Children's Hospital of Philadelphia

Virginia A. Stallings, MD
Director, Nutrition Center
2716 South Street, Room 14473
Children's Hospital of Philadelphia
Philadelphia, PA 19146
PH: (267) 425-1633

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Susan Mayne, Ph.D.
Director
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
susan.mayne@fda.hhs.gov

Frank Yiannas
Deputy Commissioner for Food Policy and Response
U.S. Food and Drug Administration
frank.yiannas@fda.hhs.gov

Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Comments on "Evaluating the Public Health Importance of Food Allergens Other Than the Major Food Allergens Listed in the Federal Food, Drug, and Cosmetic Act: Guidance for FDA Staff and Stakeholders – Draft Guidance", FDA Docket Number: FDA-2021-N-0553 ("FDA's Draft Guidance")

Dear Dr. Mayne and Deputy Commissioner Yiannas:

As a board-certified nutrition pediatrician, Professor of Pediatrics and Director of the Nutrition Center at the Children's Hospital of Philadelphia, I am writing to provide comments on the FDA Draft Guidance.

I served as report Editor and Chair of the National Academies of Sciences, Engineering, and Medicine, Committee on Food Allergies: "Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management and Public Policy." This was published by the National Academies Press, 2016 and cited as FDA Ref. 2 in the FDA Draft Guidance.

Our Food Allergy Committee's work for the National Academy found that "food allergy has two key classifications: immunoglobulin E (IgE)-mediated or non-IgE-mediated" (page 4) such as Celiac Disease. However, it should be noted that while there were certain references to Celiac

Disease in the Food Allergy Committee report, Celiac Disease was not covered in our report because it was "beyond the scope of the statement of task" for the committee, not because Celiac Disease is not an essential food safety issue for the population.

I agree with the FDA that people with Celiac Disease "face potentially life-threatening illnesses if they eat gluten, typically found in breads, cakes, cereals, pastas, and many other foods… There is no cure for Celiac Disease and the only way to manage the disease is to avoid eating gluten."

According to the NIH "Notice of Special Interest (NOSI): Accelerating Progress in Celiac Disease Research" published November 23, 2021, there are more than 3 million Americans who have Celiac Disease.

"Celiac Disease is an autoimmune disease that occurs in genetically susceptible individuals who develop an immune response to ingested gluten. This disease affects greater than 1% of the US population, and incidence appears to have been increasing over the last several decades. The only known treatment is life-long strict avoidance of all forms of wheat, rye, and barley. Although a gluten-free diet is an effective treatment in many individuals, recent research has revealed that up to 50% of individuals following a gluten-free diet are inadvertently exposed to gluten, and a substantial minority develop persistent or recurrent symptoms.

Clinical manifestations are multifaceted and include gastrointestinal (ranging from severe malabsorption to subclinical damage of the gastrointestinal tract) as well as extraintestinal (e.g., skin) expressions of disease. Additional manifestations may vary from subclinical damage of the gastrointestinal tract to refractory Celiac Disease that is non-responsive to a gluten-free diet. Although rare, Celiac Disease is associated with increased risk of gastrointestinal tract cancers and lymphomas."

While a Non-IgE-Mediated food allergy does not trigger anaphylaxis and is not *immediately* life-threatening, people with Celiac Disease face potentially life-threatening and severe adverse health effects that can arise through gluten ingestion including by way of example and not limited to: anemia, cancer, heart disease, immunological scarring, intestinal damage and malnutrition.

Nonetheless, the FDA Draft Guidance appears to be inconsistent with the conclusions of international food safety authorities and expert committees comprised of scientists, regulators, physicians, clinicians and risk managers from academia, government and the food industry including:

- Joint Food and Agriculture Organization of the United Nations/World Health Organization Expert Committee on Food Additives Evaluation of certain food additives and contaminants: 53rd report of the Joint FAO/WHO Expert Committee on Food Additives. 2000. WHO Technical Report Series 896. World Health Organization, Geneva ("1999 FAO/WHO Expert Consultation"; also referred to as the "1999 Codex Criteria" as detailed in the FDA Draft Guidance and cited as "FDA Ref. 25").
- Food and Agriculture Organization of the United Nations/World Health Organization. "Summary report of the Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens. Part 1: Review and validation of Codex priority allergen list through risk

assessment." 2021 ("2021 FAO/WHO Expert Consultation"; also referred to as "FDA Ref. 45" in FDA Draft Guidance).

For example, the 1999 FAO/WHO Expert Consultation determined:

"The revised list of those foods and ingredients known to cause food allergies and intolerance and whose presence should always be declared was identified as the following: cereals containing gluten (i.e. wheat, rye, barley, oats, spelt or their hybridized strains) and their products; Crustacea and products of these; Egg and egg products; Fish and fish products; Peanuts, soybeans, and products of these; Milk and milk products (lactose included); Tree nuts and nut products; and Sulfites in concentrations of 10 mg/kg or more."

As our Food Allergy Committee found,

"The 1999 CAC [Codex Alimentarius Commission] priority list included milk, egg, fish, crustacean shellfish, peanut, soybean, tree nuts, cereal grain sources of gluten, and sulfites. Several of these items were added because the FAO [Food and Agriculture Organization of the United Nations] Technical Consultation also considered Celiac Disease, intolerances, and sensitivity reactions in addition to immunoglobulin E (IgE)-mediated food allergies in its deliberations. For example, gluten was included because of its association with Celiac Disease." (page 284)

"In the United States, the priority list of allergenic foods was established by the Congress with the passage of the Food Allergen Labeling and Consumer Protection Act,6 7 ['For an analysis on Food Allergen Labeling and Consumer Protection Act (FALCPA) see Derr (When Food Is Poison), 2006.']. The FALCPA list mirrored the 1999 CAC list except that the FALCPA list did not address Celiac Disease and therefore did not recognize cereal sources of gluten as major allergenic foods." (page 286)

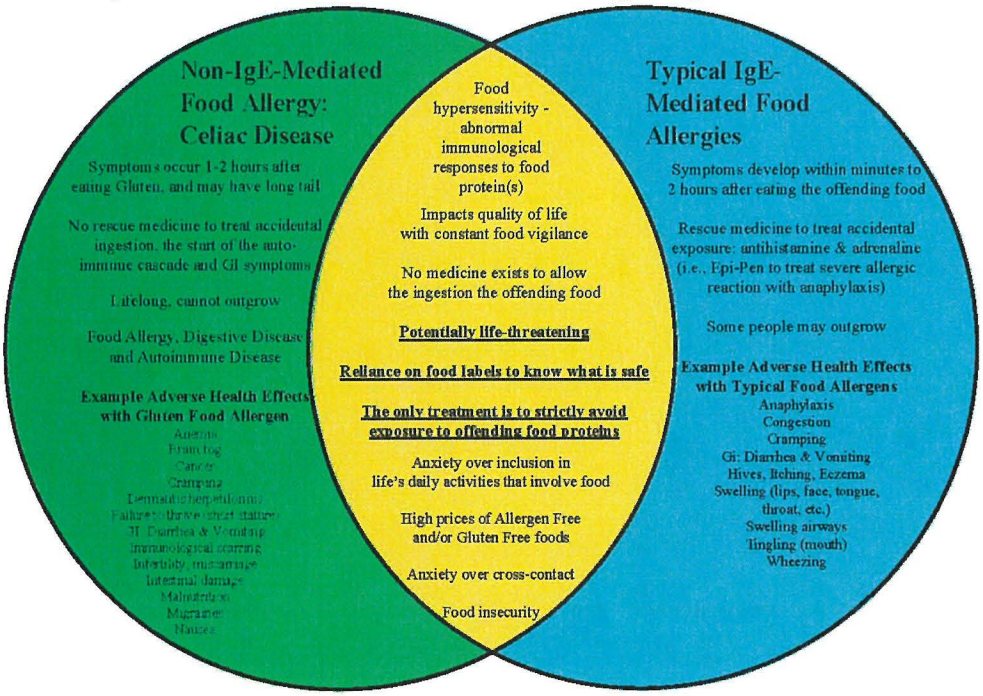
The 2021 FAO/WHO Expert Consultation, which was chaired by Dr. Lauren Jackson, Chief, Process Engineering Branch, Division of Processing Science & Technology, Institute for Food Safety & Health FDA, determined:

"Based on systematic and thorough assessments which used all three criteria (prevalence, severity and potency), the Committee recommended that the following should be listed as priority allergens: Cereals containing gluten (i.e., wheat and other Triticum species, rye and other Secale species, barley and other Hordeum species and their hybridized strains), crustacea, eggs, fish, milk, peanuts, sesame, specific tree nuts (almond, cashew, hazelnut, pecan, pistachio and walnut)."

While FDA Ref. 25 and FDA Ref. 45 are cited as sources in the FDA Draft Guidance, the FDA Draft Guidance does not include key findings by the "scientists, regulators, physicians, clinicians, and risk managers from academia, government and the food industry", and their conclusions to always declare (label) gluten on food product labels in order to provide consumer protection for the Celiac Disease community to whom ingesting gluten is just like eating poison and potentially life-threatening.

The Venn diagram below illustrates the key near-peer similarities between food allergies that are Non-IgE-Mediated Mechanisms with Celiac Disease (gluten) and typical IgE-Mediated Mechanisms: potentially life-threatening, the only treatment is to strictly avoid the food allergen(s), and consumers' reliance on food labels to know what is safe to eat.

What is Food Allergy?
The Similarities and Differences Between
Non-IgE-Mediated Mechanisms with Celiac Disease & Typical IgE-Mediated Mechanisms



Importantly, unlike food allergies with IgE-Mediated mechanisms, there is no rescue medicine (i.e., adrenaline or antihistamine) to treat accidental ingestion of gluten and the start of the auto-immune cascade in food allergy with Non-IgE-Mediated mechanisms such as Celiac Disease. Additionally, those with a Non-IgE-Mediated food allergy to gluten cannot outgrow their food allergy – Celiac Disease is lifelong (until such time as a cure may be developed).

While U.S. consumers' reactions to a top eight major food allergens (plus sesame as of January 1, 2023) and gluten vary, their consumer habits are the same -- they avoid purchasing foods that contain the allergen(s) that cause their potentially life-threatening immunological adverse reaction.

However, the key difference from a consumer protection standpoint is that under FALCPA, the labeling scheme for the top eight major food allergens in the U.S. is mandatory, but the labeling of gluten is permissive. Wheat is required to be labeled, but gluten is not. Gluten is found in wheat, barley, rye and most oats. Just because something is wheat free does not mean its gluten free. In other words, whereas sufferers of the current top nine Major Food Allergens in the U.S. rely on what ingredients are expressly included in required labeling disclosures of packaged

foods, the Celiac Disease community must rely only on what ingredients are excluded in voluntary gluten free labeling disclosures on packaged foods.

A gluten free diet is not all that is needed to treat Celiac Disease; rather a gluten free diet is all that has ever been historically available to treat Celiac Disease. Additionally, with respect to labeling food products in the United States, the voluntary gluten free labeling scheme does not sufficiently protect consumers who are on medically required and very restrictive gluten free diets.

My strong recommendation is that gluten be labeled on all packaged foods in the United States, in accordance with the 2021 FAO/WHO Expert Consultation, just like it is in more than 85 countries around the world. I respectfully request that the FDA draft guidance be revised to include evaluating gluten as a food allergen and changing the voluntary labeling rule to a mandatory labeling rule to keep the 3 million Americans with Celiac Disease safe.

Sincerely,

Virginia A. Stallings, M.D