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Separating Drugs from Supplements: In *Bayer*, Court Considers the Appropriate Substantiation Standard for Dietary Supplement Non-Disease Claims

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In recent enforcement actions by the Federal Trade Commission (FTC), courts have had the opportunity to evaluate FTC's longtime standard for substantiating evidence for dietary supplement structure/function claims--"competent and reliable scientific evidence." FTC has, in these actions, attempted to assert that supplement manufacturers must possess randomized, double-blind, placebo-controlled human clinical studies to substantiate non-disease claims in product advertising. This substantiation standard is far more restrictive than the well-established, consistent and flexible federal regulatory regime for substantiation upon which the entire dietary supplement industry has long relied. Most recently, in an FTC contempt action against Bayer, the U.S. District Court for the District of New Jersey concluded that "competent and reliable scientific evidence" does *not* require drug-level clinical trials, and that FTC cannot impose such a substantiation standard across-the-board through enforcement action against dietary supplement manufacturers.[2] As discussed further below, this decision is of critical importance to the dietary supplement industry because it confirms the appropriate standard for substantiating non-disease claims made for dietary supplements, consistent with congressional intent and longstanding guidance from both FTC and FDA.

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Different Regulatory Frameworks

Over twenty years ago, Congress enacted the Dietary Supplement Health and Education Act of 1994 (DSHEA), which amended the Federal Food, Drug, and Cosmetic Act (FDCA) to create a dietary supplement regulatory regime entirely distinct from FDA's regulation of drugs. Congress sought to "assure citizens have continued access to dietary supplements and information about their benefits."[3] Specifically, Congress made clear in DSHEA that "there is a growing need for emphasis on the dissemination of information linking nutrition and long-term good health," that "consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements," and that "the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products . . . to consumers."[4] DSHEA prohibits dietary supplements from bearing claims to diagnose, treat, mitigate, or prevent disease, but includes special provisions for dietary supplements to make structure/function claims. Under these provisions, a dietary supplement may bear claims about its effect on the structure or function of the body, or about the physiological mechanism by which the supplement works to maintain that structure or function, so long as such claims are adequately substantiated and the claims are made in accordance with other FDA requirements.

DSHEA itself does not articulate a specific substantiation standard for structure/function claims, but makes clear that dietary supplements should not be subject to the same criteria as drugs, which are intended to diagnose, treat, cure, prevent, or mitigate disease, and which often have risks that must be balanced by their benefits. The dietary supplement regulatory framework does not require the type of human clinical research that is required for drugs, where a sponsor must show that the drug can treat or mitigate disease, and that risks that are often inherent in drugs are outweighed by the disease treatment benefit. Congress recognized in enacting DSHEA that the traditional model for evaluating drugs was not generally appropriate or necessary for dietary supplements because "dietary supplements are safe within a broad range of intake, and safety problems with the supplements are relatively rare."[5]

The "Competent and Reliable Scientific Evidence" Standard

FTC has taken the lead in articulating the substantiation standard for dietary supplement structure/function claims. FDA has primary authority to regulate food and dietary supplement labels and labeling–the actual package label and any written, printed, or graphic matter that accompanies the sale of the food, often including websites–and FTC has primary authority to regulate food and dietary supplement advertising, which broadly includes virtually all non-label marketing communications, including television, web, and print advertising. Websites often are subject to the jurisdiction of both agencies.

Both FDA and FTC require dietary supplement structure/function claims to be substantiated by "competent and reliable scientific evidence." This standard has been defined primarily through FTC case law and guidance as "tests, analyses, research studies or other evidence based on the expertise of professionals in the relevant area, that have 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."[6]

The "competent and reliable scientific evidence" standard is meant to be "sufficiently flexible to ensure that consumers have access to information about emerging areas of science," while being "sufficiently rigorous to ensure that consumers can have confidence in the accuracy of information presented in the advertising."[7] FTC has historically emphasized that this is a flexible standard that depends on many factors and that "there is no fixed formula for the number or type of studies required or more specific parameters."[8] Thus, although well-controlled human clinical studies may be desirable in many circumstances, FTC has stated that results obtained in animal and *in vitro* studies could also be considered as substantiating evidence.[9] Similarly, research explaining the biological mechanism underlying the claimed effect and epidemiological evidence could be relevant.[10] Finally, FTC acknowledges that advertisers may consider whether it may be appropriate to extrapolate from the research to the claimed effect and provides that in certain circumstances it could be scientifically sound to do so.[11] FDA has issued guidance for the substantiation of dietary supplement structure/function

claims that largely tracks these FTC standards.[12]

FTC Attempts to Assert a Drug-Like Substantiation Standard for Supplement Claims

The "competent and reliable scientific evidence" standard ultimately boils down, in significant part, to what experts in the relevant field determine would be necessary to substantiate the claims being made. In recent substantiation-related enforcement actions, including most recently *Bayer*, FTC has relied upon expert testimony to require evidence that more closely resembles a rigid, drug-like standard, requiring in several instances at least one randomized, controlled clinical trial, even where FTC consent orders do not explicitly require such evidence, but instead require "competent and reliable scientific evidence."[13]

For example, in *Basic Research*, FTC attempted to enforce a consent order with a dietary supplement manufacturer by asserting that the order, which imposed a "competent and reliable scientific evidence" standard without qualification, required a randomized, placebo-controlled, clinical study to support the non-disease claims at issue; the FTC expert characterized this level of substantiation as the "ideal" support. The court rejected this standard, stating that the agreed-upon order does not require the "ideal standard." Instead, the court found that the competent and scientific evidence standard requires only "a causal connection between the evidence and the advertising claim."[14] Although the court was willing to allow FTC's expert to opine on the sufficiency of the evidence if the expert relied upon the correct standard, it refused to allow expert testimony to completely redefine the agreed-upon standard.

In *Garden of Life*, FTC attempted to hold a dietary supplement advertiser in contempt for allegedly violating a similar consent order by failing to substantiate structure/function claims such as "boosts brain development," "boosts cognitive function," "supports or boosts mental focus," "eye development," and "supports positive mood and behavior" in children.[15] Each party produced an expert to opine on whether the claims at issue satisfied the competent and reliable scientific evidence standard contained within the consent order. The court held that this battle of the experts regarding the adequacy of the trial design was insufficient to establish liability and, that FTC, by producing an expert who disagrees with another eligible expert's interpretation of a sufficient trial design, had not established by clear and convincing evidence that the advertiser had violated the consent order.[16] The court noted that to hold otherwise would require rewriting the consent order, something it was unwilling to do. On appeal, FTC attempted to argue that the advertiser's expert was not qualified because he was not an expert in "the relevant area," as is required under the competent and reliable scientific evidence standard: while FTC's expert was an expert in child cognitive and behavioral development, the advertiser's expert was an expert in pharmacology. The court refused to interpret the "relevant area" provision of the competent and reliable scientific evidence standard narrowly such that it only included child cognitive and behavioral development.[17]

Despite the refusal of the courts in *Basic Research* and *Garden of Life* to allow FTC to impose a drug-like substantiation standard in enforcing consent orders that required "competent and reliable scientific evidence," in 2014 the agency brought an enforcement action attempting to impose similar requirements in *United States v. Bayer*.[18] FTC asked the court to hold Bayer in contempt for violating a 2007 consent order that requires Bayer to "possess[] and rel[y] upon competent and reliable scientific evidence that substantiates" any claim about the efficacy of a dietary supplement product that it markets. FTC alleged that Bayer lacked such evidence for claims made for its Phillips Colon Health probiotic dietary supplement. This FTC action focused on the structure/function claims, "3 strains of probiotics to promote overall digestive health" and "helps defend against occasional gas, bloating, diarrhea and constipation," and related presentations of these claims in advertising.

FTC commissioned a gastroenterologist and professor of gastroenterology at Yale University School of Medicine to evaluate Bayer's substantiating evidence and determine whether the evidence met the competent and reliable scientific evidence standard. In rejecting Bayer's proffered evidence, FTC relied upon its expert's opinion to assert that "competent and reliable scientific evidence" for the claims at issue, regardless of whether the claims are disease claims, requires human clinical trials that (1) are randomized, placebo-controlled, and double-blind; (2) use the specific product for which the claims are made; (3) are performed in the population at which the claims are

directed; and (4) use validated methods and appropriate statistical methods to assess outcomes.[19] FTC asserted that, under this standard, Bayer could not extrapolate one ingredient's health benefits to another to substantiate its claims.[20] Bayer's expert testified that the proffered substantiation standard "would be a general rule"[21] that applies regardless of whether the products are dietary supplements or drugs. Because its expert concluded that none of Bayer's studies met this rigid standard, FTC alleged that Bayer's claims were unsubstantiated.

The *Bayer* Decision

In firmly concluding that the government had failed to demonstrate that Bayer had violated its 2007 consent order, the district court emphasized that DSHEA clearly establishes a regulatory regime and substantiation standard for dietary supplements that is quite distinct from that for drugs.[22] The court concluded not only that the government failed to give Bayer sufficient notice that the government expected drug-like substantiating evidence to substantiate Bayer's structure/function claims,[23] but also that the standard advanced by FTC was "directly contrary to DSHEA."[24] Notably, the court's analysis of the experts offered by both parties in this case could be instructive regarding future FTC action and how best to determine appropriate substantiating evidence.

Specifically, the court first considered whether FTC's expert, a gastroenterologist, had the expertise necessary to prove what experts in the field would require to substantiate Bayer's non-disease structure/function claims, and concluded that he did not, stating that a gastroenterologist who is not an expert in probiotics and does not regularly use them in his practice does not have expertise to testify to the type of evidence necessary to substantiate digestive health claims for a probiotic supplement product.[25] The court further determined that the expert's opinion did not align with the current regulatory scheme governing dietary supplement claim substantiation and that the expert had no familiarity with DSHEA, nor with FDA or FTC's implementation of DSHEA.[26] The court concluded that the expert's standard, which he testified should apply equally to drugs and dietary supplements, "is directly contrary to DSHEA, in which Congress expressly recognized 'the benefits of dietary supplements to health,' eliminated the pre-approval requirement that applies to drugs, and lowered the substantiation requirement for dietary supplements."[27]

Instead, the court concluded that Bayer's experts, one of whom is a leading expert on probiotics and probiotic-related clinical research, and the other of whom is a clinical researcher in the field of gastroenterology, were much better suited to speak to the type of evidence that could substantiate Bayer's claims.[28] Both of these experts had performed significant research on probiotics, and the court determined that they had appropriately understood and relied up on the FTC Guidance and the necessary distinction between dietary supplement structure/function claims and drug claims. The court was also compelled by the fact that neither of Bayer's experts could identify a single probiotic product currently on the market that substantiated its structure/function claims with a scientific study that would meet FTC's asserted standard.

The court further concluded that FTC's proffered substantiation standard was contrary to FTC Guidance on the matter, because it would impose a fixed formula for substantiating dietary supplement structure/function claims, while FTC and FDA have historically allowed much more flexibility, including conducting tests on similar formulations (not the exact product) and extrapolating between populations.[29] The opinion in *United States v. Bayer* thus clearly and completely supports the proposition that DSHEA created a different standard for the substantiation of dietary supplement structure/function claims than the standard for drug claims related to the treatment, prevention, or mitigation of disease, and that FTC may not seek to impose, across-the-board, drug-like substantiation standards on dietary supplements making non-disease claims, particularly based on the opinion of an expert in disease treatment rather than nutritional intervention.

The Drug/Dietary Supplement Distinction and the Public Health

The *Bayer* decision is critical in preserving the well-established flexible federal regulatory regime for dietary supplement claim substantiation provided by DSHEA. The dietary supplement industry has long relied on this standard. Holding dietary supplement marketers to a drug-like substantiation standard for structure/function claims would severely inhibit

the communication of meaningful and valuable information about the role of nutrients and health. Further, there are key differences between both the scientific evaluation of the efficacy of nutritional interventions that impact the structure or function of the body and drug interventions that treat disease, and in how such products are used by the public. These differences support distinct regulatory regimes.

The "substantial evidence" standard for drugs simply does not work well for dietary supplements, and the public health is not served by prohibiting the communication of structure/function claims to consumers unless and until drug-level clinical trial data support such claims. The health benefits of dietary supplements—which can include the maintenance of healthy body functions, the mitigation of conditions associated with natural states such as aging and pregnancy, and the treatment of symptoms not characteristic of a specific disease—are incredibly wide ranging and not always capable of being evaluated by specific endpoints through randomized, double-blind clinical studies. It is in the public's best interest to have access to information about the structure/function benefits of dietary supplements where the claims are substantiated by competent and reliable scientific evidence, even if that evidence is in the form of randomized clinical studies on a specific test population that have been extrapolated (in a scientifically supportable manner) to the general population; epidemiological evidence; *in vitro* studies; animal studies; and prospective and retrospective observational studies.

FTC and FDA understandably seek to protect consumers from being misled into purchasing dietary supplements that falsely claim to have benefits in the absence of data. Nevertheless, the restrictive scientific standard that FTC has sought to impose in recent enforcement actions goes one step too far. The *Bayer* decision confirms that the government cannot impose drug-like substantiation standards across-the-board for dietary supplements, and preserves the supplement industry's ability to make truthful and scientifically valid claims about its products.

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1. Special thanks to Grant Dixon, a third-year law student at Georgetown University Law Center, who assisted in the preparation of this article while a summer associate at Covington.
2. *United States v. Bayer Corporation*, No. 2:07-cv-00001-JLL-JAD (Sept. 24, 2015).
3. S. Rep. No. 103-410, at 17 (1994).
4. Dietary Supplement Health and Education Act of 1994, Pub. L. No. 103-417, § 2(7),(8),(13), 108 Stat. 4325, 4325 (1994) (DSHEA).
5. DSHEA § 2(14).
6. FTC, *Dietary Supplements: An Advertising Guide for Industry*, at 9 (Apr. 2001), *available at* https://www.ftc.gov/system/files/documents/plain-language/bus09-dietary-supplements-advertising-guide-industry.pdf (FTC Guidance).
7. *Id.* at 8.
8. *Id.* at 9.
9. *Id.* at 10.
10. *Id.* at 10.
11. *Id.* at 17.
12. FDA Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act (December 2008), available at: http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm073200.htm.
13. *See, e.g.*, *Basic Research, LLC v. FTC*, No. 2:09-cv-0779, 2014 U.S. Dist. LEXIS 169043, at *12–13 (D. Utah Nov. 25, 2014); *FTC v. Garden of Life, Inc.*, 845 F. Supp. 2d 1328, 1331–32 (S.D. Fla. 2012), *aff'd in part and vacated and remanded in part*, 516 F. App'x 852 (11th Cir. 2013).
14. *Basic Research* at *13.
15. *Garden of Life*, 845 F. Supp. 2d at 1331–32.
16. *Id.*
17. *Id.*
18. Brief in Support of Motion for Order to Show Cause Why Defendant Should Not Be Held in Contempt at 1, *United States v. Bayer Corp.*, No. 2:07-cv-00001-JLL-JAD (D. N.J. Feb. 17, 2015) (No. 4-1).
19. *Id.*
20. *Id.* at 18.
21. Deposition Transcript of Dr. Loren Laine at 128:21–22, *Bayer*, No. 2:07-cv-00001-JLL-JAD (No. 73-2).
22. *United States v. Bayer Corporation*, No. 2:07-cv-00001-JLL-JAD (Sept. 24, 2015).
23. *Id.* at 27.
24. *Id.* at 31.
25. *Id.* at 30.
26. *Id.* at 30-31.
27. *Id.* at 31 (citing 21 U.S.C. § 343(r)(6)).
28. *Id.* at 32.
29. *Id.* at 31-32.