

**ORAL COMMENTS TO THE FDA
FDA Open Public Hearing
March 31, 2011**

Re: FDA Advisory Committee Meeting to discuss whether available relevant data demonstrate a link between children's consumption of synthetic color additives in food and adverse effects on behavior

ILSI North America welcomes this opportunity to provide comments to FDA on whether relevant data demonstrate a link between children's consumption of synthetic color additives in food and adverse effects on behavior. ILSI North America is a public, non-profit foundation that actively collaborates with government and academia to identify and resolve scientific issues important to the health of the public. ILSI North America's programs are supported primarily by its industry membership.

In collaboration with the Life Sciences Research Organization (LSRO) and Dr. Joel Nigg, an ADHD expert at Oregon Health and Science University, available scientific evidence was reviewed. Detailed findings will be published in a peer-reviewed, meta-analysis manuscript. A preliminary analysis will be presented today.

Methods and Analysis

Our literature search identified 53 human studies. Studies were graded for relevance and usefulness. The main focus of the analysis was on studies that conducted a double/blind, placebo-controlled challenge trial using synthetic color additives. Thirteen of 16 identified studies yielded effect sizes, and 8 were relevant to gauging the percentage of children affected from within the samples selected. In summary, these studies yielded uncorrected, weighted mean $d=.33$, which was statistically reliable ($p<.01$), but the effect was not reliable in observer or objective test ratings when those were obtained. It was observed only in parent-ratings, which tend to show the largest effects due to (a) undetected failure of study blinding, or (b) parent ability to detect behaviors not detected by observers (e.g., difficult behavior at meal or bedtimes).

Limitations

The following limitations in this literature warrant consideration.

1. Children who react to dyes generally also react to other foods. Food restrictions appears to help some children, but it remains unclear whether removing dyes alone will benefit these children
2. Preselected populations: When children are preselected by reported response to an elimination diet, a behavioral response to dye challenge is observed in as many as 60% and is limited to only parental ratings, and was not observed by teacher or clinician ratings. There are two well designed population based studies, but neither provided enough information to gauge the percentage of children responding.
3. In a number of the large community studies there were many confounding food components along with synthetic food colors. Therefore, it is impossible to determine the effect, if any, that could be attributed to synthetic color additives.

4. Effects are seen only in parent ratings and the meaning of this is unclear.

Conclusions

In conclusion, based on our analysis of the literature pooled across available studies, no significance was detected in double/blind, placebo controlled studies for observer or objective test ratings and only for parent ratings was a reliable non-zero effect detected. The effects observed in community studies are confounded by inclusion of other food components-leaving it unclear how much of the community effect is attributable to FDA-approved food dyes. It is premature to make conclusions about causal associations regarding specific FDA-approved food colorings and ADHD.

Future research should be pursued to address mechanistic pathways and mode of action, as well as clinical effects above meaningful thresholds. A review paper, accepted by the journal *Pediatrics*, will address diet and ADHD methodology, and it could help to enhance the design of future studies.

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