Institute for the Advancement of Food and Nutrition Sciences

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IAFNS Food and Chemical Safety Committee

Request for Proposals

Develop and Validate a Framework for Heavy Metal Exposure Reduction in Human Diets

The Institute for the Advancement of Food and Nutrition Sciences (IAFNS) is a non-profit, 501(c)(3) scientific organization that pools funding from industry collaborators and advances science through the in-kind and financial contributions from public and private sector participants.

The IAFNS Food and Chemical Safety Committee is recognized as a scientific leader in food and chemical safety research. National and international scientific organizations apply the science provided by the Committee to address research gaps and drive decision making.

IAFNS adheres to strict procedures to maintain scientific integrity in all work we support. These requirements are described further in the attached TOP Guidelines and Guiding Principles for Scientific Integrity addendums.

Background:

Reducing the potential impact of heavy metals on health includes mitigating their presence in the food chain, however this is a complex task since metals can unavoidably enter the food supply from various routes such as soil, water, and air. There are unique factors that drive the presence of heavy metals in the supply chain for each commodity (e.g., agricultural practices and varietal characteristics) that do not allow for the application of common mitigation measures. Action levels have been set for specific heavy metals and commodity combinations (1,2), and there is currently work on-going to examine broader opportunities to mitigate dietary intake (3,4). Aligned with US and global regulatory goals to reduce dietary exposure to heavy metals, including the FDA's 'closer to zero' initiative, this project aims to establish a best practices approach for supply chain management that links an understanding of element concentrations in commodities to the most appropriate mitigation measures to reduce exposure.

This project builds on previous projects by the Food and Chemical Safety Committee that produced tools for rapid risk assessment methodology for heavy metals in human diets including a Heavy Metal Screening Tool, developed in collaboration with the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) (5,6) and an approach for the prioritization of chemical contaminants based on risk and mitigation efficacy and impact (7,8). This project will investigate how a structured approach can be developed to prioritizing heavy metals in commodities based on both risk and mitigation opportunities.

Objective:

Develop a framework for heavy metal prioritization and mitigation that incorporates knowledge on concentration ranges, together with exposure and mitigation, and validate the model with selected examples. The framework should include:

- Concentrations and variability of heavy metal(s) found within commodities and criteria for identifying when data falls outside of these ranges.
- An exposure-based prioritization of commodities which is linked to the availability of effective mitigation methods.

The Framework should consist of the following elements:

1. Development of a scheme for the prioritization for food commodity/heavy metal combinations, including:
    - A methodology to assess the variability within and between commodities, to identify 'common' ranges and criteria for when concentration data falls outside of these ranges.

- A methodology to assess exposure to enable the ranking of commodities in terms of their contribution to cumulative exposure.

2. Development of a system for the prioritization of approaches to exposure mitigation including:
    - Assessment of the root causes to heavy metal presence and accumulation, to facilitate a review of mitigation methods.
    - Evaluating available mitigation methods, including a determination of the suitability of mitigation based on efficacy and potential secondary effects such as impact on commodity availability, cost, or sustainability.
    - Assessment of future mitigation options and research needs.
    - Scope of reductions that are achievable with current and future technologies.
        - Mitigation methods to be considered include those that may be applied as a part of agronomic practices, including selection of growing location, soil treatment, and crop varietal.
        - Those that may be applied as a part of supply chain controls, including commodity processing or criteria for selection/rejection.
        - Those that may be applied in the consumer marketplace, including for example ingredient replacement or advice on consumption.
3. Validation of the above via the use of examples selected based on commodity prioritization that demonstrate root causes, scope of reductions and science gaps.

Approach

The table below provides an overview of the elements to be included in the proposed Framework, which should be developed through at least 2 worked examples.

Prioritization for food commodity-metal combinations	Prioritization of approaches to mitigation
Identification of robust data sources on occurrence and concentration.	Root cause analysis to identify the relationship between the commodity and the environmental factor that drives heavy metal accumulation, including the physicochemical and/or biochemical factors that underly these relationships.
A systematic method to capture ranges and measure of variability of the heavy metal(s) of interest.	Identification of all possible mitigation methods.
Identification of gaps in data that might be addressed.	Prioritization between mitigation methods based on multivariate inputs including but not limited to efficacy and impact on supply chains.
A method to prioritize (risk ranking) between the comparator group of commodities under study, based on contribution to consumer exposure.	Based on the information gained from the above, identification of research priorities.

The Project is anticipated to include the following elements:

1. Selection of examples.
2. Feasibility.

   a. Initial scoping of the Model, including required input parameters, fundamentals of model functioning.
   b. Testing of Model components.
3. Testing.
   a. Gathering of input data.
   b. Trial and refinement of the model.
   c. Alignment with the Stakeholder community.
4. Operation.
   a. Operate the model to provide draft outputs using the selected examples.
   b. Refinement of the model.
   c. Documentation (publication), the Framework and its operation, findings for the selected examples.

The applicant is invited to consider the most appropriate method to select examples to aid the development of the Framework, recent prioritization schemes such as by Codex might be considered (9). For illustration, a selected comparator group might be cadmium in the leafy vegetables such as lettuce, spinach, cauliflower, kale, selected based on their contribution to national leafy vegetable intake. Through the risk ranking process it might be identified that amongst this comparator group spinach contribute the greatest to cadmium exposure, so is prioritized for review of mitigation options.

As the project includes different phases to develop a risk-mitigation model, and each Phase would require distinct knowledge, we envisage that work will be undertaken by different experts working together.

Proposal Content:

The Committee requests that applicants address each of the following components in their proposal:

1. **Overview:** Please provide a short description of the proposal.
2. **Research Approach:** Please provide your approach to the research design elements as described above. Identify key research questions, primary and secondary outcomes, methodology, and analysis plan. Where appropriate, please reference the validation of proposed methods.
3. **Research Team:** Please indicate the primary and secondary investigators, plus any additional contributors or collaborators including ones from outside organizations.
4. **Anticipated Challenges**
5. **Investigator Credentials:** Please describe the experiences that make you and your team a candidate for carrying out this project. In addition, the CV of the principal investigator(s) is required.
6. **Resources:** Please describe the resources available to you to complete the project.
7. **Budget:** Please provide a budget indicating allocation of the requested funds to specific tasks, as well as a corresponding timeline to completion.
   a. Please note that IAFNS limits overhead to 10% of project costs.
   b. IAFNS will directly pay publication fees for open access.
8. **Timeline and Key Deliverables:**
   a. One or two publications in a peer reviewed journal.
   b. Periodic updates to the Food and Chemical Safety Committee.
   c. Presentation at appropriate scientific forum.

d. Timeline to completion: 9-11 months.

9. **Potential Conflicts of Interest:** List any potential conflicts of interests for all investigators, co-investigators, collaborators. We suggest using the Conflict-of-Interest Guidelines as set forth by the American Society for Nutrition: https://nutrition.org/publications/guidelines-and-policies/conflict-of-interest/

Page Limit: No more than 5 pages excluding references and investigator bios and CV.

Proposal Deadline: December 15, 2021

Submission Instructions: Please submit completed proposals to:

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nsaab@IAFNS.org

Proposal Review Process:

a) Proposals will be reviewed promptly by the Food and Chemical Safety Committee. Only projects meeting requested criteria will be considered.

b) Applicants will be notified in writing if additional information is needed.

c) Applicants will be notified of the disposition of their proposals in a timely manner.

d) Upon project initiation, the project summary, principal investigator, and budget will be published on our funded projects portal: https://iafns.org/funded-projects/

References

1. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-action-levels-poisonous-or-deleterious-substances-human-food-and-animal-feed#lead
2. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-action-level-inorganic-arsenic-rice-cereals-infants
3. https://www.fda.gov/food/cfsan-constituent-updates/fda-response-questions-about-levels-toxic-elements-baby-food-following-congressional-report
4. https://www.fda.gov/food/metals-and-your-food/closer-zero-action-plan-baby-foods#:~:text=The%20U.S.%20Food%20and%20Drug,to%20as%20low%20as%20possible.&text=the%20type%20of%20food%20crop,elements%20from%20the%20environment%2C%20and
5. Partitioning of Dietary Metal Intake—A Metal Dietary Exposure Screening Tool. Nga L. Tran*, Leila M. Barraj, Carolyn Scrafford, Xiaoyu Bi, and Terry Troxell *Risk Analysis, Vol. 35, No. 5, 2015*
6. Review of Regulatory Reference Values and Background Levels for Heavy Metals in the Human Diet. Candace Wong, Stephen M. Roberts, Imad Neal Saab (publication Pending)
7. A Risk-Based Strategy for Evaluating Mitigation Options for Process-Formed Compounds in Food: Workshop Proceedings. Paul Hanlon, Gregory P. Brorby, and Mansi Krishan. International Journal of Toxicology 2016, Vol. 35(3) 358-370
8. Evaluating the Applicability of a Risk-based Approach (Decision Tree) to Mycotoxins Mitigation. P. R. Hanlon, R. Bandyopadhyay and G. P. Brorby. Food Protection Trends, vol. 39, no. 5, pp. 406-416, Sep 2019
9. Discussion Paper on The Establishment of New Maximum Levels For Lead In Commodities According To A Prioritization Approach. Codex Committee on Contaminants in Foods. CX/CF 19/13/9 March 2019