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NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

November 19, 2018

Comment to the United States Food and Drug Administration
RE: Docket No. FDA-2018-3522 for "Use of the Names of Dairy Foods in the Labeling of Plant-Based Products"
From the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the Council for Pediatric Nutrition Professionals (CPNP)

Members of The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) are Board Certified Pediatric Gastroenterologist physicians who care for children with a broad spectrum of gastrointestinal disorders including primary nutrition and secondary nutrition disorders related to gastrointestinal, liver and other diseases. The Council for Pediatric Nutritional Professionals (CPNP) is an associated group of certified dietetic professionals serving a similar patient base. We are pleased to see the FDA request for comments regarding plant-based foods that may be labelled or used like milks. Our interest in this topic stems from increased consumption of these alternatives in recent years[1,2], our clinical experience and a large body of published literature related to adverse clinical effects when certain non-standardized plant-based beverages have been used inappropriately in lieu of standardized milk products in the feeding of infants and children[3]. Such product use places children at risk of slowed growth[4], protein-calorie malnutrition, failure to thrive and specific nutrient deficiencies, such as vitamin D[5], compromising current and future health and development. In addition, there are concerns that high intakes of some plant-based products may lead to excessive toxin intake, such as arsenic from rice-based milks[6]. Further, enterocolitis has long been known to be possible in cow milk protein intolerant infants or children fed soy formulas or milk, but may also occur with some other plant-based milk products[7-9]. Due to such concerns, the European Society for Pediatric Gastroenterology Hepatology and Nutrition recommends the use of an infant formula for the first two years of life in children who cannot consume cow milk rather than other milk substitutes[10].

The universally preferred milk for infants is human milk[11], but there are many infants fed infant formula due to maternal choice or other complex factors[12]. U.S. infant formulae are regulated under the Infant Formula Act that requires that products labelled as infant formula support healthy growth. Since introduction of the Infant Formula Act, reports of nutritional deficiencies related to US formulas have become exceedingly rare. By one year of age, most infants are weaned to some form of "milk." USDA recommendations are for intake of 2-3 servings of dairy products/day for a well-balanced,

nutritionally complete diet, which encompasses approximately 25-30% of total energy needs of 1-3 year-olds. Most infants and children tolerate cow milk-based formulae and milks with only 2-7.5% of infants and young children having true cow milk protein intolerance[13]. These infants and children suffer adverse medical consequences from consuming cow milk-based infant formulae and standardized milk products. For these children, nutritious infant formulae and alternative beverages are needed, and have become widely available. When a hypoallergenic or cow milk-free milk substitute is needed, some vegetable-based products may be attractive alternatives to consumers, but may not prove hypoallergenic and may not provide necessary nutrition. There are also aroma, taste and texture differences between alternative products and cow milk that may influence choices among hypoallergenic or plant-based cow milk alternatives[14]. Financial considerations can also play a role in substitution decisions. The cost of expensive, hypoallergenic infant formulas is not uniformly covered by health insurers, as they are nutritional products, not drugs and this may have health consequences[15]. In addition to caring for milk-intolerant infants and children who require a cow milk alternative, we increasingly see families with religious or cultural values that preclude cow milk intake, or who have strong a preference to avoid cow milk[12], which lead them to seek alternatives.

The FDA currently defines "milk" and related milk products by the product source and the inherent nutrients provided by bovine milk[16]. There is insufficient consumer recognition of why some milk alternatives meet pediatric nutritional needs and others do not. In our clinical experience, consumers and mothers understand what standardized milk products are (with varying degrees of understanding of the nutrition provided by milk), but also may see "milk" as a white beverage given to children as a source of fluid and nutrition. There are potential health risks when this second understanding leads to selection of a nutritionally inferior "milk" with resultant inadequate nutritional intake from the total diet[17,18]. The misguided substitution of a plant-based "milk" for cow milk, without adequate compensation for nutrients not supplied in those products, can place a child at risk. Breastmilk or infant formula (most commonly containing cow milk), is an infant's sole food for the first 4 to 6 months, and milk beverages continue to play an important role in providing infant and childhood nutrition because of the high nutritional value of milk with its calories, protein content, minerals and other nutrients. Substitution of a milk that does not provide similar nutrition is deleterious to a child's nutritional status[19], growth and development. Table 1 highlights nutritional differences between cow milk and plant-based nontraditional "milks." Figure 1 provides examples of plant-based "milk" and cow milk labels. Even among products based on the same plant source, there may be substantial nutrient content differences. In the absence of informative food labeling and clear standards of identity, consumers with strong dietary preferences and good intentions may be led to select a nutritionally inferior "milk," believing that one product labeled as "milk" is nutritionally equivalent to another.

Nutritional Comparison of Cow's Milk and Plant-Based "Milks"

Per 1 cup (240mls)	Cow's Milk	Vegetable Milks*								
		Almond	Cashew	Coconut	Flax-Seed	Hemp	Oat	Pea	Rice	Soy
Calories	150	30-100	25-80	45-90	55	70-170	130	115	110	90
Protein (g)	8	1-5	0-1	0-1	0	2-4	4	8	1	6
Fat (g)	8	3	2-3.5	5	2.5	5-6	2.5	5	2.5	3.5
Carbohydrates (g)	13	9-22	1-20	8-13	9	1-35	24	11	20	15
Sugars (g)	12	7-20	0-18	0-9	9	0-23	19	10	13	9
Calcium (mg)	300	300	100-450	100-450	300	400	350	450	300	400
Vitamin D (IU)	120	110	125	125	100	150	120	150	120	120

*There are variations with non-dairy milk nutrients due to different products available; averages or ranges are reported.

Figure 1. Labels of cow milk and plant-based "milks"

A. Cow milk, B. Soy milk, C. Coconut milk; D. Almond milk, E. Rice milk, F. Pea milk

Examples of adverse effects from the misuse of certain plant-based beverages have been well-documented and include failure to gain weight, decreased growth in stature, electrolyte disorders, kidney stones[20], severe nutrient deficiencies[3] including protein calorie malnutrition with edema (kwashiorkor)[21], iodine deficiency[22,23], iron deficiency anemia, rickets and scurvy, and the known risks for developmental damage related to malnutrition occurring during infancy and early childhood[24]. Tables 2, 3 and 4 reproduced from a 2017 publication by Dr. Isidro Vitoria with his permission document more than 30 such cases described in the US and international medical and nutritional literature in the past 30 years[3]. Many more such cases are seen in clinical practice, but not documented by publication.

Table II. Published clinical cases of nutritional problems associated with soy beverages consumed by infants and toddlers

Authors Year	Reasons for introduction of soy beverage	Age of introduction of soy beverage (age of diagnosis)	Characteristics of feeding	Daily intake	Laboratory findings	Diagnosis
Carvalho NF et al. (6) 2001	Taste preference Breastfeeding without vitamin D supplement	10 months (17 months)	Soy beverage, vegetables, fruits	900 ml	Ca 2.22 mmol/l P 0.55 mmol/l AP 1879 U/l VitD 19.2 nmol/l PTH 12.1 pmol/l	Rickets Failure to thrive
Fox AT et al. (16) 2004	Breastfeeding without vitamin D supplement Urticaria with infant formula at 6 months	6 months (14 months)	Breastfeeding, soy beverage, vegetables, fruits	--	Ca 1.71 mmol/l P 1.06 mmol/l AP 2054 U/l VitD 15 nmol/l PTH 44.1 pmol/l	Rickets Failure to thrive Ferropenic anemia
Imataka G et al. (17) 2004	Eczema at 3 weeks Parental decision	1 month (5 months)	Soy beverage Calcium: 28.9 mg/l No vitamin D	--	Ca 1.32 mmol/l P 1.6 mmol/l AP 2303 U/l VitD 19.9 nmol/l PTH 254 pmol/l	Hypocalcemic tetany Rickets Failure to thrive

AP: Alkaline phosphatase; Ca: Calcium; P: Phosphorus; PTH: Parathyroid hormone; VitD: 25-OH-vitamin D_3

Table III. Published clinical cases of nutritional problems associated with rice beverages consumed by infants and toddlers

Authors Year	Reasons for introduction of rice beverage	Age of introduction of rice beverage (age of diagnosis)	Characteristics of feeding	Daily intake	Laboratory findings	Diagnosis
Massa G et al. (24) 2001	Dermatitis unimproved with a soy formula (homeopathic physician)	16 weeks (33 weeks)	Rice beverage Fruits, vegetables	RB: 1.0-1.38 l	Alb 26 g/l	Kwashiorkor
Carvalho NF et al. (6) 2001	Eczema and perceived milk intolerance	13-15 months? (22 months)	Rice beverage Vegetables	RB: 1.5 l 0.3 g prot/kg/d 79 kcal/kg/d	Alb 10 g/l Zinc 32.2 µg/dl	Kwashiorkor
Liu T (25) 2001	Perceived intolerance of formula	? (4 months)	Rice beverage Vitamins	--	Alb 14 g/l TProt 29 g/l Zinc 22 µg/dl	Kwashiorkor
Novembre E et al. (26) 2003	Atopic dermatitis (naturopathic doctor)	5 months (6 months)	Rice beverage, rice cream, vegetables, fruits	RB: 660 ml 0.5 g prot/kg/d 86 kcal/kg/d	Alb 14 g/dl TProt 28 g/l	Kwashiorkor
Kuhl J et al. (27) 2004	Atopic dermatitis positive RAST to multiple foods	14 months (17 months)	Rice beverage, 1-2 tablespoons of baby food	5 g prot/d 600 kcal/d	Alb 12 g/l TProt 35 g/l Zinc 27 µg/dl	Failure to thrive Kwashiorkor
Katz K et al. (28) 2005	Breastfed 8 m Rejection of infant formula	8 months (14 months)	Rice beverage, meat, vegetables	--	Alb 14 g/l TProt 36 g/l Zinc 28 µg/dl	Kwashiorkor
Katz K et al. (28) 2005	Rejection of infant formula	2 months (7 months)	Rice beverage, baby food, iron supplementation	--	Alb 15 g/l TProt 34 g/l Zinc 31 µg/dl	Failure to thrive Kwashiorkor
Barreto-Chang OL et al. (29) 2010	Cow's milk allergy	13 months (16 months)	Rice milk (0.4 g proteins/100 ml)	--	VitD 9 nmol/l PTH 20.4 pmol/l	Failure to thrive Rickets
Tierney E et al. (30) 2010	Scalp rash	4 months (8 months)	Rice milk, bananas, sweet potatoes	--	Alb 20 g/l TProt 37 g/l Zinc 91.5 µg/dl	Kwashiorkor
Diamanti A et al. (31) 2011	Cow's milk allergy (3 cases)	3 months (4 months) 1.5 months (4 months) 3 months (5 months)	Rice beverage	--	Alb < 20 g/l TProt < 40 g/l	Kwashiorkor

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Table III (Cont.). Published clinical cases of nutritional problems associated with rice beverages consumed by infants and toddlers

Authors Year	Reasons for introduction of rice beverage	Age of introduction of rice beverage (age of diagnosis)	Characteristics of feeding	Daily intake	Laboratory findings	Diagnosis
Keller MD et al. (32) 2012	Eczema. Allergy to cow's milk, soy, egg, peanut, etc.	13 months (19 months)	Rice beverage, rice, potatoes, carrots	--	Alb 16 g/l TProt 33 g/l	Kwashiorkor
Keller MD et al. (32) 2012	Suspected cow's milk allergy (eczema, vomiting)	12 months (16 months)	Rice beverage Lentils, chick-peas, olives	--	Alb 12 g/l Hb 7 g/dl	Kwashiorkor Anemia
Fourreau D et al. (33) 2013	Suspected cow's milk allergy (naturopathic doctor)	7 months (9 months)	Rice beverage (0.1 g prot/100 ml), fruits, vegetables	RB:800-900 ml	Alb 7 g/l Hb 10 g/dl	Kwashiorkor Anemia
Fourreau D et al. (33) 2013	Suspected cow's milk allergy (parental decision)	13 months (14.5 months)	Rice beverage	RB: 300 ml	Alb 7 g/l Hb 3.5 g/dl Vit B_{12} 143 ng/l	Failure to thrive anemia
Le Louer B et al. (5) 2014	Vomiting	2 months (4.5 months)	Rice beverage	--	Hb 5.7 g/dl Alb 1.8 g/dl Zinc 3.5 µmol/l	Failure to thrive anemia
Le Louer B et al. (5) 2014	Eczema	1 months (7 months)	Rice beverage	--	Hb 8.7 g/dl Alb 1.98 g/dl Zinc 3.9 µmol/l	Failure to thrive Kwashiorkor Anemia
Mori et al. (34) 2015	Atopic dermatitis (naturopathic doctor)	4 months (6 months)	Rice milk, fruits, rice poultry and vegetable broth.	--	Alb 13 g/l TProt 30 g/l Hb 5.7 g/dl	Kwashiorkor Anemia

Alb: Albumin; Hb: Hemoglobin; PTH: Parathyroid hormone; RB: rice beverage; TProt: total protein; VitD: 25-OH-vitamin D_3.

Table IV. Published clinical cases of nutritional problems associated with almond beverages consumed by children

Authors Year	Reasons for introduction of almond beverage	Age of introduction of almond beverage (Age of diagnosis)	Characteristics of feeding	Daily intake	Laboratory findings	Diagnosis
Kanaka C et al. (36) 1992	Eczematous reaction to cow's milk formula (maternal decision)	2.5 months (7.5 months)	Self-prepared extract of almonds Cereals Fruits	98% DRI proteins 54% DRI energy	TSH 378 µIU/ml Iodine 47 nmol/l Free carnitine 12 µmol/l	Failure to thrive Iodine and carnitine deficiency
Mesa O et al. (37) 2009	--	Birth (31 days)	Almond beverage	--	Cl- 94 mmol/l Na+ 136 mmol/l K+ 3 mmol/l CO_3H- 40.3 mmol/l	Dehydration Metabolic alkalosis
Mesa O et al. (37) 2009	--	Birth (4 months)	Almond beverage	--	Cl- 74 mmol/l Na+ 124 mmol/l K+ 2.2 mmol/l CO_3H- 49.8 mmol/l	Metabolic alkalosis
Fourreau D et al. (33) 2013	Suspected gastro-esophageal reflux	12 months (13 months)	Almond beverage (17 mg sodium/100 ml; 24 mg chloride/100 ml) Yogurt Vegetables	840 ml	Cl- 69 mmol/l Na+ 127 mmol/l K+ 1.9 mmol/l CO_3H- 48 mmol/l	Metabolic alkalosis
Doron D et al. (38) 2013	Diarrhea and vomiting attributed by the mother to cow's milk protein allergy	4 months (6 months)	Almond-based home made "formula" (Almond 10 g/water 100 ml)	1,000 ml	Ca 1.4 mmol/l P 1.2 mmol/l AP 818 U/l vitD < 12 nmol/l PTH 30.3 pmol/l Hb 7.7 g/dl	Failure to thrive Rickets Anemia
Doron D et al. (38) 2013	Rash	4-5 months (8 months)	Almond-based and honey home made "formula" (20 gr almonds / 100 ml water)	600 mL	Alb 20 g/l TProt 36 g/l	Kwashiorkor
Le Louer B et al. (5) 2014	Gastro-esophageal reflux, eczema	3.5 months (5 months)	Almond and chestnut beverage	-	Alb 19.5 g/l Ca 0.64 mmol/l Zinc 7 µmol/l	Hypocalcemic tetany Malnutrition

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Table IV (Cont.). Published clinical cases of nutritional problems associated with almond beverages consumed by children

Authors Year	Reasons for introduction of almond beverage	Age of introduction of almond beverage (Age of diagnosis)	Characteristics of feeding	Daily intake	Laboratory findings	Diagnosis
Le Louer B et al. (5) 2014	Parental decision	8.5 months (16.5 months)	Almond and walnuts beverage	--	VitD < 12.5 nmol/l Ca 2.32 mmol/l P 1.71 mmol/l PTH 8.8 pmol/l	Rickets
Ellis D et al. (39) 2015	Tourette syndrome (1 case) Lactose intolerance (2 cases)	3 years 9 years 10 years	Almond milk and varied diet	700-1,000 ml	Urine oxalate 53.5, 81.5 and 97.9 mg/1.73 m²/d (27.6-35.4)	Hyperoxaluria Hematuria (2 cases) Kidney stones (1 case)
Vitoria I et al. (7) 2016	Medical indication (atopic dermatitis)	2.5 months (11 months)	Almond milk Almond flour Cereals	840 ml/d	Ascorbic acid < 10 µmol/l VitD 31 nmol/l	Scurvy

Alb: Albumin; Ca: Calcium; Hb: Hemoglobin; P: Phosphorus; TProt: total protein; VitD: 25-OH-vitamin D_3.

We believe such adverse nutritional outcomes are preventable through FDA mandated labeling of non-standardized plant-based beverages, consumer nutrition education and efforts directed to heighten health care practitioners' awareness of these nutritional issues. These challenges are not limited to the US. Codex Alimentarius similarly defines milk as coming from an animal lacteal source, but reported cases of children with nutritional compromise related to the inappropriate use of plant-based milks come not just from the US, but also from other high-income countries that use the Codex Alimentarius as the basis of their food regulation.

A food labeling challenge is that "good nutrition" has varying meanings to different segments of the population. To some, good nutrition means generally following Dietary Guidelines for the various age groups with foods that have long been part of the American diet. To others, it may relate more to the avoidance of specific foods or food components (e.g., animal-derived food products, cow milk or gluten) or the avoidance of toxins, food additives or genetically modified foods and ingredients. Food labeling needs to provide information to facilitate appropriate food choices based on personal preferences as to ingredients and ingredient sources, nutrient content and the role of specific foods in meeting daily dietary requirements, all in the small space of the food label.

Based on our clinical experience and the available relevant medical literature, we believe that labelling a product as "milk" that: 1) does not come from cow milk, or 2) does not contribute the nutritional value of milk to the diet[18,25], is not in consumers' interests. For plant-based products with a nutritional composition that requires extensive fortification[14] (e.g., calcium) to achieve a nutritional label value approximating that of "milk," it is difficult to know to what extent the actual nutritional value of milk is achieved, in the absence of bioavailability studies[18]. The biologic value of the protein source and its physical matrix relative to cow milk also needs to be considered in this regard[14,26,27]. Similarly, there may be physical stability issues with such products that require extensive shaking or special handling or instructions[14]. From a pediatric medical and nutritional standpoint, it is advisable that "milk" be: 1) milk products as currently defined by FDA, or 2) provide comparable nutritional value to standard "milk". Such labeling,

and education regarding this labeling, may reduce adverse nutritional effects from consuming nutritionally non-equivalent plant-based products labeled as “milk.”

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On behalf of the Nutrition Committee of NASPGHAN and the CPNP

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