Analysis&Perspective

Advertising and Marketing

Substantiating Claims for Over-the-Counter Drugs at FTC: How Much Is Enough?

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Pursuant to 1954 and 1971 Memoranda of Understanding, the Food and Drug Administration (''FDA'') and the Federal Trade Commission (''FTC'' or ''Commission'') coordinate regulation of claims for over-the-counter (''OTC'') drugs—FDA has primary jurisdiction over labeling (including packaging, inserts, and other promotional materials distributed at the point of sale), and FTC has primary jurisdiction over advertising (including print and broadcast ads, infomercials, catalogs, and other direct marketing materials).[1] When evaluating OTC drug advertising claims and their substantiation, FTC looks to FDA regulations and standards for guidance.

As discussed below, the Commission has required that advertisers possess at least two adequate and well-controlled, double-blind clinical studies to support advertising claims for OTC drugs. FTC based that requirement, in part at least, on the Federal Food, Drug, and Cosmetic Act's (''FFDCA'') pre-1997 requirement for at least two studies for a new drug approval. A 1997 statutory amendment, however, clarified that FDA can approve drugs based on only one clinical study. Therefore, with Congress now ensuring that FDA has flexibility with respect to evaluating substantiation for drug claims, the FTC and advertisers should have that same flexibility.

General FTC Standards for Claim Substantiation

FTC regulates advertising claims pursuant to its authority under Sections 5 and 12 of FTC Act.[2] Section 5 prohibits unfair or deceptive acts and practices in commerce, and Section 12 prohibits false or misleading advertisements for food, drugs, devices, services, or cosmetics.

To prevent deception or false advertising, FTC requires an advertiser to possess and rely upon adequate substantiation to support all claims.[3] When a claim specifically references substantiation (a so-called ''establishment claim'' such as ''tests prove'' or ''doctors recommend''), the advertiser must possess at least the stated level of substantiation. Similarly, if a claim *implies* that the advertiser has a certain type of support, the advertiser must have the amount and type of substantiation that the advertisement communicates to consumers.

In the absence of an express or implied representation about the type or amount of substantiation an advertiser has for a claim, the advertiser must have a ''reasonable basis'' to support the claim at the time the claim is made. The Commission evaluates six factors (known as the ''*Pfizer* factors'' from a 1972 FTC case against Pfizer[4]) to determine the level of proof needed to provide a reasonable basis for a claim:

(1) Type of product: When a product involves health or safety, the Commission requires a high level of substantiation.

(2) Type of claim: The Commission requires a high level of substantiation if a consumer would have difficulty determining the truth or falsity of the claim. For example, certain health conditions may not be present on a regular basis, impairing a consumer's ability to determine whether taking an OTC drug advertised to alleviate the particular condition caused any relief.

(3) Benefits of a truthful claim: In general, the Commission requires a lower level of substantiation for claims that have substantial benefits, unless the consequences of a false claim outweigh the benefits.

(4) Ease of developing substantiation for the claim: The difficulty of developing substantiation is generally not a defense to inadequate substantiation. Instead, the Commission might look to secondary, perhaps less expensive, sources for substantiation or require that the advertiser qualify its claims.

(5) Consequences of false claim: False safety or efficacy claims for an OTC drug, for obvious reasons, have a greater likelihood of consumer injury than claims for many other types of consumer products. Therefore, the

[1] Working Agreement Between Federal Trade Commission and Food and Drug Administration, 1 Advertising Law Guide (CCH) ¶ 18,080; Updated FTC-FDA Liaison Agreement — Advertising of Over-The-Counter Drugs, 1 Advertising Law Guide (CCH) ¶ 18,088.

[2] 15 U.S.C. §§ 45, 52.

[3] *See* FTC Policy Statement Regarding Advertising Substantiation, 49 Fed. Reg. 30,999 (1984).

[4] *In re Pfizer,* 81 F.T.C. 23 (1972).

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level of substantiation needed to support such claims is greater.

(6) Amount of substantiation experts in the field believe is reasonable: Most cases turn on this factor. The amount of substantiation experts in the field believe is reasonable depends on the type of claims made for a product. When industry-standard testing is available, claims should be based on such testing.

Using these factors, the Commission almost always requires safety and efficacy claims for medical products to be supported by ''competent and reliable scientific evidence,'' which is typically defined as ''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.''[5] This standard does not specify the exact type or amount of evidence needed to substantiate a claim. Rather, it provides a flexible approach that recognizes that many different types of evidence can support a claim, and also allows the nature of the evidence to evolve with advancements in science and research.

In most cases, FTC does not challenge claims permitted by FDA in a pending or final monograph or a new drug application, because FDA has already determined that adequate substantiation exists to support those claims.[6] In fact, most FTC orders for OTC drugs include a ''safe harbor'' for such claims.[7] In the case of a product subject to a final or pending OTC drug monograph, the ingredient and claim at issue must be in Category I (generally recognized as effective). Any ingredient or claim in Category II (not generally recognized as effective) or Category III (insufficient evidence to determine effectiveness) at the time of the advertisement may not be in the safe harbor.[8] Also, claims not covered by a monograph or new drug approval, such as comparative efficacy claims, require independent substantiation.

Thompson Medical: Two Clinical Trials Required

In 1984, the Commission applied the *Pfizer* factors and issued a final decision and order against Thompson Medical Co., for advertisements that claimed its product, Aspercreme, is an effective external analgesic.[9] The FDA Advisory Panel evaluating external analgesics in the OTC Drug Review had concluded that there was insufficient data to determine the effectiveness of the active ingredient in Aspercreme, triethanolamine salicylate (TEA/S), and therefore placed it in Category III;[10] FDA adopted that conclusion in the External Analgesics Tentative Final Monograph.[11]

The Commission required, among other things, at least two adequate and well-controlled, double-blind clinical studies to support any claims that Aspercreme is an effective analgesic. Importantly, when applying the sixth *Pfizer* factor, the Commission noted that FDA generally applied that standard to approve new drugs, and in its evaluation of the effectiveness of OTC drugs as part of the OTC Drug Review.[12] The Commission stated: ''We believe that advertisers of drug products subject to the joint jurisdiction of the FTC and the FDA will benefit from greater regulatory certainty if they can act with reasonable assurance that the two agencies will accept the same evidence to demonstrate the safety and efficacy of a particular ingredient. Thus, we state that advertisers who comply with the FDA's requirement of well-controlled clinical tests to demonstrate efficacy have adequate substantiation to make such claims in their advertisements.''[13] In earlier cases involving analgesics, the Commission had also required efficacy claims to be supported by at least two adequate and well-controlled, double-blind clinical trials.[14]

While *Thompson Medical* and earlier cases applied the two, double-blind clinical trial level of substantiation for claims for analgesics, the Commission has required that level of substantiation in cases involving other drugs and health-related products.[15]

Section 115 of FDAMA. As discussed above, the Commission based its requirement for two clinical trials in *Thompson Medical*, in large part, on FDA's requirement that at least two clinical trials are needed ''for drug efficacy in general.''[16]

To approve a new drug, FDA must find that there is ''substantial evidence that the drug will have the effect it purports.''[17] ''Substantial evidence'' is defined as ''evidence consisting of adequate and well-controlled clinical investigations.''[18]

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[5] *See, e.g., In re Natural Organics, Inc.*, No. 9294, 2001 FTC LEXIS 138 (Sept. 6, 2001).

[6] *See, e.g., In re Metagenics, Inc.*, 124 F.T.C. 483 (1997).

[7] The safe harbor typically provides: ''Nothing in this order shall prohibit respondents from making any representation for any drug that is permitted in the labeling for such drug under any tentative final or final standard promulgated by the Food and Drug Administration or under any new drug application approved by the Food and Drug Administration.'' *See, e.g., In re CMO Distribution Centers of America, Inc.*, No. C-3942, 2000 FTC LEXIS 71 (May 16, 2000).

[8] *See* 21 C.F.R. § 330.10(a)(5) for more detailed descriptions of these categories.

[9] *In re Thompson Medical Co.*, 104 F.T.C. 648 (1984), *aff'd*, *Thompson Medical Co. v. FTC*, 1986-1 Trade Cas. (CCH) ¶ 67,103 (D.C. Cir. 1986).

[10] 44 Fed. Reg. 69768 (Dec. 4, 1979).

[11] 48 Fed. Reg. 5852 (Feb. 8, 1983). Thompson Medical tried to argue that the FTC should not act until the FDA rulemaking for the active ingredient had been completed. The Commission, with what turns out to have been great foresight, rejected that argument and stated that while comments on the proposed rule were due on April 9, 1984, ''it is uncertain how much additional time FDA will need before resolving all of the issues presented to it by the rulemaking.'' *Thompson Medical*, 104 F.T.C. at 829. Almost 20 years later, FDA has *still not* resolved all of the issues and published a final monograph for external analgesics.

[12] *Thompson Medical*, 104 F.T.C. at 825.

[13] *Id.* at 826.

[14] *See, e.g., In re Bristol-Myers Co.*, 102 F.T.C. 21, 390 (1983); *In re American Home Prods.*, 98 F.T.C. 136, 423 (1981), *aff'd American Home Prods. v. FTC*, 695 F.2d 681 (3d Cir. 1982).

[15] *See, e.g., In re Schering Corp.*, 118 F.T.C. 1030 (1994) (challenging claims for fiber-based weight loss supplement); *In re Viral Response Sys., Inc.*, 115 F.T.C. 676 (1992) (challenging claims for device to treat colds and allergies); *In re Jerome Milton, Inc.* 110 F.T.C. 104 (1987) (challenging comparative plaque reduction claims and gingivitis treatment claims for toothpaste).

[16] *Thompson Medical*, 104 F.T.C. at 719

[17] FFDCA § 505(d)(5); 21 U.S.C. 355(d)(5).

[18] *Id.*

Prior to the Food and Drug Administration Modernization Act of 1997 (''FDAMA''),[19] FDA generally took the position that at least two studies were needed to approve a drug because of the use of the plural ''investigations.'' However, in Section 115 of FDAMA, Congress clarified that two studies were not always needed. It amended the FFDCA to clarify that: ''If the Secretary determines, based on relevant science, that data from **one** adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence.''[20]

From the legislative history of Section 115, it is clear that Congress thought that FDA should focus on the quality of the clinical trial(s), and not demand two when one, together with other evidence, is ''good enough.''

> The FDA usually interprets the requirement to demonstrate substantial evidence of effectiveness to require two adequate and well-controlled clinical studies, but has shown flexibility and approved some drugs on the basis of one adequate and well-controlled clinical study. Given scientific advancement in the past 35 years and the promise of further advancement, it is the committee's belief that the structure of a particular clinical protocol and the quality of the data underlying a new drug application should guide FDA's substantiation requirements. Therefore, the legislation confirms the current FDA interpretation that substantial evidence may, as appropriate, when the Secretary determines, based on relevant science, consist of data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained either before or after the investigation).[21]

The Commission in *Thompson Medical* also relied on FDA's standard for determining the effectiveness of drugs in the context of the OTC review, which provides that:

> Proof of effectiveness shall consist of controlled clinical investigations . . ., unless this requirement is waived on the basis of a showing that it is not reasonably applicable to the drug or essential to the validated of the investigation and that an alternative method of investigation is adequate to substantiate effectiveness.[22]

FDA did not amend this regulation in response to FDAMA, however such inaction is understandable given the flexibility provided in the regulation, and the administrative burden entailed in regulatory amendments.

Thus, the inflexible, two double-blind clinical trial minimum, demanded by the Commission in *Thompson Medical* to support claims for Aspercreme, is a higher level of substantiation than Congress believes is appropriate for FDA's approval of new drugs—indeed even possibly lifesaving drugs—in some instances.

[19] Pub. L. No. 105-115, 111 Stat. 2313 (codified as amended in scattered sections of 21 U.S.C.).

[20] FFDCA § 505(d)(5); 21 U.S.C. 355(d)(5), (emphasis added).

[21] S. REP. NO. 104-284, at 38 (1996).

[22] 21 C.F.R. § 330.10(4)(ii).

FTC Activity After FDAMA

Dietary Supplement Guide. In 1998, the Commission issued its ''Dietary Supplements: An Advertising Guide for Industry.''[23] Rather than specifying the quantity or type of studies needed to substantiate claims for dietary supplements, the Commission advised that ''[t]here is no requirement that a dietary supplement claim be supported by any specific number of studies,'' and ''the quality of the studies will be more important than the quantity.''[24] The Commission made it clear that it would evaluate ''the totality of the evidence,'' including both clinical and non-clinical data.

Recent Analgesic Product Consent Orders. We are unaware of any post-FDAMA judicial or administrative challenges to a two clinical trial requirement in an FTC order. Therefore, it is not clear how such a challenge, if brought, would be decided. It is also unclear whether the Commission would still seek such a requirement in an order.

As discussed below, one recent order involving an analgesic product does include a two-trial requirement, but it was actually initiated prior to FDAMA and it does not appear as if the advertiser has ever challenged that provision of the order. A more recent order involving an external analgesic did not include that requirement, and perhaps indicates a shift in the Commission's policy.

■ *Two Trials Required.* In June 1996 (prior to FDAMA), FTC filed an administrative complaint against Novartis Corp. and Novartis Consumer Health, Inc., the marketers of Doan's OTC internal analgesics, based on claims that Doan's pills were superior to other OTC analgesics for treating back pain. In 1998, citing *Thompson Medical*, the FTC's administrative law judge found for the Commission and adopted an order that prohibited Novartis from claiming that Doan's is more effective for relieving back pain than other OTC products unless such claim is supported by at least two well-controlled, double-blind clinical studies.[25] On appeal to the full Commission, the Commission retained the requirement for two clinical studies in the order without discussion on that issue.[26] Novartis appealed the Commission's decision to the U.S. Circuit Court for the District of Columbia. The D.C. Circuit affirmed the Commission's order in 2000.[27] As noted above, it does not appear as if Novartis challenged the two-study provision at the administrative or judicial levels, and instead challenged other provisions of the order.

■ *Two Trials Not Required.* In a recent case involving Blue Stuff, an external analgesic (like Aspercreme), FTC alleged that the advertiser lacked a reasonable basis to substantiate claims that the product relieves severe pain from specific medical conditions (claims that go beyond the scope of the Tentative Final Monograph). Through a stipulated final order, FTC did not specify the number of studies needed to support claims going forward, but rather it required the company to possess

[23] Available at http://www.ftc.gov/bcp/conline/pubs/buspubs/dietsupp.pdf.

[24] *Id.* at 10.

[25] *In re Novartis Corp.*, No. 9279, 1998 FTC LEXIS 24 (Mar. 9, 1998).

[26] *In re Novartis Corp.*, No. 9279, 1999 FTC LEXIS 63 (May 27, 1999).

[27] *Novartis Corp. v. FTC*, 223 F.3d 783 (D.C. Cir. 2000).

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the general ''competent and reliable scientific evidence'' to support such claims.[28]

Conclusion

As Congress recognized when enacting FDAMA, it is the quality, and not the quantity of clinical and other evidence that should be the focus when evaluating the substantiation for claims for OTC drug products. It is difficult to imagine that an advertising claim supported by, for example, a very large, well-controlled clinical trial, and a significant volume of supporting evidence, could be found to violate the FTC Act.

The general ''competent and reliable scientific evidence'' standard for substantiating claims for OTC drugs provides both advertisers and the Commission with flexibility to evaluate claims based on the general body of scientific evidence and the scientific community's opinion of that evidence at the time the claim is made. On the other hand, requiring any specific number of clinical trials, and specifying the type of controls used in the clinical trial (double-blind) can arbitrarily prohibit an advertiser from making truthful, nonmisleading, and indeed substantiated claims, not only to the detriment of the advertiser, but possibly to the detriment of the public as well.

[28] *FTC v. Blue Stuff Inc.*, available at http://www.ftc.gov/os/2002/11/bluestuffconsent.pdf. Recent consent orders involving other medical products have also not required two clinical studies. *See, e.g.*, *In re CMO Distribution Centers of America, Inc.*, No. C-3942, 2000 FTC LEXIS 71 (May 16, 2000); *In re Natural Organics Inc.*, No. 9294, 2001 FTC LEXIS 138 (Sept. 6, 2001) (challenging claims for drug to treat Attention Deficit/Hyperactivity Disorder); *In re True-Vantage Int'l, LLC*, No. 002-3210, 2001 FTC LEXIS 34 (Mar. 29, 2001) (challenging claims for snoring treatment); *In re Del Pharm. Inc.*, 126 F.T.C. 775 (1998) (challenging claims for lice treatment and oral cleansing product); *In re Pfizer Inc.*, 126 F.T.C. 847 (1998) (challenging claims for lice treatment).