INTOUCH SOLUTIONS®

point of view

FDA Issues Draft Guidance on Responding to Unsolicited Requests for Off-Label Information

Intouch Solutions Point of View

BACKGROUND

Two years ago, in November 2009, FDA held a **public hearing** to address five critical questions related to the use of the Internet and social media in the promotion of FDA-regulated medical products. The five (paraphrased) questions included:

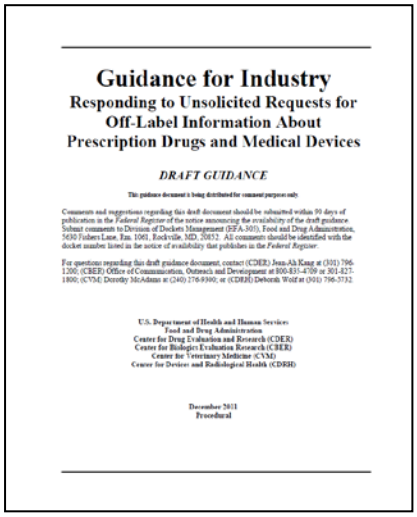
1. For what online communications are companies accountable?
2. How can companies fulfill regulatory requirements using new media, especially when there are space limitations?
3. What parameters should apply to the posting of corrective information on websites controlled by third parties?
4. When is the use of links appropriate?
5. Questions specific to Internet adverse-event reporting.

Then one year ago, **FDA outlined** which areas the agency would focus on first. Responding to unsolicited requests was at the top of that list. On Dec. 27, 2011, FDA made good on that promise. While many pharma marketers were

taking holiday vacation time, FDA quietly issued draft guidance addressing how pharmaceutical companies may respond to unsolicited requests for off-label information.

Why Is This Important?

The guidance applies to prescription drugs (including biological products), medical devices, and animal health products. Much of the guidance addresses how manufacturers should respond to questions posed in public online forums. The guidance also mentions a number of "emerging electronic media" such as Twitter, YouTube, and discussion boards that we haven't seen FDA address directly in the past.


Guidance for Industry
Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices
DRAFT GUIDANCE

Elements of the guidance address some of the questions raised at the hearing. While still in draft form, the document provides some important insights into the direction and mindset of FDA's view of the use of electronic media by pharmaceutical and medical device companies.

The full (12 pages) text of the guidance, **Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices**, can be found online on the FDA website or by clicking the image to the right. Those interested can provide suggestions and comments to FDA within 90 days.

As a service to its clients and colleagues, below Intouch Solutions has provided a summary and commentary on the draft guidance.

INTRODUCTION

FDA acknowledges, as we have all witnessed, that the rapid rise of the Internet has enabled more active and public information seeking, and the nature of this medium enables those questions and any responses to have much more visibility and longevity.

> "The Internet has revolutionized communication, information sharing, information exchange among systems, and collaboration."

Though FDA still doesn't want companies promoting drugs or devices off-label, the agency acknowledges off-label uses may be important treatment options and "may even

constitute a medically recognized standard of care." FDA also recognized that manufacturers may maintain extensive off-label-related data that may be useful to HCPs or patients seeking information.

In the document, FDA:

- Notes the distinction between online properties that are and are not under the control of the manufacturer, and the guidance covers both instances.
- Recognizes that manufacturers are qualified to respond to these requests because they are regulated and have the most accurate and current data.
- Acknowledges that, in many cases, a manufacturer is more qualified than other people who respond to queries on the Internet. In other words, they acknowledge that user-generated content may not be accurate and pharma/med device companies may be in a better position to answer off-label questions.
- Provides clear and critical differentiation between solicited and unsolicited requests (this draft guidance only addresses unsolicited requests), and between public and non-public requests/responses.

Critical Definitions

To understand the guidance, it's helpful to first understand the definitions of several critical terms and how FDA differentiates between them.

1. **Emerging electronic media** – Throughout the document, FDA discusses "emerging electronic media," noting examples such as microblogging/Twitter, YouTube chat rooms, discussion boards, and more. However, while these tools are referenced in many examples provided, the guidance is not only for online media and mentions are made of phone calls, letters, meetings, live presentations, and calls made by sales reps.

2. **Solicited requests** – Requests for off-label information that are prompted in any way by the manufacturer. A number of helpful examples that would qualify as solicited were provided for clarification:

    - The prompting by a sales rep for an HCP to request off-label information.
    - Questions asked of a paid spokesperson such as a KOL speaker or medical science liaison at a live event.
    - If a company presents information in a manner that solicits off-label requests on a business reply card, print pieces, convention booth graphics, or other promotional materials.
    - Requests made in response to a phone number, email address, URL, or username that implies availability of off-label information.

- Requests made for users to post videos on YouTube about their own uses for the product. In this case, if the call for videos itself or any videos that are posted prompt off-label questions, those will be considered solicited.
- If a company sends information to bloggers and encourages them to write about an off-label use, any resulting requests would be considered solicited.
- If a company announces results of a study via microblog (such as Twitter) that suggests the product is safe and effective for an off-label use, any resulting questions would be considered solicited.
- Requests resulting from use of a website with drop-down menus that name off-label uses or the use of search terms to generate off-label use information.

3. **Public unsolicited requests** – Requests made in a public forum, whether directed specifically to the company or not. This could include, for example, questions asked during a live forum such as a patient program, or a patient question posted in an online disease-related community or on a company's Facebook page.

4. **Non-public/private unsolicited requests** – Directed privately to a company using one-on-one communication, for example, via phone call or email.

HOW CAN PHARMA AND MEDICAL DEVICE COMPANIES RESPOND?

FDA acknowledges that companies can, if they choose to, respond to unsolicited requests for information about FDA-regulated products by providing "truthful, balanced, non-misleading, and non-promotional scientific or medical information that is responsive to the specific request." This applies, FDA notes, "even if responding to the request requires a firm to provide information on unapproved indications or conditions of use." If these rules are followed, responses don't need to meet regulatory requirements for promotional labeling or advertising.

With that baseline and the aforementioned definitions, by page seven of the document, FDA was ready to lay out how to respond to off-label queries in today's dynamic and electronic media world. Two key points to note up front:

1. The company has the choice to respond to unsolicited requests or not.
2. If the company chooses to respond, the actual response to the answer can only be provided in a private, one-on-one communication. This applies to questions posed in both a private and public setting.

Responding to NON-PUBLIC (Private) Unsolicited Requests Directed to the Pharma/Med Device Firm

1. **Be Direct**. Respond only to the person that asked the question.

2. **Be Specific**. Respond only to the specific question asked.
    - If the question is broad or unclear, the company should work to clarify and narrow down the question in order to tailor the response.
    - If there are specific risks associated with other conditions that may be relevant to the off-label use mentioned, the firm should provide that information.
3. **Be Accurate and Balanced**. Respond only with truthful, non-misleading, accurate, and balanced information.
    - If an article that was published was called into question, the company should disseminate both the original and the opposing article.
    - Responses should include complete copies of literature and not just summaries.
    - The response can include unpublished data if appropriate, but peer-reviewed journals and other independent articles are preferred.
    - Journal reprints should only be provided from journals that adhere to a policy of full disclosure of conflict of interest or bias.
4. **Science vs. Promotion**. Information provided should be scientific in nature and should not be promotional or distributed alongside material that is promotional.
5. **Deploy Appropriate Responders**. Questions should be referred to and responses should be generated from trained medical/scientific staff independent from sales or marketing departments.
6. **Provide Accompanying Materials**. When a company responds to a request, it should include the following:
    a. Appropriate FDA-required labeling (PI, medication guide, and/or client information sheet)
    b. Complete list of references for all information disseminated
    c. Several "prominent statements," including:
        - FDA has not approved this product as safe/effective for the use discussed.
        - Disclosure of the FDA-approved indication.
        - All important safety information, including any boxed warnings.
7. **Keep Records**. The following records should be maintained:
    - The nature of the request, including contact information and affiliation.
    - The information that was provided.
    - Any follow-up inquiries.

Responding to PUBLIC Unsolicited Requests Directed to Users At Large

One critical point of this section is that, essentially, responses to public requests should be made private. The conversation should be directed to a one-on-one setting so that it takes place solely between the firm and the requestor. FDA's stance is, if a reply is posted publicly, it is being communicated to individuals that didn't ask the specific question and may

therefore be considered off-label promotion. FDA also recognizes that things tend to live forever on the Web and responses can become outdated as new information becomes available.

When responding to public unsolicited requests, companies should:

1. **ID Appropriate Requests**. Companies should only respond to requests if they pertain to that company's own named product.
    a. "Can drug/device X be used for condition Y?" is appropriate to respond to; "What drug/device treats condition Y?" is not appropriate.

2. **Limit the Info**. The public response should be limited to providing only the firm's medical/scientific staff contact information, conveying the question pertains to an unapproved use.
    a. After the individual has contacted the company privately, the company is able to provide a private, detailed response and maintain records accordingly (see previous section).

> "What everybody was expecting was actual guidelines around social media. But I still think this is monumental." – *Intouch Solutions' Sr. Director of Emerging Media Jim Dayton, as quoted in* ***Advertising Age***

3. **Provide Disclosure**. Company representatives responding publicly to inquiries should clearly disclose that they are a representative of the company, and direct them to the appropriate contact.

4. **Avoid Promotion**. The public response that redirects the person to a one-on-one exchange should provide a link to FDA labeling but should not provide links to anything promotional in nature such as a brand.com website.

READING BETWEEN THE LINES: THE STORY BEHIND THE STORY

There are a lot of things this document doesn't do – namely, it is not the clear-cut social media guidance that industry has desperately been seeking. But we are excited to see FDA acknowledge the existence of – and use as examples – electronic media such as Twitter, YouTube, online discussion forums, email, and the like.

And, if one looks closely, the document does provide some insight into FDA's thinking. It may not be social media guidance, but there are some important things to note from a social media perspective:

1. **Hooray for Clarity**. While no doubt some questions remain, the direction is fairly specific in terms of not only what type of information can be used in responses, but also what information should and shouldn't be provided in both public and private forums. FDA also provides an example where the use of a link to PI is appropriate. We applaud any communication from FDA that is clear (if not concise) on direction.

2. **Time to Revisit Social Media Workflows**. The guidance, though draft, provides enough information at this point to revisit existing social media workflows that address how to respond to off-label inquiries or comments. In most cases, off-label inquiries are already routed through the appropriate channels, but FDA now lays out guidelines on how to publicly direct the queries.

3. **Offline-to-Online SOPs**. Since companies have been responding in a similar manner to requests for off-label information already, the document essentially acknowledges that – as many have done with social media – adapting offline processes for online application is the right way to go.

4. **The Unsocial FDA**. Those familiar with social media conversation norms will groan at the prospect of providing a response in a public forum in the manner in which FDA suggests. We should further assess how companies can best communicate in the manner and tone in which FDA requires without sounding like robots. Consumers won't necessarily always welcome a terse response that redirects them to a different channel. Pharma and med device companies should work hard to craft responses that meet the requirements but still sound human.

5. **Social Media Is Still an Option**. FDA did not state that a company cannot respond to requests made via the Internet or social media. Indeed, the agency acknowledged that, if done correctly, pharmaceutical companies could be in a position to further the interest of public health by doing so.

6. **Policing the Internet**. FDA also did not state that companies are REQUIRED to respond to off-label inquiries; it's the company's choice. Pharma's responsibility for policing the entire Internet was a hot topic at the 2009 hearings. This document gives us a peek into FDA's position on that topic.

All in all, FDA is recognizing the sea change that the Internet has provided in enabling the exchange of information and the empowerment of patients. And perhaps this will indeed turn out to be the first in a series of promised guidance to come out of the 2009 hearings. We will continue to monitor the topic and will keep you posted as new information emerges.

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