August 28, 2008

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Dockets 2005P-0282 (health notices on soft drinks);
99P-2630 (added-sugar DV and labeling)

Dear Sir or Madam:

Several years ago CSPI submitted petitions to the FDA concerning setting a Daily Value for added sugars (filed August 3, 1999) and requiring health notices on soft drink labels (filed July 13, 2005). We would like to provide information about research that has been conducted and expert opinions expressed since we submitted our petitions. The new information underscores the need for a Daily Value for added sugars and health notices on labels of nonalcoholic caloric beverages.

**Dietary Guidelines for Americans**

The information and recommendations in the 2005 Dietary Guidelines for Americans should be considered when the FDA evaluates CSPI’s 1999 petition calling for setting a Daily Value (DV) for refined sugars.\(^1\) The Guidelines express concern that foods, such as soft drinks, adversely affect nutritional status:

> Individuals who consume food or beverages high in added sugars tend to consume more calories than those who consume food or beverages low in added sugars; they also tend to consume lower amounts of micronutrients. Although more research is needed, available prospective studies show a positive association between the consumption of calorically sweetened beverages and weight gain. For this reason, decreased intake of such foods, especially beverages with caloric sweeteners, is recommended to reduce calorie intake and help achieve recommended nutrient intakes and weight control.\(^2\)

Importantly, the Guidelines notes that someone eating a healthy 2,000-calorie diet (with 29 percent of calories from fat) has room for only 8 teaspoons of added sugars per day.\(^3\)

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\(^1\) Generally, we ask that the FDA apply all the evidence presented in our 2005 petition to the 1999 petition.


That is similar to the 10-teaspoons-per-day amount that the U.S. Department of Agriculture has been recommending for over a decade.\(^4\)

Those strong statements in America’s basic nutrition policy argue strongly for setting a DV for refined sugars and adding a line to the Nutrition Facts label for the amount and percent-DV of those sugars in a serving of food.

**Institute of Medicine report on Dietary Reference Intakes for macronutrients**

The Institute of Medicine published a report on the health effects of macronutrients. The report states that levels of added sugars equal to 25 percent of calories or greater begin to displace intake of needed vitamins and minerals. The report advises:

> Based on the available data, no more than 25 [percent] energy from added sugars should be consumed by adults. A daily intake of added sugars that individuals should aim for to achieve a healthy diet was not set.\(^5\)

Some food-industry officials (and others) have characterized the IOM as concluding that any level of added sugars under 25 percent of calories is safe. The president of the Institute of Medicine sought to dispel that misinterpretation of the IOM report by advising the Secretary of the Department of Health and Human Services:

> This language is not meant to convey a desirable or even acceptable standard intake. The report states that persons whose intake of added sugars is 25% or more of total calories are more likely to have poorer intakes of important essential nutrients. It does not address the issue that added sugar intakes at 25% or even well below it, may well have significant implications for caloric balance and weight control. Interpretations suggesting that a sugar intake of 25% of total calories is endorsed by the Institute’s report are incorrect.\(^6\)

**Institute of Medicine report on school snacks**

In 2007 the Institute of Medicine published a report that made recommendations on the nutritional quality of snacks sold in schools.\(^7\) It concluded:

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\(^4\) USDA. The Food Guide Pyramid. Home and Garden Bulletin No. 252, Oct. 1996. USDA has recommended that people eating 1,600 calories a day eat no more than six teaspoons a day of refined sugars, 12 teaspoons for those eating 2,200 calories, and 18 teaspoons for those eating 2,800 calories (from 6 percent to 10 percent of calories). By interpolation, a 2,000-calorie diet should contain up to 10 teaspoons of sugars.


Limiting foods high in added sugars is recommended because of its association with increased calorie consumption and decreased intake of micronutrients. Decreases in micronutrient intake are strongest when added sugars exceed 25 percent of the total caloric intake. Although the committee concluded that the ideal recommendation for added sugars would be one that limits them to no more than 25 percent or less of total calories, such a recommendation for sugars could not be operationalized at this time because manufacturers are not required to list added sugars as part of the nutrition facts panel…. It should be noted that the committee considered setting the added sugars limit at 10 percent for individual foods, but it was determined that a 25-percent limit, with the exception of dairy products, would be more easily achieved, while still contributing to improvement in the eating patterns of school-age children….

It further noted that labeling added sugars on packages would help schools identify foods with less than a given amount of added sugars:8

Alternatively, USDA may want to establish guidelines for snacks and beverages that include requiring manufacturers to provide added sugars information as part of the product nutrient profile.

Because of its concerns about children’s consumption of calories, especially from added sugars, the committee recommended that beverages, except for flavored milks not contain added sugars at all.9

**Centers for Disease Control and Prevention publications on beverages**

The Centers for Disease Control and Prevention (CDC) has been concerned about the soaring rates of obesity, especially in youths. Two CDC publications remind readers that beverages are a major source of calories for some people and likely contribute to obesity. People trying to maintain or lose weight, CDC advises, should “choose water, diet, or low-calorie beverages instead of sugar-sweetened beverages” and should not “‘stock the fridge’ with sugar-sweetened beverages.”10 In a review of studies on beverage intake and weight, CDC concludes that “Although more studies need to be conducted in this area, these findings suggest that reducing the intake of sugar-sweetened beverages might be one strategy to help people manage their weight.”11 The same pamphlet advises people to “replace sugar-sweetened beverages with water or low-calorie beverages.” All in all, CDC is clearly concerned about over-consumption of sugar-sweetened beverages. The relief recommended in CSPI’s petitions would help motivate consumers to adhere to CDC’s advice.

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8 Ibid.
9 Op cit. Summary S-5 Table S-1. P. 5.
10 Centers for Disease Control and Prevention. Rethink your drink. (undated; ca. 2006)
11 Centers for Disease Control and Prevention. Does drinking beverages with added sugars increase the risk of overweight? Research to practice series, No. 3. (Sept. 2006)
Diabetes

Consumption of non-diet soft drinks and non-diet fruit “drinks” was correlated with diabetes in a cohort of almost 50,000 African American women. The more of those beverages that the women consumed, the greater the incidence of diabetes. Consuming two or more soft drinks per day was associated with a 24 percent chance of developing diabetes compared to women who drank less than one drink per day. For consumption of non-diet fruit drinks, the percentage was 31 percent.

The American Diabetes Association, an organization whose members have a vital interest in food labeling, (April 28, 2008) filed comments on the FDA’s Federal Register notice concerning the revision of reference values and mandatory nutrients on food labels {Docket No. FDA-2008-N-0040). The ADA emphasized that:

Foods high in added sugars (such as soda and sweets) are nutritionally inferior to foods high in naturally occurring sugar (such as fruit and milk)…. ADA suggests establishing a Daily Reference Value for added sugars to help guide consumers in choosing the most nutrient dense carbohydrate-containing foods. It would also be deemed acceptable to list only “added sugars” in place of “sugars” on the label. Adding information on “added sugars” will assist consumers in following the guidance of the USDA Food Guide as well as the US Dietary Guidelines.

Nutrition

A 2007 systematic review and meta-analysis of studies on soft drinks by researchers at the Yale University Department of Psychology found associations between non-diet soft drink consumption and several parameters. One of the most consistent and powerful findings is the link between soft drink intake and increased calorie consumption….Noteworthy are findings from several studies that soft drink intake is associated with a larger level of calorie consumption than can be accounted for by the soft drinks themselves….One of the most consistent and powerful findings is the link between soft drink intake and increased energy consumption. Fully 10 of 12 cross-sectional studies, 5 of 5 longitudinal studies, and all 4 of the long-term experimental studies examined showed that energy intake rises when soft drink consumption increases.

That review found smaller positive associations between soft drink consumption and BMI (body mass index) and lower consumption of milk, fruit, and dietary fiber. They cited a large, eight-year-long study of 91,249 women, saying that soft-drink consumers

(one or more servings per day) “were at twice the risk of developing diabetes as those who consumed less than one serving per month.”

A British review of associations between consumption of added sugars and micronutrient intake highlighted the difficulties of pinning down such associations. Food fortification and underreporting of intake of foods rich in sugars are two factors that complicate research. The review did not find any “clear or consistent indications of micronutrient dilution,” but recognized that the evidence “does not support any advantages in terms of micronutrient intake for the highest consumers of added sugars.”

An analysis of NHANES data for 2001-02 confirms that nonalcoholic beverages continue to provide a large percentage of refined sugars consumed by Americans. Those beverages provide 52 percent of all added sugars and 8.7 percent of total calories.

**Weight gain and obesity**

A growing body of evidence has associated soft drink consumption with increased weight gain.

- A 2006 review by researchers at the Harvard School of Public Health of various kinds of studies on sweetened beverages and weight loss found a strong relationship. They concluded that:

  In this systematic review, findings from several large cross-sectional investigations, well-powered prospective cohort studies with long follow-up and repeated measures of diet and weight, a school-based intervention targeting soda consumption, and an RCT assessing the effect of reducing sweetened beverage consumption have provided strong evidence for the independent role of the intake of sugar-sweetened beverages, particularly soda, in the promotion of weight gain and obesity in children and adolescents. Findings from prospective cohort studies conducted in adults, taken in conjunction with results from short-term feeding trials, also support a positive association between soda consumption and weight gain, obesity, or both.

  They suggested that the mechanism likely to be responsible for the weight gain is the body’s inadequate compensation for calories consumed in liquid form. The authors recommended that “Given that global incidence rates of overweight and

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obesity are on the rise, particularly among children and adolescents, it is imperative that current public health strategies include education about beverage intake,” such as what CSPI’s 2005 petition for health notices on packages recommended.

- A creative intervention pilot study by Ebbeling, et al., for 25 weeks provided free non-caloric beverages to displace sugar-sweetened beverages in the homes of adolescents.\(^{17}\) That simple intervention almost completely eliminated consumption of caloric soft drinks. Daily energy intake in the intervention group decreased significantly. In participants with an initial high BMI, the net BMI change at the end of the study was -0.75 units. Perhaps because of the small number of participants, the results were not statistically significant, but the study was consistent with other research.

- A longitudinal study of more than 3,000 black and white girls monitored beverage consumption between the ages of 9.5 and 18.6.\(^{18}\) The study found steadily decreasing milk consumption and increasing non-diet soda consumption. The researchers concluded that “Of all beverages, increasing soda consumption predicted the greatest increase of BMI and the lowest increase in calcium intake. Fruit drinks, which are essentially non-carbonated sodas, showed similar, but not significantly significant correlations with obesity and calcium intake. Further, the authors recommended “public health efforts…to promote healthful beverage choices and decreased soda consumption in adolescent girls….A concerted effort will be required by governmental institutions…to counteract the strong influence of the ‘toxic food environment’ in promoting sugar-sweetened and diet beverages.”

In commenting on that study, William Dietz, the director of the Division of Nutrition and Physical Activity of the Centers for Disease Control and Prevention, recommended “changing the environment” to promote healthier beverage choices.\(^{19}\) Setting a DV for refined sugars, listing refined sugars and the percent DV on Nutrition Facts labels, and requiring warning labels on non-diet soft drinks would be ways in which the FDA could help change the environment.

- The Yale review and meta-analysis noted above found “7 studies that examined the connection between soft drink intake and body weight in an experimental or intervention context. Five reported a positive association.”\(^{20}\) The researchers expressed surprise “that a single source of energy can have such a substantial

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impact on total energy intake. This finding alone suggests that it would be prudent to recommend population decreases in soft drink consumption.”

• A 2007 Joint FAO/WHO Scientific Update on Carbohydrates in Human Nutrition reviewed studies on the relationship between sugar-sweetened beverages and weight.21 It concluded:

Although long-term randomized controlled trials of sugar-sweetened beverages are lacking, evidence from short-term blinded randomized controlled trials, medium-term non-blinded randomized trials, and long-term prospective cohort studies indicates that reduction of consumption of sugar-sweetened beverages is beneficial for weight management.

The FAO/WHO committee as a whole affirmed, “Thus, there is justification for the recommendation to restrict the consumption of beverages high in free sugars to reduce the risk of excessive weight gain….Thus, the outcomes of the Scientific Update support the population nutrient intake goals on free sugars (that is, <10% of total energy) that were recommended by the 2002 WHO/FAO Expert Consultation (WHO, 2003).”22

• Consumption of non-diet soft drinks and non-diet fruit “drinks” was correlated with weight in a cohort of almost 50,000 African American women.23 Women who increased their consumption of those beverages increased over the observation period gained more weight than women who decreased their consumption. Also, a smaller percentage of women who consumed those beverages lost weight.

On the other hand, researchers at Archer-Daniels-Midland, a producer of high-fructose corn syrup (HFCS), analyzed several food-consumption studies sponsored by USDA (CSFII) and HHS (NHANES) and did not find any correlation between consumption of sugar-sweetened beverages and overweight or obesity.24 (However, this kind of study does not account for overweight people who might have switched from non-diet sodas to diet sodas, water, and other low-calorie beverages.) The authors cite other studies that support their finding and critique studies that found associations between consumption of sugar-sweetened beverages and weight gain and overweight or obesity.

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Another study examined beverage intake by preschool children.\textsuperscript{25} No correlation was found between soda consumption and BMI, but only 39 percent of those children consumed soda and the average child only consumed several ounces of soda per day. Thus, adding in measurement errors, the study was unlikely to be powerful enough to detect any effect of soda on weight. A British study, funded by the UK Sugar Bureau and European Soft Drinks Association, found excess risk of overweight associated with soft drink consumption, but that was only significant at the top quintile of consumption.\textsuperscript{26} The study’s sensitivity was less than several other studies, because young children (who drink relatively little soft drinks) were mixed in with older children and soft drink consumption in Britain is substantially less than half\textsuperscript{27} that in the United States.

**Metabolic syndrome**

- An eight-year-long longitudinal study of 154 girls sought to identify causes of metabolic syndrome, which is characterized by raised blood pressure, low levels of high-density lipoproteins, high blood triglyceride and glucose levels, and increased weight circumference.\textsuperscript{28} The authors examined correlations between numerous dietary elements and risk of dyslipidemias and other conditions. “The only significant difference” among the several risk groups “was in sweetened beverage intake….No consistent differences among the MetS [metabolic syndrome] risk groups were found for intakes of any other macronutrient, micronutrient, or food group or in meal and snack frequency.” The authors concluded that “the higher metabolic syndrome risk group consumed significantly more servings of sweetened beverages during childhood….This pattern suggests the possibility that consistently high intake of sweetened beverages early in life may constitute a risk factor for excessive weight gain and increased MetS risk.”

- The Framingham Heart Study has evaluated correlations between soft-drink consumption and metabolic syndrome in middle-aged adults.\textsuperscript{29} At the beginning of the study, frequent consumers of soft drinks had a higher incidence of metabolic syndrome, diabetes, dyslipidemias, and other adverse health parameters. In the course of the four-year follow-up, consumption of one or more soft drinks per day was associated with statistically significant increases in metabolic syndrome, obesity, greater waistline, and dyslipidemias. (Surprisingly, the study found that consumption of both regular and diet sodas correlated with

\textsuperscript{27} 2005 All-channel carbonated soft drink corporate shares in 95 countries. Beverage Digest. Sept. 22, 2006.
increased incidence of metabolic syndrome. The researchers speculated that diet soda’s correlation with metabolic syndrome, if real, might have been due to minor ingredients (such as caramel) in diet and regular soda. It is possible that dietary or other behaviors common to drinkers of both diet and regular sodas (such as frequent snacking, lower consumption of fiber, sedentary lifestyle, etc.) were not adequately controlled for in the models.)

Pancreatic cancer

Recent epidemiology studies have found mixed evidence on whether added sugars and/or regular soft drinks promote pancreatic cancer. Though a controlled clinical test of this hypothesis cannot be conducted, less-definitive epidemiologic evidence is of interest.

- Schernhammer et al. examined the possible relationship between soft drink consumption and pancreatic cancer in two large prospective cohorts. They found a “modest but significant increase in risk” among women, but not men. The risk was greater for women who had a BMI greater than 25 and for those who engaged in relatively little physical activity. Virtues of this study are the 20-year follow-up and updating of dietary intakes.
- Larsson et al. conducted a long-term study of almost 80,000 Swedish women, of whom 131 had developed pancreatic cancer over seven years. The highest-consuming quartile of soft-drink consumers had twice the risk of pancreatic cancer compared to the lowest-consuming quartile. The researchers suggest possible mechanisms, including increased levels of insulin and also toxic effects of glucose on the pancreatic islet.
- In contrast, the most recent large cohort study, by Bao and colleagues, did not find a positive association between total added sugars or regular soft drinks and pancreatic cancer.

Overall, these studies suggest the possibility that added sugars or regular soft drinks promote cancer of the pancreas. At the very least, they indicate the need for longer (e.g., the follow-up period in the Bao study was only 7.2 years; ideally, dietary assessments would begin in childhood) and more detailed (e.g., more frequent dietary assessments) studies. They also suggest that moderation in consumption of added sugars and non-diet soft drinks would be wise.

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Bone Density

In a study of over 2,500 men and women in the Framingham Osteoporosis Study, consumption of cola beverages was associated with lower bone density in women, but not men. Women who drink one cola a day had a 4 to 5 percent lower hip (but not spine) bone density than women who drank less than one cola per month. Non-cola soft drinks were not associated with lower bone density, though that might be because so few women drank many non-cola drinks. The cause for reduced bone density is unclear, because neither caffeine nor phosphoric acid appeared to explain the link. The lead author said, “Women concerned about osteoporosis may want to steer away from frequent consumption of cola until further studies are conducted.”

Kidney Disease

A preliminary case-control study correlated consumption of colas, but not other soft drinks, with chronic kidney disease. The researchers note that colas are typically acidified with phosphoric acid, while non-cola soft drinks are often acidified with citric acid. While a previous study had linked colas to kidney stones, the new study had two few cases of kidney stones to draw meaningful conclusions.

Gout

While Dr. William Osler prescribed low-fructose diets to prevent gout 100 years ago, little research has been done on the issue. Recently, researchers used the Health Professionals cohort of over 46,000 men to test Osler’s hypothesis. The researchers found that, after controlling for a range of dietary and other factors, consumption of non-diet soft drinks, total fructose, and fructose-containing fruit were all strongly correlated with increased risk of gout, with relative risks even exceeding 2.0. The relative risk of consuming one or more non-cola, non-diet soft drinks per day was 2.76 compared to consuming such beverages less than once a month.

Some of the same researchers also examined the relationship between soft drink consumption and serum uric acid levels, because high uric acid levels are related to occurrence of gout (which is characterized by uric acid crystals). Using data from the NHANES III survey, the researchers found that increasing non-diet soft drink

consumption was associated with a monotonic increase in uric acid levels and the incidence of hyperuricemia. Diet soda consumption did not correlate with changes in uric acid levels.

While those two studies do not prove that fructose causes gout, they are strongly suggestive and add to other concerns about fructose, sucrose, HFCS, and soft drinks.

**Beverage Guidance**

Most dietary guidelines do not distinguish between foods and beverages. Because of the special roles that beverages, including caloric carbonated and noncarbonated soft drinks, whole and reduced-fat milk, and alcoholic beverages, a team of researchers, with funding from Unilever, proposed appropriate daily consumption levels of various beverages.\(^{39}\) The “Beverage Guidance Panel” “suggested” an overall intake of 10 percent of calories from beverages, with 0 to 8 ounces daily coming from calorically sweetened beverages without nutrients (soft drinks). The panel’s “acceptable” consumption of 14 percent of calories from beverages recommended the same amount of soft drinks.

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The Center for Science in the Public Interest appreciates the FDA’s interest in reducing the adverse health consequences due to excessive consumption of soft drinks and added sugars.

Sincerely,

Michael F. Jacobson, Ph.D.
Executive Director

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