



HEALTHCARE NUTRITION COUNCIL

Improving outcomes through awareness and action

Submitted Electronically via Regulations.gov

May 11, 2023

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Protein Efficiency Ratio Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein; Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request

To Whom It May Concern,

The Healthcare Nutrition Council (HNC) is submitting comments on the U.S. Food and Drug Administration's (FDA or agency) draft guidance on "Protein Efficiency Ratio (PER) Rat Bioassay Studies" (FDA-2022-D-2424) which was published in the *Federal Register* on February 10, 2023. HNC is an association representing manufacturers¹ of enteral nutrition (EN) formulas and oral nutrition supplements (ONS), including those categorized as medical foods, and parenteral nutrition (PN). Our mission is to improve patient outcomes by advancing nutrition policies and actions that raise awareness and optimize access of essential nutrition support therapies across the continuum of care.

HNC appreciates the opportunity to submit comments in response to the FDA draft guidance and for the agency to provide this direction to industry in successfully conducting PER studies that demonstrate that a new infant formula meets the quality factor of sufficient biological quality of protein when fed as the sole source of nutrition. HNC members are seeking clarity around certain aspects of the guidance as it relates to exempt infant formulas, such as metabolic formulas and medical foods intended for infants with inborn errors of metabolism.

We acknowledge that FDA included an exemption for certain products in this guidance, but we also recognize that this will impact some exempt infant formulas as many manufacturers undergo these studies for specialty infant formula products. HNC recognizes FDA's guidance to make PER study expectations more clear which is a positive step toward helping industry follow the agency's direction. We understand that this requires FDA to devote additional resources to review PER protocols and PER studies.

We raise concerns regarding some of the modifications proposed to the AOAC method, that has been recognized by the FDA as a standardized method, that goes beyond original discussion with the final rule for infant formula good manufacturing practices (GMPs). The modification we

¹ HNC members are Abbott Nutrition, Nestlé Health Science, and Nutricia North America.



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are referring to focuses on sulfur content and suggests that companies should consider supplementing the casein diet with cysteine and methionine. This modification goes beyond regulatory requirement. HNC suggests that the inclusion of cysteine and methionine would revert the original focus of PER studies to focus on the comparison to modified casein versus just casein. We appreciate the agency's willingness to meet with firms to further discuss sulfur content, but at this time we believe the recommendation to add sulfur amino acids to the control diet needs more evaluation before making it an official guideline. The agency recognizes there have been advances made in better understanding rat nutrition over the years which is why there were modifications made to the diet to better align with the updated AOAC method. However, HNC seeks additional information and clarification on why this modification to the AOAC method is being proposed.

We recognize the challenges with PER studies that can suggest inaccuracies in review of infant formulas and exempt infant formulas. Scientists recognize challenges with the rat model such as nibble eating, low acceptance of human diets, and their uniquely high requirement for cysteine. HNC raises these concerns for increased awareness by the agency that these challenges may lead to inaccuracies with the nutrient review.

HNC believes that much of what is suggested in the guidance lacks validation, and primarily highlights speculation from the review of literature versus what has been observed from PER studies that have been conducted by manufacturers. HNC recommends that the agency provide real-world validated applications into final guidance protocols. Part of AOAC's purpose is to bring harmonization and practical application into validated methods. HNC stands ready to share examples as needed.

Although we recognize other methods are not in the scope of this guidance, we hope in the future FDA will move toward modernization of the guidance and accept other methods such as PDCAAS and DIAAS that are used globally.

HNC appreciates the opportunity to submit comments on this important guidance. For questions and how HNC can be involved with offering examples, please contact Berit Dockter MPP, RD, LD at bdockter@healthcarenutrition.org or 202-207-1112.

Sincerely,

A handwritten signature in black ink that reads "Robert Rankin". The signature is written in a cursive, flowing style.

Robert Rankin
Executive Director