July 20, 2018

RE: Response to Cochrane Review on effects of omega-3s for prevention of CVD

Dear Valued Customer:

A controversial new meta-analysis (a study of previous studies) evaluating the effects of omega-3 fatty acids on the prevention of cardiovascular disease has recently been published in Cochrane Reviews, and is generating media interest and inquiries from the public. Although the study concludes that supplemental omega-3 EPA and DHA has little to no effect on cardiovascular health, the author's conclusions are questionable for a number of reasons, including confounding factors that likely affect the study's results, and decades of scientific data that show the opposite outcome—that omega-3 fatty acids EPA and DHA do, in fact, help protect the heart.

BACKGROUND

The authors of this meta-analysis pooled data from 79 randomized clinical trials (112,059 individuals) to determine if supplementation with omega-3 from either fish (EPA+DHA) or plants (ALA) had any notable effects on cardiovascular-related problems. Results largely indicated that increasing omega-3 intake had little to no effect on cardiovascular health. The authors also concluded that previous evidence of benefits from supplemental EPA and DHA appears to come from studies with a higher risk of bias.

Although the study's authors should be complimented on their effort to further our understanding of the potential effects of omega-3 fatty acids on cardiovascular disease, their conclusions are likely inaccurate for the following reasons:

LIMITATIONS OF STUDY DESIGN

The majority of studies (68.4%) in this meta-analysis had a relatively high risk of bias.

> Just 31.6% of the 79 studies used in the meta-analysis were considered to have a low risk of bias. The study's authors therefore indirectly imply that their conclusions should be considered with great care due to the large number that were likely biased.

The meta-analysis combined studies on healthy and diseased subjects—many with pre-existing cardiovascular disease.

> Measures of cardiovascular health (obesity, blood pressure, etc.) vary greatly among 'healthy' individuals and those diagnosed with cardiovascular dysfunctions, as well as between these two groups. Important factors such as diet, exercise, chronic stress, medications, smoking, and alcohol consumption have the potential to greatly influence study measurements when not controlled. Results from this study that show little to no

influence of EPA and DHA on cardiovascular concerns are therefore expected because mixing dissimilar information likely diluted statistically significant relationships, resulting in inaccurate analyses and conclusions.

The meta-analysis combined studies performed in different countries.

Including information from individuals in different countries may have significantly reduced the likelihood of finding any meaningful relationship between EPA and DHA supplementation and cardiovascular dysfunctions because cardiovascular risk factors vary among cultures and socio-economic classes.

The meta-analysis contradicts a substantial body of previously published research demonstrating specific cardiovascular benefits of EPA and DHA in <u>both</u> laboratory studies and clinical investigations.

Cardiovascular benefits of omega-3s have been found using a broad range of study types, including meta-analyses, randomized control trials (RCTs), observational studies, and laboratory (animal and in vitro) studies. Because this study did not evaluate data across a variety of study types, all conclusions should be viewed as extremely limited in scope.

CONCLUSION

Taken together, these issues related to experimental design suggest that the conclusions of this meta-analysis are limited and potentially inaccurate, and that we should take extreme care when considering them as a guide to omega-3 supplementation.

Presently, *thousands* of published articles in peer-reviewed journals have demonstrated the value of omega-3 EPA and DHA to cells and tissues throughout the body, and a multitude of clinical studies have shown benefits of EPA and DHA for cardiovascular dysfunctions. In light of this evidence, Nordic Naturals believes that comprehensive and effective health-care decisions are best made when considering all information available.

Thank you for your continued support of the Nordic Naturals brand.

Sincerely,

Scott Minton, PhD
Scientific Advisor