ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

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Margaret A. Hamburg, M.D.
Commissioner, U.S. Food and Drug Administration
C/O Division of Dockets Management (HFA–305)
5630 Fishers Lane, Rm. 1061 Rockville, MD 20852

Re: Proposed Rule for FDA 21 CFR Part 101: Food labeling: Revision of the Nutrition and Supplement Facts Labels

Dear Commissioner Hamburg:

The American Society of Nephrology (ASN), the world's leading organization of kidney health professionals, represents nearly 15,000 health professionals who are dedicated to treating and studying kidney disease and to improving the lives of patients affected by kidney disease. ASN appreciates the opportunity to provide comments on the *FDA Food labeling Revision*. ASN is a not-for-profit organization dedicated to promoting excellence in the care of patients with kidney disease. Foremost among ASN's concerns is the ease of use and safety of food labels for the more than 20 million Americans affected with kidney disease.

In summary, ASN recommends that FDA:

- Include Chronic Kidney Disease (CKD) in all lists of important chronic diseases affecting public health
- Finalize its proposal to highlight the importance of sodium in the nutritional label
- Leave potassium listed in the main content portion of the label, as opposed to moving it to the footnote list of minerals
- Make labeling of phosphorus content a mandatory part of the label
- Consider distinguishing between naturally-occurring phosphorus content versus added phosphates, similar to the proposed changes for distinguishing between naturally-occurring sugar content of food versus added sugar
- Define upper limits of tolerability and intake for phosphorus in special populations such as people with kidney disease

I. <u>1, p 11885. Rates of Chronic Disease:</u>

The proposed *FDA Food labeling Revision* lists several important chronic diseases that constitute the leading causes of death and disability in the United States, conditions that poor diet is a contributing factor associated with in term of morbidity and mortality. ASN believes that FDA should include Chronic Kidney Disease (CKD) in this list of along with cardiovascular disease, cancer, obesity and hypertension in its final rule regarding the Revision of the Nutrition and Supplement Facts Labels, and similarly highlight the significant public health burden of kidney disease in subsequent proposed rules and other documents.

Kidney disease affects more than 20 million Americans, nearly 500,000 of whom rely on lifesaving dialysis. The incidence of CKD and dialysis has been steadily increasing over the last two decades. According to the Centers for Disease Control and Prevention, kidney disease is the eighth leading cause of death, and patients with kidney disease are at a much high risk of cardiovascular disease. While the leading cause of kidney disease is diabetes, more than 50 percent of patients who require dialysis developed kidney failure due to a variety of other causes, ranging from genetic disorders to alterations in glomerular or tubular function.

The kidney is important in metabolism and regulation of many nutrients. For example, people with kidney disease are much more likely to retain sodium than people without kidney disease. Further, the kidney is involved in the homeostasis of micronutrients such as potassium, calcium, vitamin D, and phosphorus—and for the millions of Americans with kidney disease, carefully regulating consumption of these micronutrients is critical to preventing progression to kidney failure and, for those whose kidneys have failed, to maintaining the best possible health and quality of life. The nearly 15,000 health professionals who constitute ASN's membership instruct patients with kidney disease to carefully read food labels in order to avoid adverse consequences of inappropriate intake of sodium, potassium, and phosphorus. Recognizing the importance of diet in the management of kidney disease, ASN strongly recommends that FDA include kidney disease in addition to the other chronic diseases listed in this opening section in the final rule.

2. p 11886 h. Dietary Recommendations, Consensus Reports, and National Survey Data. h. IOM Sodium Intake in Populations Report.

ASN commends FDA for highlighting the importance of sodium intake on the proposed label, especially considering the significance of sodium intake to the health of people with kidney disease. As noted above, the kidney regulates sodium and water metabolism and is integrally involved in the development of hypertension. Patients with kidney disease are encouraged to reduce sodium intake to assist in managing hypertension, volume overload and edema, and the proposed changes to the label will be instrumental in empowering patients to take more control over their sodium consumption. Ultimately, this change may help improve the lives of millions of Americans with kidney disease who are working, in partnership with their nephrology health professionals, to better slow the progression of their kidney disease or minimize its effect on living a normal, healthy life.

C. Factors for Mandatory or Voluntary Declaration of Non-Statutory Nutrients. 1. Factors Considered. b. Public Health Significance.

ASN was disappointed FDA made no mention of dietary phosphorus intake in the proposed rule, and did not propose any changes to with regard to how phosphorus content is reflecting in the nutrition label. This omission is a significant missed opportunity. Phosphorus can occur naturally in the form of food, or as a component in commonly-used food additives. The kidney is responsible for the homeostasis of phosphorus through an effect of several hormones that increase the urinary excretion of phosphorus. While these mechanisms of enhancing urinary phosphorus excretion are effective in maintaining normal blood phosphorus levels until very late in the course of the progression of kidney disease, the persistent elevation of these hormones cause bone disease, heart disease, and are associated with mortality in patients with CKD.

Consequently, restricting dietary phosphorus intake is an important therapeutic strategy in patients with kidney disease. However, the increasing use of additives and the lack of mandatory labeling of phosphorus content pose significant—and often insurmountable—

challenges to patients and their families in adhering to these important recommendations. Two recent scientific meetings highlighted the importance of kidney patients' phosphorus regulation: A scientific consensus symposium sponsored by the National Kidney Foundation in 2012 (published in[1]) and a symposium at the Annual Meeting in Experimental Biology in 2013 at a session entitled "Dietary Phosphorus Excess: A risk factor in chronic bone, kidney and cardiovascular disease" sponsored by the American Society of Nutrition and American Society of Nephrology (published in[2, 3]).

Furthermore, recent studies also indicate that in patients without kidney disease, there is increased mortality in those with the highest quartile of phosphorus levels, even if those levels are within the normal range (Reviewed in [3]). ASN contends that the emerging data support phosphorus as a serious public health problem in the United States, and the society urges FDA to designate phosphorus as a mandatory, not a voluntary, listing on the nutrition label.

The proposed rules states that when FDA is determining if mandatory or voluntary labeling is indicated "First we consider whether there is evidence of a relationship between the nutrient and a chronic disease, health-related condition, or health-related physiological endpoint. Second, we consider whether there is evidence of a problem related to health in the general U.S. population." Widespread practices of processing of meat and fish products increases the phosphorus content above the naturally-occurring levels in the protein itself [8].

Studies of patients with kidney disease demonstrate that high phosphorus intake, whether in the form of additives or meat, leads to changes in hormones that are shown to be associated with mortality[4-7]. In particular, individuals that consume processed foods with phosphorus additives (most commonly in the form of sodium phosphate and its derivatives) have increased urinary sodium and phosphorus compared to similar foods without additives, indicating significant absorption of these nutrients from the additives[9]. In one study of patients on dialysis, simply instructing patients to avoid processed foods (where most additives are found) led to a reduction in blood phosphorus levels that allowed reduction in phosphate binder prescriptions[10].

Another study found that over 45% of the best-selling grocery items contained phosphorus additives[11], and these items typically cost less and are eaten more commonly in individuals of lower socioeconomic status[12]. The use of phosphate containing food additives has increased substantially over the last several years. Analyses of processed foods that contain phosphate additives indicate that these increase the food phosphorus content by 70%[13]. Analyses of meat and poultry products demonstrate that additives increase both the phosphorus and potassium intake by two to three fold, respectively[14], both leading to adverse consequences in patients with CKD.

ASN strongly recommends that FDA make labeling of phosphorus content a mandatory part of the label as opposed to a voluntary part of the label. This change would be ideally be further subdivided into natural content of phosphorus versus added phosphates, similar to the proposed changes for distinguishing between sugar content of food versus added sugar as detailed in Section II Proposed Rule, D. Carbohydrates, 2. Sugars and 3. Added Sugars (p 11902). In the Section II Proposed Rule, H. Essential Vitamins and Minerals of Public Health Significance, Essential Vitamins and Minerals that are Mandatory (p 11921) the rule discusses the role of upper limits of safety on additives that are "Generally regarded as safe".

The data described above supports that phosphate additives should also have an upper limit of safety. The proposed rule does not plan changes to micronutrients such as phosphorus. However, given the considerable evidence that the micronutrient of phosphorus is associated

with adverse outcomes in kidney disease—which affects more than 20 million Americans—and the fact that phosphorus is a widespread, unregulated food additive—ASN believes that labeling the micronutrient be mandatory. Furthermore, ASN recommends that FDA define upper limits of tolerability and intake in special populations such as people with kidney disease.

M. Format:

ASN commends the FDA for improving the format of the proposed food label, specifically increasing the prominence of calories and serving size. This will assist consumers in weight loss, and determination of true sodium intake. However, the ASN objects to moving potassium labeling to a footnote, rather than its current location in the main label as detailed in section 4 (page 11957). While we agree that potassium is a mineral, its risk to health is substantial. Importantly for patients with CKD, excessive potassium intake can lead to increased mortality in dialysis patients[15]. Thus, the ASN recommends leaving potassium content in the main label, rather than minimizing its importance by listing it in the mineral section along with many other potentially less toxic substances.

The ASN thanks the FDA for the opportunity to comment on the Food Label Propose Rule. References are listed below and on the following page.

Sincerely,

Sharon M. Moe

Sharon M. Moe, MD
President, American Society of Nephrology

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