FDA Policies On Dissemination of Information Relating to New Uses of Approved Products

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Foundational Principles

• Policy Considerations
• General rule: no off-label promotion
• Exceptions:
  – Responses to unsolicited requests
  – Scientific exchange
  – Reprints
  – Industry-supported scientific and educational activities
Policy Considerations

• Limitations of Labeling
  – Approved labeling includes only the information FDA deems necessary for safe and effective use (21 C.F.R. § 201.56)
  – Emergence of valuable new uses necessarily outpaces regulatory processes
    • Time needed for FDA to review supplemental applications
  – Clinical decisions must be individualized and must rely on a more heterogeneous mix of information that includes labeling and other sources
Policy Considerations

• Delicate Balance
  
  – FDA policies should “strike the proper balance between the need for an exchange of reliable scientific data and information within the health care community, and the statutory requirements that prohibit companies from promoting products for unapproved uses”

General Rule

- No off-label promotion, meaning:
  - FDCA § 505(a), 21 U.S.C. § 355(a): No new drug may be introduced or delivered for introduction into interstate commerce without a new drug application (NDA) or abbreviated NDA
    - Government must point to labeling causing “newness” to arise within the “new drug” definition
    - “Labeling” definition is limited
  - FDCA § 502(a), 21 U.S.C. § 352(a): A drug shall be deemed to be misbranded if its labeling is false or misleading in any particular
    - Government must demonstrate that “labeling” is “false or misleading”
    - “Labeling” definition is limited
    - Government must demonstrate that a statement by or on behalf of the company creates a new “intended use”
Responses to Unsolicited Requests

Companies may . . . disseminate information on unapproved uses in response to unsolicited requests for scientific information from health care professionals. Scientific departments within regulated companies generally maintain a large body of information on their products. When health care professionals request such information, companies can provide responsive, non-promotional, balanced scientific information, which may include information on unapproved uses, without subjecting their products to regulation based on the information. This policy permits companies to inform health care professionals about the general body of information available from the company.

“A sponsor . . . or any person acting on behalf of a sponsor . . . Shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.”

21 C.F.R. § 312.7(a).
Scientific Exchange

• Examples of scientific exchange:
  – “publishing results of scientific studies”
  – “letters to the editor in defense of public challenges”
  – “investigator conferences”

• Statements made in the exchange of scientific information should:
  (1) make clear that the drug is investigational; (2) make no claims that the drug has been proven to be safe or effective; and (3) be truthful and nonmisleading when measured against available information on the drug—and fairly represent available information—as set forth in materials such as investigators’ brochures and patients’ informed consent sheets.

Dissemination Per Reprints Guidance (Jan. 2009)

• Provides pathway for dissemination of (inter alia) reprints of medical and scientific journal articles relating to new uses of approved new drugs
  – Regulatory technique: recommendations for the types of reprints and the manner of their dissemination (e.g., if sales representative distributes reprints, questions about off-label uses should be directed to non-sales personnel within the company)

• Necessary in view of sunsetting of analogous FDAMA provision
  – Could not include requirement to submit supplemental application because guidance, as a legal matter, cannot be binding

• Reprint carriers and other ancillary promotional activity/communications remains subject to FDA regulation

Source: www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm
Industry-Supported Scientific and Educational Activities

- In December 1997, FDA finalized guidance identifying 12 factors the agency would consider in determining whether a manufacturer, through its support of scientific and educational activities, created a new use for a drug for which adequate directions and new drug approval would be required. 62 Fed. Reg. 64,074.

- On July 30, 1998, the D.D.C. enjoined FDA from seeking to limit any pharmaceutical manufacturer’s ability to (inter alia) suggest content or speakers to an independent program provider in connection with a CME program or other symposium, regardless of whether off-label uses are to be discussed. Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51, 74-75 (D.D.C. 1998).

Industry-Supported Scientific and Educational Activities

• FDA then issued a notice setting forth the agency’s current stance on industry support for scientific and educational activities. 65 Fed. Reg. 14,286 (March 16, 2000).
  – “Manufacturers that support CME may wish to become familiar with the CME guidance document, which details the factors FDA intends to take into account in exercising its enforcement discretion in relation to industry-supported scientific and educational activities. The CME guidance document, however, does not itself have the force and effect of law.”
Industry-Supported Scientific and Educational Activities

• In 2002, FDA issued a letter rejecting a citizen petition filed by WLF challenging the 2000 Federal Register document, and requesting that the agency follow the terms of the injunction issued by the district court in the WLF litigation (but vacated by the court of appeals).

  “. . . FDA can bring actions for alleged violation of these statutory requirements, whether the product is approved for any use or not, relying on proof of . . . sponsorship of CME . . . to demonstrate the manufacturer’s intent. . . . If evidence of . . . sponsorship activity forms part of the basis of FDA’s claim, the trier of fact will consider the context of that activity and any other indicators of independence in assessing the manufacturer’s objective intent. . . . FDA is unlikely to initiate an enforcement action where the only evidence of an unapproved intended use is the . . . sponsorship of CME.”
Industry-Supported Scientific and Educational Activities

“... The description of this safe harbor does not mean that FDA necessarily will bring an action in any case not clearly falling in the heartland of the CME guidance. The decision to bring any action will be made on a case-by-case basis, taking into account all of the facts and circumstances, as is the case in any exercise of prosecutorial discretion. Neither the presence nor absence of any of the factors discussed in the CME guidance is necessarily dispositive in FDA’s determination of whether it has adequate evidence to support a charge of misbranding, although ... FDA will consider these factors in its overall assessment of a manufacturer’s activities.”