Reviewer's report

Title: An Increase in Dietary n-3 Fatty Acids Improves Bone Health in Humans

Version: 2 Date: 6 November 2006

Reviewer: Marlena Kruger

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General
The paper is well written and the methodology sound. But there are a few issues that need to be addressed. This is not a “stand-alone: study as it forms part of a larger study investigating cardiovascular health. This could have compromised the current study. The study population was very small, with few women and mostly men. Though it is stated in the results that when compared results for the women were not different from those for the men, there is still a possibility that the women could have responded differently. Bone markers are highly variable and the response of only three women is not significant enough to justify the statement that there was no difference; the small group could have resulted in the lack of observing a difference.

NTx is highly variable and the “real” effect would be an observed effect of at least 10-20%. Intraperson variance is also high and can be up to 15% from one day to the other. So it is possible that though the presented results are statistically significant it is not “real”. Several studies have been done and published by Prof Richard Eastel’s lab on the variability of the resorption markers NTx and CTx, and these need to be taken into consideration when doing a power calculation.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Methodology:
How was the study population selected from the larger study? Was it random and what were the criteria? Why were only three women included?
A wash-out period of 3 weeks is too short for bringing membrane fatty acid composition back to baseline. It should have been 6 weeks. Any comments?
What was the intra-assay CV for NTx?

Results:
The percentage change in NTx is within reported intraperson variation. The observation may not be real. Any comments?
Plasma levels of cytokines are also highly variable for individual people. The small number of samples (16) used to draw a correlation between TNFalpha and NTx makes it questionable. Could the graph showing the correlation be included in the results?

Discussion:
The discussion is too long, and can be shortened significantly.
Page 11; there is reference to studies done in humans with evening primrose oil, with no mention of fish oil. The statement is therefore not correct as there have not been any human studies done using only evening primrose oil. All studies used a combination of EPO and fish oil, or fish oil only. Please correct.
Page 13: There is mention of the synthesis of PGE1 after supplementation with EPA. PGE1 is synthesised from GLA not EPA. The latter gives rise to PGE3.
In the same paragraph it is stated that production of PGE1 is expected to reduce osteoclast activity, why?? There are no references given.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Well written and presented, so no corrections.

Discretionary Revisions (which the author can choose to ignore)
None
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.