

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: Docket 2004D-0466

Dear Sir or Madam:

Pharmavite LLC wishes to submit comments on the draft Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug and Cosmetic Act, which availability was published in the Federal Register on November 9, 2004. Pharmavite LLC is a major manufacturer and distributor of dietary supplements in the United States.

We would like to preface our comments with the acknowledgement of the overriding principle of all label statements, including statements of nutritional support (which have become commonly known as “structure/function claims”), which is that they must be truthful and not misleading. Recent court decisions, most notably *Pearson v. Shalala* and *Whitaker v. Thompson*, show that through the use of qualifying language there can be a great deal of latitude in crafting claims that are truthful and not misleading in the context of the degree of scientific substantiation that supports them. We applaud the FDA’s efforts in its intention to establish a Guidance for Industry, which we believe will ultimately serve the purpose of enabling a better-educated American public to make choices in bettering and maintaining their health.

We believe the draft Guidance is a good approach, particularly in the way it gives specific examples of the degree of substantiation the FDA would consider appropriate. We find it similar to the Federal Trade Commission’s “Dietary Supplements: An Advertising Guide for Industry,” which we have found to be very useful. There are many commonalities between labeling and advertising and we encourage the continued cooperation between the FDA and FTC in harmonizing their standards. We further encourage the FDA to consider adopting the FTC standard of “competent and reliable scientific evidence” as a basis for substantiation.

Before we comment on the four specific issues cited in the draft Guidance, we find one major aspect of claims that did not seem to be specifically addressed, and that is the principle of “qualification:” the wording of the claim to accurately represent the strength of the underlying substantiation. This criterion is inherent in the principle of qualified health claims, and also is pervasive throughout the FTC Advertising Guide. We believe that consumers understand and strongly consider such qualifying language when claims are being evaluated. For example, a consumer could have a very different interpretation of the claims “nutrient X supports vascular system health,” “nutrient X helps support vascular system health,” and “nutrient X may help support vascular system health.” Each of these three statements may be truthful and not misleading depending upon the respective degree of substantiation supporting it. We therefore encourage FDA to recognize the role and benefit of appropriate qualifying language in developing truthful and non-misleading claims for dietary supplements.

Following are our comments on the four areas requested by the FDA:

1. The meaning of the claim(s) being made

We agree that a claim may carry implications that go beyond the technical meaning of the claim. When there is obvious ambiguity about those implications, we agree that properly conducted consumer testing is an appropriate and sufficient mechanism to determine how the claim and its implications are interpreted by the average consumer.

2. The relationship of the evidence to the claim

Claims are generally best supported by evidence that relates to the specific dosage level and condition of use of the dietary ingredient. However, we believe that reasonable extrapolations may be made for conditions outside those that may be found in clinical evidence, provided the claim makes that distinction clear. For example, suppose high quality clinical studies show a positive effect of nutrient X on the health of the vascular system at levels of 100, 150 and 200 mg/day. They could serve as substantiation for a claim of “nutrient X supports vascular system health” on products containing a recommended use of 100 to 200 mg/day of nutrient X. If, for technical or other reasons, a marketer markets a product containing a recommended dosage of 75 mg/day of nutrient X, an appropriate claim could be “at the level in this product, nutrient X may support vascular system health” provided the substantiating data indicate a linear dose response without a threshold effect and there is no evidence that the nutrient is not supportive of vascular health at that level. In other words, we believe extrapolations may be made when formulating claims, provided the claims, through such qualifying language, adequately convey the strength and applicability of the data.

There is an issue related to this area on which we would like to state an opinion. A large proportion of clinical studies applicable to dietary ingredients are typically conducted with an endpoint that shows that a body system or component that is in an abnormal state is brought back to a normal condition after ingestion of the dietary ingredient in question. For example, high quality studies may show nutrient Y may improve immune system function through modulating some quantifiable aspect (such as activity of a particular type of cell) in populations whose immune systems are slightly compromised (such as feeling the onset of a cold). We believe this data could support a claim that “nutrient Y supports (or maintains) immune system function,” to a target market of people with immune systems that are not compromised, and wish to remain so. In other words, in the case where a nutrient may be shown to bring the functioning of a body system from a slightly compromised state back to an optimal state, it can be reasonably inferred that the same nutrient could help support or maintain a body system in an optimal state.

3. The quality of the evidence

One, but not necessarily the only “gold standard” for clinical data is a randomized, double blind, parallel group, placebo-controlled design. It is also preferable that the data show reproducibility. However, other data may adequately substantiate claims, provided the claim indicates the level of support. For example, if preclinical (animal) studies show an effect of nutrient X on vascular system health, and the applicability of the data to humans is likely but not established, an

appropriate claim could be “animal studies suggest nutrient X may support vascular system health.” Comparable qualifications could be appropriate in claims based on other data, such as epidemiological, with limitations. We believe this would allow the consumer to evaluate the potential benefits of products based on emerging science, and is consistent with the position the FDA has taken with respect to qualified health claims and the position the FTC has taken with respect to advertising claims.

4. The totality of the evidence

We agree for a claim to be truthful and not misleading, the totality of the evidence must be considered when crafting the claim. Again, this may be an area where qualifying language may be useful or necessary to adequately describe the nature of the totality of the evidence. We encourage the FDA to recognize the benefit and acceptability of appropriately qualified claims for dietary supplements in describing the degree of scientific evidence supporting the claim. It is industry’s responsibility to evaluate and assess all relevant evidence, and to make objective judgments regarding applicability to claims.

This concludes our comments. If you have any questions or would like further information on any of these topics, please do not hesitate to contact me.

Sincerely,

David Kropp
Director, Regulatory Affairs
Pharmavite LLC