April 15, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane Rm. 1061
Rockville, MD 20852

Re: Amended Comments of the Medical Information Working Group for the Food and Drug Administration Transparency Task Force, Docket No. FDA-2009-N-0247, 75 Fed. Reg. 11893 (Mar. 12, 2010)

Dear Sir/Madam:

On April 12, 2010, the Medical Information Working Group submitted a response to FDA's request for comments on ways to increase transparency between FDA and the regulated industry, published in the Federal Register on March 12, 2010, 75 Fed. Reg. 11893. Please find attached our amended comments, which are substantively unchanged but include Eli Lilly and Company among the manufacturers in support.

Sincerely,

/s/Alan R. Bennett

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Re: Amended Comments of the Medical Information Working Group for the Food and Drug Administration Transparency Task Force, Docket No. FDA-2009-N-0247, 75 Fed. Reg. 11893 (Mar. 12, 2010)

Dear Sir/Madam:

The following comments and recommendations are being submitted on behalf of The Medical Information Working Group (MIWG),[1] in response to FDA's request for comments on ways to increase transparency between FDA and the regulated industry, published in the Federal Register on March 12, 2010, 75 Fed. Reg. 11893. In that document, FDA specifically asked for comments on how it can make improvements in "[p]roviding useful and timely answers to industry questions about specific regulatory issues." Id. at 11894. As discussed in more detail below, we respectfully request that FDA implement an advisory opinion process that would provide timely binding advice[2] in response to a specific request on proposed promotional and scientific exchange practices. We believe that doing so would not only encourage greater industry compliance but also lead to the improved communication of important health information.

Once a product is approved for a particular use, the law permits health care professionals to prescribe or use the product in ways that are different than those approved by FDA. Indeed, the legal recognition of off-label use is an accepted and necessary corollary of the FDA's public health mission to regulate products without directly interfering in the practice of medicine, and it is generally recognized that off-label use can result in significant benefit to patients so long as it is appropriate and informed. While physicians may prescribe or use products in a manner different from that approved by the FDA, the Agency restricts how manufacturers can communicate information about unapproved uses and prohibits manufacturers from promoting those uses. Unfortunately, statutes, regulations, FDA guidance documents, and other agency policies are frequently unclear in this regard and may become even more difficult to interpret as technology and business practices evolve. Deciding whether a particular activity

[1] The MIWG is an informal working group of prescription drug and medical device manufacturers that was formed to consider issues relating to the federal government's regulation of truthful, non-misleading, scientifically substantiated manufacturer communications about products subject to FDA jurisdiction. The members of the MIWG in support of these comments include: Allergan, Inc., Amgen Inc.; Bayer Healthcare Pharmaceuticals; Eisai, Inc.; Eli Lilly and Company; GlaxoSmithKline; Genentech Inc.; Johnson & Johnson; Novo Nordisk, Inc.; Pfizer Inc.; and Sanofi-Aventis U.S. LLC. The group has previously submitted comments to FDA on Guidance for Industry: 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.

[2] Although the opinions themselves would be binding, we recognize that the Agency will occasionally need to amend opinions in light of changed circumstances. In such a case, we suggest that amendment occur only after appropriate public notice.

is violative or permissible in light of FDA regulation and policy requires companies to maintain large regulatory staffs, and even then there is often disagreement within a company.[3] Although companies seek to achieve compliance, rules can be both vague and evolving.[4] The lack of clarity surrounding regulation of these issues, as well as an understanding that FDA cannot possibly anticipate every scenario when developing regulations or guidance, can result in unnecessary self-censorship by manufacturers. We believe that implementation of an advisory opinion process would help facilitate the effective communication of useful scientific information to the public while at the same time maintaining appropriate regulatory controls.

Advisory opinions encourage compliance with the law by permitting parties to "double-check" their legal interpretations before acting "at-risk" to commit time and resources to activities that might later be alleged to be illegal. At the same time, the issuance of advisory opinions allows agencies to develop a robust, publicly available set of fact-dependent recommendations without engaging in the labor-intensive and time-consuming task of formal rulemaking or guidance development. Complementing, rather than replacing, broad-based legal guidance, advisory opinions afford parties the unique opportunity to seek detailed agency input on issues relevant to their business practices. While regulations and formal guidance generally set forth the legal rules to be followed, advisory opinions can provide a specific roadmap to compliance for requestors and can serve as helpful examples for the public at large about "real-world" activities. Agencies with advisory opinion processes include, among others, the Office of Inspector General (OIG) at the Department of Health and Human Services, the Centers for Medicare and Medicaid Services (CMS), the Securities and Exchange Commission (SEC), the Federal Election Commission (FEC), and the Federal Trade Commission (FTC).

Although FDA currently has a regulation that provides for an advisory opinion process, it is seldom used. We believe, moreover, that the existing process is not conducive to the issuance of opinions on many promotional issues. Among the problems with the existing regulation, it requires that requests relate to issues of "general applicability" rather than specific proposed business practices, does not require FDA to respond to the request in a timely manner, and does not distinguish between the legal effect of opinions for the requestors and the general public. 21 C.F.R. § 10.85(a). At the same time, FDA regulations regarding presubmission and preapproval of promotional materials (e.g., 21 C.F.R. § 202.1(j)) are similarly inadequate because they allow for FDA input on individual advertising or labeling pieces, as opposed to business practices. Companies and individuals seeking advice on a course of action requiring prompt attention in the context of promotion therefore have no avenue by which to seek advice. We therefore request that FDA implement a special advisory opinion process through which individuals or companies can seek guidance with respect to specific proposed business practices relating to promotional and scientific exchange activities that adheres to the parameters discussed below.

Scope. We recommend the implementation of an advisory opinion process that would focus on issues relating to promotional and scientific exchange practices concerning drugs

[3] See Wayne L. Pines, Regulation of Promotion and Distribution, in A Practical Guide to Food and Drug Law and Regulation (Kenneth R. Pina & Wayne L. Pines, eds., 3rd ed. 2008) 321.

[4] See id.

and medical devices. In our view, providing an advisory opinion process focused on promotional and scientific exchange practices would more closely mirror the advisory opinion processes administered by agencies such as the OIG and others, and it would fulfill an unmet need with regard to the current state of FDA guidance on these issues. In an ever-vigilant enforcement environment governed by vague statutes and regulations, the development of robust recommendations—even if nonbinding except as to the requestor—promises to serve the public interest and enhance compliance.

In addition, we believe that, for the advisory opinion process to hold the greatest public benefit and to ensure the most effective use of FDA resources, individuals and companies should outline a specific, proposed course of action in their requests. The more details provided in the request, the more helpful FDA's advice will be to the requestor. For example, a company could seek the Agency's opinion on whether specific types of communications with payors are "non-promotional," or whether a company's recordkeeping system for unsolicited requests is appropriate. As with the advisory opinion processes of other agencies, however, we believe that individuals and companies should refrain from submitting requests regarding questions of general legal interpretation, actions undertaken by parties other than the requestor, or conduct by the requestor that has already occurred or is occurring on an ongoing basis.

Requesting Parties and Legal Effect. Because advisory opinions are inherently fact-bound, moreover, they should be legally binding only with respect to the requestors. For other parties, advisory opinions may serve as nonbinding recommendations.

Public involvement and availability of opinions. As with the advisory opinion processes of other federal agencies, the mechanism for advisory opinions on promotional issues should allow for public comment. Specifically, we recommend that, upon receiving a request, FDA publish a notice in the Federal Register briefly summarizing the issues raised in the request and solicit public comment, to be taken under advisement during the preparation of the advisory opinion. Further, we suggest that, once FDA issues an opinion, it post both the request and the opinion on its website in an easily searchable format similar to that available for FDA guidance documents.

Timeframe. FDA's general regulation on advisory opinions, 21 C.F.R. § 10.85, does not provide a deadline by which requests must be answered by FDA. To encourage companies and individuals to seek FDA's advice before engaging in activities about which they are unsure, FDA should provide comprehensive and substantive responses to such requests in a timely manner. A review of the advisory opinion processes of other federal agencies indicates that the timeframe between the request and issuance of the opinion ranges from 60 to 120 days. Cognizant of the labor required in considering the issues and drafting the opinion, as well as the desirability of public input, we suggest that FDA issue an advisory opinion within 90 days of accepting the request for filing.

Reasonable fee. We believe that this process—including FDA's timely response to detailed industry questions, the availability of robust public guidance regarding business practices, and the ability to rely on the expertise of agency staff— has significant advantages for all parties. However, we recognize that the implementation of a special advisory opinion process would require the expenditure of limited agency resources. The MIWG would be willing to

discuss a system that charged a reasonable fee for the review of advisory opinion requests and the development and issuance of advisory opinions in response to those requests.[5]

As described, we believe that the establishment of an advisory opinion process focused on advertising and promotion issues would be of great benefit to the public health, to industry, and to FDA itself. We therefore respectfully request that FDA adopt a process consistent with the considerations outlined above.

Respectfully submitted,

/s/Alan R. Bennett

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[5] We recognize that Congress likely would need to authorize the imposition of such a fee. Such an authorization could be discussed as part of the reauthorization of the Prescription Drug User Fee Act, which expires September 30, 2011.