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FDA Revises Draft Guidance Concerning Distribution of Scientific and Medical Publications for Drug and Device Manufacturers

Updating policies established in a 2009 Guidance, the Food and Drug Administration (FDA) has released a draft version of a proposed 2014 Guidance addressing the use of medical publications in promoting "off label" uses of approved drugs and devices. The draft 2014 Guidance, announced by the FDA in a March 3, 2014, Federal Register notice, expands upon but neither revokes nor materially amends existing policies. Although the spirit and substance of the proposed guidelines mirror, to a significant degree, the 2009 Guidance, the revisions add a new discussion of clinical practice guides (CPGs) and treat articles, reference texts, and CPGs separately. Manufacturers have sought greater clarity from the agency concerning permissible practices in educating doctors about off-label uses.

Specifically, the proposed new section on CPGs incorporates the Institute of Medicine's (IOM's) standards for CPG "trustworthiness." In keeping with IOM standards, a CPG must:

1) be based on a systematic review of the existing evidence;

2) be developed by a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups;

3) consider important patient subgroups and patient preference;

4) be based on an explicit and transparent (publicly accessible) process by which the CPG is developed and funded that minimizes distortions, biases, and conflicts of interest;

5) provide a clear explanation of the logical relationships between alternative care options and health outcomes, provide clearly articulated recommendations in standardized form, and provide ratings of both quality of evidence and the strength of recommendations; and

6) be reconsidered and revised when important new evidence warrants modifications of recommendations. CPGs are subject to similar standards as articles and texts, such as providing the guide in unabridged form, separate from any promotional materials, and manufacturers are to affix clear disclosures to the CPGs along the same lines required for texts.

As background, Section 401 of the Food and Drug Administration Modernization Act (FDAMA) described various conditions under which a drug or medical device manufacturer could disseminate medical and scientific publications discussing unapproved uses of approved drugs and cleared or approved medical devices to healthcare professionals and certain healthcare-related entities. That section was interpreted as providing a "safe harbor" for manufacturers that complied with the conditions set forth under Section 401 and its implementing regulations. Because the statutory provisions were subject to a "sunset" in 2006, the FDA stepped in and developed a nonbinding "guidance" to establish a set of practices manufacturers could follow to ensure legal compliance.

Generally speaking, the 2009 Guidance described criteria concerning the editorial guidelines for journals or medical texts appropriate for potential distribution (*e.g.*, the journal must be peer-reviewed and published by an organization

with an editorial board composed of independent experts) and placed conditions on the manner in which the texts were distributed (*e.g.*, the articles must be distributed in their full, unabridged form, without highlighting or otherwise isolating sections relating to the drug's or device's potential off-label use). This Guidance specified that the information relayed should address adequate and well-controlled clinical investigations that are considered scientifically sound by experts and must not be false or misleading or pose a significant risk to the public health. Where, for example, an article contained results that have been repudiated by a substantial number of other studies or where the FDA had expressly found the research methodology to be flawed, an article might be considered "misleading," and its distribution could expose a manufacturer to FDA scrutiny. Even where a study met these editorial and scientific standards, manufacturers were advised to provide full bibliographies and copies of representative studies reaching contrary results. Additionally, publications were to be provided entirely separately from any promotional materials and with clear disclosures concerning, among other things, the scope of the FDA's approval and any role the manufacturer may have played in funding the study.

Since the issuance of the 2009 Guidance, drug and device manufacturers have filed petitions with the FDA, seeking additional clarification. The revised draft 2014 Guidance, for which the FDA has solicited comments, presents recommended practices for drug or medical device manufacturers and their representatives to follow if they choose to distribute scientific or medical journal articles, scientific or medical reference texts, or CPGs that discuss unapproved or uncleared uses of legally marketed drugs and devices.

The recommendations regarding articles adhere closely to those in the 2009 recommendations, with similar requirements as to editorial guidelines, manner of dissemination, and disclosures. The revised guidelines do, however, address reference texts separately, requiring that drug and device manufacturers that distribute such texts ensure that the texts satisfy various editorial standards (including being the most current edition and being available through general sales channels rather than manufacturer-funded publications). Additionally, manufacturers are to affix stickers or marks prominently, identifying the manufacturer and stating that some of the uses discussed in the text may not be approved or cleared by the FDA. In situations where a reference text is distributed in its entirety but one or more individual chapters devote primary substantive discussion to an individual product or products, the text must be disseminated with the approved product labeling for the drug or device.

Stakeholders are invited to submit comments, and the detailed recommendations are likely to evolve through the public comment process. Importantly, when finalized, the 2014 Guidance will be just that: guidance. While it will provide a limited safe harbor to manufacturers that comply with all the recommendations, the Guidance will not be binding, and failure to comply with the recommendations will not have the legal effect of a statutory violation.

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