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RE: Comments on Sodium, Low-Calorie Sweeteners, Stearic Acid, Fructose, and Added Sugars and Fiber from ILSI North America

Dear Dr. Olson and Ms. Rihane,

The North American Branch of the International Life Sciences Institute appreciates the opportunity to share ILSI North America supported scientific research, published recently by experts in nutrition research, dietary assessment, and epidemiology. ILSI North America is a public, non-profit organization that actively collaborates with government and academia to identify and resolve scientific issues important to the health of the public. The organization carries out its mission by sponsoring relevant research, professional education programs and workshops, seminars and publications, as well as, providing a neutral forum for government, academic, and industry scientists to discuss and resolve scientific issues of common concern for the well-being of the general public.

The research summarized here addresses potential benefits, as well as, realistic approaches to diet patterns aligned with the two "overarching concepts" articulated in the *Dietary Guidelines for Americans 2010* (namely, "maintain calorie balance over time to achieve and sustain a healthy body weight" and "focus on consuming nutrient-dense foods and beverages") [1]. These over-arching priorities remain highly relevant to the scientific evaluations currently being conducted by the 2015 Dietary Guidelines Advisory Committee (DGAC 2015) [2]. ILSI North America's Sodium, Low-Calorie Sweeteners, Dietary Lipids, and Carbohydrates Committees supported the work forming the basis of the comments provided here.

1) Sodium intake in the context of overall dietary patterns: Health outcomes related to sodium intake continue to prove to be a multi-factorial problem. The work by ILSI North America on sodium intake indicates that overall quality of the diet is more effective in improving health outcomes compared to restricting sodium to low levels [3,4,5].

2) <u>Calorie Balance:</u> Scientific evidence from a recently completed, comprehensive meta-analysis of randomized clinical trials shows the potential of low-calorie sweetened foods and beverages in helping maintain calorie balance [6].

3) <u>Stearic acid health effects:</u> Stearic acid and oleic acid have comparable effects on markers of hemostasis [7].

4) <u>Fructose consumption and fatty liver disease:</u> From a recently completed systematic review and meta-analysis, there is a lack of evidence that fructose consumption has any different effect on non-alcoholic fatty liver disease than any other monosaccharides at typical intake levels [8].

5) <u>Added sugars and fiber</u>: Evidence does not support differentiating naturally present, as compared to “added” sugars and fibers [9-12].

Summary of New Evidence

1) <u>Sodium intake in the context of overall dietary patterns</u>

The *Dietary Guidelines for Americans 2010* states that the sodium goal is to “reduce daily sodium intake to less than 2,300 milligrams and further reduce intake to 1500 milligrams per day among persons who are 51 and older and those of any age who are African American or have hypertension, diabetes, or chronic kidney disease, which includes about half of the U.S. population” [1]. However, foundational studies show the world-wide range of mean sodium intake, as measured by 24-hour urinary sodium concentration from 190 datasets, is 2,622–4,830mg/d, and is determined by physiological needs [13]. In the United States, reaching an intake of 1,500 milligrams/day would require reduction in mean sodium intake of 50% among women and 67% among men [3] and thus, based on current mean intake levels, presents a significant challenge for effective single-nutrient interventions.

In contrast to the recommendations within the 2010 DGAs, sodium intakes ≤2300 mg/day have not been shown to improve health outcomes as demonstrated by the IOM report, “Sodium Intake in Populations: Assessment of Evidence”, released in 2013 [14]. Work, also in line with ILSI North America’s findings, (published in *Hypertension*) indicates that following the DASH diet, rich in fruit and vegetables, is effective at decreasing blood pressure and managing hypertension, even at 3000 mg/day of sodium, well above the currently recommended intake level [15].

The following evidence summarized from recently published, ILSI North America sponsored research highlights the importance of the overall quality of the diet, while taking into consideration sodium intake and its balance with other nutrients, when attempting to improve health outcomes.

- **“Food pattern modeling shows that the 2010 Dietary Guidelines for sodium and potassium cannot be met simultaneously”** [4]

Modeling sodium and potassium targets simultaneously based on U.S. diet patterns shows challenges in meeting lower sodium and higher potassium goals. “The theoretical feasibility of meeting sodium and potassium guidelines while simultaneously maintaining nutritional adequacy of the diet was tested using food pattern modeling based on linear programming…" and dietary data from the National Health and Nutrition Examination Survey 2001-2002. Dietary patterns for six age, gender sub-groups and modeling scenarios were evaluated before and after an across-the board 10% reduction in sodium content of all foods in the Food and Nutrition Database for Dietary Studies.

- "The 2300-mg/d sodium guideline was theoretically compatible with the potassium guidelines (4700 mg/d) for all sex-age groups." Notably, "…women older than 50 years could reach the 4700-mg/d potassium goal only at the maximum level of sodium. For the remaining women and younger men, only a few Na-K combinations were compatible with nutritionally adequate diets…"

- "The 1500-mg/d sodium guideline was theoretically compatible with the potassium guideline (4700 mg/d) only for men older than 50 years and no other group…"

- Across-the-board 10% Na reduction in the food database "had minimal impact on the low energy food patterns. The feasibility of reaching the sodium goals by women was not affected. By contrast, the reduction in sodium content of the food supply led to food patterns for men that were significantly reduced in sodium content; however, the sodium and potassium guidelines could not be met simultaneously."

- The authors concluded: "If the level of sodium is set too low, the other nutrient requirements cannot be met; hence the sodium goal becomes incompatible with nutrient-adequate diets." And 10% across-the-board reduction in the food supply "proved to be ineffective."

➢ **"Sodium to potassium ratio and food choices of U.S. adults"** [5]

The health benefits of maintaining an appropriate ratio of sodium to potassium through a balanced dietary pattern have been demonstrated repeatedly. Analysis of current U.S. diets illustrates the importance of nutrient dense food choices to achieve lower sodium to potassium ratios in the U.S. population.

- Fewer than 2% of adults met the recommended Na/K ratio of 0.49 (based on 2300 mg Na/4700 mg K), in NHANES 2007-2010. Mean Na/K ratio was 1.5 (SEM 0.01) for adult men and 1.4 (SEM 0.01) for adult women.

- "Among individuals with Na/K <1.0 vs. Na/K ≥1.0, milk and dairy foods contributed 8% vs. 6% of daily Na and 12% vs. 9% of daily K." Note that consumers with lower Na/K ratios (<1.0) had higher percent of both Na and K intakes from milk and dairy foods, compared to consumers with higher Na/K ratios. Because nutrient dense milk and dairy foods contributed importantly to potassium intakes, the individuals' overall dietary Na/K intake ratio was better, even though milk and dairy foods contributed a relatively greater portion of sodium to their diet compared to consumers with high Na/K ratios.

- Similarly, "…fruit and vegetables contributed 12% vs. 6% of total daily Na and 25% vs. 18% of daily K, respectively for individuals with Na/K <1.0 vs. Na/K ≥1.0."

- The authors state, "These data highlight the importance of food choices to achieve improved sodium to potassium ratios in the U.S. population."

In summary, recent evidence aligns with past studies to show the importance of dietary patterns, such as DASH, and the consumption of nutrient dense food to improve health outcomes, and promote overall health.

2) <u>Calorie Balance: Low calorie sweeteners offer potential to help manage body weight, BMI, fat mass, and waist circumference.</u>

- **"Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies"** [6]

Maintaining calorie balance is an issue for the majority of Americans, regardless of age [1]. In a recent comprehensive meta-analysis by Miller and Perez, evidence from 15 randomized clinical trials (RCT) indicates that substituting low-calorie sweeteners (LCS) for regular-calorie versions "results in a modest weight loss, and may be a useful dietary tool to improve compliance with weight loss or weight maintenance plans" [6]. Evidence from the body of RCT's is particularly important since it differs from observed associations in prospective studies among free-living, self-selecting subjects. In the observational studies (n=9), which lack randomization, it is not possible to completely adjust for the multiple biases and confounding factors associated with self-selecting LCS.

For this meta-analysis, low-calorie sweeteners included nonnutritive and bulk sweeteners used in foods, beverages, tabletop or experimental capsule. Details on the study inclusion criteria, data extraction, and data analysis can be found in the full manuscript, which was published online June 18, 2014 in the *American Journal of Clinical Nutrition*. Pooled summary estimates are expressed as weighted group mean differences for the RCT and weighted group mean correlation for the prospective observational studies.

- Among randomized clinical trials (n=15), low calorie sweeteners reduced body weight (weighted group mean differences - 0.80 kg, 95% CI: -1.17, -0.43) relative to the comparator arm, BMI (-0.24 kg/m2, 95% CI: -0.41, -0.07), fat mass (-1.10 kg, 95% CI: -1.77, -0.44), and waist circumference (-0.83 cm, 95% CI: -1.29, -0.37). All were statistically significant at the $p<0.05$ level (as shown by the 95% CI).

- Results were directionally similar when stratified by children and adults. For example, body weight change among children was -1.06 kg (95% CI: -1.57, -0.56) and among adults -0.72 kg (95% CI: -1.15, -0.30).

- In contrast to randomized trials, prospective observational studies (n=9) among free-living subjects showed self-selected LCS use at baseline was not associated with fat mass, was modestly associated with positive change relative to the comparator arm in BMI (weighted group mean correlation 0.03, 95% CI: 0.01, 0.06) and directionally, but not statistically, for weight gain (0.02, 95% CI: -0.01, 0.06).

In summary, this meta-analysis shows that had prospective studies (with un-accounted for residual biases and confounding factors) been used as evidence for dietary guidance, the conclusions may have missed the potential benefit on body weight and composition shown in randomized clinical trials. Differing results are also suggestive that advice related to consumer behavior may be relevant to reinforce that LCS be used in replace of higher calorie options, in order to realize the demonstrated potential to help maintain calorie balance for weight management. Based on findings from the meta-analysis of randomized clinical trials, Miller and Perez state that the findings “provide suggestive evidence that LCS do not, contrary to past hypotheses, increase the desire or inclination to consume more sweet foods.”

3) <u>Stearic acid health effects: Stearic acid and oleic acid have comparable effects on markers of hemostasis.</u>

➢ **“Impact of stearic acid and oleic acid on hemostatic factors in the context of controlled diets consumed by healthy men”** [7]

Since the publication of the first edition of the Dietary Guidelines for Americans, it has been understood that stearic acids have a neutral effect on serum lipids. However, questions on stearic acid’s effect on thrombosis still persist. As dietary guidance and regulations have promoted limiting *trans* fat intake, there is a need for *trans* fatty acid alternatives and stearic acid may be a viable alternative due both to its physical characteristics, as well as its neutral or beneficial cholesterolemic effects compared to other saturated or *trans* fatty acids. Data from a recently published randomized crossover study [7], responds directly to a request made in the 2010 Dietary Guidelines Advisory Committee Report which addresses the need for more research on metabolic effects of stearic acid, particularly when replaced for unsaturated fatty acids in the diet. The outcome measures of hemostasis included: factor VII which has a major role in thrombus formation, plasminogen activator inhibitor-1 (PAI-1) the major regulator of fibrinolysis, and plasmin alpha-2-antiplasmin complex (PAP) a marker of activation of the fibrinolytic system. This study offers the following messages:

- “Stearic acid and oleic acid had a similar impact on the plasma concentration of factor VIIc, PAI-1 and PAP.”
- Even at consumption at “high amounts (≥ 10% of energy), there was no evidence of adverse effects of stearic acid on the hemostatic factors reported herein.”
- “Overall, data from controlled studies suggest that intake of [stearic acid] STA, in amounts as high as 9% of energy and potentially up to 14% of energy, results in little or no adverse effect on hemostatic risk factors.“

In summary, these data on markers of hemostasis, along with previously published results on lipids and inflammation demonstrate that stearic acid and oleic acid had comparable effects on markers of hemostasis and stearic acid is a suitable and perhaps more healthful replacement for *trans* fatty acids in food applications.

4) **<u>Fructose consumption and fatty liver disease: There is a lack of evidence that fructose consumption has any different effect on non-alcoholic fatty liver disease than any other mono-saccharides at typical intake levels.</u>**

➢ **"Fructose, high fructose corn syrup, sucrose, and nonalcoholic fatty liver disease or indexes of liver health: a systemic review and meta-analysis"** [8]

Total sugar consumption in regards to calorie intake is a subject of continued discussion, but potentially of greater concern is the discussion that various monosaccharides disproportionately contribute to negative health outcomes. Concerns have been raised about the concurrent temporal trend between simple sugar intakes, especially of fructose or high fructose corn syrup (HFCS), and rates of nonalcoholic fatty liver disease (NAFLD) in the United States. ILSI North America commissioned this review and analysis to examine the effect of different amounts and forms of dietary fructose on the incidence or prevalence of NAFLD and indexes of liver health in humans.

The evidence-based review of the published literature shows a lack of evidence that fructose consumption has any different effect on nonalcoholic fatty liver disease than any other monosaccharides at typical intake levels. Indeed the data point to confounding of any health outcome effects by overconsumption of total sugars in most trials.

In summary, the authors stated: "[o]n the basis of indirect comparisons across study findings, the apparent association between indexes of liver health … and fructose or sucrose intake appear to be confounded by excessive energy intake" [8]. Specific indexes of liver included: liver fat, hepatic de novo lipogenesis, alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transpeptase. Therefore, they concluded: ''overall, the available evidence is not sufficiently robust to draw conclusions regarding effects of fructose, HFCS, or sucrose consumption on NAFLD."

5) **<u>Added sugars and fiber: Evidence from published papers does not support differentiating naturally present sugars and fibers as compared to "added sugars" or "added fiber."</u>**

➢ **"Added sugars" are not distinguishable structurally from those occurring naturally in a food and evidence does not support differentiating by health benefit** [9, 10]

Dietary Guidelines for Americans 2010 has a strong focus on differentiating naturally present sugars from those "added" to food. It does so despite concluding that "[a]lthough the body's response to sugars does not depend on whether they are naturally present in foods or added to foods, sugars found naturally in foods are part of the food's total package of nutrients and other helpful components. In contrast, many foods that contain added sugars often supply calories, but few or no essential nutrients and no dietary fiber" [1]. Focusing on a single source of carbohydrate adds unnecessary complexity and detracts from the emphasis on holistic diet patterns for which "[s]trong evidence shows that eating patterns that are low in calorie density improve weight loss and weight maintenance, and also may be associated with lower risk of type 2 diabetes in adults" [1].

- In a 2012 overview of global dietary guidelines for sugars, the authors concluded: "Clearly, excess energy intake in any form results in weight gain; therefore, moderating sugar intake so as to not exceed daily energy requirements can help to reduce the risk for obesity. It is not clear, however, if diets lower in added sugars necessarily result in better or more balanced diets based on currently available scientific evidence" [9].

- To address the issue of whether added sugars leads to unbalanced micronutrient intakes, ILSI NA sponsored a project to update data on intakes of selected micronutrients at 5% increments of added sugars (from 0 to >35% of energy intake) using NHANES 2003–2006 data [10]. As reported in the publication:
  - "Nutrient intake was less with each 5% increase in added sugars intake above 5-10% [of energy intake]."
  - "Higher added sugars intake were associated with higher proportions of individuals with nutrient intakes below the [Estimated Average Requirement] EAR, but the overall high calorie and low quality of the U.S. diet remained the prominent issue."
  - The authors concluded that "[h]igh levels of added sugars intake occur among only a small proportion of the population and cannot explain the existing problem of poor nutrient intake in the U.S. population as a whole."

➢ **Regardless of whether fiber is "added" or naturally occurring, it has potential to provide a range of beneficial physiologic effects** [11-12]

Although the *Dietary Guidelines for Americans 2010* states: "Fiber is sometimes added to foods and it is unclear if added fiber provides the same health benefits as naturally occurring sources" [1], evidence does not support this broad generalized statement.

- At the 2010 Vahouny Symposium on Dietary Fiber, global fiber experts met to build scientific agreement on the scientific definition of fiber. Three categories of fiber were recognized, including "those occurring naturally in food as consumed; those obtained from food raw material by physical, enzymatic, or chemical means; and those that are synthetic in origin", with the latter two categories requiring a demonstrated physiologic benefit to health. Additionally, they readily agreed that some specific health endpoints are well-established physiologic effects attributed to fiber (e.g., reduced blood total cholesterol and blood pressure). The experts also agreed that "substantiation of the beneficial nature of any proposed effects is a case-by-case basis in relation to the individual food ingredient" [11].

- In 2013, Dilzer et al. summarized physiologic benefits associated with fiber and aligned them with credible global authoritative health organizations that recognize various physiologic benefits [12]. Moreover, the authors concluded that scientific findings "suggest that increasing intake of fiber-containing foods may offset energy balance, but adding fiber to foods may improve alignment with current dietary guidelines [that] emphasize calorie control for weight maintenance." And finally, they point out the challenges of "counseling for behavior change to replace low-fiber foods with higher-fiber foods"; making the case that adding fiber to foods is a relevant means to increase fiber intakes.

In summary, focusing on single dietary components, like added sugars and added fiber, lack substantial supportive evidence and may distract from the simple dietary guidance to choose a diet pattern low in caloric density characterized by high intake of vegetables, fruits and dietary fiber.

In conclusion

Recently published and presented scientific evidence summarized herein: supports the importance of dietary patterns, such as DASH, and the consumption of nutrient dense food to improve health outcomes rather than multiple single-nutrient health outcome approaches; demonstrates the potential benefit of substituting low-calorie sweeteners for regular calorie sweeteners to maintain calorie balance; shows that intake of stearic acid results in little or no adverse effect on hemostatic risk factors; provides a perspective showing insufficient evidence to conclude effects of high fructose corn syrup or sucrose on nonalcoholic fatty liver disease, and addressed lack of evidence and complexity of differentiating natural versus added sugars and fibers.

The ILSI North America Sodium, Low-Calorie Sweeteners, Lipids, and Carbohydrates Committees appreciate the opportunity to provide evidence for consideration by the Committee.

Sincerely,

Eric Hentges, Ph.D.
Executive Director
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Enclosures: References 6-8 (others available through hyperlinks).

References

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