

FDA Issues Revised Draft Reprints Guidance

On February 28, 2014, the Food and Drug Administration (“FDA”) released a revised draft guidance for industry entitled “*Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices*” (“Revised Reprints Guidance”). In the March 3, 2014, Federal Register [notice](#) announcing the availability of the Revised Reprints Guidance, FDA noted that comments are due on May 2, 2014.

The Revised Reprints Guidance proposes changes to FDA’s January 2009 final guidance “*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*.” (“2009 Guidance”). Both the 2009 Guidance and its new revision address the practices a manufacturer should follow when distributing scientific and medical publications to health care professionals that include information on unapproved new uses (i.e., “off-label uses”) for an approved or cleared product. While many of the concepts set forth in the 2009 Guidance remain as to journal reprints, the Revised Reprints Guidance provides distinct treatment for dissemination of reference texts and, importantly, adds specific recommendations for the distribution of “clinical practice guidelines (“CPGs”),¹ which were not addressed at all in the 2009 Guidance.

FDA explicitly indicated that the Revised Reprints Guidance is in direct response to two pending citizen petitions² filed by members of the Medical Information Working Group (MIWG), an *ad hoc* coalition of drug and device manufacturers to which Ropes & Gray LLP serves as one of the outside counsel. Further, as discussed below, FDA’s *Federal Register* notice states that the agency will continue to address other requests set forth in the MIWG’s citizen petitions.

I. Key Changes in the Revised Reprints Guidance

While the Revised Reprints Guidance indicates some additional regulatory flexibility by permitting the distribution of CPGs, other key changes suggest that FDA is looking to restrict certain reprint distribution practices. Below we describe the important features of the Revised Reprints Guidance.

- ***Allowance of CPG Distribution:*** In contrast to the 2009 Guidance, which is silent on the subject, the Revised Reprints Guidance expressly allows manufacturers to distribute CPGs that include information on off-label uses for approved or cleared products. FDA would allow distribution of only those CPGs that incorporate the [Institute of Medicine’s \(IOM’s\)](#) standards for “trustworthiness”³ and thus are aimed at ensuring that CPGs are informed by a “systematic review of evidence” and an assessment of the benefits and risks of “alternative care options.” Like the requirements for other scientific and medical publications from the 2009 Guidance, CPGs would have to be accompanied by standard disclaimers as to risks of off-label uses, along with financial disclosures related to any of the CPG authors, and relevant context and bibliographic information.

¹ The Revised Reprints Guidance defines CPGs as statements that include recommendations intended to help clinicians make decisions for individual patient care, including in circumstances where there are few or no approved drugs or devices indicated for the patient’s condition or the approved therapies have not proven successful for the individual.”

² See [July 2011 Citizen Petition](#) FDA-2011-P-0512; [September 2013 Citizen Petition](#) FDA-2013-P- 1079.

³ FDA clarifies that standards for CPG “trustworthiness,” incorporated in the Revised Reprints Guidance, are taken directly from IOM’s Congressionally mandated study that focused on “the best methods used in developing clinical practice guidelines in order to ensure that organizations developing such guidelines have information on approaches that are objective, scientifically valid, and consistent,” results of which are set forth in its report, Robin Graham, et al., Institute of Medicine of the National Academies, Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, [Clinical Practice Guidelines We Can Trust](#) (2011).

- *Distribution of CPGs and Reference Texts in Their Entirety or Individual Sections*: While the Revised Reprints Guidance retains the requirement that a journal article should be distributed only in an “unabridged” form, it expressly allows the distribution of CPGs and reference texts either in their entirety or in individual sections (e.g., chapters) that include information on unapproved uses. If a manufacturer chooses to distribute an individual section of a text or CPG, it must be the complete, unabridged section. Further, the Revised Reprints Guidance provides that a CPG addressing one disease state, rather than multiple disease states, should be disseminated only in its entirety.
- *Meta-Analysis and Non-Clinical Research Information Limited to Medical Device Reprints*: The 2009 Guidance permits distribution of reprints and texts that “address adequate and well-controlled clinical investigations,” including historically controlled studies, pharmacokinetic (“PK”) and pharmacodynamic (“PD”) studies and meta-analyses of a specific clinical hypothesis, without any distinction between medical device and drug reprint practices. The Revised Reprints Guidance draws such a distinction. Drug reprints are limited to information that addresses adequate and well-controlled studies, whereas device reprints also can discuss “significant investigations other than adequate and well-controlled studies, such as meta-analyses, if they are testing a specific clinical hypothesis” and “significant non-clinical research (such as well-designed bench or animal studies).” As currently written, the Revised Reprints Guidance implies that drug manufacturers cannot distribute reprints discussing meta-analyses, PK or PD studies and other significant non-clinical research.

II. Impact of MIWG Petitions on FDA’s Regulation of Manufacturer Communications

In addition to announcing the availability of the Revised Reprints Guidance, FDA’s *Federal Register* notice explains that the agency is continuing to consider the specific requests set forth in the MIWG’s pending citizen petitions. Specifically, in July 2011, seven MIWG member companies filed a citizen petition requesting FDA to clarify its regulatory approach to four types of manufacturer communications about off-label uses: (1) responses to unsolicited requests; (2) scientific exchange; (3) communications with formulary committees and payors; and (4) the dissemination of third-party CPGs. In response, on December 28, 2011, FDA issued a draft guidance entitled “[Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices](#)” and opened a [public docket](#) on the concept of “scientific exchange.” In September 2013, MIWG filed a second citizen petition requesting FDA to respond fully to all four requests in the July 2011 petition and further requesting FDA to undertake a comprehensive review and modification of its entire regulatory approach to manufacturer communications, particularly in light of three recent cases⁴ highlighting the constitutional and statutory limitations of FDA’s regulatory authority.

The *Federal Register* notice acknowledged that the agency has not yet reached a final determination on the issues presented in the MIWG’s citizen petitions. But the notice indicated FDA intends to address a number of those issues. For example, the *Federal Register* notice explicitly lays out FDA’s responses to-date regarding some of the issues raised in MIWG’s citizen petitions, including (1) creating a public docket to solicit public input on the concept of scientific exchange; (2) considering comments on the 2011 unsolicited requests draft guidance and (3) considering draft guidance on industry interactions with formulary committees and payors, including presentation of health care economic information. Both the notice and the Revised Reprints Guidance, however, were silent on recent First Amendment case law and its potential impact on FDA regulation.

⁴ See *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011); *FCC v. Fox Television Stations*, 132 S. Ct. 2307 (2012); *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

It remains to be seen whether any regulatory changes made by FDA will result in additional flexibility or additional scrutiny over manufacturer communications regarding truthful, non-misleading information about unapproved uses for approved or cleared products.

If you would like to discuss the foregoing or any other related matter, please contact the FDA Team: [Greg Levine](#), [Alan Bennett](#), [Al Cacozza](#), [Joy Liu](#), [Paul Rubin](#), [Kellie Combs](#) or your usual Ropes & Gray advisor.