Hyperactivity Disorder" that dismissed "restricted diets" as an example of "the types of treatment that have not been scientifically shown to be effective in treating the majority of children or adults with ADHD."¹³⁶ A few anecdotal success stories, said the NIMH, cannot substitute for scientific evidence. "Until sound, scientific testing shows a treatment to be effective, families risk spending time, money, and hope on fads and false promises." Elsewhere, though, the pamphlet acknowledges that the 1982 NIH consensus panel found that dietary treatment could "help about 5 percent of children with ADHD, mostly either young children or children with food allergies." (The basis of that "5 percent" statement is unclear.) It is true that diet may not be effective in "the majority" of children with ADHD, but that does not mean it should not be employed by the minority.

Children and Adults with Attention Deficit/Hyperactivity Disorder (CHADD)

CHADD, the largest self-help group concerned with ADHD and one that assists a

great many families, dismisses any role of food additives:

Dietary intervention has long been claimed to be a useful treatment for an array of children's learning, behavior, and attention problems. Advocates claim that removing food additives, such as preservatives and colorings, from the diet will improve most or all of a child's learning and attention problems. Numerous studies have debunked the notion of an additive-free diet as a treatment for ADD.¹³⁷

CHADD has been a vigorous proponent of drug treatment for ADHD. To make methylphenidate less expensive and more available, the group petitioned the DEA to reclassify it as a less risky controlled substance.¹³⁸ CHADD has been criticized for failing to disclose a conflict of interest that might have influenced its advice on treatments. About 20 percent of the organization's budget in some years reportedly was underwritten by Ciba-Geigy (now Novartis), the maker of Ritalin.¹³⁹ CHADD was reported to have received from drug companies more than \$1 million in grants and services. The DEA charged, "The relationship between Ciba-Geigy and CHADD raises serious concerns about CHADD's motive in proselytizing the use of Ritalin."¹⁴⁰ CHADD in a recent year received about \$30,000 from Novartis and ten percent of its income overall from the drug industry.¹⁴¹

National Center for Learning Disabilities: Learning Disabilities Association of America

The National Center for Learning Disabilities states: "... in spite of some claims, ADHD has not been proven to result from too much TV, food allergies, excess sugar intake ..."

Another organization, the Learning Disabilities Association of America, grants a little credence to diet's potential effect: "Several nutritional approaches have been proposed. The Feingold Diet appears to work at best for 1-2 percent of children with ADHD. Too much refined sugar can increase hyperactivity in some children." No evidence for either statement is provided.

Nutrition Foundation

The Nutrition Foundation sponsored some of the early research on the Feingold hypothesis, and it created a National Advisory Committee on Hyperkinesia and Food Additives. In 1980, the foundation issued its final report, which concluded:

Instead, the evidence that the total Feingold diet produces improvement in the behavior of hyperactive children is equivocal. The mild and entirely subjective changes that have been reported are not, in our opinion, clinically important.... It is our opinion that the studies already completed provide sufficient evidence to refute the claim that artificial food colorings, artificial flavorings, and salicylates produce hyperactivity and/or learning disability.¹⁴²

The committee did acknowledge that one child in each of three studies may have been affected by colorings, but said those effects were not definitely proven. The committee consistently tried to explain away positive findings, but failed to address weaknesses in studies said to have negative findings. The Nutrition Foundation described itself as "a public, non-profit institution ... dedicated to the advancement of nutrition knowledge," but it was financed largely by makers of processed foods. (The Nutrition Foundation was subsequently absorbed by the International Life Sciences Institute, another industry group.)

American Academy of Pediatrics

The leading organization of physicians who specialize in children's health problems dismisses any link between diet and hyperactivity. In its *Pediatric Nutrition Handbook* for physicians, the academy states: "Double-blind controlled studies of the Feingold diet, which eliminates all artificial colorings and flavorings, have not supported the thesis that additives are a significant causative factor."¹⁴³ On its web site, the academy states:

Special diets. These are based on the unproven idea that certain foods cause ADHD.... While there is scientific evidence that these diets do not work, many parents strongly believe they help.... Remember, no special diet alone can solve the problems of ADHD and should not be used as the only treatment for your child's behavior.¹⁴⁴

William Klish, the former chairman of the academy's Committee on Nutrition, wrote: "Foods do not appear to be related to ADHD even though the concept has persisted for many years."¹⁴⁵ Whenever the hypothesis that diet affects hyperactivity "is tested in well designed blinded placebo-controlled clinical studies," wrote Klish, "the results are negative."

American Medical Association

In 1998, the American Medical Association's Council on Scientific Affairs reviewed the treatment of ADHD without discussing diet.¹⁴⁶ On its KidsHealth web site, the AMA states:

In addition to drug and psychosocial therapies, there also exists a long history of other treatments, including herbs, vitamins, minerals, biofeedback, and dietary solutions. Many of these therapies, although appealing, have not been proven in therapeutic trials to be effective.¹⁴⁷

American Academy of Child and Adolescent Psychiatry

This professional organization states:

Since the mid-1970s, the advocates of dietary treatment of behavioral problems have been remarkably persistent despite the lack of scientific evidence. Families who insist on trying a diet should be permitted to do so, provided the diet is nutritionally sound, because initial attempts to dissuade them may disrupt the therapeutic alliance.¹⁴⁸

A working group of that organization stated:

Given the minimal evidence of efficacy and the extreme difficulty of inducing children and adolescents to comply with restricted diets, they should not be recommended.¹⁴⁹

Sugar Association—American Academy of Family Physicians Foundation

A pamphlet on hyperactivity published by the Sugar Association, an industry group, was "favorably reviewed" by the American Academy of Family Physicians Foundation (AAFPF).¹⁵⁰ "Questions Most Frequently Asked About Hyperactivity," published in the early

1990s, dismisses any notion that diet affects behavior. In response to the questions "Is there a dietary relationship to hyperactivity? Should I restrict certain foods from my child's diet?" the pamphlet states:

The answer to both questions is "No." Folklore linking certain foods such as food additives, colorants and refined sugars with hyperactivity in children began in the early 1970s.... In over 20 studies, including those supported by the Food and Drug Administration, science has been unable to support these claims. Results of the most recent research indicate there is no dietary connection to increased incidence of ADHD or intensity of symptoms in children already affected with the disorder. Restricted diets for the purpose of manipulating behavior problems are not recommended.

The AAFPf's review was done by Esther H. Wender, professor of pediatrics at Albert Einstein College of Medicine. Wender did a study, supported in part by the Sugar Association, that actually found that sucrose (table sugar) reduced attention to tasks in children with ADHD, but not other children.¹⁵¹

In a second pamphlet, "Fast Facts About Hyperactivity," that also was "reviewed favorably" by the AAFPf, the Sugar Association states:

It used to be thought that ADHD could be caused or made worse by food additives and/or sugar in the diet. **The truth is...** Scientific studies do not support any connection between diet and ADHD. Forbidding children with ADHD to eat certain foods will not change their behavior, and is not recommended.

The American Academy of Family Physicians, a respected medical organization, diminishes its credibility by endorsing self-serving industry propaganda.

American Council on Science and Health (ACSH)

In a 1979 report titled "Diet and Hyperactivity: Is There a Relationship?" ACSH stated:

The current evidence indicates that a few hyperkinetic children, on the order of a fraction of one percent, may experience adverse reactions to one or several of the large number of artificial food colors and thousands of artificial flavors...¹⁵²

Returning to the topic a decade later, another article in ACSH's newsletter called the Feingold diet "now-disproven."¹⁵³

ACSH calls itself a nonprofit "consumer education association," but it is funded largely by food and chemical companies and consistently defends those companies' practices and products. Sponsors include Kraft, Anheuser-Busch, Monsanto, Pfizer, PepsiCo, Procter and Gamble, the National Soft Drink Association, and many others.

Researchers

One of the best known and most widely quoted researchers on ADHD is Russell A. Barkley, director of psychology and professor of psychiatry and neurology at the University of Massachusetts Medical Center in Worcester, Massachusetts. In his popular book *Taking Charge of Hyperactivity*, Barkley largely dismisses the link between additives or foods and hyperactivity:

Most of the substantial amount of research done over the next decade was simply unable to support Feingold's claim. In fact, only a very small number (5% or less) of mainly preschoolers showed a slight increase in activity or inattentiveness when consuming these substances.... In 1983, Drs. Kenneth Kavale and Steven Forness with the University of California published a review of 23 studies investigating the Feingold diet. They concluded that diet modification was not effective for treating hyperactivity.¹⁵⁴

The authoritative-sounding study by Kavale and Forness is flawed, because it averages together the reactions of all the children, rather than looking at the effect on each child's behavior. The benefits experienced by subgroup of responders are masked when they are averaged in with a larger group of non-responders.

Alan J. Zametkin, a leading NIMH researcher on the neurobiology of ADHD, stated in the *Journal of the American Medical Association*:

Many carefully controlled studies have failed to find any substantive link between food additives and ADHD. Support for this finding is well summarized in Barkley's definitive textbook ... as well as in the 1980 report of the National Advisory Committee on Hyperkinesia and Food Additives.¹⁵⁵

It is puzzling that Zametkin chose to cite that advisory committee, which was sponsored by the food industry, and not the NIH's own 1982 consensus conference, which concluded that some children are affected by diet.

Josephine Elia (University of Pennsylvania School of Medicine), Paul J. Ambrosini (MCP-Hahnemann University), and Judith Rapoport (NIMH) authored in the *New England Journal of Medicine* a major review of the treatment of ADHD and focused entirely on drugs, dismissing other approaches in a single sentence: "Controlled studies have not proved the effectiveness of ... restrictive or supplemental diets."¹⁵⁶

The drumbeat of statements from naysayers, some with vested interests, has created a conventional wisdom that diet has no effect on behavior and that Feingold's hypothesis has been disproved. As early as 1986, Bernard Weiss, a neurotoxicologist at the University of Rochester who has studied the effect of diet on behavior, observed that "most clinicians and scientists remain unaware of the evidence supporting [Feingold's] claims, because of an effective publicity campaign by the Nutrition Foundation and because of their unfamiliarity with the pertinent literature."¹⁵⁷ Whatever the underlying reason, it is clear that many authorities appear to be unfamiliar with evidence that some children are adversely affected by diet.

Appendix 4: Is Your Child Sensitive to Food Ingredients?

Some children with ADHD or other behavioral problems are sensitive to one or more substances in food. Testing different diets on your child may be rewarded with improvements in behavior, without the potential side effects (and costs) of stimulant drugs. Preschool children and children who suffer from asthma, hives, hay fever, or similar symptoms might be the most likely to benefit from dietary changes.

Numerous studies have demonstrated that some children are sensitive to artificial colorings, which are listed on food and vitamin labels with names like Red 40 and Yellow 5. The simplest experiment you could try would be for several weeks to eliminate foods that contain artificial colorings and see if your child's behavior improves. Those foods are relatively easily avoided and usually not very nutritious.

If you are more ambitious, you could put your child on the Feingold diet, which eliminates not only artificial colorings, but also artificial flavorings, artificial sweeteners (acesulfame-K, aspartame, saccharin, sucralose), and several preservatives (BHA, BHT, and TBHQ). Those additives sometimes are used in vitamin supplements, toothpastes, and drugs—including Ritalin. The Feingold diet also excludes foods that contain salicylates, such as apples and oranges (see box below). Almost no research has been

done to investigate the behavioral effects of either additives other than artificial colorings or salicylate-containing foods, but many parents believe that eliminating some or all of those ingredients has helped their children. (You can obtain practical assistance for keeping your child on the Feingold diet, lists of acceptable brand-name foods, and other information from the Feingold Association, whose address is on page 14.)

After you've decided which foods you will eliminate, you should start a notebook to keep track of your child's behavior before and after you change his or her diet. Prepare a score sheet based on common characteristics of ADHD (see box on page 2), but modify it to include your own child's most troubling behaviors, which may include sleep disturbances and aggressiveness. Note when behavioral problems arise and which foods your child recently had eaten. For each day, rate the various behaviors on a scale of 0 (no problem) to 3 (severe problem). You also can ask your child's teacher if he or she has noticed any improvement in behavior, but don't say that you're changing your child's diet unless you need his or her assistance to provide your child with special snacks. Considering how erratic most children's behavior is, correctly linking improved or worsened behavior to diet is not an easy task.

If those first changes do not improve your child's behavior, you can try more restricted diets. Several studies indicate that certain foods—including wheat, eggs, milk, chocolate, corn, and soybeans—adversely affect some children's behavior. You could eliminate one food at a time for a week or two each, or you could try eliminating several simultaneously (also continue to exclude the artificial colorings and perhaps other additives). If your child appears to

Salicylate-containing Foods (partial list)*

almonds	coffee	peaches
apples	cucumbers and pickles	peppers (bell, chili)
apricots	currants	plums, prunes
berries (all)	grapes, raisins	tangerines
cherries	nectarines	tea
cloves	oranges	tomato
aspirin (acetyl salicylate) and medications that contain it		
oil of wintergreen (methyl salicylate; mint flavoring)		

*Reactions to these foods are based on unconfirmed reports, not controlled studies.

be sensitive to a certain food, try reintroducing it into his or her diet. Your child is probably sensitive to it if he or she reacts adversely to it repeatedly. You should only undertake an elimination diet with assistance from an allergist, especially if your child has eczema or other allergies (severe reactions might occur when a food is reintroduced). If your child is sensitive to milk or other major source of nutrients, you should consult a dietitian to get suggestions of other foods that will provide your child with all the necessary nutrients. If the food does not trigger symptoms, a different food or something other than diet might be the problem. It is also possible that your child might be able to eat a provoking food in smaller quantities or infrequently.

The Feingold Association suggests that, if its basic diet does not improve behavior, corn sugar (glucose or dextrose) and corn syrup, MSG (monosodium glutamate) and HVP (hydrolyzed vegetable protein), and sodium nitrite (in luncheon meats) also should be eliminated. Again, those changes are based on reports from parents, rather than from controlled studies.

Some research suggests that a severely restricted diet, called the "few-food diet," improves behavior in high percentages of children. That diet excludes all food additives (including artificial colorings, flavorings, and sweeteners, MSG, and preservatives) plus:

- ✓ caffeine (colas and other soft drinks, coffee, tea)
- ✓ chocolate

- ✓ corn products (and corn sugar and corn syrup)
- ✓ dairy foods
- ✓ eggs
- ✓ nuts
- ✓ oranges, grapefruit
- ✓ soybeans/tofu
- ✓ wheat

The few-food diet also eliminates other foods that an individual child is suspected of being affected by.

On this diet, children can eat fresh meat and poultry, any vegetable (except corn and soy foods), fruits and fruit juices (including pineapple and pear, but not orange and grapefruit), rice, and oats. If you see an improvement in behavior after your child has been on that diet for one or two weeks, reintroduce one food every few days to identify as many foods as you can to which your child is not sensitive.

Adhering to a severely restricted diet for even a short while requires a tremendous commitment from both parents and children and may be more appropriate in a research setting than for typical families. If a highly restricted diet does appear to help your child, and your child remains on it for an extended period of time, you'll need to work with a dietitian to ensure that your child is getting all the necessary nutrients.

Finally, if your child does not seem to benefit significantly from any restricted diet, then you should discuss with your pediatrician other treatment options, including behavioral counseling and/or medications.

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