



LETTER

Letter to the Editor Regarding Critical Differences Between Dietary Supplement and Prescription Omega-3 Fatty Acids: A Narrative Review

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Key Summary Points

The authors of the review have reproduced figures from two previous publications that show the results of omega-3 dietary supplement quality assessment which has not been carried out in a correct manner.

These reproduced results are misinterpreted with respect to the quality requirements set by industry for dietary supplements and pharmaceutical products, because methods assessing these requirements have not been followed correctly.

The authors failed to cite a replication study reporting conflicting results from one of the cited studies used to substantiate their position.

Recent literature showing good to excellent quality of dietary supplements available to consumers has been omitted.

Digital Features To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.12489782>.

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Dear Editor,

By means of this writing, we would like to react to the recently published article “Critical Differences Between Dietary Supplement and Prescription Omega-3 Fatty Acids: A Narrative

Review” by Hilleman, Wiggins, and Bottorff [1]. Although this is a narrative review, it should consider the totality of the available scientific evidence and be as objective as possible. While this review is fraught with inaccuracies (e.g., efficacy, safety, regulatory, etc.), it is the misrepresentation of dietary supplement oil quality that is particularly troublesome and thus the focus of our comments. Specifically, the review failed to acknowledge results from a publication which calls into question the data and interpretation of one of the cited references.

The authors define omega-3 finished product quality by referring to the quality standards for eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) omega-3 ingredient oils and finished products that are established by the Global Organization for EPA and DHA Omega-3s (GOED) (<https://www.goedomega3.com/goed-monograph>). These quality criteria are as strict or stricter than those set by regulatory agencies in the countries where both supplements and pharmaceutical omega-3 products are sold to consumers. GOED’s membership encompasses the majority of omega-3 oil producers worldwide, including producers of omega-3 oils used in both dietary supplement and pharmaceutical products. What most readers of this journal likely do not know is that the omega-3 oil ingredients for both pharmaceutical and dietary supplements are produced by the same companies, most of which are members of GOED.

In Hilleman et al.’s review, the results and interpretation shown in Figs. 1b and 2b are incorrect for the reasons described below. According to the authors, “variable content of EPA and/or DHA, and inconsistencies with labeled quantities have been documented (Fig. 1) [57–61]”. While this is true, the authors failed to mention recent studies that report high to excellent dietary supplement product quality in various geographies when executed by laboratories that know how to analyze these sensitive products (e.g., Sprague et al. [2]). The results shown in Figs. 1b and 2b are from Albert et al. [3], but a study that fully replicates those findings (Bannenberg et al. [4]) and finds them to be incorrect in several aspects is not cited.

The replication, conducted by multiple independent laboratories, showed that nearly

all dietary supplements available to consumers were in compliance and adhered to applicable regulations in New Zealand (the country where the products were purchased for Albert et al. [3]). The replication revealed that the original researchers at the time of study execution did not know how to properly handle and analyze omega-3 oils. For example, a method for quantifying EPA and DHA in water-rich biological fluids, but unsuitable for oils, was used, and inadvertent oxidation of samples was shown to have likely occurred during sample preparation. The applicable regulatory framework was also not considered when reporting on compliance.

Suggesting that omega-3 dietary supplements are of inferior quality compared to one specific pharmaceutical product, which is marketed by the company that paid for the writing and publication costs of this review (see the acknowledgements), is negligent and contributes a bias to the review. While we are not questioning the high quality of the pharmaceutical product, it deserves mention that the three supposedly oxidized dietary supplements shown in Fig. 2b, reproduced from a study by Mason and Sherratt [5], likely correspond to finished products that contain a flavor. Flavoring frequently interferes with the colorimetric assays used for measuring oxidation and causes false positive signals, erroneously leading to these excessive values shown. This is a technical limitation not familiar to either the researchers when the study was performed, or to the authors of the current review.

Peroxide values, *para*-anisidine values, and the composite Totox numbers were further normalized by the authors to 1 g EPA + DHA, which is not the way these quality parameters are meant to be expressed (for example, see the GOED Voluntary Monograph cited earlier). Since most dietary supplements typically contain concentrations of EPA + DHA between 20% and 60% of this pharmaceutical product (which is a 97% EPA-ethyl ester concentrate), such normalization is further inflating the oxidation values of the three shown dietary supplements.

All sources of EPA/DHA omega-3 fatty acids are suitable to address the high incidence of insufficient dietary intake of these important

fatty acids, or contribute to improving health, whether from food, supplementation or pharmaceutical products. Accurate reporting and reviewing is critical, and there is no need for detraction or inciting any competition between different forms of omega-3 fatty acids. GOED will be pleased to provide further information on EPA/DHA omega-3s to any readers of this journal.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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