CENTER FOR Science IN THE Public Interest
Your Food and Health Watchdog

August 17, 2022

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: FDA-2021-N-0553; Evaluating the Public Health Importance of Food Allergens Other Than the Major Food Allergens Listed in the Federal Food, Drug, and Cosmetic Act; Draft Guidance for FDA Staff and Stakeholders; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request

To Whom it May Concern:

The Center for Science in the Public Interest (CSPI), Your Food and Health Watchdog,[1] respectfully submits this comment on the above-referenced draft guidance (The Draft Guidance).[2]

The Draft Guidance offers a framework to determine if a particular food allergen is of importance for public health, consisting of four factors: 1) evidence of IgE-mediated food allergy, 2) prevalence in the U.S. population, 3) severity, and 4) potency (the amount of the allergen that produces symptoms).

While the framework is potentially useful, we are concerned that an overly strict interpretation of the standards described in the guidance would create unnecessary barriers to prioritizing new allergens. We are also concerned that FDA has failed to commit to requiring labeling disclosures and other regulatory protections for allergens prioritized under the framework. We urge the agency to lay out a plan to proactively consider new allergens and develop controls for allergens prioritized under the proposed framework. Finally, we also urge FDA to develop an approach to prioritizing food intolerances not covered by the current guidance.

[1] CSPI is a non-profit consumer education and advocacy organization that has worked since 1971 to improve the public's health through better nutrition and safer food. CSPI has long advocated for clear labeling and sensible regulation of allergens in food.
[2] Evaluating the Public Health Importance of Food Allergens Other Than the Major Food Allergens Listed in the Federal Food, Drug, and Cosmetic Act; Draft Guidance for FDA Staff and Stakeholders; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request, 87 Fed. Reg. 23181 (April 19, 2022) [The Draft Guidance].

I. Background on FDA Authority to Require Controls for Allergens of Public Health Importance

As FDA has recognized, more than 160 foods have been identified as causing food allergies in sensitive individuals.[3] Yet, while all of these allergens pose risks, not all such risks are equal in public health importance, with some more likely than others to cause serious and even life-threatening reactions.

FDA, with oversight and support from Congress, has worked for years to prioritize the most important allergens for controls that minimize risks, including mandatory labeling and control of cross-contact risks. Efforts to develop a priority list at FDA began as early as 1992, when the agency published a policy statement that provided "examples of foods that commonly cause an allergenic response" which included "milk, eggs, fish, crustacea, mollusks, tree nuts, wheat, and legumes (particularly peanuts and soybeans)."[4] In 2001, the agency published Compliance Policy Guidance (CPG) 555.250, stating the agency's policy for labeling and controlling cross-contact risks, which targeted a list of eight priority allergens: peanuts, soybeans, milk, eggs, fish, crustaceans, tree nuts, and wheat, which the agency understood to cause 90 percent of all food allergies.[5] In 2004, Congress supported efforts already underway at the agency by codifying the eight-allergen list into the definition of "major food allergen" in the Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA), and requiring such major allergens to be declared on labels whenever present in foods.[6]

In developing the "major" allergens list, Congress never intended to reduce FDA's ability to continue to adapt the list of priority allergens in response to new scientific evidence. Indeed, Congress affirmed and expressly provided the agency authority to require labeling for additional allergens. Specifically, FALCPA added section 403(x) to the Federal Food, Drug and Cosmetic Act, which authorized the agency to require additional allergens to be labeled even if they fall outside the "major" allergens list.[7]

The authority granted by Congress and longstanding expertise of FDA make the agency well-positioned to periodically update the priority allergens list, incorporating the latest scientific evidence to ensure that the most significant risks are being addressed. A 2017 report by the National Academies of Sciences, Engineering and Medicine (NASEM) affirmed the need for the US and other countries to update such priority lists, recommending that "…public health authorities in individual countries decide on a periodic basis about which allergenic foods should

[3] The Draft Guidance at footnote 6.
[4] In that year, the agency published a policy statement provided "examples of foods that commonly cause an allergenic response" which included "milk, eggs, fish, crustacea, mollusks, tree nuts, wheat, and legumes (particularly peanuts and soybeans)." Statement of Policy: Foods Derived from New Plant Varieties. 57 Fed. Reg. 22,984, 22,987 (May 29, 1992)
[5] CPG Sec. 555.250 Statement of Policy for Labeling and Preventing Cross-contact of Common Food Allergens. April 19, 2001. https://www.fda.gov/media/71940/download. Accessed August 15, 2022.
[6] Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA). Pub. Law 108-282, Title II.
[7] *See* 21. U.S.C. § 343(x).

be included in their priority lists based on scientific and clinical evidence of regional prevalence and severity of food allergies as well as allergen potency."[8]

Despite the need for periodic, evidence-based updates, FDA actions following the passage of FALCPA have been slow, piecemeal, and largely driven by advocacy from outside stakeholders, including CSPI. For example, the agency's only use of section 403(x) was in 2009, when the agency cited this section as one of several authorities supporting mandatory labeling of carmine/cochineal extract as an allergenic color additive, an action taken in response to a petition that CSPI had submitted 11 years earlier.[9] More recently, FDA deliberated for six years on a 2014 petition from CSPI requesting that sesame be labeled as an allergen. While the agency eventually issued a draft guidance in November 2020 providing "voluntary recommendations" to manufacturers regarding sesame labeling,[10] it never exercised its authorities under 403(x) or other provisions to require labeling and food safety controls for sesame.

In 2021 Congress responded to FDA's inaction by passing the FASTER Act, which made sesame the 9th "major" allergen.[11] The Act also instructed FDA to take additional proactive steps to prioritize new allergens, directing the agency to develop a plan for updating the priority allergen list. This plan was to take the form of a report back to Congress with "recommendations for the development and implementation of a regulatory process and framework that would allow for the timely, transparent, and evidence-based modification of the definition of 'major food allergen.'"[12] The draft guidance appears to partially address that statutory requirement by creating a framework for prioritizing allergens of public health importance, but does not indicate how the framework might lead to the updating of the definition of "major food allergen" or ensure the labeling disclosures and other the regulatory controls that accompany that designation.

II. While the Draft Guidance Offers a Useful Framework, it Also May Create Unnecessary Barriers to Prioritizing New Allergens of Public Health Importance

The Draft Guidance offers a useful framework in that it indicates the types and quality of evidence that FDA will consider in determining whether a food allergen is of public health importance. We generally agree that the four factors identified are all important considerations for prioritizing new allergens (but not necessarily food intolerances, which we discuss *infra*).

We also appreciate that FDA has indicated it will take into account well-documented community-acquired reports, which can provide important evidence of IgE-mediated food allergy and its severity and potency. CSPI has recently published several such reports

[8] Stallings VA, Oria MP, eds. Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management, and Public Policy. Washington DC: The National Academies Press; 2017.
[9] Listing of color additives exempt from certification; food, drug, and cosmetic labeling: cochineal extract and carmine declaration. 74 Fed. Reg. 207 (January 5, 2009).
[10] Voluntary Disclosure of Sesame as an Allergen: Guidance for Industry. November 2020. https://www.fda.gov/media/13521/download. Accessed August 15, 2022.
[11] Food Allergy Safety, Treatment, Education, and Research Act of 2021. Pub. Law 117-11.
[12] *Ibid.*

documenting adverse events associated with food risks, including a report on adverse events related to sesame.[13,14,15]

At the same time, we are concerned that overly strict interpretation of criteria in the guidance would create unnecessary barriers to prioritizing new allergens when sufficient evidence indicates they warrant prioritization. FDA has indicated it will take a wholistic, case-by-case approach to interpreting the evidence, leaving ample room for the agency to take a stricter or more permissive interpretation of the level of evidence needed to warrant prioritization. If the agency sets the bar too high, its framework has the potential to unnecessarily delay designating new priority allergens, resulting in preventable harm.

While we agree with the agency that the quality of studies should be taken into account when assessing the evidence, absence of an ideal evidence base in one or more factors should not serve as a reason to delay protecting the public if the strength of the evidence for one or more of the other factors is high. We note that FDA did not apply the framework proposed in the guidance in prioritizing the original major eight allergens in CPG 555.250. In that instance, the agency's prioritization was supported by national prevalence assessments without consideration of other factors such as severity or potency.[16] Similarly, when FDA required carmine/cochineal to be declared as a color additive in 2009,[17] relying in part on its authority from section 403(x), the decision was based on reports of severe allergic reactions, including anaphylaxis, to carmine/cochineal in food and cosmetics, without reference to the other factors. We are encouraged that the agency has recognized in the guidance that there may be circumstances, such as the introduction of a novel, poorly-studied food or ingredient in the food supply, under which regulatory action could be warranted in the absence of a robust evidence base supporting each factor described in the guidance.

We urge the agency to be liberal in applying flexibility more generally, and in particular when weaknesses in one factor can be compensated by considering compelling evidence to support one or more of the other four factors. The approach employed by the agency should not be so stringent that it prevents FDA from identifying new priority allergens.

[13] Markon AO, Jones OE, Punzalan CM, Lurie P, Wolpert B. Caffeinated energy drinks: adverse event reports to the US Food and Drug Administration and the National Poison Data System, 2008 to 2015. Public Health Nutr. 2019;22(14):2531-2542.
[14] Greenthal E, Lurie P, Doyon S. Opioid exposure associated with poppy consumption reported to poison control centers and the U.S. Food and Drug Administration. Clin Toxicol. 2021;59(8):746-755.
[15] Nguyen K, Greenthal E, Sorscher S, Lurie P, Spergel JM, Kennedy K. Adverse events and labeling issues related to suspected sesame allergy reported in an online survey. *Ann Allergy Asthma Immunol.* 2021;S1081-1206(21)01303-X.
[16] CPG Sec. 555.250 Statement of Policy for Labeling and Preventing Cross-contact of Common Food Allergens. April 19, 2001. https://www.fda.gov/media/71940/download. Accessed August 15, 2022.
[17] Listing of color additives exempt from certification; food, drug, and cosmetic labeling: cochineal extract and carmine declaration. 74 Fed. Reg. 207 (January 5, 2009).

III. FDA Should Develop a Systematic Plan to Update Labeling and Other Controls for Allergens of Public Health Importance

As described in the first section of the draft guidance, FDA is well-positioned to periodically update the priority allergen list with the latest scientific evidence. Yet, while the guidance outlines a framework for designating new allergens of public health importance, it fails to offer a plan for how the agency will then address the risks posed by such allergens.

We urge the agency to amend the guidance, or publish an additional statement, indicating the steps FDA will take under section 403(x) and other authorities to address the risks posed by allergens deemed to be of public health importance under the framework proposed in the guidance.

In addition, the guidance does not indicate how FDA will meet the FASTER Act requirement to provide "recommendations for the development and implementation of a regulatory process and framework that would allow for the timely, transparent, and evidence-based modification of the definition of 'major food allergen.'' As already discussed above, this term is currently defined by statute as the list of 9 allergens. Amending this definition to add a new allergen, as Congress did recently with sesame, has the effect of extending labeling and other controls to cover the new allergen, addressing the risks posed by that allergen. To meet the requirements of the FASTER Act and ensure consistent treatment of priority allergens, we urge FDA to recommend to Congress that the definition of "major food allergen" be modified to allow FDA to designate new "major food allergens" by regulation, employing the framework proposed in the guidance.

The agency has also not laid out an approach to proactively review the evidence to identify new allergens of public health importance, meaning FDA may intend to rely outside groups to request new allergens for prioritization. We urge FDA to develop a systematic method to proactively review the scientific evidence and identify and prioritize new allergens, rather than relying on petitions from outside stakeholders to prompt agency action. This could include a systematic, proactive review of databases that include reports of adverse events tied to foods (e.g., National Poison Data System, NEISS-CADES), as well as any ongoing cohort studies that could inform prioritization of new allergens. FDA should also consider whether specific subpopulations have a particularly high exposure to specific allergens based on dietary practices, and ensure that community surveys are representative. Such a plan will help ensure that the agency's response to new evidence of allergen risks is systematic, timely, and effective in protecting consumers.

IV. FDA Should Develop an Approach to Prioritizing Food Intolerances Not Attributed to IgE-mediated Food Allergy

While IgE-mediation is an appropriate criterion for identifying and assessing food allergies, this factor is not an appropriate mechanism for assessing the public health importance of other intolerances and sensitivities (e.g. gluten sensitivity), which can also be of importance for public health. We urge the agency to develop a means to evaluate requests to prioritize these risks, a description that can be undertaken either in this guidance or in a separate policy document.

V. Conclusion

We generally support the Draft Guidance's approach to laying out a systematic framework for considering new allergens of public health importance, and urge the agency to apply the proposed framework flexibly. However, the current guidance falls short in that the agency has failed to commit to requiring labeling disclosures and other regulatory protections for the allergens that have been prioritized. We urge the agency to lay out a plan to proactively develop protections for new allergens as new evidence emerges, request authority from Congress to add such allergens to the "major food allergens" list, and develop a process for prioritizing food intolerances that are not IgE-mediated.

Signed,

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