IFT Comments to FDA Food Allergen Threshold RFI FDA-2026-N-1304-0001

The Institute of Food Technologists (IFT) appreciates the opportunity to provide information on the Food Allergen Threshold Request for Information. IFT is a global organization whose members are committed to advancing the science of food. We believe science is essential to ensure the global food system is equitable, sustainable, safe, and nutritious. We commend the Food and Drug Administration (FDA) for issuing this Request for Information (RFI) on Food Allergen Thresholds to improve food allergen management.

To prepare this response, input was gathered from IFT scientific members with expertise in food safety and food processing, including the Toxicology & Safety Evaluation Division and the Codex Team that observes the Codex Committee on Food Labeling. The comments below are organized around the four topics outlined in the RFI.

1. ***Available data and concepts for establishing risk-based thresholds for application in various food allergen management and risk assessment situations***

   IFT supports the conceptual approach, and sufficient available data exists to move forward with initial implementation of risk-based Food Allergen Thresholds for food allergen risk assessment and management based on the FAO/WHO defined science-based thresholds. FDA implementation of allergen thresholds would greatly improve the current approach used by industry entities practicing various types of Allergen Advisory Statement (AAS) or Precautionary Allergen Labeling (PAL), which is the term used within the Codex framework. The Codex Committee on Food Labeling (CCFL) has aligned around a framework for PAL using allergen thresholds that the US FDA should consider leveraging in development of an improved framework for the US industry.

   Use of the "reference dose" (RfD) should be employed, and appropriate use of RfD in setting thresholds can help assure appropriate allergenic population risk control based on scientifically sound statistical assessment of determination of the Eliciting Dose (ED) and whether ED01 or ED05 is most appropriate for a given allergen regarding the US population. The FAO/WHO technical report on Threshold RfD recommendations, upon which the CCFL approved the Codex allergen threshold levels to be used, uses the ED05, which may or may not be appropriate in all cases for the US population. These assumptions should be reviewed by the FDA. Likewise, the FAO/WHO report that developed the RfD levels also used a p50 (50th percentile value from the general population distribution of the single-eating occasion intake of a food that is used to estimate the Reference Intake Amount or

RfA). IFT raised concern at the recent CCFL 49 meeting about the use of p50 for the setting of the RfA delivering an adequate level of protection, and the WHO representative pointed to the FAO/WHO Food Allergen Expert Committee Report #3 as providing sufficient reason to not question the use of that level. The specific language from the report (found on page 36) is as follows:

"Following the discussions of the second meeting (see section 8 of the second report) (FAO and WHO, 2022b) and Figure 3, RfDs based on UAP exposures at ED05 improved the overall ability of FBOs to assess analytical-based action levels and to apply risk-based approaches for determining the need or otherwise for PAL compared to RfDs based on UAP exposures at lower eliciting dose (ED) levels. Another important factor in using RfDs in a risk assessment context for establishing action levels is total estimated product consumption. Since food consumption patterns vary across the world, this approach allows action levels to be derived that reflect regional differences. This was illustrated in section 8 of the second report using the 75th percentile of consumption which provided extended compliance in previously published analyses within the framework of the iFAAM project (Blom et al., 2019). However, the appropriateness of the 75th percentile resulted from analyses using the ED01 as RfD. Since these analyses were performed, threshold datasets have been improved as have threshold modelling methods (Remington et al., 2020; Houben et al., 2020) and the current RfDs recommended by the Expert Committee were based on the ED05 (FAO and WHO, 2022b). ***More recent analyses showed that for compliance with the ED05, the 50th percentile of consumption could be as reliable as a consumption marker with similar statistical uncertainty****. At the third meeting, it was determined to use the 50th percentile of general population single-eating occasion consumption for the derivation of action levels at the RfDs based on ED05. The Expert Committee further incorporated into their recommendations the action levels for the priority allergens, using approaches applied to other food hazards. The action levels were calculated for different intakes of the affected food (containing potential unintended allergen), ranging from 10 g to 1 000 g in 10 g increments".*[1]

FDA should take a closer look at this assumption in developing the Allergen Threshold RfD levels for the US population, as it does not align with the current US FDA approach used for chemical contaminant food safety:

[1] Risk assessment of food allergens: part 3: review and establish precautionary labelling in foods of the priority allergens: meeting report

FDA Guidance for Industry: Recommendations for Submission of Chemical and Technological Data for Direct Food Additive Petitions states: "The petitioner should provide, at minimum, a mean EDI (to represent the "average" consumer) and the EDI at the 90th percentile (to represent the "high" consumer)".[2]

As stated in the IFT Conference Room Document comments at the Codex Committee on Food Labeling, CCFL 49 (CRD 13);
"It would seem more appropriate to suggest a higher percentile consumption figure to ensure a greater proportion of the potentially allergenic populations are protected in realistic exposure scenarios, including those who are high consumers of various food. In addition, clarification/guidance should be included on how to obtain appropriate food consumption data for determining action levels in a particular country and on how to proceed if those data are not available."[3]

A detailed evaluation of US food consumption intake data for relevant food allergens is recommended to determine whether the 50th percentile approach used by FAO/WHO in developing RfD levels is appropriate for US consumer protection. IFT member scientists have questioned use of the mean level as potentially insufficient protection for US consumers and have indicated that the higher consumption level used by the FDA for Submission of Chemical and Technological Data for Direct Food Additive Petitions may be more appropriate, considering differences in intake by the US population versus the global approach used by FAO/WHO, among other rationales.[4]

IFT believes that setting appropriate and population-relevant thresholds is the best basis for generating guidance for AAS / PAL use by industry and the necessary risk assessments derived from them, but a revisit to the FAO/WHO RfD analysis as outlined above is encouraged.

Regarding analytical capabilities for establishing allergen risk-based thresholds, the following points warrant emphasis:

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[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-recommendations-submission-chemical-and-technological-data-direct-food-additive#intake

[3] fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-714-49%252FCRDs%252FCompiled%2BCRDs%2B07-18%252Ffl49_crd13.pdf

- Analytical method capability must be considered alongside clinical threshold evaluation. Detection limits (LOD/LOQ) and method sensitivity directly impact the ability to enforce thresholds.
- ELISA-based methods, widely used in industry, can be influenced by matrix effects, processing conditions (e.g., heat hydrolysis, fermentation), and protein extractability, all of which can lead to underestimation or non-detection of allergens. Therefore, FDA guidance should include directions on appropriate testing methodologies for conducting risk assessments. The issue was discussed in depth at the recent Codex CCMAS meeting.[5]
- Variability introduced via sampling, subsampling, and heterogeneous allergen distribution remains a contributing factor to test uncertainty and should be incorporated into threshold-based allergen risk assessments. Additionally, increased dilutions required for high-concentration samples can introduce additional measurement uncertainty, which should be transparently communicated by FDA in sampling guidelines.

2. ***Options using risk-based thresholds for effective communication and labeling strategies to ensure consumers can make informed decisions***

- Threshold implementation must consider fitness-for-purpose of analytical methodologies, including matrix-specific verification by laboratories when manufacturer validation data is insufficient or too generalized.
- Analytical Laboratories should clearly communicate the methodological limitations, including cross-reactivity (e.g., conserved proteins such as tropomyosin or parvalbumin) and inability to differentiate allergen sources.
- Instead of using generalized disclaimers, analytical laboratories conducting testing for manufacturers should use structured communication with their clients, including intended use of the analytical results (e.g., regulatory compliance vs. internal risk verification).
- Harmonized reporting approaches (e.g., qualitative and quantitative outputs for swabs vs. ELISA) are essential to avoid misinterpretations.

3. ***Practical considerations for the use of risk-based thresholds in manufacturing, procurement, and assessment of product safety***

In order to apply thresholds in manufacturing situations, practical tools should be incorporated into FDA guidance:

- Action levels that match what test methods can measure (e.g. ELISA or lateral flow tests). If the threshold is set at a level that testing cannot reliably detect with an understanding of sampling variability and error, it will not be useful for conducting proper risk assessments.
- Matrix complexity (e.g., high fat levels, food processing techniques, use of protease enzymes and hydrolyzed ingredients) significantly affects extraction efficiency and detection reliability, requiring matrix-specific verification by ingredient end-users.
- Swab-based methodologies are subject to high variability (e.g., pressure, swab type, surface characteristics) and are best suited for qualitative assessment vs. quantitative threshold enforcement.
- Laboratories should establish clear policies and procedures for submitted samples (e.g., dilution ranges, matrix considerations) and communicate these directly with customers.
- Access to representative positive control samples for various high manufacturing use of ingredients and high consumption finished products of concern (e.g., pre-clean samples) can improve method selection and reduce method applicability.
- Simple decision guides will be useful, such as:
    - Tests consistently below X ppm protein for a particular allergen recovered from the food matrix indicate that current mitigation controls are working.
    - With results at or above x ppm allergenic protein, an investigation will need to occur and documentation of corrective actions (e.g., product holds, further sampling and testing). FDA should provide examples for industry of best practice approaches to conducting these investigations to help drive industry consistency.

- Most small manufacturers and many mid-sized manufacturers do not have trained toxicologists or protein scientists on staff and will be reliant on various support systems to conduct risk assessments. They will need FDA, possibly in partnership with others (e.g., industry groups) to provide:
    - Standard supplier questionnaire templates that ask the proper questions about allergen controls relative to thresholds.

  - Simple risk matrices and decision trees that can be used without requiring advanced science degreed staff.
  - Guidance on where and when to sample for the design of updated allergen controls for manufacturer food safety plans.

- Operational Challenges
  - Standard curve modeling (e.g., 4PL/5PL) and data processing tools will be critical for accurate quantification and must be verified by end users, even when supplier-provided software is used.
  - Allergen risk communication among food ingredient suppliers, finished goods manufacturers, and laboratories providing data needs to be part of the documentation retention process for all parties. FDA guidance on expectations and best practices regarding these communications, developed in concert with industry groups, would be beneficial.
    - Acceptance criteria for assay performance (e.g., curve fit, R^2, OD range) and ongoing monitoring of standard curve stability will be essential for maintaining data reliability.
  - Lack of detailed matrix information from test kit providers remains a key limitation. Improved transparency in validation data by providers should be required by FDA for those test kit manufacturers.
  - Differences in laboratory practices, operator variability, and data interpretation highlight the need for standardized training and guidance for all involved parties. Something similar to standardized FDA Low-Acid Canned Food training programs may be useful to consider as part of the implementation.
  - Requirements for ingredient supplier documentation and communications to finished goods manufacturers needs to explicitly be defined by FDA (e.g., required level of historical test data, ingredient production system cleaning validations and multi-allergen use of ingredient production systems)

4. ***Potential opportunities and barriers for adopting and implementing food allergen thresholds***

- FDA should consider how best to fit the use of allergen thresholds into existing manufacturer requirements for food safety, including conducting hazard analysis, preventative control setting, monitoring, and verification under FSMA. Thresholds should be incorporated as part of the holistic system, not as a stand-alone, separate component (e.g., allergen cross-contact could be evaluated in the hazard analysis using the threshold as the benchmark for "likely to cause harm").
- Integration of analytical method performance with clinical threshold data to enable practical, risk-based allergen management by industry.
- Development of standardized verification frameworks for end users to ensure methodological suitability across diverse food matrices. FDA can work with industry groups to develop these frameworks and appropriate reference information/samples for ongoing use.
- Improved ongoing collaboration between verification method developers, regulators, and industry to align expectations.
- Recognize that science is continuously evolving and therefore build plans for updates/changes to the various components of the allergen threshold system, starting with the threshold setting and the appropriate verification tools for use. New data on allergen sensitivity, need for a potential "tier 2" of allergens based on new scientific data or changes to US population sensitivity, changes to food crops and new clinical studies are some of the numerous changes that could be expected and the FDA implementation needs to build such thinking into how it approaches updates and revisions. Potentially, FDA could set a planned review period (e.g., every 5 years) to capture and feed back into the system whatever changes are necessary. That way, tool developers, laboratories, industry and end consumers would have a reliable timetable to expect updates as opposed to occurring ad hoc.
- Specific barriers for consideration include:
    - Limited availability of matrix-specific validation data.
    - Variability in analytical performance and method error across test tools and laboratories
    - Challenges in detecting allergens in highly processed or hydrolyzed food matrices that may interfere with testing
    - Economic affordability of test kits/laboratories for small and mid-sized food manufacturers
    - Requirements for mini-scale (e.g., home based) food producers

- Challenges for food importers from global manufacturers of various scales with implantation, particularly if the US approach varies dramatically from Codex Alimentarius.
- Resource requirements for laboratory and industry implementation
- FDA Resource needs for both implementation and ongoing management & updating of the program.
- Risk of over-reliance on analytical results without consideration of sampling uncertainty and real-world variability issues.

Concluding Comments

FDA implementation of risk-based allergen thresholds would be a major step forward in improving food safety and regulatory consistency across the food industry and a significant enabler for the more than 30 million US consumers who have varying degrees of allergen sensitivity. It would be particularly beneficial for those with medium-to-high allergen sensitivity when fully implemented. However, successful implementation depends upon FDA continually aligning clinical data with real-world capabilities and recognizing the limitations of analytical methods, along with the continuing advancement of scientific information on allergenicity. Use of allergen thresholds would bring a new level of transparency for consumers and provide a more standardized approach to allergen management for industry.

We welcome the opportunity to support the FDA in their continued development of allergen thresholds. If you have any questions about our comments, please contact me at arosales@ift.org.

Sincerely,

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Footnotes:

1 Risk assessment of food allergens: part 3: review and establish precautionary labelling in foods of the priority allergens: meeting report

2 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-recommendations-submission-chemical-and-technological-data-direct-food-additive#intake

3 fao.org/fao-who-codexalimentarius/sh-proxy/pt/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-714-49%252FCRDs%252FCompiled%2BCRDs%2B07-18%252Ffl49_crd13.pdf

4 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-recommendations-submission-chemical-and-technological-data-direct-food-additive#intake

5 fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-715-45%252FFINAL%252520REPORT%252FREP26_MASe.pdf (See Paragraphs 105-117 of the document)