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Life Sciences Health Industry Alert

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Commentary: FDA's New Good Reprint Practice Rule

The Food and Drug Administration's new Good Reprint Practice ("GRP") Guidance went into effect January 2009. The GRP Guidance establishes criteria that FDA will now use to determine whether the distribution of medical or scientific reprints and reference texts about off-label uses of a drug or device would constitute impermissible promotional activity under the Food, Drug and Cosmetic Act.

The GRP Guidance in some ways liberalizes, and in other ways tightens, the criteria applied previously by the FDA to determine whether and to what extent a manufacturer could distribute medical or scientific information about the off-label use of its product. For example, before finalizing the GRP Guidance, FDA had indicated that the distribution of certain off-label information may be appropriate, in some circumstances, by a company's medical affairs representatives, but probably not by sales or marketing representatives whose actions could suggest a promotional intent. FDA also cautioned that such distribution should be in response to unsolicited requests from health care professionals. Put another way, FDA expected reprints to be distributed in a manner typical for the exchange of scientific and medical information among professionals, such as continuing education programs, seminars at educational institutions or professional conferences, or by a company's medical staff at the unprovoked request of a physician, but not proactively distributed by sales representatives. Under the new GRP Guidance, however, there is no mention of unsolicited requests, or who should or should not provide the reprints to a health care professional. Implicit in this omission is that a company can proactively disseminate certain reprints and reference texts through any person in the company, including sales representatives. Such activity, therefore, should not lead FDA to conclude that the distribution is impermissible promotion *so long as* the reprints and the manner in which they are distributed meet the criteria set forth in the GRP Guidance.

At the same time, the GRP Guidance appears to tighten FDA's previous criteria by requiring companies to, among other things, disclose financial arrangements with any of the authors of a reprint. Specifically, companies are expected to reveal the nature and amount of the financial interest, including compensation, if provided. FDA expects companies to affix prominently and permanently such information on the reprint. In addition, companies are expected to identify any person who has provided funding for the study or studies discussed in a reprint if they know the person (apparently even if there is no formal or legal relationship between the person and company). The Guidance does not state, however, that the amount of funding should be specified.

Although the GRP Guidance is "final," meaning it is in effect and can be relied on, please keep in mind that the Guidance is not a regulation, but only FDA's recommendations about ways to avoid an FDA conclusion that the company's activities amount to impermissible promotion of an off-label use. A different approach might also be acceptable, but as we know from experience, deviations from an FDA Guidance (especially one that has been vetted for years as this one has, *i.e.*, since 1997), should not be implemented lightly.

Despite the apparent finality of this Guidance, we may still see a change to the policy in the near future. At least one powerful member of Congress, Rep. Henry Waxman (D-Calif.), has asked the FDA to reconsider the Guidance document, complaining that it is too lenient and permits companies, in effect, to promote off-label. Rep. Waxman may be reacting to the likelihood that sales and marketing representatives would be the ones to deliver the reprints, proactively, and not pursuant to an unsolicited request. Because the new Democratic administration is more supportive of government regulation and enforcement, we believe there is a strong likelihood that the FDA will not only reconsider the GRP Guidance, but will also ultimately rescind it or revise it to tighten the criteria for permissible dissemination. Rep. Waxman and Sen. Kennedy (D-Mass.) are significantly involved in choosing the next FDA Commissioner, as well as the next Chief Counsel (a Kennedy staffer is rumored to be in line for Chief Counsel and a former Waxman staffer is rumored to be a possible choice for Commissioner), so we should be prepared for FDA to take a very narrow view of what activity should be allowed under the First Amendment right to "Commercial Free Speech." However, until FDA rescinds, stays, or revises the GRP Guidance, it will continue to be FDA's current policy

and, if followed, should not lead to any enforcement action by FDA.

Good Reprint Practice Checklist

To qualify for the safe harbor under FDA's Good Reprint Practice Guidance, a scientific or medical reprint and/or medical or scientific reference text (referred to collectively as "reprint") and the manner in which it is disseminated, should *not be false or misleading*, and should meet the following criteria:

- Publishing organization has an editorial board.
- Publishing organization uses independent experts to review, and objectively selects, rejects, or provides comments about proposed articles.
- Publishing organization has a publicly stated policy that it follows of full disclosure of any conflict of interest or biases for all authors, contributors, or editors.
- The reprint has been peer-reviewed.
- The reprint is not published or distributed as a special supplement or publication that has been funded in whole or in part by any of the manufacturer(s).
- A reprint is generally available through independent distribution channels where medical textbooks or periodicals are sold (*e.g.*, bookstores, subscription, Internet), and not distributed primarily by the company.
- The reprint has not been written, edited, excerpted, or significantly influenced by, or published specifically for, or at the request of, a manufacturer or any individuals having a financial relationship with the manufacturer.
- The information addresses scientifically sound, adequate and well-controlled clinical investigations. For example, such studies may be:
  - Historically controlled studies
  - Pharmacokinetic (PK) and pharmacodynamic (PD) studies
  - Meta-analyses, if they are testing a specific clinical hypothesis
- The reprint is not characterized as definitive or representative of the weight of credible evidence if the weight of credible evidence, or a significant number of other studies, contradict the article or reference-text's conclusions.
- The reprint has not been withdrawn by the journal or disclaimed by the author.
- The FDA has not informed the company that the clinical study described in the reprint is not adequate and well-controlled.
- The reprint does not pose a significant risk to the public health, if relied upon.
- The reprint is *not*
  - A letter to the editor
  - An abstract of a publication
  - A report of Phase 1 trials in healthy subjects
  - A publication with little substantive discussion of the relevant investigation or data
- The reprint is unabridged, not marked, highlighted, summarized, or characterized in any way, except for specified disclosure statements.
- The following disclosure statements are prominently displayed and permanently affixed:
  - "The [specify] uses described in the reprint have not been approved or cleared by FDA, as applicable to the described [drug or medical device] product."
  - "The [Company Name] has an interest in the [drug or medical device] that is the subject of the reprint or reference text."
  - "The following author(s) have a financial interest in the product [and/or manufacturer]." *[If applicable]*
  - "The following author(s) is receiving compensation from the manufacturer [or has a financial interest in the Company or product or both]. (Describe *affiliation*, the nature and amount of the financial interest or compensation.) *[If applicable]*
  - "[Name of Person] is known to the company and has provided funding for the study discussed in the reprint." *[If applicable]*

- "The significant risks or safety concerns known to [Company Name] concerning the unapproved use, and that are not discussed in the journal article or reference text, are as follows: [insert risks/safety information]."

- The following items "accompany"* the reprint:
  - The approved product labeling is attached.
  - A comprehensive bibliography of publications discussing adequate and well-controlled clinical studies about the unapproved use of the drug or medical device (unless already included in the reprint).
  - A representative publication, if it exists, that reaches contrary or different conclusions regarding the unapproved use.

- The reprint is distributed separately from promotional material

  E.g., if a sales representative delivers a reprint to a physician in his office, the reprint should not be physically attached to any promotional material the sales representative uses or delivers during the office visit and should not be the subject of discussion between the sales representative and the physician during the sales visit. Similarly, while reprints may be distributed at medical or scientific conferences in settings appropriate for scientific exchange, reprints should not be distributed in promotional exhibit halls or during promotional speakers' programs.

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* The Supreme Court defines "accompany," within the context of drug labeling, to mean "to supplement or explain," but that "no physical attachment is necessary" and that the "textual relationship is significant." *Kordel v. U.S.*, 335 U.S. 345 (1948). FDA has not defined what it means by the word "accompany" in the Good Reprint Practice Guidance. If interpreted consistently with the Supreme Court's definition, materials could accompany a reprint even if provided separately, so long as the textual relationship is significant, and the material is easily accessible and provided in temporal proximity to the reprint. It is unlikely, however, that FDA will adopt such a liberal interpretation.

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