FDA Regulation of Promotion & Advertising

Part 3: Disseminating Scientific Information

ComplianceOnline Seminar
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Overview

• **Tension** – FDA, approved labeling and the First Amendment

• **Manifestations**
  – Scientific information exchange – concern – improper influence by company on content of educational activity
  – Off-Label promotion (to be discussed in Part 6)
  – Our approach – *disregard “Caronia” for now*

• **Guidance** -- *Industry-Supported Scientific and Educational Activities* [Hot link] -- 1997
1997 Scientific Exchange Guidance

- To be “safe,” must be both independent and non-promotional
  - if so, not subject to FDA jurisdiction
- Unapproved uses – not permissible if program is subject to “substantive influence” by regulated industry
- Factors influencing “independence” determination
  - Content influence -- whether and to what extent company can
    - speaker or moderator selection or recommendation, especially if speaker has promoted company’s products or were subject of complaints as to past presentations that were biased or misleading in favor of company

» ... continued ...
1997 Scientific Exchange Guidance …

• Factors influencing “independence” determination

… continued …

➢ topic selection, e.g., via targeting points for emphasis
➢ scripting done

– Disclosures to audience –

➢ company funding of project
➢ relationships between company and speakers (e.g., financial, employee)
➢ whether any unapproved uses would be disclosed

– Program Focus

➢ intent to be free of commercial bias (not clear how proved)
➢ Title and content really match
1997 Scientific Exchange Guidance …

• Factors influencing “independence” determination

… continued …

– Program Focus … continued

➤ Balanced discussion of all treatment modalities

– Relationship with provider –

➤ e.g., if provider believes continued financial support is dependent on having programs about company products

➤ intertwining ownership or control of provider with company

– Provider involved in sales & marketing – including provider employees

– Provider’s Demonstrated Failure to Meet Standards – of independence, balance, objectivity, or scientific rigor
1997 Scientific Exchange Guidance …

• Factors influencing “independence” determination

… continued …

– Multiple presentations – of same material – could be factor; FDA recognizes there are benefits to repeated info
– Audience selection – how done can influence
  ➢ generated by company Sales & Marketing – e.g., to reward big “rx writers” or Key Opinion Leaders (KOLs)
– Opportunities for discussion – if not present, not good
– Post-event dissemination of information – except if done via unsolicited request or thru independent provider
– Ancillary promotional actions –
  ➢ exhibit materials
  ➢ Sales & marketing presentations
1997 Scientific Exchange Guidance …

- **Factors influencing “independence” determination**
  
  … continued …

  - **Complaints** – any raised that company tried to influence content

- **Document independence**
  
  - Contract between company and provider that provides for independence and that provider will be solely responsible for managing program

- **Promotional vs. non-promotional**
  
  - If supported activity is not about the company’s products OR competitive products, is not promotional
Good Reprint Practices
January 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 [Hot Link]

• Genesis of guidance
  – FDAMA § 401 – had added § 551 of Act (sunsetted in late 2006) – on off-label use dissemination; led to promulgation of 21 CFR Part 99 (also now void) – if complied, could not be used as evidence of intent of off-label use – “safe harbor”
    ➢ limited to HCPs and certain healthcare entities (e.g., PBMs)
    ➢ sunsetting – led to guidance in 2009
FDA -- Legal Analysis of Unapproved Use

• **Drug**
  – approved drug marketed for an unapproved use is an unapproved drug for that use – violation of § 505(a) – is a “prohibited act” under § 301(d) of Act
  – unapproved drug that is marketed lacks adequate directions for use in violation of § 502(f) of Act – is a prohibited act under § 301 of Act to market misbranded drug

• **Medical Device** – if promoted for unapproved or uncleared use is also misbranded and adulterated
  – marketing = prohibited act
Permissible Reprints -- Types

• **Published by an organization that has an editorial board** that:
  – uses experts with demonstrated expertise in the subject of the article under review by the organization and who are independent of the organization to review and objectively select, reject, or provide comments about proposed articles; and
  – that has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization;

• **Must be peer-reviewed** -- and published in accordance with the peer-review procedures of the organization; and

• **Not be in the form of a special supplement or publication that has been funded** in whole or in part by one or more of the manufacturers of the product that is the subject of the article.
Permissible Reprints -- Types

• **Excluded characteristics**

  – Can’t be primarily distributed by a drug or device manufacturer,
    
    ➢ Should be generally available in bookstores or other independent distribution channels (e.g. subscription, Internet) where medical textbooks or periodicals are sold;

  – Can’t be written, edited, excerpted, or published specifically for, or at the request of, a drug or device manufacturer; or

  – Can’t be edited or significantly influenced by a drug or device manufacturer or any individuals having a financial relationship with the manufacturer.
Content

• **Required** – to address 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.
  – These can include historically controlled studies, pharmacokinetic (PK) and pharmacodynamic (PD) studies, and meta-analyses if they are testing a specific clinical hypothesis

• **Excluded** –
  – Be false or misleading
  – Pose a significant risk to the public health, if relied upon
Distribution Manner

• Unabridged reprint, copy of an article, or reference publication – note– does not have to be solicited
• Not be marked, highlighted, summarized, or characterized by the manufacturer in any way
  – except for disclosures required by the guidance
• Be sent with the approved labeling for product
• Be sent with a comprehensive bibliography --
  – discussing adequate and well-controlled clinical studies published in medical journals or medical or scientific texts about the use of the drug or medical device covered by the information disseminated (unless the information already includes such a bibliography)
Distribution Manner …

- **Sent with a representative publication, when such information exists, that reaches contrary or different conclusions regarding the unapproved use;**
  - especially where the conclusions of articles or texts to be disseminated have been specifically called into question by another published article(s) or text(s)

- **Must not include any promotional information**
  - can be delivered by sales rep, but must be free of any promotional info and can’t be discussed by rep
  - can be handed out at a medical or scientific conference, must not be in exhibit halls or during a promotional presentation
Disclaimers Required

• Reprint must be accompanied by a “prominently displayed and permanently affixed statement” disclosing:
  – that the uses described in the information have not been approved or cleared by FDA, as applicable to the described drug or medical device;
  – the manufacturer's interest in the drug or medical device that is the subject of the journal reprint or reference text;
Disclaimers Required …

- Reprint must be accompanied by a “prominently displayed and permanently affixed statement” …
  - any author known to the company as having a financial interest in the product or company or who is receiving compensation from the company, along with the affiliation of the author, to the extent known by the company, and the nature and amount of any such financial interest of the author or compensation received by the author from the company;
  - any person known to the company who has provided funding for the study; and
  - all significant risks or safety concerns known to the manufacturer concerning the unapproved use that are not discussed in the reprint.
Responding To Unsolicited Requests for Off-Label Information
December 2011 – Draft Guidance

• **Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices**  *[Hot Link]*

  – Applies to
    - approved drugs and biologics (human and animal)
    - approved and cleared devices
    - Off-label also includes deviating from intended uses in device classifications for devices that are 510(k) exempt
  – Not applicable to investigational products
  – Dissemination of info on off-label uses – can be seen as “evidence of a new intended use” – without approval/clearance – violates law
December 2011 – Draft Guidance …

- Applies to unsolicited requests made directly or indirectly – e.g., in public internet sites
- If respond consistent with guidance, FDA will not use the response as “evidence of the firm’s intent that the product be used for an unapproved or uncleared use.”
- Responses – not expected to comply with normal disclosure of information rules for advertising or labeling
- Solicited requests – not subject to draft guidance, but can be evidence of intent by firm of an off-label use for its product – implied message of guidance – DON’T
December 2011 – Draft Guidance …

• FDA – Acceptable to reply to unsolicited requests for off-label info on FDA-regulated medical products:
  – “by providing truthful, balanced, non-misleading, and non-promotional scientific or medical information that is responsive to the specific request, even if responding to the request requires a firm to provide information about unapproved or uncleared indications or conditions of use.”

• Response – whether to a private or public solicitation – should be in a private, one-on-one communication, to the person who requested.
Private Requests – Responding

• **Two key aspects of response:**
  – Should be in a private, one-on-one communication, to the person who requested.
  – Response should be “tailored to answer only the specific question(s) asked.”
    ➢ if get a broad question, should try to narrow the focus
    ➢ however, if risk info exist that relates to the question, but is not directly on point to the question, should include
      ▪ **Example:** question about use in pregnancy and diabetes; risk info exists on fetal harm when used in arthritis – disclose fetal harm issue even though off-label use asked about was re diabetes
Private Requests – Responding …

• **Response must be “truthful, non-misleading, accurate and balanced”**
  – must include info that would cast doubt or are non-supportive of off-label info
  – should include complete copies of articles referenced
  – to “extent possible,” should rely on peer-reviewed journals, medical texts, and independent sources of info.
    - but, can use “data on file”
    - journals – should be from those with full disclosure info on authors as to conflicts and biases

• **Must be “scientific” in tone**
Private Requests – Responding …

• Should be generated by medical or scientific personnel – independent of sales or marketing

• Responders – should be trained on how to reply (consistent with the guidance)

• Info to send with response:
  – FDA approved labeling, including any patient labeling
  – “Prominent statements”
    ➢ FDA has not approved/cleared the off-label info enclosed
    ➢ As to what uses are FDA approved/cleared
    ➢ All important safety info re product, including boxed warning
    ➢ complete list of references
Private Requests – Responding …

• Recordkeeping
  – Nature of request for information
  – Name, address and affiliation of requestor
  – What was provided to the requestor
  – Any follow-up requests or inquiries from requestor
Public Requests -- Responding

• Only respond if it is specifically about your product (and not just your competitor’s) – even if you have info on your product that would respond to the request

• Public response – limited – just provide contact information – scientific or medical -- for more info
  – but, FDA wants you to say in your public response that the request relates to an off-label use
  – contact info -- be specific (e.g., e-mail address; phone; fax)
  – assumption – until you then get a private inquiry, nothing more you can do
  – “public responder” – must make clear they are with the company
Public Requests -- Responding

• Public response … continued …
  – must be non-promotional
  – must include info on how to access just the approved labeling and not any other website that is promotional
    ➢ the URL for labeling must be non-promotional (e.g., can’t be www.bestforgout.com)
End of Part 3 – Disseminating Scientific Information