

June 18, 2014

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: Docket No. FDA-2012-N-1210 and RIN 0910-AF22

Dear Dr. Hamburg,

The undersigned organizations who are dedicated to preventing and improving treatment of kidney disease appreciate the opportunity to comment on Food Labeling: Revision of the Nutrition and Supplement Facts Label (FDA-2012-N-1210). One in three Americans over age 20 — 73 Million people — is at risk for kidney disease because of high blood pressure, diabetes, or a family history of kidney disease and more than 20 million Americans already have kidney disease. Our organizations applaud the efforts of the FDA to provide consumers with more detailed information that they need to make more informed nutritional decisions to live healthier lives. Kidney disease, like obesity, is a public health problem that leads to increased morbidity and mortality. However, patients with kidney disease who follow a special diet have improved outcomes. Nutritional recommendations for patients with kidney disease are markedly different from the general public and nutrition education efforts need to be supported by more transparent, informative and clearer food labeling. This can be accomplished by listing specific measurements of nutrients, which helps the average consumer as well as the consumer who requires a specialized diet. For these reasons we strongly endorse the FDA's proposal to include the amount of potassium and calcium in milligrams (mg) on food labels. However, we urge the FDA to also include phosphorus content on the food label as this information is essential for patients with kidney disease and more studies each day demonstrate that phosphorus additives also affect the health of the general public.

Controlling potassium and calcium intake for people with CKD

While most Americans need to increase their potassium and calcium intake individuals with CKD need to limit their intake. Including potassium and calcium amounts in milligrams provides essential information to people with CKD. Too much potassium and calcium increases the risk of cardiovascular events in people with CKD. In 2006 the National Kidney Foundation and the Academy of Nutrition and Dietetics¹ conducted a survey of people with CKD to see how useful the nutrition labels were for them. Eighty-three percent of the total respondents indicated that they read the food label for the amounts of nutrients when they decide to buy or eat a food or beverage. Eighty-nine percent of Americans believe it would be useful to have potassium content on the Nutrition Fact Panel. More than half (58% of respondents) had decided at some time not to buy a food or beverage because the amount of potassium was not listed. Similarly, two thirds of the survey participants responded that they did not know how much calcium was contained in a serving of food that is described on the food label as 25% DV. These findings were provided to the FDA in 2007 in response to the previous proposed food labeling revisions. We expect this recent proposal, to include the actual units of both potassium and calcium, will help those with CKD who are educated about their dietary needs make better informed decisions about the foods they consume.

¹ At the time called the American Dietetics Association

The importance of disclosing phosphorus units on the food label

Our organizations were disappointed that the FDA failed to mention dietary phosphorus intake in the proposed rule, and did not propose to add phosphorus content to the nutrition label. This omission is a significant missed opportunity. Phosphorus can occur naturally in various forms of food, or as a component in commonly-used food additives. The proposed rule 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 increase the phosphorus content above the naturally-occurring levels in the protein itself.²

The kidney is responsible for the homeostasis of phosphorus through the effect of several hormones that increase the excretion of phosphorus in the urine. While these mechanisms of enhancing urinary phosphorus excretion are effective in maintaining normal blood phosphorus levels until very late in the course of progressive kidney disease, the persistent elevation of these hormones causes bone disease, heart disease, and are associated with mortality in patients with CKD. Furthermore, recent studies also indicate that higher levels of phosphorus can increase mortality in patients without kidney disease, even if those levels are within the normal range.³ For individuals with obesity, reducing phosphorus intake has also been associated with less urine albumin excretion (UAE). UAE is one of the first signs of kidney disease.⁴ We contend that the emerging data support phosphorus as a serious public health problem in the United States, and we urge the FDA to designate phosphorus as a mandatory, not a voluntary, listing on the nutrition label.

We contend that 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 from adhering to these important recommendations. Two recent scientific meetings highlighted the importance of patients with kidney disease phosphorus regulation: A scientific consensus symposium sponsored by the National Kidney Foundation in 2012⁵ 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.⁶

² Lou-Arnal LM., et al. The impact of processing meat and fish products on phosphorus intake in chronic kidney disease patients. *Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia* 2013;33:797-807.

³ Nadkarni GN and Uribarri J. Phosphorus and the kidney: what is known and what is needed. *Advances in nutrition* 2014;5:98-103.

⁴ Chang, Alex, et al. Association of a Reduction in Central Obesity and Phosphorus Intake With Changes in Urinary Albumin Excretion: The PREMIER Study. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 2013; 62:5: 900-907.

⁵ Block GA, Ix JH, Ketteler M, et al. Phosphate homeostasis in CKD: report of a scientific symposium sponsored by the National Kidney Foundation. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 2013;62:457-473.

⁶ Gutierrez OM. The connection between dietary phosphorus, cardiovascular disease, and mortality: where we stand and what we need to know. *Advances in nutrition* 2013;4:723-729.

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.^{7 8 9 10} 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.¹¹ 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.¹²

Another study found that over 45% of the best-selling grocery items contained phosphorus additives,¹³ and these items typically cost less and are eaten more commonly in individuals of lower socioeconomic status.¹⁴ The use of phosphate containing food additives has increased substantially over the last several years.¹⁵ Analyses of processed foods that contain phosphate additives indicate that these increase the food phosphorus content by 70%.¹⁶ Analyses of meat and poultry products demonstrate that additives increase both the phosphorus and potassium intake by two to three fold, respectively¹⁷, both leading to adverse consequences in patients with CKD.

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.” Our organizations strongly recommend 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 ideally be further subdivided into natural content of phosphorus versus added phosphates, similar to the

⁷ Moe SM, Zidehsarai MP, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. *Clinical journal of the American Society of Nephrology : CJASN* 2011;6:257-264.

⁸ Isakova T, Gutierrez, et al. Postprandial mineral metabolism and secondary hyperparathyroidism in early CKD. *Journal of the American Society of Nephrology : JASN* 2008;19:615-623.

⁹ Isakova T, Gutierrez, et al. Pilot study of dietary phosphorus restriction and phosphorus binders to target fibroblast growth factor 23 in patients with chronic kidney disease. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association* 2010.

¹⁰ Takeda E, Yamamoto H, Yamanaka-Okumura H, Taketani Y. Increasing dietary phosphorus intake from food additives: potential for negative impact on bone health. *Advances in nutrition* 2014;5:92-97.

¹¹ Carrigan A, et al. Contribution of food additives to sodium and phosphorus content of diets rich in processed foods. *Journal of renal nutrition: the official journal of the Council on Renal Nutrition of the National Kidney Foundation* 2014;24:13-19.

¹² Sullivan C, et al. Effect of food additives on hyperphosphatemia among patients with end-stage renal disease: a randomized controlled trial. *JAMA : the journal of the American Medical Association* 2009;301:629-635.

¹³ Leon JB, et al. The prevalence of phosphorus-containing food additives in top-selling foods in grocery stores. *Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation* 2013;23:265-270 .

¹⁴ Gutierrez OM, et al. Associations of Socioeconomic Status and Processed Food Intake With Serum Phosphorus Concentration in Community-Living Adults: The Multi-Ethnic Study of Atherosclerosis (MESA). *Journal of renal nutrition: the official journal of the Council on Renal Nutrition of the National Kidney Foundation* 2012.

¹⁵ Calvo MS, et al. Assessing the health impact of phosphorus in the food supply: issues and considerations. *Advances in nutrition* 2014;5:104-113.

¹⁶ Benini O, et al. Extra-phosphate load from food additives in commonly eaten foods: a real and insidious danger for renal patients. *Journal of renal nutrition: the official journal of the Council on Renal Nutrition of the National Kidney Foundation* 2011;21:303-308.

¹⁷ Sherman RA, Mehta O. Phosphorus and potassium content of enhanced meat and poultry products: implications for patients who receive dialysis. *Clinical journal of the American Society of Nephrology : CJASN* 2009;4:1370-1373.

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).

The evidence described above supports the need for phosphate additives to also have an upper limit of safety on food labels. The proposed rule does not plan changes to micronutrients such as phosphorus. However, given the considerable evidence that 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 associated with mortality and morbidity in the general public as well—our organizations believe that labeling the micronutrient be mandatory. Furthermore, we recommend, separately from the food labeling process, that FDA define upper limits of tolerability and intake in special populations such as people with kidney disease.

We appreciate the opportunity to comment on this important proposed regulation.

Sincerely,

Alport Syndrome Foundation

American Association of Kidney Patients

American Kidney Fund

American Society for Nephrology

American Nephrology Nurses Association

American Renal Associates

American Society for Apheresis

American Society of Diagnostic and Interventional Nephrology

American Society of Transplant Surgeons

Dialysis Patient Citizens

Home Dialyzors United

The IGA Nephropathy Foundation of America

National Kidney Foundation

National Renal Administrators Association

Nephrology Nursing Certification Commission

PKD Foundation

Renal Physicians Association

Renal Support Network