American Society for Nutrition
Excellence in Nutrition Research and Practice

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,

The American Society for Nutrition (ASN) appreciates the opportunity to comment on the proposed rule, "Investigational New Drug (IND) Applications; Exemptions for Clinical Investigations to Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic". Established in 1928, ASN is a non-profit organization dedicated to our mission of advancing the science, education, and practice of nutrition. ASN has more than 8,000 members around the world, working throughout government, clinical practice, academia, and industry, to conduct research to achieve the ASN vision of "A Healthier World Through Evidence-Based Nutrition".

ASN has long communicated[1] that the current IND application and review processes are not appropriate for human research on food, nutrients, and dietary supplements since a drug development model cannot accurately be applied to foods or their components, and that INDs should not be necessary for food studies that will not result (nor are intended to result) in the development of new drugs or drug claims. ASN fully supports the Agency's efforts to allow IND exemptions for clinical studies evaluating health benefits of a food product or dietary supplement for human consumption, provided those studies meet the safety and exemption criteria set forth by FDA.

Exemptions from INDs for clinical investigations of lawfully marketed food products that are not intended to result in the development of new drugs or drug claims 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 that often accompany INDs, allowing for more human nutrition research, clinical trials, and product innovation. IND application 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.

[1] https://asn-cdn-remembers.s3.amazonaws.com/7ae4fa5a6772968856c8cb8e9466a228.pdf; https://asn-cdn-remembers.s3.amazonaws.com/3a359c2a938d59152137205370bff49a.pdf

9211 Corporate Blvd., Suite 300 | Rockville, MD 20850
T: 240.428.3650 | F: 240.404.6797
info@nutrition.org | www.nutrition.org

Scientific evidence supports that many foods and nutrients impart health benefits as components of food products which impact the risk and development of chronic diseases. In fact, the White House National Strategy on Hunger, Nutrition, and Health[2] includes the pillar Integrate Nutrition and Health, which seeks to prioritize the role of nutrition in disease prevention and management. While the role of an IND is to ensure that a product is reasonably safe for use in humans, many foods and nutrients have Generally Recognized as Safe (GRAS) status under the conditions of their intended use in human or animal food. When the scientific objectives of a clinical investigation of a conventional food or dietary supplement are not intended to result in a new drug or drug claim, but the product will continue to be intended for consumption as a conventional food or supplement, an IND should not be necessary.

As such, 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. These clinical investigations are solely to better understand the health effects of lawfully marketed foods on human health and the products will continue to be intended for consumption as a food or supplement, not as a drug. ASN therefore encourages 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, as it applies to IND exemptions for clinical investigations of lawfully marketed food products or supplements. There may be unintended consequences and confusion with regards to exemptions for clinical investigations that are not designed or meant to evaluate drug use in the eyes of the studies' sponsors and sponsor-investigators. For example, use of these terms may confuse institutional review boards (IRB), who may continue to err on the side of caution and require a written IND exemption from FDA, even when self-determined exemptions are adequate.

In the proposed rule, "lawfully marketed" means the product is marketed in the United States as a food or cosmetic consistent with the FD&C Act and any applicable FDA regulations but no guidance is given for food products still in development. ASN requests 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.

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[2] https://www.whitehouse.gov/wp-content/uploads/2022/09/White-House-National-Strategy-on-Hunger-Nutrition-and-Health-FINAL.pdf

ASN supports the criteria for a self-determined exemption from an IND and the FDA-determined exemption process. ASN requests that FDA provide clarification on the expected 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. It would be helpful if FDA could provide a timeline for the FDA-determined exemption process so that sponsors and sponsor-investigators can have a better understanding of when a response might be provided for their study planning purposes.

ASN also requests that FDA-determined exemption cases be handled by and ultimately decided by the Center for Food Safety and Applied Nutrition (CFSAN), rather than the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER). 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.

It would also be useful for FDA to further clarify the timeline for implementation of this proposed rule into a final rule, and when the final rule might go into effect, for research being planned. It has been more than seven years since the FDA issued a stay of portions of the final guidance for clinical investigators, sponsors, and IRBs for IND requirements for certain types of clinical studies on conventional foods. ASN hopes to see movement towards implementation of the final rule for IND exemptions for food studies happen at a more expedited pace.

Thank you for your attention to this important research issue. ASN appreciates FDA's efforts to offer IND 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. Please contact Sarah Ohlhorst, MS, RD, ASN Chief Science Policy Officer (240-428-3647; sohlhorst@nutrition.org) if ASN may provide additional information.

Sincerely,

Martha A. Belury, PhD, RDN
2022-2023 President, American Society for Nutrition