

Food & Drug

E-ALERT

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FDA Issues Final Guidance on “Good Reprint Practices”

On January 13, 2009, the Food and Drug Administration (FDA) issued final guidance regarding “Good Reprint Practices.”¹ The guidance applies to the distribution of medical or scientific journal articles and reference publications that discuss unapproved new uses of approved drugs, licensed biological products, and approved or cleared medical devices. While the final guidance largely follows the approach and principles set forth by FDA in an earlier draft guidance, there are several substantive changes and additions that manufacturers should carefully consider.

I. Background

On February 15, 2008, FDA issued a draft guidance that set forth the agency’s views regarding “Good Reprint Practices.” This draft guidance was issued following the expiration of Section 401 of the Food and Drug Administration Modernization Act (FDAMA) of 1997,² which had created a statutory “safe harbor” for the dissemination of medical and scientific information concerning unapproved uses of approved drugs and biologics. FDA provided for a 60 day comment period following publication of the draft guidance, and the agency received comments from industry organizations, public interest groups, lawmakers, and numerous other stakeholders.

FDA maintains that this new guidance does not change the agency’s legal authority to determine whether distribution of medical or scientific information constitutes promotion of an unapproved new intended use. The final guidance, unlike the draft, also stresses the importance of having new indications and intended uses approved or cleared by FDA and the agency “encourages sponsors of medical products to seek such approvals or clearances.” FDA explains in the guidance, however, that the dissemination of truthful and non-misleading medical and scientific information regarding unapproved uses of approved medical products to healthcare professionals and healthcare entities is supported by important public health and policy considerations—namely, “the public health value to healthcare professionals of receiving truthful and non-misleading scientific and medical information.”

II. Key Changes in the Final Guidance Relative to the Draft Guidance

The final guidance contains several substantive changes from the draft guidance, many of which reflect concerns and suggestions provided in comments to FDA.

1. The final guidance defines “healthcare entity” to include hospitals, professional medical organizations, drug formulary committees, and health plans. This definition clarifies that publications covered by Good Reprint

¹ 74 Fed. Reg. 1694 (Jan. 13, 2009). See <http://www.fda.gov/oc/op/goodreprint.html>.

² FDCA §§ 551-557, codified at 21 U.S.C. § 360aaa. The FDAMA provision was subject to a sunset provision and expired on September 30, 2006.

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Practices may be distributed to these organizations, in addition to healthcare professionals.

2. The final guidance elaborated on the types of studies that would be considered “adequate and well-controlled investigations,” and thus eligible for distribution under Good Reprint Practices. Traditionally, the term “adequate and well-controlled” investigations referred to the pivotal studies necessary to obtain FDA approval of a drug or medical device. FDA’s final guidance, however, provides that adequate and well-controlled studies may include “historically controlled studies, pharmacokinetic (PK) and pharmacodynamic (PD) studies, and meta-analyses if they are testing a specific clinical hypothesis.”

3. The final guidance differs in its description of the types of publications that would be considered “false or misleading.” The draft guidance provided several examples of the types of publications that would be considered false or misleading (and thus ineligible for distribution), including a publication that “is inconsistent with the weight of credible evidence.” Under the final guidance, however, it appears that an article that is inconsistent with the weight of credible evidence could be distributed consistent with Good Reprint Practices, so long as that article is not “characterized as definitive or representative.” The intent of this change is not clear given that manufacturers generally are prohibited from characterizing a distributed article as “definitive or representative,” and reprints generally do not themselves contain claims that a study is definitive or representative.

4. The final guidance alters the recommendation that manufacturers distribute a “representative publication ... that reaches contrary or different conclusions regarding the unapproved use.” The draft guidance provided that manufacturers should distribute a representative, contrary publication if the conclusions of the distributed publication had been specifically called into question by other articles or texts. The final guidance calls for the distribution of a contrary publication “when such information exists,” but “especially those in cases” where the conclusions of distributed publication have been specifically called into question. This new language arguably broadens the circumstances when distribution of a publication that reaches “contrary or different conclusions” is recommended.

5. The draft guidance provided that the publication be accompanied by a prominently displayed and permanently affixed statement disclosing any financial interest that the author of the publication had in the product or the company distributing the publication. The final guidance adds that this disclosure should include “the nature and amount” of any such financial interest or any compensation received by the author from the manufacturer. FDA did not provide further guidance on how the amount of the financial interest should be calculated, the relevant time period to consider, or other details on how this disclosure should be accomplished.

6. As with the draft guidance, the final guidance closes with a statement reflecting FDA’s view that if a manufacturer complies with the draft guidance, the agency “does not intend to consider the distribution ... as establishing intent that the product be used for an unapproved new use.” The draft guidance, however, conditioned this “safe harbor” on the condition that “there is no unlawful promotion of the product.” The final document drops that language, but states that “if a manufacturer engages in other conduct that unlawfully promotes an unapproved use of a medical product -- whether or not the manufacturer also engages in conduct in conformance with the recommendations in this guidance -- such other conduct may result in enforcement action.” This language suggests that if a manufacturer complies with Good Reprint Practices, but engages in other misconduct, the agency could take enforcement action with respect to the other misconduct. It is not clear whether FDA would consider the dissemination of reprints (in accordance with the final

guidance) as additional evidence of intent in an enforcement action with respect to the other unlawful promotion.³

III. Conclusion

While the final Good Reprint Practice guidance provides some additional clarity regarding the distribution of off-label publications, it is unlikely to quell the controversy surrounding the distribution of reprints. Already, key lawmakers such as Representative Henry Waxman have criticized the final guidance as too lenient and have encouraged the Obama administration to revoke or revise the guidance. Earlier, however, advocacy groups such as the Washington Legal Foundation had asserted that the draft guidance was too restrictive and threatened to challenge the guidance on constitutional grounds if it was finalized.

Even putting aside the possible modification of the Good Reprint Practices guidance under the new administration, the final guidance itself still contains many areas of ambiguity that will require careful consideration and judgment. Companies should consider the recommendations provided in the guidance document and incorporate these strategies into their overall compliance program.

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³ In its Notice announcing the availability of the guidance, FDA stated that "many comments suggested that FDA continue to require presubmission of the articles and suggested other mandatory review practices." 74 Fed. Reg. at 1694. The agency declined to adopt these suggestions, because "given the sunset of section 401 of FDAMA, these [requirements] were not within FDA's authority and thus outside the scope of the guidance." *Id.*