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Academy of Nutrition  
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LEADING THE SCIENCE AND  
PRACTICE OF CLINICAL NUTRITION

March 8, 2023

Food and Drug Administration  
Office of Policy  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

Re: Docket No. FDA-2019-N-2650; Investigational New Drug Applications; Exemptions for Clinical Investigations to Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic.

To Whom it May Concern,

We the undersigned organizations with a vested interest in food and nutrition research appreciate the opportunity to comment on the proposed exemptions for Investigational New Drug (IND) applications for clinical investigations to evaluate products lawfully marketed as a conventional food or dietary supplement. We appreciate FDA's efforts to develop the proposed rule with the goal of reducing the burden of INDs for clinical investigations evaluating certain drug uses of foods or supplements that are not intended to result in the development of new drugs or drug claims while maintaining adequate safeguards for human subjects.

Exemptions from INDs for clinical investigations of lawfully marketed food products that are not intended for drug development will alleviate limitations on human nutrition research and remove burdens to investigators, such as the need for significant human and financial resources and delayed research projects, allowing for more human nutrition research, clinical trials, and product innovation. These exemptions will more readily allow for nutrition research in the U.S. to support future health claims designed to help consumers make healthier food choices and for nutrition research to support federal dietary recommendations and policies, such as the *Dietary Guidelines for Americans* and Dietary Reference Intakes.

We are concerned, however, that the proposed rule does not address the following key considerations.

- 1) FDA should clarify that clinical investigations assessing lawfully marketed foods and supplements are not studies of "drug uses" when the product will continue to be intended for consumption as a food or supplement, not as a drug.

- a. It is of concern that the proposed rule uses language describing clinical investigations of lawfully marketed foods as studies to evaluate a food's use as a drug ("*when the product is to be studied to evaluate its use as a drug*") when IND exemptions are being proposed for clinical investigations of foods that will not result, nor are intended to result, in the development of new drugs or drug claims. The products will continue to be intended for consumption as a food or supplement, not as a drug. These clinical investigations are solely to better understand the health effects of lawfully marketed foods on human health. The undersigned organizations therefore encourage FDA to further clarify use of the term "drug use" within the proposed rule or to remove this terminology altogether for the purposes of these proposed exemptions.
- 2) FDA should clarify IND exemption applications for foods and supplements that are not yet "lawfully marketed" (i.e., products under development or products being reformulated).
  - a. The undersigned organizations request that FDA provide an exemption pathway both for products that are already lawfully marketed in the U.S. as a food and also for products that could be lawfully marketed in the U.S. as a food based on composition and ultimate intended use. We request that FDA provide further clarification for exemptions for conventional foods and dietary supplements for human consumption under development or products being reformulated that have not yet been lawfully marketed to the public to help manufacturers better understand how exemptions may apply to clinical investigations of these food products.
- 3) FDA should clarify the timeline for the FDA-determined exemption process to ensure that research is not unnecessarily delayed.
  - a. The undersigned organizations request that FDA provide clarification for the timeline for FDA-exemptions. We encourage FDA to streamline the FDA-determined exemption process as much as possible so that significant human and financial resources, such as are often required for the completion of IND paperwork, are not necessary. We encourage FDA to consider a timeline that supports timely responses to sponsors and sponsor-investigators so as not to impede or delay the start of food and supplement research studies.
- 4) FDA should determine that the Center for Food Safety and Applied Nutrition (CFSAN) is the most appropriate FDA Center to review IND exemption applications related to foods and supplements, rather than Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER).
  - a. The undersigned organizations requests that FDA-determined exemption cases be handled by and ultimately decided by CFSAN the rather than CDER or CBER. Nutrition has many complexities that are best understood by experts dedicated to food and nutrition when food, nutrient, or dietary supplement-related research is involved. This is especially relevant and pertinent given the current redesign of FDA's Human Foods Program to provide improved coordination of and a clear line of authority for all food-related aspects of FDA.

Thank you for your attention to this important research issue. The undersigned organizations appreciate FDA's efforts to offer Investigational New Drug application exemptions for clinical investigations to evaluate products lawfully marketed as conventional food or dietary supplements since it has a significant potential impact on food and nutrition research.

Sincerely,

Academy of Nutrition and Dietetics  
American Society for Nutrition  
American Society for Parenteral and Enteral Nutrition  
Institute of Food Technologists