FDA Releases Final Guidance for Substantiation of Dietary Supplement Claims


Section 403(r)(6)(A) of the Federal Food, Drug, and Cosmetic Act (FDCA), as amended by the Dietary Supplement Health and Education Act of 1994 (DSHEA), requires that a manufacturer making nutritional deficiency, structure/function, or general well-being claims in dietary supplement labeling have substantiation that the claim is truthful and not misleading. Because DSHEA establishes no particular or distinctive substantiation standard, FDA relies on general antideception law standards established under the misbranding provisions of the FDCA and related consumer protection laws in characterizing the nature, quality, and amount of scientific evidence that typically is necessary to substantiate health benefit claims for dietary supplement products.

FDA’s Substantiation Standard

FDA intends to apply a standard for the substantiation of dietary supplement claims that is consistent with the Federal Trade Commission (FTC) standard of “competent and reliable scientific evidence.” FDA observes that this standard has been defined in FTC case law as encompassing “tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.” The agency notes that there is no pre-established formula defining the amount or type of studies that are needed to substantiate a claim, but states that, like the FTC, FDA will consider the norms accepted in the relevant research fields in consultation with experts from the appropriate disciplines. FDA states that it may accord some

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3 See, e.g., 21 U.S.C. §§ 321(n) and 343(a).
5 Under the governing statutory schemes, FDA has exclusive jurisdiction over the safety, and primary jurisdiction over the labels and labeling, of dietary supplements under the FDCA, while the FTC has primary jurisdiction over advertising and other non-labeling promotional activities for dietary supplements under the FTC Act. FDA’s Substantiation Guidance draws significantly upon FTC substantiation principles derived from consumer protection cases litigated under the FTC Act and FTC’s guidance entitled, “Dietary Supplements: An Advertising Guide for Industry,” issued in April 2001, served as a model for the new FDA Guidance. (available at http://www.ftc.gov/bcp/edu/pubs/business/adv/bus09.pdf).
deference to any existing standard for substantiation developed by a government agency or other authoritative body.

FDA recommends that, in determining whether the substantiation standard has been met with competent and reliable scientific evidence, firms should consider the following issues:

- The meaning of the claim(s) being made;
- The relationship of the evidence to the claim;
- The quality of the evidence; and
- The totality of the evidence.

**Identifying the Meaning of the Claim**

FDA states that, in order to determine what information is needed to substantiate a claim for a dietary supplement, a firm must first understand the meaning of the claim and clearly identify each express and implied claim. When a claim may have more than one reasonable interpretation, FDA recommends that a firm have substantiation for each interpretation. FDA asserts that it is important that the overall “message,” as well as individual statements, be substantiated.

**The Relationship of the Evidence to the Claim**

FDA emphasizes that scientific evidence must substantiate the claim made in labeling in the actual context of the specific dietary supplement product that the firm is marketing. The agency recommends that companies consider the following threshold questions in evaluating whether the scientific evidence is sufficiently related to the specific dietary supplement product to support claims in product labeling:

1. **Have the studies specified and measured the dietary supplement that is the subject of the claim?**

FDA recommends that study conditions of use be similar to those recommended in labeling for the dietary supplement product bearing the claim the study is meant to substantiate, including with respect to formulation, serving size, length and frequency of exposure.

**FDA Example:** A study demonstrating that an ingredient is effective when used topically generally would not be useful to substantiate a claim for a dietary supplement, which is, by definition, a product that is intended for ingestion.  

**FDA Example:** Clinical studies based on conventional foods may not provide competent and reliable scientific evidence for dietary supplement claims. FDA states that nutrients in food may exhibit a different effect when taken in the form of a dietary supplement, or the effect achieved in the food study may be attributable to other substances in the food.

2. **Have the studies appropriately specified and measured the nutritional deficiency, structure/function, or general well-being that is the subject of the claim?**

FDA recognizes that certain biomarkers may serve as surrogate clinical endpoints. Scientific evidence showing beneficial effects on a specific biomarker can support dietary supplement claims where the validity of the biomarker has been established, and where the evidence can be generalized to support the health benefit claimed for the supplement.

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**FDA Example:** Studies showing that an amino acid improves blood flow generally would not be adequate to support claims that an amino acid product “improves blood circulation” and “improves sexual performance.”

3. **Were the studies based on a population that is similar to that which will be consuming the dietary supplement product?**

FDA stresses the need for the study population to resemble the population to which the dietary supplement is marketed in material respects. The agency indicates that appropriately designed foreign research may be sufficient to substantiate claims, but warns that population differences with respect to dietary intake patterns and other factors affecting general health can confound results and limit the value of evidence for claim substantiation purposes.

**FDA Example:** A study involving young adults may not support claims for a product marketed for conditions manifested only in the elderly.

**FDA Example:** A study showing benefits from a supplemental mineral product in foreign subjects consuming diets deficient in that mineral could not be extrapolated to substantiate claims promoting the same benefit for the general U.S. population which does not have such a mineral deficiency.

4. **Does the claim accurately convey to consumers the extent, nature, or permanence of the effect achieved in the relevant studies and the level of scientific certainty for that effect?**

FDA advises companies to consider whether the scientific evidence concerning the extent, nature, and permanence of the benefits observed in study populations can be generalized to support particular benefits from consuming the dietary supplement product when used as directed in labeling. Additionally, claims should not overstate the level of scientific support for the claim.

**FDA Example:** A claim such as “Recommended by Scientists” in connection with the product’s claim would give consumers the impression that there is a body of qualified experts who believe that the claim is supported by evidence. Consumers might also reasonably interpret the statement as meaning there is general scientific consensus regarding the claim.

**The Quality of the Evidence**

FDA states that scientific quality is based on several criteria concerning study design and research methods with respect to study populations (e.g., presence of a placebo control), data collection (e.g., dietary assessment method), statistical analyses, and outcome measures. The agency asserts that the “gold” standard is the randomized, double blind, placebo-controlled clinical trial design, although the agency notes that clinical trials of this type may not always be possible, practical or ethical to undertake. FDA believes that clinical intervention studies can provide evidence to substantiate the effect of a dietary supplement because they can evaluate the direct effect of a product in the human body, whereas observational studies have a more limited capacity for distinguishing relationships attributable to a dietary supplement or ingredient and the health outcomes being evaluated.

According to FDA, substantiating evidence should consist of information derived primarily from human studies. The agency would generally consider the following types of information to be background information and may not be adequate to substantiate a
claim independently: animal studies, in vitro studies, testimonials and other anecdotal evidence, meta-analyses, review articles, comments and letters to the editor, and product monographs.

FDA highlights factors that contribute to the quality of studies, including: adequate and well-defined study design; appropriate, representative population in large enough sample size to detect a significant effect; adequate and appropriate assessment of intervention or exposure and outcomes; appropriate statistical analyses and data assessment; and peer review (although FDA clarifies that publication in a peer-reviewed journal is not required for studies to substantiate a claim). FDA refers to several systems available to rate the quality of scientific evidence, and cites in particular the Agency for Healthcare Research and Quality ("AHRQ") Evidence Report/Technology Assessment Number 47 entitled “Systems to Rate the Strength of Scientific Evidence.”

The Totality of the Evidence

FDA emphasizes that the strength of the total body of scientific evidence is the critical factor in assessing whether a claim is substantiated. The agency advises firms to consider criteria such as quality, quantity (number of various types of studies and sample sizes), consistency, relevance of exposure, and persuasiveness. FDA notes, however, that there is no general rule for how many studies, or what combination of types of evidence, is sufficient to support a claim.

The agency stresses the need to consider all relevant research, both favorable and unfavorable. Ideally, the substantiating evidence should agree with the surrounding body of evidence, but where there are conflicts or inconsistencies, a firm should determine whether there are plausible explanations for these discrepancies. Where multiple studies exist, FDA will consider whether the studies that have the most reliable methodologies suggest a particular outcome.

Covington & Burling LLP has considerable experience helping dietary supplement companies ensure that their claims are adequately substantiated. We would be pleased to provide further assistance regarding these matters.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our food & drug practice group:

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7 AHRQ Publication No. 02-E016, April 2002.