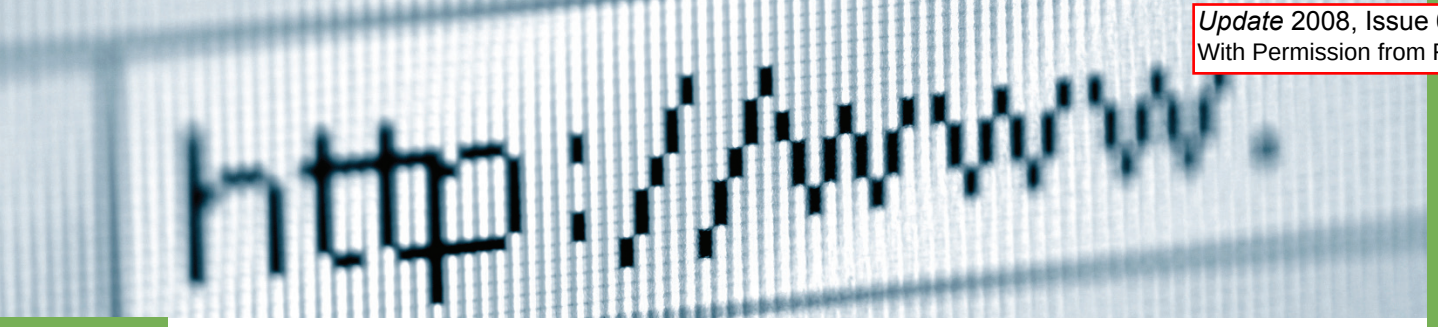

New Internet Promotion Options Pose Risks for Drug Manufacturers

by Maura Martin

Drug companies today use the Internet in new and innovative ways to provide information on and promote their products to consumers. Increasingly, companies utilize search engine optimization techniques, as well as interactive new media such as blogs, YouTube, and Wikipedia. However, companies should proceed with caution in using these creative promotional media, as they may inadvertently violate the Federal Food, Drug, and Cosmetic Act (FDCA)[1] in doing so.

Even as technology has radically changed the ways that drug companies promote their products, the Food and Drug Administration (FDA) has not articulated an official policy on Internet promotion. Perhaps the closest thing to a "formal" policy on Internet promotion is the agency's response to a citizen petition in which it said that it would approach Internet materials on a case-by-case basis.[2] However, the manner in which the agency has in the past applied its principles on promotion to these new forms of Internet promotion, as well as recent public statements made by agency employees, can provide some insight into how the agency regards promotion using these new media.

The agency has already issued warning letters addressing search optimization issues, and, in at least one case, FDA prevailed in a case in which it argued that choice of website metatags, considered in conjunction with a company's other promotional materials, can be evidence of intended use.[3] In addition, Kristin Davis, the Deputy Director of the Division of Drug Marketing, Advertising and Communications (DDMAC) in FDA's Center for Drug Evaluation and Research (CDER), addressed drug companies' use of YouTube, blogs, and Wikipedia to promote their products.[4] Using these piecemeal sources of information on FDA's views, one can begin to understand how the agency views use of new technologies, including blogs, YouTube and Wikipedia, for promotion of FDA-regulated products.

Response to WLF Citizen Petition

In November 2001, FDA responded to a citizen petition filed on behalf of the Washington Legal Foundation (WLF), in which WLF asked FDA to "formally adopt a rule, policy, or guidance stating that information presented or available on a company's Internet website, including hyperlinks to other third party sites, does not constitute 'labeling,'" as defined by the FDCA. The FDCA defines "labeling" as "all labels and other written, printed or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."[5] WLF also requested that such a rule, policy, or guidance specify that such information may, but does not necessarily, constitute advertising.

In its response, FDA stated its position that information available on a company's website may constitute labeling. The agency cited *Kordel v. United States*, in which the United States Supreme Court broadly interpreted the definition of labeling. The Court held that labeling is something that supplements or explains an article, and that it is not necessary for the labeling to be physically attached to the article.[6] Rather, according to the Court, the textual relationship between the labeling and the article was considered to be most significant.

Based on this authority, FDA explained, the agency had interpreted "labeling" to include "[b]rochures, booklets . . . motion picture films, film strips . . . sound recordings, . . . and similar pieces of printed, audio, or visual matter descriptive of a drug . . . which are disseminated by or on behalf of its manufacturer, packer, or distributor . . . ."[7]

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Based on this precedent, FDA concluded in its citizen petition response that "information about FDA-regulated products that is disseminated over the Internet by, or on behalf of, a regulated company can meet the definition of labeling in section 201(m) of the FDCA." FDA stated as an example that, if a company promotes a regulated product on its website and allows consumers to purchase the product from the website, the website would most likely be "labeling." In addition, the agency stated that "some product-specific promotion presented on non-company websites that is very much similar, if not identical, to messages the agency has traditionally regulated as advertisements in print media (e.g., advertisements published in journals, magazines, periodicals, and newspapers) would be viewed as advertising."

FDA declined to provide any rule or guidance on this issue, reasoning that it would be quickly outdated because of the ongoing rapid changes in the Internet and its use and that such a rule or guidance "may stifle innovation and create greater confusion." As a result, FDA stated that it would "continue to use a case-by-case approach based on the specific facts of each case." FDA also stated that it was willing to discuss a company's specific plans for content on its website or linking to content on a third-party website.

Search Engine Optimization

Drug companies seeking to draw traffic to their sites use search engine optimization techniques, including metatags, to achieve a high ranking on a search results page after a particular search term is entered. Companies can also pay to have a link to their websites advertised on search results pages. Because a company can control what search terms will produce a highly visible link to its website on the results page, companies run the risk of engaging in what FDA may consider to be off-label promotion. For example, if a drug company's website is highly ranked on a search results page after a consumer enters as a search term a disease that the drug is used off-label to treat, FDA may find this problematic.

FDA's basic position is that the promotion of off-label uses for approved new drugs is illegal. FDA typically uses one or two legal theories under the FDCA to proceed against promotion of off-label uses. First, the agency contends, such promotion misbrands a drug because it "is evidence of" a new "intended use" for which adequate directions must be provided in labeling. According to FDA, without approval of the off-label use, the labeling necessarily lacks such directions, and the drug is misbranded.[8] Second, FDA asserts, promotion of off-label uses causes a drug to be an illegal "unapproved new drug."[9]

In 2004, the New Jersey district court granted the government a permanent injunction prohibiting the defendants, Lane Labs-USA and Andrew J. Lane, from promoting products containing shark cartilage, rice bran treated with Shiitake mushroom, and glycoalkalid for the treatment of cancer, skin cancer, and HIV/AIDS.[10] The court noted that the website selling these products contained the metatags "alternative cancer therapies," "non-toxic cancer therapy," "cancer treatment," "brain tumors," "breast cancer," "colon cancer," "leukemia," "skin cancer," and "prostate cancer," among others.

FDA's district offices in Philadelphia, Seattle and New York have issued warning letters that cite companies for promoting off-label, taking into account the companies' use of certain metatags.[11] On May 21, 2008, the Philadelphia district office sent a warning letter to Millennium Health LLC, after the company made claims on its website and cited an article to market its product, Ellagic Acid, to prevent and treat cancer. The district office stated that Millennium Health had used the metatag "alternative medicine for cancer prevention" to bring consumers to its website.

Similarly, FDA's Seattle district office sent a warning letter to JHS Natural Products on May 20, 2008 objecting to promotion of its product, "Pectasol," for the prevention and treatment of cancer through article citations and claims on its website. Again, the district office cited the fact that the company had used the metatag "alternative cancer treatment" to bring consumers to its website through Internet searches.

In 2006, FDA's New York district office sent a warning letter to Robert Sargent for marketing an erectile dysfunction product, Vigor-25, on a website. After citing all of the claims made on the website to describe the intended use of the product, FDA pointed out that "[t]hese claims are further supplemented by a metatag that you use to bring consumers to your website. This metatag includes the words 'herbal sex enhancement.'"

These examples make clear that companies should carefully choose their metatags and cautiously utilize other search optimization techniques to avoid creating new intended uses in violation of the FDCA.

Uses of Interactive New Media: Blogs, YouTube and Wikipedia

FDA has also sent a warning letter to a company for an FDCA violation involving an advertisement on YouTube. On September 25, 2008, DDMAC issued a warning letter to Shire Development, Inc., citing a company for the first time for such a violation.[12] A video was posted on YouTube that featured the testimonial of celebrity Ty Pennington, which promoted the use of Shire's attention deficit

hyperactivity disorder (ADHD) drug, Adderall XR. Pennington stated, "Once I got on medication it's just amazing the transformation I made." He claimed that Adderall XR "gave [him] the confidence to achieve [his] goals," and implied that the drug helped him to "communicate with people," "fit in," and not feel "alienated." According to Shire, the posting was made in error and was not intended to be posted on YouTube.[13] Instead, the video was intended to be a link to a Shire website with more information and links about Adderall XR and other ADHD medications.

Despite the error, DDMAC still determined that the "video overstates the efficacy of Adderall XR by implying that this product will 'transform' patients' lives and improve their 'confidence.'" DDMAC found that Pennington's "claims imply an impact on aspects of a patient's life that are much broader than those actually impacted by Adderall XR treatment." FDA stated that it was "not aware of substantial evidence or substantial clinical experience demonstrating that treatment with Adderall XR has a beneficial effect on these behaviors and feelings." The warning letter also asserted that Shire did not submit the video to FDA for pre-review, as required by regulation.

Kristin Davis, the Deputy Director of DDMAC, directly addressed issues associated with YouTub, as wall as other new forms of interactive media, including blogs and Wikipedia, at the Food and Drug Law Institute (FDLI) Advertising and Promotion Conference on September 8-9 of this year.[14] Davis indicated that the same promotional standards apply whether the manufacturer is making a statement directly or through a consumer promoting the product via YouTube, a blog, or Wikipedia. Testimonials must still be supported by substantial evidence, particularly if a consumer's actual results do not reflect the average patient experience as described in the prescribing information. In addition, patient testimonials on YouTube or Wikipedia or in blogs should include risk information from the prescribing information, and should avoid minimizing risks associated with the product. Davis told companies that they are responsible for any company-dispensed material, regardless of where that material ends up.

To address some of these issues, Davis suggested that, if companies want consumer videos discussing their products on YouTube, then they should have the consumer submit the video to the company first for screening before it is posted. She also recommended to companies with blogs on their websites to use time delays and monitoring to control the blog content. With respect to Wikipedia, Davis urged companies to closely observe content related to their products, because the content is user-generated and can be changed by anyone with Internet access. Davis said that companies have a responsibility to ensure that Wikipedia content is "accurate and non-misleading."

Conclusion

Although FDA has stated that it may treat "information about FDA-regulated products that is disseminated over the internet by, or on behalf of, a regulated company" as labeling, questions still remain about FDA's authority over these types of Internet communications, including whether such communications are labeling, advertising, or neither. In addition, Davis's statements at the FDLI conference about FDA's authority to hold companies responsible for content on third party sites are also questionable. In particular, both of these positions may arguably violate the First Amendment. Until these unsettled questions are answered, companies should carefully review information posted on their websites and monitor third-party sites to minimize exposure to regulatory action by FDA.

1 21 U.S.C. §§ 301 *et seq*.
2 Letter from Margaret M. Dotzel, Ass. Comm'r for Policy, FDA , Responding to Citizen Petition from Daniel J. Popeo and Paul D. Kamenar, Washington Legal Foundation, Docket No. 2001P-0187 (Nov. 1, 2001), available at http://www.fda.gov/ohrms/dockets/dailys/01/Nov01/110901/01p-0187_pdn0001.pdf.
3 *United States v. Lane Labs-USA, Inc.*, 324 F. Supp. 2d 547, 557 (D.N.J. 2004).
4 *See* Carlene Olsen, Wiki-How: FDLI Panel Cautions Firms on New Media Use, [The Pink Sheet], at 24 (Sept. 15, 2008).
5 21 U.S.C. § 321(m).
6 335 U.S. 345, 350 (1948).
7 21 C.F.R. § 202.1(l)(2).
8 *See* 21 U.S.C. § 352(f)(1) (requirement of adequate directions for use); 21 C.F.R. §§ 201.5 (FDA drug labeling regulations, defining "adequate directions for use"), 201.128 (same, defining "intended use").
9 *See* 21 U.S.C. § 355(a) (prohibition against introducing or delivering for introduction into interstate commerce a new drug unless an NDA or ANDA approval is effective with respect to such drug); 21 U.S.C. § 321(p) (defining "new drug" to mean "Any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . ."); 21 U.S.C. § 321(m) (definition of "labeling").
10 *United States v. Lane Labs-USA, Inc.*, 324 F. Supp. 2d 547 (D.N.J. 2004).
11 Letter from Thomas D. Gardine, Philadelphia District Dir., FDA to Millennium Health LLC (May 21, 2008), Letter from Charles M. Breen, Seattle District Dir., FDA to John Seleen, Pres., JHS Natural Products (May 20, 2008), Letter from Otto Vitillo, Acting Dir. New York District, FDA to Robert Sargent (July 11, 2006).
12 Letter from Thomas Abram, R.Ph., MBA, Dir., DDMAC, FDA to Angus Russell, CEO, Shire Development, Inc. (Sept. 25, 2008), available at http://www.fda.gov/cder/warn/2008/AdderallXR_Letter.pdf
13 *See* Carlene Olsen, FDA's Advertising Enforcement Turns Its Focus to YouTube, ADHD Drugs, [The Pink Sheet], at 12 (Oct. 6, 2008).
14 *See* Carlene Olsen, Wiki-How: FDLI Panel Cautions Firms on New Media Use, [The Pink Sheet], at 24 (Sept. 15, 2008); *see also* 21 C.F.R. § 10.85(k) (providing that a statement given orally by an FDA employee is "an informal communication that represents the best judgment of that employee at that time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed").