American Society for Nutrition
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November 26, 2013

Janet Woodcock, M.D., Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Rockville, MD 20993-0002

Re: Docket No. FDA-2010-D-0503; Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND

Dear Dr. Woodcock,

The undersigned organizations write to express our concerns with the September 2013 Final Guidance for Clinical Investigators, Sponsors, and Institutional Review Boards (IRBs): Investigational New Drug Applications (INDs). Of utmost concern is that the food and nutrition research community was not given an opportunity to review and provide input on the language related to *Conventional Food* and *Studies Intended to Support a Health Claim* before the final guidance was issued. We request that the U.S. Food and Drug Administration (FDA) reevaluate Section VI, Part D of the guidance and thus, reissue this portion of the guidance with an opportunity for interested parties to provide comment. Ultimately, this portion of the guidance should be revised so that additional clarity is provided on the rationale behind when an IND is required for human research on foods, nutrients and dietary supplements.

Based on our interpretation of the document, it is our understanding that if a food or dietary supplement manufacturer or distributor intends to make a claim that classifies the product as a drug (i.e., to treat, cure, mitigate, or prevent disease), then the research to support such a claim would need to be conducted under an IND. The purpose of this letter is to raise concerns about requiring an IND for studies that will not result (nor are intended to result) in the development of new drugs or drug claims. The guidance presents multiple concerns for the food and nutrition research community, including many possible unintended consequences, which are outlined below.

- Given the lack of clarity in the examples provided, university and medical facility IRB's may find it difficult to discern when INDs are *NOT* required. It is expected that IRBs will err on the side of caution and will enforce the recommendations in this final guidance for most clinical nutrition studies. Thus, investigators might be required to prepare an IND even when one is not needed per the guidance.
- The increased paperwork, time and uncertainty in filing INDs for clinical nutrition studies are new research barriers for investigators. The delay in the start date of

9650 Rockville Pike | Bethesda, MD 20814
T: 301.634.7050 | F: 301.634.7892
info@nutrition.org | www.nutrition.org

clinical nutrition studies while IND paperwork is processed will reduce the productivity of investigators and their subsequent potential for funding. This is of particular concern given that the IND will not result in a drug or drug claim.

- The guidance creates particular complexities for multi-site clinical studies in that INDs will need to be shared. Data safety monitoring boards (DSMBs) must also be involved for multi-site clinical trials, and DSMBs for all sites of clinical trials must interpret the guidance in the same way.
- Federal agencies beyond FDA may not provide funding for certain clinical nutrition studies that do not have an IND.
- Research in many emerging areas, including bioactives found in foods, pre/probiotics, and functional and medical foods, could be significantly and inappropriately reduced given the increased burden and the fact that in many situations the research is not expected to result in development of a drug.
- Research to support credible health claims and other product claims designed to help consumers make healthier food choices may be diminished.
- The implications of filing an IND for studies on products that are intended to be marketed as foods (not drugs) are not clear. Until this guidance was issued, studies to substantiate health claims have been conducted without an IND and have been used by FDA in its decision-making process for health claims. Essentially all studies submitted in health claim petitions since the enactment of the 1990 Nutrition Labeling and Education Act (NLEA) have likely been conducted without an IND.
- Filing an IND typically disqualifies a substance from becoming a new dietary ingredient (NDI). Consequently, clinical nutrition research on food components such as bioactives found in foods would be difficult to conduct, and may not be feasible to conduct, especially in view of the concern that IRBs are likely to err on the side of requiring INDs.
- The guidance may unintentionally encourage certain dietary supplements and/or food components to be marketed without adequate clinical research on their physiological effects.
- Due to the new research and marketing barriers, the food and dietary supplement industries may decide to conduct certain clinical nutrition research studies outside of the U.S., thus harming the U.S. research enterprise and economies.

Thank you for your attention to this important research issue. We would appreciate an opportunity to meet with the appropriate FDA officials to discuss our concerns in more detail and hear how they will be addressed. Sarah Ohlhorst, MS, RD, ASN Director of Government Relations, will contact the Center for Drug Evaluation and Research (CDER) office to follow-up on this request. In the meantime, please don't hesitate to contact her at sohlhorst@nutrition.org or 301.634.7281 should you have any questions.

Sincerely,

American Academy of Pediatrics
American Society for Nutrition
American Society for Parenteral and Enteral Nutrition
Institute of Food Technologists
International Life Sciences Institute North America
International Scientific Association for Probiotics and Prebiotics
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

CC: Karen Midthun, M.D., Director, U.S. Food and Drug Administration Center for Biologics Evaluation and Research

Michael Landa, J.D., Director, U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition