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Client Alert

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FDA's Good Reprint Practices and Product Liability: A Lottery Ticket That Must Be Used Carefully

The Food and Drug Administration recently finalized its guidance document entitled, "Good Reprint Practices for the Distribution Of Medical Journal Articles and Medical Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (the "GRP Guidance)," which describes the conditions under which FDA will allow drug and device companies to proactively disseminate certain off-label use information. Because dissemination of off-label information has the potential to affect product liability exposure, it's worth examining the content of the GRP Guidance carefully. To illustrate the point, I note that the GRP Guidance and the recent sermon of my pulpit Rabbi share similar characteristics. Both focus on the potential of good news, but also offer a note about caution in saying too much.

I am sitting in synagogue listening to my well-respected pulpit Rabbi when he relates a joke he heard; a man is pulled over by a state police officer. The officer informs the driver, "Your license number was drawn in a special lottery, and you won $1 million." The driver responds, "Even though I don't have my license?" and his wife, in the passenger seat, offers, "Officer, don't listen to a word he says, he's drunk." The man in the back seat chimes in, "How did he know this is not our car?" I won't attempt to convey my Rabbi's moral message from this tale but, for some reason, it made me think of FDA's GRP Guidance. My mind works in mysterious ways. While the guidance offers pharmaceutical and medical device manufacturers guidance about disseminating specific kinds of off-label information according to proscribed conditions, companies must be careful and cautious in recognizing the potential trapdoor of product liability exposure if they say too much.

Background

On February 15, 2008, FDA issued a draft GRP Guidance to provide manufacturers with guidelines regarding the dissemination of peer-reviewed scientific journal articles that discuss unapproved uses of drugs or medical devices. FDA finalized this document on January 12, 2009 with a few changes.[1] While not legally binding, the Guidance provides FDA's current thinking on the subject.

Section 401 of the Food and Drug Administration Modernization Act of 1997 described certain conditions under which a manufacturer could disseminate

[1] Guidance for Industry: Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices U.S., http://www.fda.gov/oc/goodreprint.html, January 2009.

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information regarding off-label uses. FDA promulgated implementing regulations and codified the regulations at 21 C.F.R. Part 99. FDA published a March 16, 2000 Federal Register Notice stating that the regulations in 21 C.F.R. Part 99 constituted a "safe harbor" for manufacturers that complied with them. 65 Fed. Reg 14286. On September 30, 2006, Section 401 of FDAMA ceased to be effective because that section of FDAMA expired. Therefore, the regulations at 21 C.F.R. Part 99 are no longer applicable.

Under the GRP Guidance, the scientific or medical journal article must be published by an organization that has an editorial board consisting of experts in the subject area of the article. The organization should adhere to a policy of full disclosure of any conflict of interest or bias of any author, contributor, or editor associated with the article. The article must be peer-reviewed and published in accordance with sound scientific and peer-reviewed principles. The distribution of special supplements or publications that have been funded by one or more of the manufacturers of a product mentioned in the publication is prohibited. Further, a scientific or medical reference publication that is distributed generally should be available in bookstores or other independent distribution channels where medical textbooks or periodicals are sold.

The GRP Guidance does not apply to the following publications, which are not considered scientifically sound and are not consistent with the Guidance: (1) letters to the editors; (2) abstracts of a publication; (3) reports of Phase I clinical trials; or (4) reference publications that contain little or no substantive discussion of the relevant investigation.

The information contained in such publications must address adequate and well-controlled clinical investigations that are considered scientifically sound by experts with sufficient training to evaluate the safety or effectiveness of the drug or device. The referenced clinical investigations can include historically controlled studies, pharmacokinetic (PK) and pharmacodynamic (PD) studies, and meta-analyses if they are testing a specific clinical hypothesis. (This inclusion was added in the final guidance version.) The information cannot be false or misleading, such as an article or reference text that is inconsistent with the weight of credible evidence derived from adequate and well-controlled clinical studies. An article should not have been withdrawn by the author, disclaimed by the journal, or derived from a clinical investigation FDA found to be inadequate or not well-controlled. The information also must not present a significant risk to the public health, "if relied upon" (this phrase was added in the January 2009 version.)

The GRP Guidance states that drug and medical device manufacturers may distribute a scientific or medical reference publication, so long as:

- the article was not written, edited, excerpted or published specifically for, or at the request of, a drug or device manufacturer;
- the publication has not been edited or "significantly influenced" by a drug or device manufacturer or any individuals with a financial relationship with the company;
- the scientific information is distributed in the form of an unabridged reprint, copy of article, or reference publication without being marked, highlighted, summarized, or characterized by the manufacturer in any way (except to provide for permitted accompanied disclosures);
- the information is accompanied by the approved labeling for the drug or medical device;
- it is not primarily distributed by a drug or device manufacturer, but should be generally available in

bookstores or other independent distribution channels where medical textbooks or periodicals are sold;
- the material is accompanied, when such information exists (a phrase added in the January 2009 final guidance), by a comprehensive bibliography of publications discussing adequate and well-controlled clinical studies published in a medical journal or scientific text about the product covered by the information disseminated (unless the information already includes such a bibliography);
- the information is disseminated with a representative publication, when such information exists (this phrase was added in the final guidance), that reaches contrary or different conclusions regarding the unapproved use; especially those in cases where the conclusions of articles or texts to be disseminated have been specifically called into question by another article(s) or text(s); and
- the reprint is distributed separately from information that is promotional in nature.

According to the GRP Guidance, a journal reprint or reference publication should be accompanied by a prominently displayed and permanently affixed statement disclosing:
- that the uses described in the information have not been approved or cleared by FDA, as applicable to the described drug or medical device;
- the manufacturer's interest in the drug or medical device that is the subject of the journal reprint or reference text;
- any author known to the manufacturer as having a financial interest in the product or manufacturer or who is receiving compensation from the manufacturer, along with the affiliation of the author, to the extent known by the manufacturer, and the nature and amount of any financial interest of the author or compensation received by the author from the manufacturer (slightly revised from the draft guidance version);
- any person known to the manufacturer who has provided funding for the study; and
- any significant risks or safety concerns known to the manufacturer concerning the unapproved use that are not discussed in the journal article or reference text.

In issuing the guidance, FDA stated that it recognizes "the important public policy reasons for allowing manufacturers to disseminate truthful and not misleading medical journal articles and medical or scientific reference publications on unapproved uses of approved drugs and approved or cleared medical devices to healthcare professionals and healthcare entities." However, FDA states that it retains the authority to determine whether the distribution of an article or publication constitutes the promotion of a "new use" or whether such distribution causes a product to be adulterated or misbranded, in violation of federal law.

Product Liability Issues

While the GRP Guidance has its detractors, including some members of Congress and public interest groups, many in industry feel they have won the lottery. FDA has provided a roadmap by which drug and device companies can proactively disseminate certain off-label information with little fear of FDA enforcement. However, not all government authorities have recognized the GRP guidance as the winning lottery ticket.

Even FDA has cautioned that discussions or dissemination beyond the GRP guidance create potential risk.

Companies must recognize that when they decide to disseminate off-label information, they are consciously deciding to distribute materials about the product's unapproved use, even if the intentions are good. FDA has not determined that the off-label use is safe and effective for, had it done so, the use would likely be on-label. FDA continues to issue enforcement letters to companies that distribute promotional materials that broaden a product's approved indication. Such letters can be used in court as evidence in a product liability case. The plaintiff's lawyer closes his argument to the judge and jury with, "Little Johnny was injured due to the company's unlawful promotion," and holds up an FDA Warning Letter for the judge and jury to see. Even without such a letter, through discovery, the injured party can find promotional materials that a company disseminated and, if there is off-label information that can be connected to the injury, the company will be on the defensive and the ability to rely on the possible preemptive effect of the product's approved labeling is significantly diminished. Therefore, companies must remain mindful and vigilant to ensure any materials that discuss off-label information are carefully reviewed before dissemination.

While the GRP guidance may appear to be a lottery ticket, companies must be careful not to drive without their proverbial license, must remain sober, and have lawful ownership and responsibility of their vehicle, i.e., their product. Indeed, it is important to recognize that the GRP guidance is not a license to violate the law. Nor should companies be lulled into a false sense of security, merely because FDA has issued a guidance providing some freedom to "drive" more aggressively. The GRP guidance does not immunize companies from potential product liability exposure. There are many other cops on the beat, including FDA and state common law requirements, and product liability risks remain. What you say can be used against you in a court of law.

Maybe my Rabbi was right – saying less can sometimes be the most appropriate option.

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