

August 30, 2024

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**Re: CRN Comments on Draft ODS Strategic Plan 2025-2029**

On behalf of the Council for Responsible Nutrition (CRN),<sup>1</sup> we submit these comments in response to the draft Office of Dietary Supplements (ODS) Five-Year Strategic Plan for 2025-2029. We appreciate the appointment of Dr. Stefan Pasiakos as the director of Office and his vision for establishing ODS as the premier organization for advancing dietary supplement research. We cannot agree more that ODS is in the best position to foster growth in dietary supplement science and knowledge in the U.S. and would serve as an excellent model for other countries. We commend and support the three cross-cutting themes of diverse populations, healthy lifespan, and resilience in the ODS research agenda. These themes align with the concept of Whole Person Health and emphasis on health restoration, resilience, and disease prevention outlined in the strategic plan of the National Center for Complementary and Integrative Health (NCCIH),<sup>2</sup> a key partner for ODS within NIH. We appreciate that ODS has led the effort to coordinate resilience research across the NIH through its Trans-NIH Resilience Working Group and ODS's continued commitment to supporting the application of resilience science to dietary supplement research to understand mechanisms by which dietary supplements and their ingredients promote health across the lifespan. The ODS draft strategic plan for the next five years clearly outlines how the Office intends to accomplish goals through coordination, collaboration, and partnership. We fully support the strategic plan and appreciate that Dr. Pasiakos named dietary supplement trade organizations as partners in reaching strategic goals. We look forward to continued engagement with ODS beyond the strategic plan process into the implementation phases.

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<sup>1</sup> **The Council for Responsible Nutrition (CRN)**, founded in 1973, is a Washington, D.C.-based trade association representing 200+ dietary supplement and functional food manufacturers, ingredient suppliers, and companies providing services to those manufacturers and suppliers. In addition to complying with a host of federal and state regulations governing dietary supplements and food in the areas of manufacturing, marketing, quality control and safety, our manufacturer and supplier members also agree to adhere to additional voluntary guidelines as well as to CRN's Code of Ethics. Visit [www.crnusa.org](http://www.crnusa.org). Follow us on X (formerly Twitter) [@CRN\\_Supplements](https://twitter.com/CRN_Supplements) and [LinkedIn](https://www.linkedin.com/company/crnusa).

<sup>2</sup> National Center for Complementary and Integrative Health. NCCIH Strategic Plan FY 2021–2025: Mapping the pathway to research on whole person health. National Center for Complementary and Integrative Health. Available from: <https://www.nccih.nih.gov/about/nccih-strategic-plan-2021-2025>.

*Are there additional emerging public health issues that ODS can help address?*

#### Women's health across the lifespan

As alluded to in the plan, we emphasize the importance of additional research to understand, through a health equity lens, the associations between dietary supplement use and women's health across the lifespan. For example, dietary supplement use and its contribution to meeting the unique nutrient needs of lactating women is under-researched. ODS should support research in this area and educate consumers and healthcare providers on the unique nutritional requirements of this life stage, as well as the impact that dietary supplement use during the post-partum period can have on the nutrient content of breast milk. Consumers and healthcare providers would benefit from guidance on appropriate supplements to address these requirements.

*Are there partnerships ODS should pursue, both inside and outside of government, to advance research on dietary supplements?*

#### USDA and HHS

We recommend ODS to expand partnership with USDA and HHS to support research underlying the scientific questions about the relationships between supplementation of specific nutrients and maternal and child health that the 2020 Dietary Guidelines Advisory Committee did not review due to time constraints. Initially, six nutrients (folate, omega-3 fatty acids, iron, iodine, vitamin D, and vitamin B12) from supplements were to be included in the review; however, the Committee prioritized review of folate and omega-3 fatty acid supplementation during pregnancy and lactation and iron and vitamin D supplementation during infancy. It remains important to explore the relationships between the identified nutrients from supplements and maternal and child health outcomes. However, it is possible that not enough evidence is available for systematic reviews on these topics, given that these topics were not included in the scientific review of the 2025 Dietary Guidelines Advisory Committee. Recently, the U.S. Preventive Services Task Force issued an evidence report pointing to limited data on the association between iron status and maternal and infant health outcomes while concluding that prenatal routine iron supplementation reduces iron deficiency and iron deficiency anemia during pregnancy.<sup>3</sup> ODS should support research to help answer the scientific questions related to dietary supplements that were posed during the development of the 2020-2025 Dietary Guidelines for Americans.

In addition, ODS should consider supporting additional research on the role of other bioactive compounds that are potentially beneficial for infant and maternal health including choline, lutein and zeaxanthin. Choline's role in fetal brain growth and development is well established.<sup>4</sup> Emerging research demonstrates maternal choline supplementation during pregnancy positively impacts cognitive

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<sup>3</sup> Cantor AG, Holmes R, Bougatsos C, Atchison C, DeLoughery T, Chou R. Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. Published online August 20, 2024. doi:10.1001/jama.2024.13546.

<sup>4</sup> Jaiswal A, Dewani D, Reddy LS, Patel A. Choline Supplementation in Pregnancy: Current Evidence and Implications. Cureus. 2023 Nov 8;15(11):e48538. doi: 10.7759/cureus.48538.

outcomes in offspring.<sup>5,6,7</sup> Recent research indicates lutein and zeaxanthin intake provides benefits for infant neural and ocular development and overall maternal health.<sup>8,9,10,11</sup>

### Industry researchers and trade organizations

We applaud ODS for harnessing many strategic partnerships within government to advance research on dietary supplements. We appreciate the ODS strategic plan has identified that collegial partnerships with industry researchers, among others, help “expand the range of subject matter expertise, enhance initiative collaborations, allow for pooled resources, and provide opportunities for feedback and dialogue.” We recommend establishment of an industry advisory council with a range of companies as well as trade organizations to support a continuous feedback loop with the goal of developing and disseminating best practices and knowledge to better the health of populations in the U.S. Moreover, we encourage ODS to seek public-private partnerships to facilitate funding of research. The Botanical Safety Consortium has helped advance the development of scientific tools to evaluate the safety of botanicals<sup>12</sup> and demonstrates that public-private partnerships are a worthwhile approach to advancing specific areas of dietary supplement research.

In addition to expertise in nutrition, industry scientists can offer valuable insight into the practical aspects of dietary supplement formulation and manufacturing. For example, CRN and our members have previously shared our perspective on the types and levels of nutrients for inclusion in prenatal multivitamins.<sup>13</sup> Factors including consumer preferences for “non-pill” delivery formats, inconsistency in recommended levels from health authorities and expert groups, the expanding list of nutrients with demonstrated benefits and requirements during pregnancy, all play a role in determining appropriate product formulations. This input was well received by academic researchers and has led to constructive

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<sup>5</sup> Nevins J, Beckman K, Bahnfleth C, et al. Maternal choline supplementation during pregnancy improves executive functioning in children at age 7 y (E10–06). *Curr Dev Nutr*. 2018; 2(nzy043): 3-4. doi:10.1093/cdn/nzy043.

<sup>6</sup> Bahnfleth, C. L., Strupp, B. J., Caudill, M. A., & Canfield, R. L. (2022). Prenatal choline supplementation improves child sustained attention: A 7-year follow-up of a randomized controlled feeding trial. *The FASEB Journal*, 36(1), e22054. <https://doi.org/10.1096/fj.202101217R>.

<sup>7</sup> Obeid R, Derbyshire E, Schön C. Association between Maternal Choline, Fetal Brain Development, and Child Neurocognition: Systematic Review and Meta-Analysis of Human Studies. *Adv Nutr*. 2022;13(6):2445-2457. doi:10.1093/advances/nmac082.

<sup>8</sup> Mahmassani HA, Switkowski KM, Scott TM, et al. Maternal Intake of Lutein and Zeaxanthin during Pregnancy Is Positively Associated with Offspring Verbal Intelligence and Behavior Regulation in Mid-Childhood in the Project Viva Cohort. *J Nutr*. 2021;151(3):615-627. doi:10.1093/jn/nxaa348.

<sup>9</sup> Anderson MJ, Romaguera D, Saint-Amour D, Fossati S, Fochs S, Pey N, Vrijheid M, Julvez J. Lutein and Zeaxanthin Intake during Pregnancy and Visual Function in Offspring at 11-12 Years of Age. *Nutrients*. 2022 Feb 18;14(4):872. doi: 10.3390/nu14040872. PMID: 35215522; PMCID: PMC8876686.

<sup>10</sup> Addo EK, Allman SJ, Arunkumar R, et al. Systemic Effects of Prenatal Carotenoid Supplementation in the Mother and her Child: The Lutein and Zeaxanthin in Pregnancy (L-ZIP) Randomized Trial -Report Number 1. *J Nutr*. 2023;153(8):2205-2215. doi:10.1016/j.tjnut.2023.05.024.

<sup>11</sup> Addo EK, Gorka JE, Allman SJ, et al. Ocular Effects of Prenatal Carotenoid Supplementation in the Mother and Her Child: The Lutein and Zeaxanthin in Pregnancy (L-ZIP) Randomized Trial - Report Number 2. *Ophthalmol Sci*. 2024;4(5):100537. Published 2024 Apr 24. doi:10.1016/j.xops.2024.100537.

<sup>12</sup> Mitchell CA, Dever JT, Gafner S, et al. The Botanical Safety Consortium: A public-private partnership to enhance the botanical safety toolkit. *Regul Toxicol Pharmacol*. 2022;128:105090. doi:10.1016/j.yrtph.2021.105090.

<sup>13</sup> Eric D. Ciappio, Nastaran Faghini, Laura Harkness, Susan H. Mitmesser, Alpa V. Shah, Andrea W. Wong, Challenges in Formulating a Prenatal Dietary Supplement: A Perspective from Industry Scientists, *The American Journal of Clinical Nutrition*, Volume 118, Issue 3, 2023, Pages 729-730, ISSN 0002-9165, <https://doi.org/10.1016/j.ajcnut.2023.06.018>.

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dialogue which has the potential to impact the nutrient intakes of millions of Americans.<sup>14</sup> We are aware that ODS is planning a workshop in early 2025 on prenatal supplementation and emphasize the need to include industry scientists in this event and other related initiatives.

#### *Additional Comments*

- We support the Office's plan to use population sciences to help identify nutrient and bioactive deficiencies. We suggest consideration of menaquinone or vitamin K2 as an under-researched area. Vitamin K2 is not widely available from foods and has been linked to promotion of cardiovascular and bone health. Therefore, it is important to monitor vitamin K2 intake and status in the U.S. population. More research is needed to support the assessment of dietary intake of vitamin K2 from food databases and the development of biomarkers of vitamin K2 and testing methodology. This basic research will help inform studies of the health effects of vitamin K2 in diverse populations across the lifespan. In addition, we highlight an opportunity for ODS to help further research currently being funded by the National Institute on Aging on the development of methodologies to measure nicotinamide adenine dinucleotide (NAD+) in humans in support of Research Priority 1.<sup>15</sup>
- We encourage ODS to continue regularly updating the fact sheets when new information becomes available. For vitamin D, in particular, the CRN-Foundation's Vitamin D & Me website ([www.vitamindandme.org](http://www.vitamindandme.org)) contains educational information on vitamin D and health supported by research. We strongly encourage ODS to review and include information from the Vitamin D & Me site in ODS education initiatives.
- We applaud ODS for providing valuable health information related to dietary supplements for diverse populations, including those that read English and Spanish. To advance health equity, we stress the importance of providing information in multiple languages so that trusted and credible information can be shared with as much of the U.S. population as possible.

Thank you for this opportunity to provide feedback.



Andrea Wong, Ph.D.

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<sup>14</sup> Sauder KA, Couzens GL, Bailey RL, et al. Reply to E Ciappio et al. *Am J Clin Nutr.* 2023;118(3):731-732. doi:10.1016/j.ajcnut.2023.06.019.

<sup>15</sup> Department of Health and Human Services. Notice of Funding Opportunity: Development and Validation of Harmonized Methodologies to Measure NAD+ and Related Metabolites in Clinical Trials (U01 Clinical Trial Required). <https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-24-039.html>.