

Science Board to the FDA
October 7, 2019

Color Additives and Behavioral Effects in Children

In 2011, FDA convened its Food Advisory Committee (FAC) to consider whether available relevant data demonstrate a link between children's consumption of synthetic color additives in food and adverse effects on their behavior. The FAC concluded that a causal link between children's consumption of synthetic color additives and behavioral effects had not been established. However, the FAC recommended further research to investigate potential developmental and neurotoxic effects in children from exposure to these substances and a comprehensive exposure assessment for these color additives (Ref. 1).

In the U.S., the color additives of primary concern are the FD&C color additives, namely Blue 1, Blue 2, Green 3, Red 3, Red. 40, Yellow 5, and Yellow 6. All these color additives are permitted for use in foods generally at levels consistent with good manufacturing practices. Additionally, all these color additives must come from a batch certified by FDA before they may be used in food to ensure conformance with the prescribed identity and purity specifications. FDA's labeling regulations require that foods containing these color additives must declare the name of the color additive in the statement of ingredients on the product label. Consumers who wish to avoid these color additives may use the information found in the ingredient statement when choosing food products.

Since the 2011 FAC, FDA has conducted and published a comprehensive exposure assessment for all seven FD&C color additives based on levels present in food (Ref. 2). The exposure estimates for these color additives, including for children, are well below FDA's established acceptable daily intake levels for these color additives. FDA also has conducted an updated search of the scientific literature for relevant studies on color additives and Attention Deficit/Hyperactivity Disorder (ADHD) that have published since the 2011 FAC. The search identified the following four studies: (1) a meta analyses study by Nigg et al. in 2012 on the role of diet and food colors in ADHD, (2) a meta analyses study by Sonuga-Barke et al. in 2013 on dietary and psychological interventions as treatment for ADHD, (3) a double-blind, placebo-controlled clinical study in children with color additive mixtures by Lok et al. in 2013, and (4) a systematic review of several meta-analyses of clinical studies on various dietary factors, including color additives, and their possible role in ADHD by Pelsser et al. in 2017 (Refs. 3-6). FDA's review of the first three studies are provided as references (Refs. 7-9)¹.

FDA is asking the Science Board to consider the following questions:

- (1) Does the latest science establish a link between consumption of FD&C color additives in food by children from the general population and adverse effects on their behavior?

¹ The study by Pelsser et al. was not reviewed by FDA in time for this meeting. However, the study authors concluded that their review showed that the effect-size of artificial food color (AFC)-free diets on ADHD was small to medium such that dietary intervention that excludes AFCs should not be advised as general ADHD treatment.

- (2) Does the latest science establish that the use of artificial food color exclusions is an efficacious dietary intervention in the nonpharmacological treatment of children with ADHD and related problem behaviors?
- (3) Since the 2011 FAC, are there any new considerations in terms of design characteristics of a study intended to test the hypothesis that there is a causative link between individual color additives and ADHD in children?
 - a. Have there been any new tools developed since the 2011 FAC that could potentially be used in the conduct of such a study?

References:

1. Quick Minutes: Food Advisory Committee Meeting March 30-31, 2011
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3. Nigg, J., Lewis, K., Edinger, T., Falk, M., “Meta-Analysis of Attention-Deficit/Hyperactivity Disorder or Attention-Deficit/Hyperactivity Disorder Symptoms, Restriction Diet, and Synthetic Food Color Additives,” *Journal of the American Academy of Child & Adolescent Psychiatry*, 51(1):86-97, 2012.
4. Sonuga-Barke, E., Brandeis, D., Cortese E., Daley, D., Ferrin, M., Holtmann, M., Stevenson, J., “Nonpharmacological Interventions for ADHD: Systematic Review and Meta-Analyses of Randomized Controlled Trials of Dietary and Psychological Treatments,” *American Journal of Psychiatry*, 170:275-289, 2013.
5. Lok, K., Chan, R., Lee, V., Leung, P., Leung, C., Leung, J., Woo, J., “Food Additives and Behavior in 8- to 9-Year-Old Children in Hong Kong: A Randomized, Double-blind, Placebo-Controlled Trial,” *Journal of Developmental and Behavioral Pediatrics*, 2013, 34:642–650.
6. Pelsser, L., Frankena, K., Toorman, J., Pereira, R., “Diet and ADHD, Reviewing the Evidence: A Systematic Review of Meta-Analyses of Double-Blind Placebo-Controlled Trials Evaluating the Efficacy of Diet Interventions on the Behavior of Children with ADHD,” *PloS One* (open source), 12(1): e0169277. doi:10.1371/journal.pone.0169277.
7. FDA Review and Analysis Report on Nigg, et al., 2012.
8. FDA Review and Analysis Report on Sonuga-Barke et al., 2013.
9. FDA Review and Evaluation Report on Lok, et al., 2013.