GLOBAL ORGANIZATION FOR EPA AND DHA OMEGA-3S

19 December 2024

Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality
ATTN: EPC SEADs Coordinator
5600 Fishers Lane, Mail Stop 06E53A
Rockville, MD 20857
epc@ahrq.hhs.gov

RE: Request for Supplemental Evidence and Data (SEAD) Submission for *Dietary Saturated Fat Replacement and Plasma Lipid and Cardiovascular Events*

Dear EPC SEADs Coordinator:

GOED, the Global Organization for EPA and DHA Omega-3s, represents the worldwide EPA and DHA omega-3 industry, with a membership built on a quality standard unparalleled in the market. Members must comply with quality and ethics guidelines that ensure they produce quality products that consumers can trust. Our 200+ members and partners represent the entire supply chain of EPA and DHA omega-3s, from fisheries and crude oil suppliers to refiners, concentrators and finished product brands. Our mission is to use science-based information to promote consumption of and enable access to quality EPA & DHA from all sources for a positive impact on public health.

Given our mission, we appreciate the opportunity to provide comments (i.e. supplemental evidence and data (SEAD)) on the research protocol for ***Dietary Saturated Fat Replacement and Plasma Lipid and Cardiovascular Events.***[1]

We will focus on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) as it relates to the key questions. While your request is specific to providing supplemental evidence and data on the research protocol, we would like to provide commentary to address a specific concern.

EPA and DHA, the two main omega-3 long-chain polyunsaturated fatty acids of marine origin, have shown promise for the prevention of cardiovascular disease (CVD), and the evidence for a protective effect is covered in, for example, the meta-analyses of Hu *et al* and Bernasconi[2] *et al*. These benefits and their supporting evidence are described in detail in a separate letter to be sent in response to the "Request for supplemental evidence and data submission for Dietary Intake of Polyunsaturated Fatty Acids and Plasma Lipid and Cardiovascular Events."

[1] https://effectivehealthcare.ahrq.gov/products/saturated-fat-replacement/protocol
[2] In the interest of full disclosure, we consider it necessary to mention that the first author is a GOED employee and a co-signer of the current letter.

To date, most interventional trials have been designed with EPA/DHA as an addition to the regular diet, and not as a replacement. However, a relevant question remains regarding whether the observed benefits were due to a replacement effect, or to an independent action of EPA and/or DHA. We believe the latter to be the case.

As background, the Dietary Guidelines for Americans, 2020-2025[3] contains a key recommendation to limit saturated fat intake to less than 10% of caloric intake but Shan *et al* used NHANES[4] data to estimate that the actual intake of saturated fat in 2016 was approximately 12% of the total caloric intake. Assuming a 2000 Kcal/day diet, this corresponds to more than 25 g of saturated fat per day. The usual intake of EPA+DHA in 2003-2008, also according to an analysis of NHANES data, was estimated to be 113 mg/day. Even in clinical trials when higher dosages were provided to the treated group, the use of a supplement or drug was not intended to change the participants' diet or their intake of other fats. Regardless of the purpose or dosage, EPA+DHA intake was only a minor fraction of the usual saturated fat intake.

We believe that this is a strong argument supporting the hypothesis that the reported cardiovascular benefits of EPA+DHA intake derive from the biological action of these fatty acids, rather than from a probably negligible replacement effect. For this reason, we are concerned that your pursuit of the second key question as it relates to EPA and DHA may have the untoward effect of minimizing the benefits of EPA & DHA unless the results are put into proper context.

References

Hu Y, Hu FB, Manson JE. Marine Omega-3 Supplementation and Cardiovascular Disease: An Updated Meta-Analysis of 13 Randomized Controlled Trials Involving 127 477 Participants. *J Am Heart Assoc*. 2019;8(19):e013543. doi:10.1161/JAHA.119.013543

Bernasconi AA, Wiest MM, Lavie CJ, Milani RV, Laukkanen JA. Effect of Omega-3 Dosage on Cardiovascular Outcomes: An Updated Meta-Analysis and Meta-Regression of Interventional Trials. *Mayo Clin Proc*. 2021;96(2):304-313. doi:10.1016/j.mayocp.2020.08.034

U.S. Department of Agriculture and U.S. Department of Health and Human Services. *Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020.*

Shan Z, Rehm CD, Rogers G, et al. Trends in Dietary Carbohydrate, Protein, and Fat Intake and Diet Quality Among US Adults, 1999-2016. *JAMA.* 2019;322(12):1178-1187. doi: 10.1001/jama.2019.13771

[3] https://www.dietaryguidelines.gov/sites/default/files/2020-12/Dietary_Guidelines_for_Americans_2020-2025.pdf
[4] https://www.cdc.gov/nchs/nhanes/

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GOED appreciates the opportunity to provide feedback on this protocol. We remain at your disposal should any questions arise.

Sincerely,

Aldo Bernasconi, PhD
Vice-President, Data Science
aldo@goedomega3.com

Harry B. Rice, PhD
Vice-President, Regulatory & Scientific Affairs
harry@goedomega3.com

Kaitlin Roke, PhD
Director, Scientific Communication and Outreach
kaitlin@goedomega3.com