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Client Alert

FDA & Life Sciences Practice Group

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FDA Releases Revised Draft Guidance on the Distribution of Scientific and Medical Publications About Unapproved Uses: *Guidance Clarifies Prior Guidance and Addresses Reference Texts and Clinical Practice Guidelines*

On March 3, 2014, the U.S. Food and Drug Administration (FDA) released a revised draft guidance entitled, "Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices" ("Revised Draft Guidance").[1] This guidance revises the 2009 guidance, "Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference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." Consistent with longstanding FDA policy, if manufacturers distribute scientific or medical publications as recommended in the Revised Draft Guidance, FDA does not intend to use the distribution as evidence of the manufacturer's intent to promote the product for an unapproved new use. The deadline for public comments on the Revised Draft Guidance is May 2, 2014.

In the Revised Draft Guidance, FDA confirms the recommendations outlined in the 2009 guidance for the distribution of scientific and medical journal articles, while clarifying several recommendations, particularly as they apply to device manufacturers. FDA also provides specific recommendations regarding the distribution of reference texts and clinical practice guidelines ("CPGs") in response to stakeholder requests.

FDA Confirms and Clarifies the 2009 Guidance Recommendations

- The Revised Draft Guidance specifies that FDA's recommendation against "marking," "highlighting," "summarizing," or "characterizing" the scientific or medical publication may encompass both written and **oral statements** made by, or on behalf of, the manufacturer. For example, "if during a sales call to a physician, a sales representative summarizes or characterizes the article to emphasize portions of the article that suggest the manufacturer's drug may be safe or effective for an unapproved use, this might be used as evidence of intended use."

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- The Revised Draft Guidance contains several important clarifications for device manufacturers:
    - FDA specifically includes the sponsor of a **510(k)-exempt** product within the definition of a "manufacturer" that is subject to the Revised Draft Guidance, stating: "[M]anufacturer means a person who manufacturers a drug or device or who is licensed by such person to distribute or market the drug or device, or a representative of such a person. The term might also include the sponsor of the approved, licensed, cleared, or 510(k) exempt drug or device."
    - While reiterating the recommendation that disseminated publications should describe "adequate and well-controlled clinical investigations that are considered scientifically sound by experts with scientific training and experience to evaluate the safety or effectiveness of the drug or device," FDA elaborates on the acceptability of "**significant non-clinical research**" relating to medical devices.[2] The Revised Draft Guidance states: "In the case of devices, significant investigations other than adequate and well-controlled studies, such as meta-analyses, if they are testing a specific clinical hypothesis, and journal articles discussing significant non-clinical research (such as well-designed bench or animal studies) may be consistent with this guidance."
    - For **510(k)-cleared devices**, FDA recommends that a statement of the cleared indications for use, in lieu of the approved labeling suggested for other products, should be distributed with the scientific or medical publication.
- FDA revises the definition of "**healthcare entity**" to specify "pharmacy benefits managers, health insurance insurers . . . and Federal or State governmental agencies involved in the provision of health care or health insurance," in addition to the hospitals, professional medical organizations, drug formulary committees, and health plans identified in the 2009 guidance.

FDA Provides Specific Recommendations on the Distribution of Scientific or Medical Reference Texts

Noting that scientific or medical reference texts typically discuss a wide range of topics (*e.g.*, diagnosis, pathophysiology, treatments, and pharmacology) and are longer than journal articles, FDA sets forth recommendations that specifically address their distribution. The Revised Draft Guidance states that **a reference text distributed in its entirety** by a manufacturer should:

- Be based on systematic review of existing evidence;
- Be published by an independent publisher that is not substantially dependent on financial support from manufacturers and that publishes scientific or medical education content;
- Be the most current version;
- Be authored, edited, and/or contributed to by experts with demonstrated expertise in the area;
- Be peer-reviewed by experts with relevant expertise and published in accordance with peer-review procedures that are easily accessible or available upon request;
- Be sold through usual and customary independent distribution channels for scientific and medical educational content directed at healthcare providers and students;
- Be distributed separately from promotional information;
- Contain a prominent and permanently affixed statement on the front cover that identifies the distributing manufacturer, discloses that some uses described are not approved or cleared by FDA, and states that the author(s) of some chapters may have a financial interest in the manufacturer, unless otherwise verified; and
- In situations where a reference text is distributed in its entirety but one or more individual chapters have substantive discussion about the manufacturer's product(s), be distributed with product labeling or the 510(k)-cleared indications for use statement.

When a manufacturer distributes **an individual chapter(s) of a reference text that contains discussion of unapproved/uncleared uses of the manufacturer's product**, the chapter(s) should:

- Come from a scientific or medical reference text that comports with the Revised Draft Guidance;
- Be unaltered or unabridged and extracted directly from the text;
- Be disseminated with other unaltered or unabridged chapters, when necessary to provide context, *e.g.*, chapters that provide related or supportive information;
- Contain a prominent and permanently affixed statement identifying the same information required for reference texts distributed in their entirety, but specific to the distributed chapters, and with an added disclosure of all the significant risks and safety concerns associated with the unapproved/uncleared use(s) discussed in the chapter(s); and
- Be distributed with approved labeling or cleared indications for use.

FDA Provides Specific Recommendations on the Distribution of Clinical Practice Guidelines ("CPGs")

The Revised Draft 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." FDA observes that CPGs, like reference texts, are often longer and cover a wider range of topics than a typical journal article.

FDA incorporates the Institute of Medicine's standard for CPG "trustworthiness," and recommends that CPGs, at a minimum, should:

- Be based on systematic review of existing evidence;
- Be developed by a knowledgeable, multi-disciplinary panel of experts and representatives from key affected groups;
- Consider important patient subgroups and patient preferences;
- Be based on an explicit and publicly accessible process for the development and funding of the CPGs that minimize distortions (*e.g.*, reliance on incomplete data), biases, and conflicts of interest;
- Provide a clear explanation of the logical relationships between alternative care options and health outcomes, provide clear recommendations in standardized form, and provide ratings of quality of evidence and strength of recommendations; and
- Be reconsidered and revised when important new evidence warrants modification on recommendations.

FDA recommends that CPGs discussing only one disease state should be disseminated in their entirety. **CPGs distributed in their entirety** should**:**

- Be the most current version;
- Be distributed separately from promotional information;
- Contain a prominent and permanently affixed statement on the front page of the CPG that identifies the manufacturer, discloses that some uses described are not approved or cleared by FDA, and states that the author(s) may have a financial interest in the manufacturer, unless otherwise verified; and
- Be distributed with product labeling and the cleared indications for use statement if one or more sections devotes primary substantive discussion to an individual product or products.

If a manufacturer distributes an **individual section(s) of a CPG**, the section(s) should:

- Come from a CPG that comports with the recommendations of the Revised Draft Guidance;
- Be unaltered or unabridged and extracted directly from the CPG;
- Be disseminated with other unaltered or unabridged chapters when needed to provide context such as related or supportive information;
- Contain a prominent and permanently affixed statement on the front page of each section that identifies the same information recommended for CPGs distributed in their entirety, but specific to the distributed sections, with an added disclosure of all significant risks and safety concerns associated with the unapproved use(s) discussed in the section(s); and
- Be distributed with approved labeling or cleared indications for use.

Comments on the Revised Draft Guidance may be submitted online at http://www.regulations.gov or by mail to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

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[1] U.S. Food and Drug Administration, Revised Draft Guidance for Industry on Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices; Availability; Notice, 79 Fed. Reg. 11,793 (March 3, 2014).
[2] In a footnote, the 2009 guidance noted: "In the case of medical devices, journal articles or reference publications discussing significant non-clinical research may be consistent with this guidance."