



The Role of RCTs in Substantiating Dietary Supplement Claims

By Rend Al-Mondhiry, Council for Responsible Nutrition

For over a decade, one of Federal Trade Commission's (FTC) highest priorities has been targeting deceptive health-related advertising in the area of dietary supplements. As authorized by the Federal Trade Commission Act (FTCA), the agency requires that product claims be truthful, not misleading and adequately substantiated with "competent and reliable scientific evidence." Until 2010, FTC applied this standard to health benefit claims, including those made by dietary supplement companies, in a broad

and flexible manner. It did not require a certain type or quantity of testing to establish a product's efficacy or safety. However, the FTC's initial loss in *FTC v. Lane Labs* led to a shift in the agency's enforcement strategy toward a more rigid standard. Two years later companies are still left with many questions, and in some cases they have turned to the courts for answers.

Section 5 of the FTCA provides FTC with broad authority to prohibit "unfair or deceptive acts or practices"; Sections 12 through 15 specifically prohibit the dissemination of false advertising with regard to food or drugs.¹ In carrying out this mandate, FTC adheres to the basic principles that advertising claims, both express and implied, must be: 1) truthful and not misleading, and; 2) have adequate substantiation which must be established prior to the dissemination of the advertisement. The key component of this latter requirement is "competent and reliable scientific evidence", which FTC defines as "tests, analyses, research, studies, or other evidence that have been



Rend Al-Mondhiry is Regulatory Counsel at the Council for Responsible Nutrition (CRN), where she provides legal counsel and advice to CRN's staff and members in the areas of legislation, regulatory compliance and advocacy, and international policy development with respect to dietary supplements and nutrition issues.

conducted and evaluated in an objective manner by qualified persons, that are generally accepted in the profession to yield accurate and reliable results.”²

The standard appears to permit a fairly wide range of evidence to support a claim regarding a product’s efficacy or safety. However, FTC’s application of this standard in recent enforcement actions against dietary supplement manufacturers seems to create a higher threshold for substantiation for certain health claims. A new and modified definition of “competent and reliable evidence” in consent orders put supplement companies on notice that FTC was no longer analyzing health claims with the same mindset as it had in the past – but without the certainty that an official rule or guideline change typically provides.

Redefining “Competent and Reliable Evidence”

The shift in FTC’s approach to substantiation traces back to the well-known case *FTC v. Lane Labs*. In 2009, a New Jersey district court held that supplement manufacturer Lane Labs-USA, Inc. (“Lane Labs”), was not liable for violating a previous consent order requiring competent and reliable scientific evidence.³ The court found that Lane Labs provided “credible medical testimony” and appropriately relied on scientific articles and studies in support of the products at issue.⁴ Therefore, the court was unwilling to find Lane Labs in violation of the order based merely on the fact that FTC disputed the credibility of this evidence. The FTC appealed this decision and, on remand, the district court ultimately ruled in favor of the agency on most allegations.⁵ However, this initial setback led to a tightening of the agency’s interpretation of competent and reliable scientific evidence.

Shortly thereafter, FTC announced it would begin including “more precise” language in future consent orders. The agency articulated three goals related to this change: 1) clearer guidance regarding the required scientific evidence, 2) harmonization with FDA laws and regulations and, 3) addressing “outlier studies” whose results appear inconsistent with the majority of scientific evidence specific to that field.⁶ Meeting these goals, in FTC’s view, would help ensure the enforceability of its orders and further prohibit deceptive claims.

Within a year of *Lane Labs*, the agency issued two consent orders that provided more specific substantiation provisions, including a new definition of “competent and reliable scientific evidence.” In the *Iovate* and *Nestle* orders, certain health claims (in these cases, rapid weight loss, treatment of diarrhea and reduced absences from school), would require:

“at least two adequate and well-controlled human clinical studies of the product, or of an essentially equivalent product, conducted by different researchers, independently of each other, that conform to acceptable designs and protocols and whose results, when considered in light of the entire body of relevant and reliable scientific evidence, are sufficient to substantiate that the representation is true.”⁷

In the *Iovate* order, another case involving dietary supplements, FTC further clarified that these human clinical studies must be “randomized, double-blind, placebo-controlled, and conducted by persons qualified by training and experience to conduct such stud[ies].”⁸ Both orders also require FDA approval prior to making future disease prevention or treatment claims, either through FDA regulation (i.e., authorized health

claim) or under the FDA drug approval or OTC monograph process.

While this modified definition applies only to the categories of claims at issue in these cases and the companies subject to the orders, this move by FTC has many in the supplement and food industry concerned and questioning the agency’s next steps. The requirement of two randomized, double-blind, placebo-controlled clinical trials, or the “two RCT standard”, continues to appear in consent orders involving weight loss claims made by supplement companies. But would FTC apply the standard more broadly and eventually begin analyzing other claims using the modified standard, along with the FDA pre-approval provision, and extend it to companies not operating under a consent order? And, depending on FTC’s interpretation of “essentially equivalent product”, do supplement companies need to conduct their own RCTs or could they rely on existing studies?

RCTs – Always the “gold standard”?

Requiring RCTs to support health claims is not a new concept, but this method has limits. RCTs are often referred to as the “gold standard” for substantiation because they can provide a high level of accuracy and reliability, depending on the product and the claim. In the context of drugs, there are no means other than RCTs to achieve the level of certainty required to establish efficacy or safety. However, this methodology is far less utilized in the field of nutrition science because the necessary parameters may be difficult to achieve. For example, contrasting nutrient intervention groups with a placebo group may not be feasible when studying the effect of a nutrient in the human body. Drugs generally have a single targeted effect and work within a

shorter period of time, making it easier to contrast with a true placebo group. In contrast, nutrients work together in complex ways, their effects take much longer to manifest, and achieving a “zero exposure” (i.e., placebo) group is extremely difficult; in some cases it may be unethical, or not possible.⁹

In noting the distinction between evidence-based nutrition and evidence-based medicine, experts in this field contend that assessing the totality of the available evidence is the best approach when establishing the relationship between nutrients and human health effects.¹⁰ This takes into account in vitro, in vivo, animal, and various types of human studies which may or not include RCTs - all of which can serve as the basis for a food- or supplement-based health claim. This approach also aligns with FTC’s current guidelines for the industry which, although under question in light of recent consent order language, remain intact and in force. In fact, the traditional definition of “competent and reliable scientific evidence” clearly embraces the use of test, studies, etc. “that are generally accepted in the profession to yield accurate and reliable results.” Therefore, moving forward the agency should consider both the methodology that is “generally accepted” by experts in this field, and the inherent limits of RCT-based evidence in the nutritional (food or supplement) context.

For the time being, it is unclear whether *Iovate* and its kin actually signify a move towards a new policy change that will eventually encompass a broader range of claims. FTC claims this is merely a clarification of existing policy to aid enforceability¹¹, but the industry has been skeptical of this response. Although FTC rightly has a

great deal of discretion when drafting orders, the agency’s latitude with regard to enforcement is not without limits. And viewed along-side the provisions requiring FDA approval, it appears that FTC is shifting toward a more drug-like standard for dietary supplement claims – despite its earlier position cautioning against overly broad or burdensome restrictions on food and supplement claims that can “deprive consumers of useful information and impede their ability to exercise informed choice.”¹² Moreover, if these stringent standards for substantiation are in fact a policy change rather a clarification, the legality of such a move in the absence of notice-and-comment rulemaking is also questionable.

POM Wonderful Takes On FTC

All of these issues, and specifically the applicability of the two RCT standard to certain health claims, are at center stage in the ongoing litigation between FTC and POM Wonderful LLC (“POM”), a maker of supplements and juice products. Shortly after *Iovate* and *Nestle*, POM filed a complaint against FTC alleging that the new requirements in these orders violate the agency’s rule-making procedures, encroach on the authority of FDA, and violate POM’s First and Fifth Amendment rights.¹³ FTC swiftly responded with its own complaint and a proposed consent order, charging that POM’s disease claims regarding its supplement and juice products were not supported by competent and reliable evidence.¹⁴ Notably, the proposed order does not include the two RCT standard, nor does a lack of RCTs serve as the basis for FTC’s complaint. Rather, POM argues that the agency is applying its modified standard, including the FDA pre-approval requirement, “universally” to all food

and dietary supplements which directly contradicts years of agency practice and existing law, and also violates POM’s free speech and due process rights.¹⁵

Following a lengthy procedural history, the Administrative Law Judge (ALJ) issued an Initial Decision in May 2012. The ALJ sided with FTC on some issues, finding that POM’s disease-related claims lacked adequate substantiation. However, he rejected FTC’s contention that RCTs and FDA pre-approval are legally required to make such claims. The ALJ found that for claims that a product treats or reduces the risk of disease “made in connection with a food, or food-derived product [i.e., supplement] that is safe, and that is not being offered as a substitute for medical treatment, double-blind, randomized, placebo-controlled clinical trials, such as those required by the Food and Drug Administration, are not required.”¹⁶ The ALJ also rejected FTC’s attempt to require POM to obtain prior FDA approval for certain claims in future, holding that this requirement “would constitute unnecessary overreaching.”¹⁷ These determinations represent a win not only for POM, but the supplement and food industry as a whole. The language in this decision echoes the concerns of many in the supplement industry – these products are not drugs and therefore should not be assessed using the same scientific standards as drugs. In the interest of protecting consumers, all companies must be held to a standard that assures products are safe and claims are truthful and not misleading. But claims for products such as dietary supplements, which are intended to support overall health rather than serve as medical treatment, should not be subject to an inflexible evidentiary

standard that fails to take into the totality of the evidence (which or may not include RCTs) and the accepted norms in the field.

Following the initial *POM* ruling, both sides submitted notices of appeal seeking review before the full Commission. Oral arguments are scheduled for August 23, and based on the history of this case, an appeal of the Commission's decision is likely. While the *POM* case may have a long road ahead, the ALJ's initial findings along with the concerns of nutritional science experts have re-ignited the debate regarding RCTs and the limits of FTC's discretion in enforcement actions.

What's Next?

On the heels of *POM*, FTC suffered another setback. After a Florida district court denied FTC's motion to hold supplement manufacturer Garden of Life in contempt for violating a consent decree, it then rejected the agency's attempt to modify the decree to include the two RCT standard and FDA pre-approval provisions. Similar to *Lane Labs*, the court found that a disagreement between the parties' experts regarding competent and reliable evidence is not a sufficient basis for modifying the decree.¹⁸

Finally, it is noteworthy that the agency's long-standing guidelines for the dietary supplement industry have yet to be modified to include the prescriptive provisions at the

center of the dispute. The agency has given some indication that it plans to revise these policies in the near future but until that time, more court challenges may be on the way. Δ

1. Federal Trade Commission Act, ch. 311, 38 Stat. 717 (1914), (codified as amended at 15 U.S.C. § 41 – 64).
2. FTC, *Dietary Supplements: An Advertising Guide for Industry* (1998), available at <http://business.ftc.gov/documents/bus09-dietary-supplements-advertising-guide-industry>.
3. See *FTC v. Lane Labs-USA, Inc.*, No. 00-CV-3174, 2009 WL 2496532, (D.N.J. Aug 11, 2009)
4. *Id.* at *8.
5. See *FTC v. Lane Labs-USA, Inc.*, 624 F.3d 575 (3d Cir. 2010); *FTC v. Lane Labs-USA, Inc.*, No. 00-CV-3174 (D.N.J. Nov. 18, 2011).
6. David C. Vladeck, Director, Bureau of Consumer Protection, FTC, Remarks Before the Council for Responsible Nutrition's Annual Symposium for the Dietary Supplement Industry, *Priorities for Dietary Supplement Advertising Enforcement* (Oct. 22, 2009), available at <http://www.ftc.gov/speeches/vladeck/091022vladeckcrnspeech.pdf>.
7. See *FTC v. Iovate Health Sciences USA, Inc.*, Case. No. 10-CV-587 (W.D.N.Y. July 29, 2010) (Stipulated Final Judgment), available at <http://www.ftc.gov/os/caselist/0723187/100729iovatestip.pdf>; Nestlé HealthCare Nutrition, Inc., FTC File No. 092-3087, Agreement Containing Consent Order (July 14, 2010), available at <http://www.ftc.gov/os/caselist/0923087/100714nestleorder.pdf>.
8. *FTC v. Iovate*, at 4.
9. Blumberg J, Heaney RP, Huncharek M, Scholl T, Stampfer M, Vieth R, Weaver CM, & Zeisel SH (2010). Evidence-based criteria in the nutritional context. *Nutrition Reviews*, Vol. 68 (8), 478-84;
10. *Id.*
11. Julie Brill, FTC Commissioner, Keynote Speech Before the National Advertising Review Council and Council of BBB's National Advertising Division Annual Conference, "What's New in Comparative Advertising, Claim Support and Self-Regulation" (Oct. 4, 2010), at 5-7, available at <http://www.ftc.gov/speeches/brill/101004nadspeech.pdf>.
12. Federal Trade Commission Staff Comments Before the Department of Health and Human Services Food and Drug Administration, *In the Matter of Food Labeling: Health Claims; Dietary Guidance*, Docket No. 2003-0496 (2004), available at <http://www.ftc.gov/os/2004/01/040126fdacomments.pdf>.
13. *POM Wonderful LLC vs. FTC*, No. 10-CV-01539 (U.S. Dist. Ct., D.C., filed Sept. 13, 2010).
14. *In the Matter of POM Wonderful, et al.*, FTC File No. 082-3122, Docket No. 9344 (Sept. 24, 2010) (Administrative Complaint), available at: <http://www.ftc.gov/os/adjpro/d9344/100927admincmplt.pdf>.
15. *POM Wonderful LLC vs. FTC*, at 2.
16. *In the Matter of POM Wonderful, et al.*, FTC File No. 082-3122, Docket No. 9344 (May 17, 2012) (Initial Decision) at 5, available at: <http://www.ftc.gov/os/adjpro/d9344/120521pomdecision.pdf>.
17. *Id.* at 323.
18. See *FTC v. Garden of Life, Inc.*, No. 06-80226 (U.S. Dist. Ct., S.D. Fla., filed February 27, 2012); *FTC v. Garden of Life, Inc.*, No. 06-80226 (U.S. Dist. Ct., S.D. Fla., filed May 25, 2012).