U.S. FOOD & DRUG ADMINISTRATION

Discussion Paper Development of an Enhanced Systematic Process for the FDA's Post-Market Assessment of Chemicals in Food

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I. Background and Purpose

The U.S. Food and Drug Administration (FDA or we) is working to establish an enhanced systematic process for the post-market assessment of chemicals in food, including food additives, color additives, generally recognized as safe (GRAS) substances, substances used in contact with food, and those chemicals present as unintentional (for example, environmental) contaminants.

This discussion paper broadly outlines a general approach for such a systematic process that would allow the FDA to proactively identify and target chemicals currently in the food supply for assessment in a structured manner based on risk. The purpose of this discussion paper is to obtain public comment on the process to assist in developing the post-market chemicals program we will establish under the new FDA Human Foods Program.

Recognizing that the FDA Human Foods Program will be monitoring large amounts of information related to chemicals in food, some post-market assessments will be more complex and resource-intensive than others. Therefore, this process outlines two different types of assessments: Focused and Comprehensive.

Note: FDA compliance-related activities and actions taken in response to urgent public health matters (for example, the FDA's assessment of a chemical suspected or implicated in a foodborne illness outbreak investigation) are not within the scope of this discussion paper.

II. Process

For All Chemicals

We envision the post-market assessment process to start with a review of information, which would include food chemical Signal Monitoring, Triage, and a Fit for Purpose Decision process used to determine which type of Assessment (Focused or Comprehensive) is warranted.

1. **Review of Information**
    a) **Food Chemical Signal Monitoring**
        - The FDA will identify new information through monitoring of multiple sources.
        - Possible sources of information include new submissions to the FDA, scientific publications, international and U.S. regulatory activities, adverse event reports, news reports and trade press, and social media.
    b) **Triage**
        - The FDA will conduct a preliminary quality and impact assessment of information obtained through food chemical signal monitoring to determine the need for post-market assessment.
    c) Fit for Purpose Decision
        - The FDA will decide whether to conduct a Focused or Comprehensive Assessment. We will make this decision based on the likely complexity of the assessment needed, taking into account a number of factors (see Section III: Fit for Purpose Decisions below). For example, if we identify a

single new small study on a chemical, the assessment is likely to be Focused. However, if we identify multiple new studies or otherwise have reason to suspect an assessment will be complex or of significant public interest, the assessment is likely to be Comprehensive.

Once a decision has been made about whether to conduct a Focused or Comprehensive Assessment based on the review of information, we envision that the steps in each respective process will be as follows:

Focused Assessments

Focused Assessments will be limited in scope and will be conducted by the FDA without formal external engagement during the process, unless required by law. As such, we expect that Focused Assessments will generally be completed more quickly than Comprehensive Assessments. Focused Assessments will range in scope, but typically will be completed within 4 months to 1 year (not including risk management review and actions, if warranted).

1. **Scope/Problem Formulation**
    - The FDA will define the chemical substance or substances and establish the scope of the review.
2. **Scientific (Risk and Safety) Assessment**
    - The FDA will assess whether new information about a chemical suggests a possible safety concern.
    - We will determine if substances or ingredients intentionally added to food continue to meet the “reasonable certainty of no harm” standard or if actual or estimated exposures exceed a safe level.
    - We will determine if information on a contaminant(s) suggests a public health concern.
3. **Risk Management Review**
    - FDA subject matter experts will determine whether action is necessary to protect public health and outline possible mitigation strategies and associated benefits to public health. The FDA will identify resource needs to implement potential risk management actions.
    - We may also identify the need for additional research or the need for a full comprehensive assessment.
4. **Communication of Conclusions and Implementation of Risk Management Action(s)**
    - The FDA will communicate conclusions and take any appropriate risk management actions. Depending on conclusions, the chemical may be referred for prioritization as part of a Comprehensive Assessment.

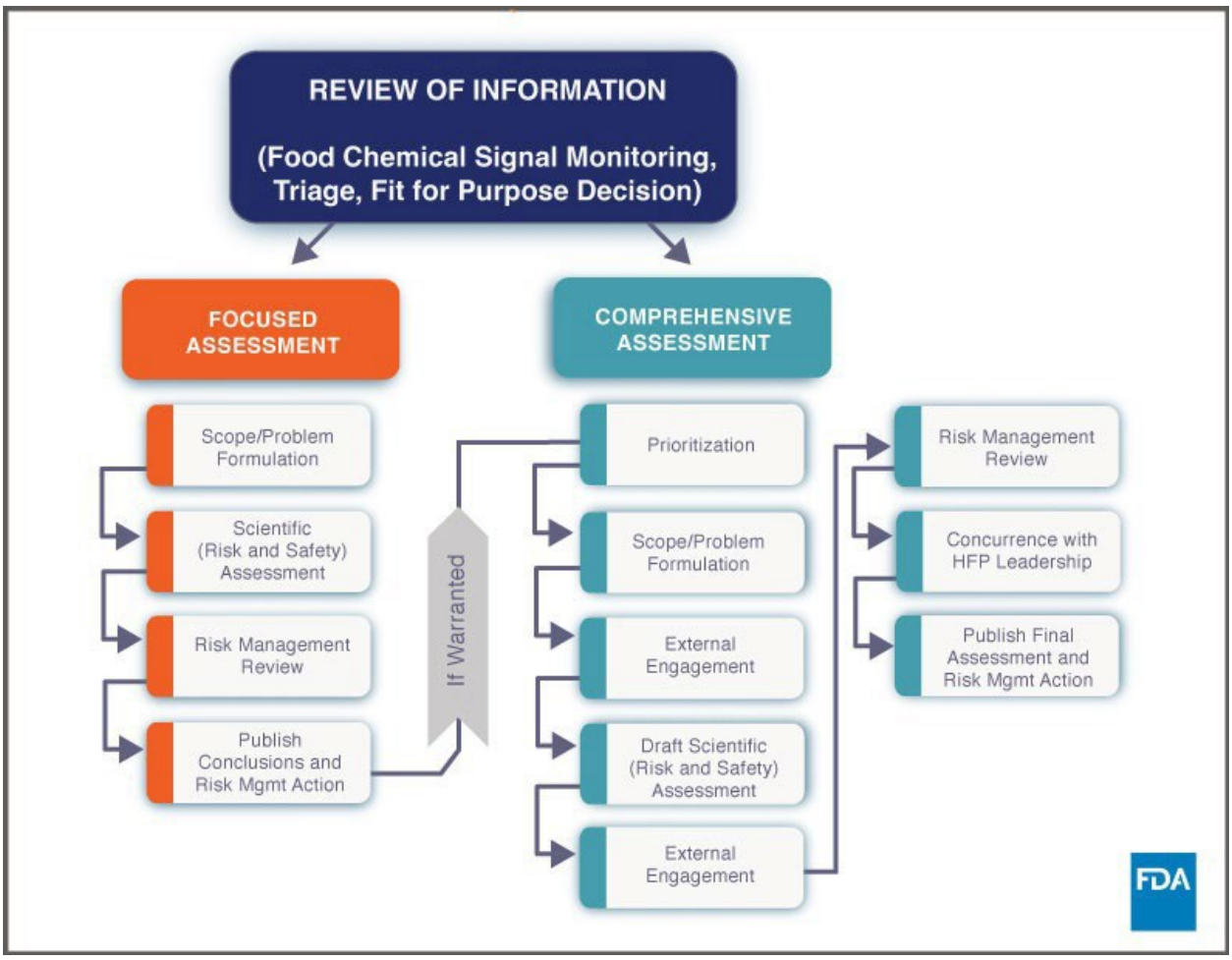
Comprehensive Assessments

Comprehensive Assessments will be more complex and resource intensive than Focused Assessments and may take years to complete. We envision incorporating external engagement (including through peer review, where appropriate) in the Scope and Draft Scientific (Risk and Safety) Assessment steps, and risk communication will be critical throughout this process.

1. **Prioritization**
    - A team of FDA experts will rank individual chemicals selected for Comprehensive Assessment based on pre-established criteria to determine their relative priority against other chemicals in food. Prioritization is covered in more detail in Section IV of this document.
2. **Scope/Problem Formulation**
    - The FDA will define the chemical substance or substances and establish the scope of the review.
      We will engage the public to help identify new information and data to inform our work.
3. **Draft Scientific (Risk and Safety) Assessment**
    - After considering relevant external feedback gathered in the Scope/Problem Formulation stage, the FDA will assess whether available information about a chemical suggests a safety concern.
    - Risk and Safety Assessments may include the following:
        i. Assessment of the hazard(s): evaluation of the nature of adverse health effects associated with the identified hazard(s) and population(s) of concern.
        ii. Assessment of the anticipated dietary exposure: characterization of the dietary exposure of the population and relevant subpopulations.
        iii. Assessment of the risk from exposure to the hazard(s): integration of dose/response and dietary exposure to estimate likely risk to relevant populations.
        iv. Identification of data gaps or research needs to support the scientific assessment.
    - We will determine if substances or ingredients intentionally added to food continue to meet the “reasonable certainty of no harm” standard or if actual or estimated dietary exposures exceed a safe level.
    - For contaminants, we will assess the risk of the contaminant in food to determine if the presence needs to be limited or reduced to assure safety.
    - We will engage the public on the Draft Scientific (Risk and Safety) Assessment.
4. **Risk Management Review**
    - After the Draft Scientific (Risk and Safety) Assessment, the FDA will determine whether action is necessary to protect public health and, if so, available options for risk management. The FDA will identify the associated public health benefits of each option and resource needs for implementation. We may request new data from industry or other stakeholders, collect new analytical or exposure information, or conduct exposure or safety studies.
5. **Concurrence with FDA Human Foods Program (HFP) Leadership**
    - FDA experts responsible for conducting the Draft Scientific (Risk and Safety) Assessment and Risk Management Review will brief leadership in the FDA Human Foods Program on their scientific conclusions, available options for risk management, and recommendation(s) for Risk Management Action(s).
6. **Make Public Final Assessment and Risk Management Action**
    - After consideration of any external and internal feedback we receive, the FDA will make public the Final Scientific Assessment.
    - The FDA will initiate any Risk Management Actions needed (including regulatory measures such as recommending recalls and taking enforcement actions).
    - Depending on the risk management action, there may be opportunity for public comment. For instance, if the FDA decides to revoke a regulation authorizing the

use of a food additive, we would follow the applicable procedures for publication in the Federal Register notice and an opportunity for public comment before issuing a final rule.

Process Flow Chart 1



III. Fit for Purpose Decisions

Following Signal Monitoring/Detection and Triage, we envision that FDA experts will conduct a cursory review to determine whether the information warrants additional review and if we should conduct a Focused or Comprehensive Assessment to address the information identified in the signal based on a number of factors. We envision that the answers to the following questions will help determine if an assessment should be Focused or Comprehensive:

- Will the assessment require significant resources outside of the Office of Post-market Assessment (for example, lab work, data collection) that require prioritization of risk within the new FDA Human Foods Program?

- Is there scientific consensus and/or strong weight of evidence about the substance suggesting its potential to impact the prevailing conclusion of reasonable certainty of no harm under the conditions of use in food?
- Have multilateral organizations, U.S.-bilateral organizations and/or scientific organizations recently reviewed the risks associated with the food substance and identified potential safety concerns?
- Is there evidence of a change in dietary exposure indicative of an impact to consumer health?
- Is the substance of significant public health interest?
- Are there statutory deadlines or other required timelines for the FDA to make its determination?

IV. Prioritization of Risk

The FDA seeks to develop an objective post-market assessment prioritization of risk process that is sufficiently flexible while ensuring the process is science-based, data-driven, systematic, and reproducible. The FDA envisions to use a Multi-Criteria Decision Analysis (MCDA) method. Using the MCDA approach, the higher the total score (for example, sum of criteria, including weighting, if used), the higher the priority for that chemical for further review, with the primary focus being risk to public health (risk ranking).

The MCDA method is similar in approach and criteria to the method used by the U.S. Environmental Protection Agency (EPA) for prioritization of chemicals for risk evaluation (see: Prioritizing Existing Chemicals for Risk Evaluation | US EPA) with a scoring method similar to FDA's Risk Ranking Model for Traceability (see: FDA Risk-Ranking Model).

For public health ranking, we tentatively envision that a chemical that would receive a higher public health score is one for which:

- The toxicity of the chemical is severe with potentially life-threatening adverse health effects (for example, cancer);
- Changes in exposure have occurred: for example, contamination data indicate significantly higher levels than previously documented, and/or consumption of the foods in which the chemical is found has increased, and/or there has been a significant increase in production volume of the chemical compared to the previous assessment;
- The chemical is found in or could be present in food intended for vulnerable subpopulations (for example, infants); and
- Newly available information, data, or science indicates a potentially significant impact on the conclusions of the previous assessment of the chemical.

Additional criteria that may be considered includes, for example, interest and/or attention to this chemical by other organizations or the public.

V. External Engagement

Transparency and external engagement are important parts of our planned process for post-market assessment of chemicals in food. The FDA envisions engaging the public during two important parts of the Comprehensive Assessment process: Scope/Problem Formulation and

Draft Scientific (Risk and Safety) Assessment. There may also be instances where we seek external peer review of Focused Assessments on an ad hoc basis.

The method of this solicitation may depend on the particular regulatory program(s) and requirements for those specific program(s). For example, the requirements for food additive and color additive petitions are prescribed in 21 CFR part 171 and 21 CFR part 71, respectively, and the requirements for citizen petitions are outlined in 21 CFR 10.30. However, for Comprehensive Assessments conducted on our own accord (for instance, not in response to a petition), the FDA is considering when and how to best engage the public in a way that balances the need for increased transparency and public input with resource considerations. Any regulatory actions will be subject to any applicable public notification and comment period requirements. We are reviewing how other agencies and programs (for example, EPA's TSCA Program) engages the public as the FDA develops its own program.

VI. Questions for the Public

We appreciate public input on the process outlined in this document. In particular, we welcome feedback on the following questions:

1. When and how should the FDA engage the public on post-market assessments?
2. Is the frequency and mechanisms of the envisioned public engagement described in Section V of this document appropriate? If not, please provide alternative areas for engagement/communication, additional information that you believe should be shared publicly, and rationale for the change.
3. Should the FDA integrate an advisory committee review into our post-market assessment process? If yes, at what stage, and what should the committee's role be?
4. Are the Fit for Purpose Decision Tree questions in Section III of this document appropriate? If not, what questions would you add or how would you modify the questions to be more appropriate to the task?
5. Is the Prioritization of Risks scheme the FDA outlines in Section IV of this document appropriate for ranking food chemicals, (including contaminants, food ingredients, and those substances used in contact with food) for post-market assessments? If not, please explain why and how you would modify the Prioritization of Risks scheme. Please provide supporting rationale for the changes.
6. Is the FDA's two-pronged approach of Focused Assessments and Comprehensive Assessments appropriate to assess public health risks of chemicals in food? If not, please explain why and provide an alternative process, including rationale for such alternative(s).

Please submit your comments regarding the questions in this discussion paper to Regulations.gov Docket No. FDA-2024-N-3609 by December 6, 2024.