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March 28, 2012

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Docket Number FDA-2011-D-0868

Dear Sir or Madam:

Hogan Lovells US LLP files these comments to FDA's *Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices*, published on December 30, 2011 (the "Draft Guidance"). We submit these comments in the interest of clients that routinely engage in non-promotional exchange of medical and scientific information in response to unsolicited questions from healthcare professionals ("HCPs"). We appreciate the efforts of the four FDA centers that collaborated on the Draft Guidance.

As a law firm that regularly counsels pharmaceutical and biotechnology companies on promotional and non-promotional activities, we understand the tremendous complexity presented by the public exchange of off-label medical and scientific information. Since 1982, when FDA first offered the industry guidance on how to respond to unsolicited questions, the pharmaceutical industry has, with the assistance of law firms like Hogan Lovells, carefully scrutinized the two most important—and sometimes conflicting—sources of law: the agency's sparse guidance and judicial decisions clarifying the scope of First Amendment rights. To assure that the industry faithfully follows the law, pharmaceutical companies have gone to great lengths. These include: developing medical affairs functions within companies, hiring and deploying medical science liaisons and reimbursement assistance professionals, and creating databases of scientific and clinical literature regarding drug products.

Although the agency has said the Draft Guidance "updates and clarifies" past policies, *see* Draft Guidance at line 23, a number of the positions taken would diminish the appropriate availability of reliable, objective, and scientific information regarding drug products. That is troubling because it conflicts with the agency's expressed goals and intentions around permitting companies, who have "robust and current" information about their products, to respond to unsolicitied requests for information about those products in order to advance the public health. *See, e.g.,* Draft Guidance at lines 83-90. But the problems run deeper still. Many of the new positions may prompt changes in carefully developed industry practices that provide for controlled, non-promotional communications that have, to date, contributed to the public health through the free flow of scientific information. Moreover, some of the Draft Guidance's recommendations are simply not practical to implement on a widespread and consistent basis. Finally, the Draft Guidance reflects an anachronistic

understanding of First Amendment law. Since FDA issued its last statement about unsolicited requests, the Supreme Court and several federal courts have fundamentally recalibrated the ability of government to regulate truthful speech of this sort. *See, e.g., Sorrell v. IMS Health, Inc.* (S. Ct. 2011). The Draft Guidance should therefore be revised to reflect the careful balance between regulation and truthful scientific exchange that the federal courts have recognized over the past few years.

With these concerns in mind, we respectfully urge the agency to reconsider and clarify elements of the Draft Guidance with respect to 1) "public" responses at meetings held between manufacturers and HCPs, 2) the materials that should accompany a response, and 3) the role of toll-free customer service numbers in prompting requests for off-label information.[1]

A. **Responding to Questions in a "Public" Forum**

1. The definition of "public"

Perhaps the policy position in the Draft Guidance that has drawn the most attention is FDA's statement that "[r]egardless of whether the initial unsolicited request for off-label information was made in a non-public or a public forum, a firm that chooses to respond should provide the final response . . . only to the individual who requested the information as a private one-on-one communication." Draft Guidance at lines 209 – 213. The agency defines a "public forum" to include a "live presentation" where a question is directed at a "firm's representative." *Id.* at lines 131-32. We believe this construct – where privately-sponsored promotional speaking events involving approximately a dozen participants are considered "public" – will cause substantial confusion among HCPs in attendance and will result in less information being available to those HCPs.

Critically, FDA's definition of "live presentations" as "public" is a misclassification. The vast majority of promotional presentations sponsored by drug manufacturers are indeed private. They are by invitation only, access is restricted by the sponsoring company, the meetings are held in settings such as private rooms in restaurants or hotels, the presentations are not recorded or broadcast by the company, and they are designed to meet industry standards as a setting appropriate for educational purposes. FDA appears to be taking the position that, in the context of speaker programs, anything more than one-on-one is a public exchange even if that is not the case as a factual matter. In terms of public access, speaker programs more closely resemble private meetings in a practitioner's office. *See* Draft Guidance at lines 119-120 (defining a "non-public" request as one that "is directed privately to a firm…").

FDA's proposed definition of "public" is problematic because it interferes with the ability of a speaker to respond to unsolicited requests in a meaningful, non-burdensome manner. Typically, if manufacturers anticipate off-label questions at speaker programs, the medical affairs function will draft scientifically-supported talking points to answer what it reasonably anticipates will be the most

[1] FDA's expressed intention is that the Draft Guidance "does not address requests for information about medical products that are not currently approved or cleared for any purpose." Draft Guidance at lines 28-29. We do not read this statement as limiting companies' ability to respond to unsolicited questions about investigational products, but merely as a statement of the scope of the Draft Guidance. We welcome the agency's effort to clarify the scope of the scientific exchange regulation, which we believe currently allows responses to questions about investigational products. *See* 76 Fed. Reg. 81508 (December 28, 2011)(Communications and Activities Related to Off-Label Uses of Marketing Products and Use of Products Not Yet Legally Marketed: Request for Information and Comments.)

frequently asked off-label questions, and train speakers on how to deliver limited, supported, and objective responses. These responses acknowledge that a use is off-label, and provide a focused, high-level, neutral and balanced response. If manufacturers are no longer able to provide these substantive responses, or provide them in a targeted, non-burdensome manner, there is a risk that the HCPs in attendance may simply choose to rely on the personal clinical experience of others in attendance, whether or not that experience is backed by scientifically rigorous data. Based on our experience with speaker programs, we believe that the policy approach that is most likely to result in a response that is focused, objective, balanced, and scientifically rigorous, *see* Draft Guidance at lines 260-284, is one based on data gathered, analyzed, and drafted by the host company that is presented to the audience in a concise and targeted manner by a trained speaker. Simply put, a rule that does not allow an exchange that is open and data-driven will stifle speech and could lead to confusing or incomplete responses by speakers and will not advance the public health.

As an alternative, FDA should craft a more accurate definition of "public." For example, presentations that result in enduring materials such as webinars available for replay or videos posted to sponsoring organizations' websites might legitimately be considered "public." Similarly, events that are open to the public and advertised – such as patient seminars or on-line chats with experts – better fit the term "public." Limiting responses to unsolicited questions in these settings would address FDA's concern about materials that may become outdated (Draft Guidance at lines 367-369) without restricting a fulsome exchange in a truly private and controlled setting, such as a promotional speaking event or an in-service training at a private clinic – which are not properly considered "public forums."

2. Practical Considerations Regarding the Proposed One-on-One Individualized Responses

The practical hurdles to FDA's suggested one-on-one responses policy are substantial. We believe there are several options for delivering a one-on-one individualized response, each of which raises considerable hurdles:

- A company could require the presenter at a promotional dinner to hold all off-label questions until the end when the presenter would meet individually with audience members to take questions. But, would this instruction be deemed be a solicitation of an off-label question?
- A company could require the speaker to defer all questions until after the main program, where they would be fielded either by the speaker or a company medical representative at the back of the room. But would the company be responsible for assuring that the answer was provided out of earshot of other attendees? What if two or more members of the audience wanted to hear the answer? Would the company be required to establish a separate room for the purpose of providing one-on-one answers?

The problems do not end there. Were companies to adopt either of these approaches, how would it monitor these individualized responses for scientific rigor, objectivity, and balance? Does the "one-on-one" rule apply to other private settings where unsolicited requests are frequently made, such as events for clinical investigators or meetings between a company's senior executives and key opinion leaders?

Finally, companies routinely interact in private, small-group settings with HCPs and participate in back-and-forth exchanges about scientific information. The most prominent are those with insurance plans and formulary committees, the vast majority of which rely on the Academy of Managed Care Pharmacies (AMCP) framework for providing the complete set of information deemed relevant to

coverage determinations. Under this system – which has been in place for close to a decade – plans request a full dossier of information on a drug before a meeting. This allows the plan to gather information about all the potential uses that patients and providers will ask the plan to reimburse. Meetings between plans and companies usually involve several participants with unique roles – account managers to discuss a potential contract's financial terms and medical liaisons to discuss clinical data – but rarely present opportunities for "individual" exchanges. Insurance plans and large providers are sophisticated customers with very specific needs, and FDA should continue to allow these informational exchanges.

Because an individual one-on-one rule for live presentations and small meetings would be both unworkable and indeterminate, we urge FDA to reevaluate this policy position. A better approach than the "individual one-on-one" response would be a "one entity-to-one entity" framework. Under an "entity discussion" framework, FDA should encourage company "back up" slides for responding to anticipated off-label questions so long as those slides are objective, balanced, and scientifically rigorous; the company has a reasonable belief that those questions will be asked; and the speaker is adequately trained in narrowing the response and quickly returning to the on-label portion of the presentation. This approach – which the industry has implemented for years – is most likely to assure that the responses meet FDA's recommendations for appropriateness, and provide information that will advance the public health rather than generate the potential to confuse or mislead the requestor.

B. **The Materials that Should Accompany a Response**

FDA recommends that companies provide voluminous information to requestors when responding to unsolicited requests. In Section V.5.3, the agency suggests that responses:

- Should include both positive and negative results;
- Should include "complete copies of scientific reprints, technical literature, or other scientific and medical information responsive to the request, not just summary documents or abstracts prepared by" the responding manufacturer;
- May include unpublished data that are responsive; and
- Should rely to the greatest extent possible on peer-reviewed journal articles from organizations with conflict of interest policies.[2]

At the February 2012, Drug Information Association "Marketing Pharmaceuticals 2012" workshop, Jean-Ah Kang, Special Assistant to the Director, Office of Prescription Drug Promotion (OPDP), maintained that all materials analyzed to develop the response would need to be disseminated to the requester after receiving an oral response.[3]

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[2] Meeting these recommendations may substantially increase manufacturers' costs. A reasonable, less burdensome alternative would allow companies to document the support for standard responses through citations to the literature or allow companies to distribute abstracts of peer-reviewed publications that are available to the requestor through on-line databases such as PubMed.

[3] In one place, the Draft Guidance qualifies that materials must accompany "information distributed" in response to a question (line 260) – implying that a written response triggers the recommendation for voluminous accompanying materials – elsewhere the Draft Guidance implies that "complete copies" are always necessary – "the response should include…". Draft Guidance at line 268. Although we disagree with the clarification provided by Ms. Kang for the reasons set out here, changes to the draft document are in order simply to clarify this point.

Although the intention behind these standards may be laudable, they are more likely to confuse the requestor than provide a narrowly tailored response. Many marketed drug products have been the subject of hundreds of peer-reviewed publications. A common question could require a company to provide dozens of peer-reviewed journal articles in response. Even if the question were appropriately narrowed by the company representative, a response that included a handful of journal articles would not be narrowly tailored. Though companies do not necessarily object to disseminating this information, the costs and administrative burdens associated with this provision, such as obtaining multiple copyright clearances and managing the logistics to hand-deliver, mail, or e-mail a large number of articles, are substantial. And, the dissemination recommendation presents substantial enforcement hurdles. If responses to unsolicited requests are provided in one-on-one settings by paid speakers or employees, how would the sponsoring company assure that the necessary supporting materials are delivered to the requestor?

In addition to suffering from all these shortcomings, such a position would appear to be in tension with the recent district court decision striking down FDA's mandate of graphic warnings on cigarette packages as compelled speech. *See R. J. Reynolds v. F.D.A.* (D.D.C. 2012); *but see Discount Tobacco City & Lottery v. U.S.* (6th Cir. 2012). OPDP's requirement that companies disseminate vast quantities of medical literature can only be described as compelled speech that must meet a higher standard of scrutiny. The Draft Guidance offers no consideration of a less burdensome approach nor does it explain why this compelled speech is required to satisfy an important governmental interest.

C. **Solicited Requests**

In the Draft Guidance, FDA notes that "[i]f a firm… presents statements or contact information in promotional pieces in a manner that solicits requests for off-label medical or scientific information (e.g., "Product X continues to be evaluated in more than 50 trials in a broad range of conditions and patient" and "Call 1-800-… for more information")… [then] requests made in response to these types of requests would be considered solicited requests." Further, at the "Marketing Pharmaceuticals 2012" workshop, FDA representatives suggested that this rationale would also apply to a menu option related to medical information (e.g., "for medical information, press 3") delivered to callers via a 1-800 product service number.

Including an option for obtaining medical information among other options such as reporting an adverse event or discussing patient assistance programs, should not be considered to prompt requests for off-label information. Importantly, a menu option does not invoke a topic (e.g., unapproved uses, alternative dosing, etc.). Toll-free numbers are important vehicles to provide patients and HCPs with access to important services and information related to a company's products – separating out different service functions such as reimbursement support to a different telephone number would not advance FDA's interests in avoiding solicited questions, but could substantially burden patients, HCPs, and companies as they work together to meet patient's health

needs. In fact, it is our understanding that FDA's Office of Surveillance and Epidemiology expects sponsors of drugs with REMS that have Elements to Assure Safe Use to have a single toll-free number that patients and HCPs can use to report issues with, or obtain information about, the drug product. Accordingly, we request that FDA clarify that presenting one toll-free number, with a menu option related to medical information, is permitted and that the use of one toll-free number does not transform every call to that number for medical information into a solicited request.

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We appreciate the opportunity to comment on this important Draft Guidance. Thank you for your consideration and for your efforts in finalizing the draft.

Sincerely,

Meredith Manning

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