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VIA ELECTRONIC DELIVERY

February 28, 2006

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: Docket No. 2005N-0354

Dear Sir or Madam:

Eli Lilly and Company (Lilly) respectfully submits the following written comments regarding the September 13, 2005 Federal Register notice announcing a Public Hearing on Consumer-Directed Promotion of Regulated Medical Products.

Lilly is a leading, innovation-driven corporation committed to developing a growing portfolio of best-in-class and first-in-class pharmaceutical products that help people live longer, healthier, and more active lives. We are committed to providing *Answers that Matter* – through medicines and information – for some of the world's most urgent medical needs.

Given the increasingly complex health care system, Lilly knows that patients are seeking more information about diseases and treatments, asking questions, evaluating information, and actively participating in health care decision-making. Lilly believes that direct-to-consumer (DTC) advertising provides many benefits, including raising awareness of diseases and conditions that are often undiagnosed, untreated or under-treated. As a company responsible for developing new, innovative medicines, Lilly understands its duty to provide information that is truthful, accurate and balanced. In the spirit of providing *Answers that Matter* in all consumer communications, Lilly established the following principles in 1998 to help serve as a guide in upholding the corporate responsibility that accompanies the creation and execution of DTC communications.

- We will educate physicians and other health care professionals about Lilly medications before advertising them to the public.
- We will involve patients and health care professionals in the advertisement development process to obtain their perspective and input regarding DTC campaigns.
- We will adhere to all applicable laws, regulations and standards regarding DTC advertising. This includes creating advertising that provides clear, accurate and

2005N-0354

C 16

responsible information that is fair and balanced in both the benefits and risks associated with the medications.

- We will not knowingly create advertising that contains false, misleading, exaggerated or unbalanced statements or visuals.
- If reminder advertisements are used, we will provide ways to easily access more information about our medications as well as how to recognize and understand the conditions being treated by those medications.
- We will create DTC campaigns that reinforce the patient/physician relationship by encouraging patients to seek additional information and guidance from health care providers.
- We will create DTC campaigns that educate and encourage appropriate use of Lilly medications.
- We will not target advertising directly to individuals under the age of eighteen.

In August 2005 Lilly announced its support of the Pharmaceutical Research and Manufacturers Association's (PhRMA) guiding principles for direct-to-consumer advertising. Lilly committed to act in accordance with, or exceed, the principles and to be in full compliance with the principles within 60 days. Lilly also announced a higher standard for Cialis DTC television broadcast advertisements by committing to target advertisements to programs with at least 90 percent adult viewers and avoid advertising during programs where a large number of younger viewers could be present.

Evidence-based policy decisions

The benefits of direct-to-consumer promotion have been widely documented and several surveys show strong consumer support for direct-to-consumer promotion of medical products. Despite such evidence, there are many questions regarding the consumer's ability to understand and comprehend the benefits and risks communicated in direct-to-consumer promotion. Indeed, the role of the FDA in protecting public health requires these questions to be asked and answered. However, the manner in which these answers are ascertained is of the utmost importance. It is paramount to making good policy decisions that stakeholders utilize an evidence-based approach for answering questions regarding the presentation of information on benefits and risks in direct-to-consumer promotion. Such an approach requires adequate consumer research to determine from the many possible approaches the most comprehensible way to communicate to consumers. An evidence-based approach is critical to the foundation of good policy decisions and essential if subjectivity and interpretive differences are to be minimized.

Benefits of Direct-to-consumer Advertising

The information-seeking health care consumer

Access to information is a key to patient-centered health care. Direct-to-consumer promotion plays a critical role in increasing disease state awareness and treatment availability, and it

directs the consumer to appropriate resources and information. Many patients feel compelled to do their own health care research, likely due to a number of factors, including the widespread availability of such information on the Internet, as well as limited time with physicians during their actual visit. According to the 2004 Manhattan Research Cybercitizen report, of all US adults:

- 39% look for information before they have any symptoms
- 41% look for information before they visit the doctor
- 51% look for information before they begin taking a prescription medication

In addition, patients want active involvement in treatment decisions for themselves and their family. In March 2005, the Blue Cross & Blue Shield Association reported the following information from a study conducted by the RAND Corporation:

- 60% of American consumers have searched for information to help them make treatment decisions in the past 12 months, with about one third saying the information affected their treatment choice
- 52% of patients want to make the final call on treatment decisions

Direct-to-consumer information provided by health care management organizations, manufacturers and government agencies is essential to meet the needs of increasingly sophisticated, information-seeking health care consumers.

Impact of direct-to-consumer promotion on health seeking behavior

Direct-to-consumer promotion, although not a primary source of information, is often a motivating factor or trigger in sparking patient interest in a health condition or prescription treatment.

According to a November 2004 FDA report¹ summarizing survey findings about patient and physician attitudes and behaviors associated with promotion of prescription drugs:

- In 2002, 43% of respondents reported that advertisements caused them to look for more information, either about the drug or about their health.
- The most commonly reported sources of this additional information were health care providers: 89% reported obtaining information from their doctors.
- Far more people look for information about side effects than about benefits (61% vs. 10%)
- Direct-to-consumer promotion and other sources did appear to play a role in generating questions for the doctor. About 1/3 of respondents indicated that a direct-to-consumer advertisement had generated a question for their doctor.

Further, the FDA report states: "There have been concerns that DTC advertising has the potential to create general expectations of receiving prescriptions. Our research does not provide strong support for this concern. Only 6% of respondents said they expected a

¹ See K. Akin et al., "Patient and Physician Attitudes and Behaviors Associated with DTC Promotion of Prescription Drugs – Summary of FDA Survey Research Results" Final Report (Nov. 19, 2004), www.fda.gov/cder/ddmac/researchka.htm.

prescription because of an advertisement they saw on TV, and 5% said their expectations stemmed from an advertisement in a magazine.”

In addition, evidence suggests that patients who are knowledgeable about health care issues make better patients. According to a March 2004 Harris Interactive Strategic Health Perspectives report, 82% of physicians agree with the statement: “Patients who are eager to learn about their health are generally better patients.” In the recent FDA summary report, over 90% of respondents who questioned their doctor about a specific drug reported that their doctor welcomed their questions, and 83% reported that the doctor responded as if their questions were a normal part of the visit.

Direct-to-consumer advertising does not lead to inappropriate prescribing

Many opponents of DTC advertising claim that such advertising leads to inappropriate prescribing of prescription medications due to increased pressure placed on prescribers by patients. Such claims are not supported by empirical evidence. Approximately one-third of every 100 adults in the United States have talked to a prescriber about an advertised product. Yet only about five percent of adults received prescriptions for advertised medications after they asked for those products².

Research reported on by Weissman et al. shows that patients who mention an advertised drug during a clinic visit saw their physician for clinically important conditions such as high cholesterol or high blood pressure, and many of these visits resulted in new diagnoses for significant health problems such as hyperlipidemia and heart disease. In addition, physician visits prompted by a DTC advertisement often result in care that goes beyond the prescribing of drugs, such as follow-up tests and visits. When researchers studied the outcomes of these visits, they failed to find significant negative health consequences among those subjects who took the advertised drug. In fact, the researchers found a small advantage in the relief of side effects among patients who switched their medications to an advertised drug after their visit³.

Additionally, empirical work by Iizuka and Jin⁴ found that DTC advertising contributes to an increase in the number of physician visits. This finding supports the notion that DTC advertising has an important, positive effect on public health by encouraging patients to talk with their physician or other health care professional. Further, researchers found a modest increase in the amount of time the physician spends with patients prompted to visit their physician as a result of a DTC advertisement. This increased interaction time demonstrates that physicians are spending more time with patients who, after viewing a DTC advertisement, are likely seeking information about an underlying condition and available treatment options.

² Schommer JC, Singh RL Hansen RA. Distinguishing characteristics of patients who seek more information or request a prescription in response to direct-to-consumer advertisements. *Research in Social and Administrative Pharmacy*, 2005 (1), 231-250.

³ Weissman JS, Blumenthal D, Silk AJ, Zapert K, Newman M, Leitman R. Consumers' reports on the health effects of direct-to-consumer drug advertising. *Health Aff.* 2003 Jan-Jun; Suppl Web exclusives: W3-82-95.

⁴ Iizuka, T., Jin, G.Z., 2005. The effects of prescription drug advertising on doctor visits. *Journal of Economics & Management Strategy* 14 (3), 701-727.

Such interactions should not be viewed as patient pressure but rather as patient participation in health care decision-making. Most importantly, however, Iizuka and Jin found that DTC advertising has no effect of the physician's choice of a prescription drug within a therapeutic class.

This latter point has also been evaluated by Rosenthal et al. who investigated the effects of DTC advertising and detailing on the aggregate sales of prescription drugs. They found that DTC advertising has a significant effect on total class sales, but generally does not have any significant impact on market shares within each class⁵. These findings underscore the effect of DTC advertising in motivating patients to seek information about medical conditions and available treatment options, but once the conversation begins, the physician's role is paramount. Clearly, it is the preeminent role of the physician – and to a growing extent third party payors through formularies, therapeutic substitutions, and preferred status for generic medications – to determine whether or not treatment is needed and, if treatment is needed, which treatment is right for an individual patient.

Communication/comprehension of benefits and risks

FDA-conducted surveys⁶ of patients and physicians suggest that patients do not believe DTC advertisements provide enough risk information and that physicians think patients do not understand the risks and possible negative consequences of advertised drugs. The FDA is interested in hearing why consumers and health care providers may believe that risk information is not being communicated as clearly as benefit information in DTC advertisements, even though that information is present.

Research conducted by Day⁷ suggests that consumers have difficulty comprehending the information presented in DTC advertisements. Day's findings include:

- A lower reading grade level for the presentation of benefit information than for risk information.
- The serial positioning or location of risk information within the body of the advertisement favors the recall of benefit information.
- The use of "chunking" to cluster like information and separate it from surrounding information is frequently used to communicate benefit information and rarely used to communicate risk information.
- The reading speed is much quicker for risk information than for benefit information.

⁵ Rosenthal, M.B., E.R. Berndt, J.M. Donohue, and R.G. Frank, 2002, Promotion of Prescription Drugs to Consumers, *New England Journal of Medicine*, 346(7), 498–505.

⁶ See K. Aikin et al., "Patient and Physician Attitudes and Behaviors Associated with DTC Promotion of Prescription Drugs – Summary of FDA Survey Research Results" Final Report (Nov. 19, 2004), www.fda.gov/cder/ddmac/researchka.htm.

⁷ See R. Day, "Comprehension of Benefits vs. Risks: Fair Balance in DTC?" Presentation at FDA public meeting on direct-to-consumer promotion, Washington, D.C., November 1-2, 2005, www.fda.gov/cder/ddmac/dtc2005/Day.pdf

- The use of certain advertising techniques to divide the viewer's attention during the presentation of important information.

Additional research conducted by Glinert et al.⁸ suggests that for medications with a complex risk profile, placing risk information at the end of the advertisement and using captions to support oral messages improved the recall of risk information, improved the perception that the advertisement had greater informational content and lessened aspects of information overload for the advertisement. This pattern of findings was not found for medications with a less complex risk profile. This distinction in findings between medications with different risk profiles highlights the need for flexibility in communicating benefit and risk information in DTC communications. A "one size fits all" approach may not be appropriate.

These research findings appear to shed light on how to address the issues raised by the FDA. However, they fail to take into account the existing regulatory framework for DTC advertising. Therefore, as noted by the FDA, compliant advertisements include the required risk information; typically the major contraindications, warnings, precautions, and most common side effects. This approach generally results in advertisements that include a litany of risk concepts, some of which are more relevant to the physician – and to the physician-patient interaction once the decision has been made by the physician to prescribe – than to what a consumer should be expected to learn from a DTC advertisement. Current FDA regulations create several obstacles that prohibit the use of suggested techniques to create emphasis (assuming that such techniques would indeed achieve a "reasonably comparable prominence" and a "fair balance" between benefit information and risk information).

DTC advertisements should focus only on the information a patient needs to know at that juncture to determine whether to discuss with his or her physician the treatment advertised and should not be expected to fully educate patients about each specific risk. A more comprehensible approach may be to focus more appropriately on a few, more relevant risk concepts and encourage consumers to have a conversation with their physician by providing information that generates a productive dialogue between the patient and the physician. Does it make sense that a statement about a side effect that might rarely occur in a very small percentage of the treated population would receive the same – if not more – amount of time, words, and prominence as a statement about who should never take the advertised medication because of severe, life-threatening results that may occur should the wrong patient take the wrong drug at the wrong time? This does not mean that less time, or fewer words, or less prominence would be allocated to communicating important risk information. Such an approach would allow for the consideration of the techniques suggested by Glinert et al. and Day for achieving a "reasonably comparable prominence" and "fair balance" between the communication of benefit information and risk information.

Lilly believes the communication of benefit and risk information through DTC advertisements is an important public health tool that should be designed to encourage the appropriate use of

⁸ Glinert LH, Schommer JC. Television advertisement format and the provision of risk information about prescription drug products. *Research in Social and Administrative Pharmacy*, 2005 (1), 185-210.

prescription drugs and to protect and advance the public health. While there has been much attention placed on the appropriate method for communication of risk, we believe a discussion of risk presentation should never occur in isolation. It is the appropriate balance of benefit and risk information that is necessary to allow consumers to make informed decisions about their health.

While the pursuit of more consumer-friendly advertisements is important, consumers are not and should not be in a position to make prescription medicine decisions on their own. This basic premise must guide all attempts to enhance or improve communication of drug information to consumers. Health care professionals receive extensive training over many years and are licensed to prescribe medication based on this training. An advertisement should lead to a meaningful discussion with a health professional but must not take the place of the learned intermediary.

Improving Communication of Benefits and Risks in the Brief Summary in DTC print advertisements

Research suggests that the current format for communicating risk information in consumer-directed print advertisements is less than optimal. Research conducted by FDA suggests that an increasing number of consumers read little or none of the brief summary in its current format⁹. Furthermore, additional research by Slaughter et al. suggests that almost half of consumers did not recall the brief summary¹⁰. These results emphasize the need for focused efforts to improve the format for communicating risks to consumers.

The FDA introduced the concept of "less is more" in the draft guidance entitled "Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements." Lilly believes that a "less is more" approach to the communication of important risk information may increase comprehension and retention in consumer-directed print advertisements. However, we believe that only well-designed consumer research can fully articulate the appropriate content and format that would provide the most useful information to consumers. Lilly conducted consumer research for various print advertisements in an effort to obtain useful information and support the development of evidence-based policy. The results of this study, along with Lilly's specific comments regarding the draft guidance were submitted on August 10, 2004.

⁹ See K. Aiken, "The Impact of Direct-to-Consumer Prescription Drug Advertising on the Physician-Patient Relationship," Presentation at FDA public meeting on direct-to-consumer promotion, Washington, D.C., 22-23 September 2003, slide 5, www.fda.gov/cder/ddmac/aiken/sld005.htm (15 April 2004). To the question, "How much of the brief summary do you read?" 56 percent responded a little/none in 1999, and 73 percent responded a little/none in 2002.

¹⁰ See E. Slaughter, "Consumer Reaction to DTC Advertising of Prescription Medicines, 1997 to 2002," Presentation at FDA public meeting, Washington, D.C., 22-23 September 2003, www.fda.gov/cder/ddmac/PIslaughter/index.htm (13 April 2004). In that study, 46 percent of respondents were not aware of or did not recall a brief summary.

While a "less is more" approach to disclosing product risk information would likely benefit patients, there is concern that such an approach could present product liability issues for sponsors. The FDA draft guidance states, "In the circumstances described [in section III of the guidance], FDA does not intend to object to consumer-directed print advertisement for a prescription drug on the ground that it does not present risk information in compliance with the brief summary requirement." This language may suggest that while FDA does not believe the options outlined in the guidance fully comply with the Code of Federal Regulations, the agency will use its enforcement discretion in this area. Lilly believes that the approaches contained in the FDA draft guidance fulfill the requirements outlined in 21 CFR 202.1 (e)(1). Therefore, we recommend that the final document communicate the consistency of this guidance with regulatory requirements. If, however, the FDA does not believe the outlined approaches fulfill the regulatory requirements, the Agency should amend the applicable regulations.

Use of the package insert with consumer-directed promotional labeling pieces

The Federal Register notice requests comments on whether including the package insert with consumer-directed promotional labeling is the best way to meet the requirement that promotional labeling include adequate directions for use. As the FDA points out, the package insert is written in technical language intended for health care professionals and its value for consumers is questionable. Lilly agrees that the use of a document intended for communicating highly complex and technical information to health care professionals is not the most informative way to communicate this information to consumers. Lilly believes that the current regulations allow for a more consumer-friendly approach for satisfying the adequate directions for use requirement and that the results from comprehensive research with consumers should support policy changes addressing this issue.

Coupons, money back guarantees, buy-one/get-one free offers

In the Federal Register notice, the FDA raises the question of the appropriateness of the use of certain strategies such as coupons, free samples, free trials, and money-back guarantees to influence consumers. It is important to note that with any of these marketing programs, a patient must obtain a prescription written by a physician or other health care professional—patients cannot send in a coupon and expect to receive a prescription without first consulting with their physician or other health care professional to determine the appropriateness of the medication advertised prior to receiving a prescription. There are also certain patient benefits from such programs. The financial incentive of a 30-day trial coupon could serve to remove a barrier which may be preventing a patient from seeking treatment; programs to provide future free products might motivate patients to refill an existing prescription; and a free sample could ease patients' concerns about spending money on a product that might not work for them.

FDA's focus is and should be on evaluating the content of DTC advertisements, with particular emphasis on determining if the advertisement is false or misleading, or otherwise

endangers public health. If these tactics are carried out in accordance with applicable laws and regulations, we see no need for additional regulations or guidelines further restricting the use of such marketing strategies.

Use of new communication technologies – video news releases, audio news releases and print “advertorials”

The Federal Register notice states that, at times, TV and radio stations do not make it clear to consumers that video news releases (VNRs), audio news releases (ANRs), and print “advertorials” are generated by regulated industry. If these communications are carried out in accordance with applicable laws and regulations, we believe additional regulations or guidelines requiring additional disclosures or further restricting the use of these media vehicles are unnecessary.

We agree that all promotional materials provided to the news media should contain the appropriate balance of benefit and risk information regarding the product discussed. However, it is important to distinguish between advertorials and news vehicles such as VNRs and ANRs.

Advertorials are paid advertising created to look like newspaper or magazine articles. The company that produces the advertorial essentially buys advertising space and, in return, the media outlet uses the advertorial as is (advertorials are typically camera-ready for placement in the newspaper). Media outlets will always require, and should require, that the piece include clear reference to the fact that it is paid advertising and not generated by the editorial department so as to not mislead the reader.

VNRs and ANRs are tools to provide the editorial departments of news outlets product-related news in a format that is “user friendly” for the news station (i.e., video or audio tapes). They are created as a news story to enable the station to use the VNR or ANR as is. However, a critical distinction between these tools and an advertorial is that the company is not paying the media outlet to run these news releases. The editorial department has final control of whether to use the news release at all, and if so, whether to use sections of it as part of their own news story. Again, ANRs and VNRs that contain promotional content should include a balanced presentation of benefit and risk information and typically offer the station additional footage and/or audio that allows for additional options to choose from. Even if the news outlet would choose to use a VNR or ANR as is, it would have to meet their editorial standards for accuracy, balance and news value.

Conclusion

In an increasingly complex, patient-centered health care system it is important for all stakeholders to place the needs of the patient at the forefront of all our thoughts and actions. Patient-focused health care information that offers a balance of benefit and risk information is

Eli Lilly and Company
February 28, 2006
Page 10 of 10

a first step to ensuring that the right drug is available for the right patient at the right time. Lilly appreciates the opportunity to provide comments on these critically important issues and looks forward to continuing dialogue with the FDA. Thank you for your consideration of our comments.

Respectfully submitted,

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