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Subject: “Estimated Daily Intake and Safety of FD&C Food Colour Additives in the US Population,” by Bastaki et al., published in *Food Additives & Contaminants: Part A* contains significant errors and reaches incorrect conclusions

Dear Dr. Gilbert:

The recent study funded by members of the International Association of Color Manufacturers (IACM) and written by IACM staff, members, and consultants touting the safety of food dyes is so riddled with inaccuracies and misleading statements that it should be retracted and disregarded (Bastaki et al. 2017, hereinafter “Bastaki”). Each of its conclusions is incorrect. The Corrigendum only partially and inadequately addresses the errors. Bastaki mischaracterizes the relationship between the study’s exposure estimates and actual concentrations measured analytically by the US Food and Drug Administration (FDA), systematically underestimates food dye exposure, and relies on acceptable daily intake (ADI) estimates that are based on outdated animal studies that are incapable of detecting the kinds of adverse behavioral effects reported in multiple double-blind clinical trials in children. Bastaki ignores the nine recent reviews (including three meta-analyses) drawing from over 30 such double-blind clinical trials that all conclude that excluding food dyes, or adherence to a diet that eliminates food dyes as well as certain other foods and ingredients, reduces adverse behavior in some children (Arnold et al. 2012, Arnold et al. 2013, Faraone and Antshel 2014, Nigg et al. 2011, Nigg and Holton 2014, Schab and Trinh 2004, Sonuga-Barke et al. 2013, Stevens et al. 2011, Stevenson et al. 2014). While Bastaki has been revised to delete the incorrectly reported doses used in the Southampton study, it makes misleading statements about the Southampton study.

We address each erroneous conclusion in turn, below.

First, the authors conclude that “use levels reported by industry are consistent with the concentrations measured analytically by the US Food and Drug Administration.” In fact, the results estimated by Bastaki (based on industry surveys) are much lower than the levels of dyes actually measured in products by the FDA (Doell et al. 2016). For example, Bastaki estimates 2 ppm as a “typical use” level for FD&C Yellow 5/tartrazine in juice drinks, and 48 ppm as a maximum (Table 2A). The FDA (Doell et al.) tested 38 juice drinks, 13 (34%) of which contained FD&C Yellow 5/tartrazine, at levels ranging from 1.0 to 44.8 ppm, with a mean of 14 ppm and a median of 11 ppm. The mean and median levels of FD&C Yellow 5/tartrazine in juice drinks tested by FDA are more than five times the typical use claimed by Bastaki. Since the concern with adverse behavioral effects is from acute exposure to dyes (exposure in a given serving or meal), it would not be appropriate to include drinks that do not contain dyes (in this case, FD&C Yellow 5/tartrazine) when determining the mean or median. Nevertheless, even if

one did, the mean value derived from the FDA measurements (4.8 ppm) is more than twice that of the “typical” value of 2 ppm reported by Bastaki.

Obviously, industry surveys produce results that are less valid than actual measurements by government scientists.

Such differences are significant, given the FDA study’s conclusion in Doell et al. that juice drinks are by far the largest contributor to exposure to FD&C Yellow 5/tartrazine for children aged 2-5 (comprising almost 30% of exposure for that group), and are also major contributors to exposure to those dyes for the US population in general and teenage boys aged 13-18 in particular, the other population groups that Doell et al. chose for exposure estimates. Yet Bastaki suggests that juice drinks would be an insignificant source of intake, contributing about 2% of the typical exposure for 2-to-5-year-olds (Table S2). The FDA (Doell et al.) reports that there was FD&C Yellow 5/tartrazine in 21% of juice drinks tested, but Bastaki reports that approximately 9% of fruit/flavored still drinks as well as beverage concentrates contain FD&C Yellow 5/tartrazine (Figure 1).

A likely reason that Bastaki underestimates the frequency with which food labels list FD&C colour additives as ingredients is its reliance on the Mintel database of finished product labels, which contains only *new* labels published between January 2011 and February 2015 (including new products launched, new formulations, and new packaging of existing products). Because many companies are responding to consumer demands to eliminate dyes, reliance only on new labels likely systematically underestimates exposure, compared to the complete array of labels currently in the marketplace.

We compared information from the Label Insight database, a cloud-based database that enables access to complete and accurate product information beyond what’s typically found on the label, for a single product category (energy drinks), and after ensuring data accuracy and currency, found a far higher proportion of energy drinks that contain FD&C Red 40 (8.7%) than reported by Bastaki (1.1%).

Also, it is unclear whether the industry’s survey was limited to the United States. Bastaki states that “[t]he data compilation was representative of colour use within IACM’s membership and covered the main foods where colours are used.” IACM’s membership extends beyond the United States. Many companies doing business in Europe reformulated products to eliminate certain dyes in response to the European Union requirement that foods containing dyes used in the Southampton study (McCann 2007) be labeled with a warning that they “may have an adverse effect on activity and attention in children.” Including information from Europe would underestimate exposures for the United States.

Another possible reason why Bastaki underestimates frequency of color additives in foods is its practice of disaggregating products (e.g., apple pie) into the ingredients used to make the products (e.g., flour, butter, apples, sugar), combined with its use of the US Environmental Protection Agency’s What We Eat In America Food Commodity Intake Database, which does not include non-nutritive ingredients like dyes.

Second, Bastaki concludes that “exposure to food-colour additives in the United States by average and high-intake consumers is well below the Acceptable Daily Intake (ADI) of each colour additive as published by the Joint WHO/FAO Committee on Food Additives (JECFA) and allows wide margins of safety.” (Bastaki makes no mention of the US Food and Drug Administration’s ADIs, which are different from, although similar to, JECFA’s ADIs for color additives.) Such a statement has little meaning, considering that both the JECFA’s and FDA’s ADIs are based on old chronic toxicity studies in animals, which, as experts on an FDA advisory committee noted, are “completely insensitive” for assessing neurobehavioral outcomes, “have no value in assessing any kind of neurological responses,” and may result in a “significant risk that the ADIs are set too high ... are erroneous, they’re incorrect” (US FDA Food Advisory Committee, 2011).

The inadequacy of the JECFA’s and FDA’s ADIs is also illustrated by comparing the sum of the FDA’s acceptable daily intakes of currently used certified color additives in the United States (560 mg for a 35-pound child) with the challenge doses used in clinical trials that triggered behavioral reactions in some children; 26-36 mg of dyes was frequently used (Lefferts 2016), and some studies find effects at as little as 1 or 2 mg (Rowe and Rowe 1994).

It is easy for children to consume high levels of synthetic dyes. For example, using FDA data (Doell et al.) and serving sizes from manufacturers, Little Debbie Swiss Rolls have 32 mg of total synthetic dyes per serving, a 20 oz. bottle of Powerade Orange has 36 mg, and a snack consisting of one serving of Orville Redenbacher’s Cheddar Cheese Microwave Popcorn and 8 oz. of Hawaiian Punch Fruit Juicy Red contains 36 mg of dyes.

The FDA (Doell et al.) estimates that 100 percent of children aged 2 through 5 in the United States are exposed to FD&C Blue 1, FD&C Red 40, FD&C Yellow 5, and FD&C Yellow 6. Besides triggering adverse behavior in some children, synthetic food dyes frequently disguise the absence of nutritious ingredients and make unhealthy foods more appealing.

Finally, even though the Bastaki study was recently revised to delete one of its preposterous conclusions and an inaccurate statement regarding the Southampton study, it still makes misleading statements in an attempt to dismiss the results of the Southampton study, which led to a series of actions by the British government to lower consumer exposure to food dyes and a requirement for warning labels on most dyed foods throughout Europe. Specifically, the revisions delete Bastaki’s blatantly false conclusion that “for children to reach the intake assumed in the Southampton study, they would have to consume *at least 30 times* more foods and beverages daily than the high consumers (95%) *and* the foods would have to contain four different colours at maximum use levels, a clearly unrealistic scenario.” And the revisions delete the untrue statement that “[i]n the Southampton study, children were given a combination of four colours and a preservative at daily amounts equal to each ADI, with totals adding up to very high levels of intake.” Bastaki now misleadingly asserts that “[t]he results of this exposure assessment and the exposure estimates obtained by Doell et al. (2016) easily demonstrate that the Southampton study design tested levels above conservative intakes for the US population.”

In fact, the doses given in the Southampton study (McCann et al. 2007) were about two orders of magnitude less than amounts equal to each ADI, and the amounts are within the range of

exposures reported by the FDA in Doell et al. More specifically, in the Southampton study, 3-year-olds were given between 2.5 and 7.5 mg of each of four dyes, for a total of 20 mg of dyes in Mix A and 30 mg of dyes in Mix B. The FDA (Doell et al.) reported that for 2-to-5-year-olds, average consumption of FD&C Red 40 ranged from 2.6 to 15.3 mg under different exposure scenarios and up to 38.8 mg for 90th percentile consumers (using two-day consumption data). For FD&C Yellow 5 and FD&C Yellow 6, consumption was as high as 5.5 mg and 6.2 mg on average, and 12.7 mg and 14.2 mg at the 90th percentile, respectively. In contrast, an amount equal to each ADI for a three-year-old child weighing 15 kg would total 330 mg for Mix A and 270 mg for Mix B.

For all these reasons, we respectfully request a retraction of this deeply misleading study.

Sincerely,

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