

1<sup>st</sup> March, 2007

Dear Valued Retailer,

As you will no doubt have seen in recent newspaper coverage, a new meta-analysis study has been published in the Journal of the American Medical Association (JAMA) entitled '*Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention, Systematic Review and Meta-Analysis*'.

Unfortunately the study itself is flawed and the resulting headlines and articles are therefore misleading for the millions of consumers who use antioxidant supplements.

The study in question is a meta-analysis, so the first thing to note is that this is not new clinical research. This type of study analyses data from existing studies in a given field, and therefore represents nothing more than a new interpretation of existing data.

As one of the world's leading experts on antioxidant research we have asked Dr Richard Passwater to comment on the article published in JAMA.

Dr Passwaters' response:

- This is not a clinical study but a review of certain SELECTED previous studies. Such meta analysis are only as good as the clinical trails selected and reason for inclusion and exclusion. This meta analysis has worse inclusion criteria than the Miller meta analysis of a couple of years ago that was eventually discredited.
- The trials selected appear to be mostly "secondary event" trials wherein someone has -- for example -- had a heart attack and was then entered into a short term trial at second heart attacks used for the endpoint. These trials are characterized by being low-dose, short-term and treatment of existing disease. These trials tend not to be a measure of prevention (prevent the first heart attack, etc.), nor are they long-term (it takes 2 years for the preventive effect of vitamin E to manifest itself, as an example) nor are they high-dosage.
- This meta analysis purports to be a study of chronic supplementation (over a long time), yet includes a study on vitamin A of a one-time, single-dose of 200,000 IU. This is just one example of acuteness rather than chronic intake. There are several problems with inclusion criteria that make the study invalid.

- The conclusion seems so out of context of the body of science that it is suspect. A meta analysis carries very little scientific weight whereas some of the studies that do show preventive and life-extending effect are better studies (not meta analysis, but clinical data).
- **This poorly designed meta analysis does not undo the overwhelming majority of studies showing the safety and effectiveness of antioxidant supplements that have withstood the test of time. This study will not withstand the test of time.**
- In the past, we have found such negative finding meta analysis to have excluded cases where benefit was found. They dreamed up reasons for excluding these trials. The vitamin E meta analysis of 2 years ago is an example.
- "Healthy consumers can still feel confident that they can still safely take their antioxidant supplements. This meta analysis does not change the basic facts that antioxidant supplements are safe and effective."
- The one key point of a valid meta analysis is to compare and combine studies that are EXTREMELY similar. This new meta analysis combines studies that are EXTREMELY DISSIMILAR !!!

These comments are also reflected in responses from the American Council for Responsible Nutrition (CRN) and Patrick Holford, which are included with this letter for your information. I hope this background on the study will help you to be able to answer enquiries from your customers, but please feel free to call the technical team if you need any further information on this issue.

With very best regards,

A handwritten signature in black ink, appearing to read 'P. Chamberlain', with a horizontal line extending to the right.

Paul Chamberlain  
Solgar Vitamin and Herb, UK