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May 10, 2004

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

Re: Docket No. 2004D-0042; *Draft Guidances for Industry on Improving Information About Medical Products and Health Conditions*

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) welcomes the opportunity to comment on the Food and Drug Administration's (FDA's) *Draft Guidances for Industry on Improving Information About Medical Products and Health Conditions*, Docket No. 2004D-0042. 69 Fed. Reg. 6308 (Feb. 10, 2004). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier and more productive lives. Investing more than \$30 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

PhRMA companies devote substantial resources not only to discovering and developing new medicines, but also to informing and educating healthcare professionals and patients about the availability, proper usage and risks associated with those medicines. PhRMA thus has a keen interest in FDA's policies on disseminating information about medical products and health conditions. PhRMA's detailed comments on the two draft guidance documents applicable to pharmaceutical products -- *Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements (Brief Summary Guidance)* and *"Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms (Disease Awareness Guidance)* -- are provided below.

### The Value Of DTC Communications

As an initial matter, PhRMA is pleased that FDA's draft guidance documents recognize the tremendous value of DTC advertisements in conveying useful health information to patients. The purpose of DTC advertising is to inform and educate consumers about treatable conditions, the symptoms that may help them identify those conditions, and the innovative therapies available to treat such conditions. Research

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demonstrates that DTC advertising helps educate patients about medical conditions and treatment options, encourages dialogue between patients and physicians, prompts large numbers of Americans to discuss illnesses with their physicians for the first time, and promotes improved compliance with physician-prescribed treatments.

In light of the documented, pervasive patterns of under-treatment of serious medical conditions, such as asthma, depression, high cholesterol, diabetes, and many others, such outreach to patients is desperately needed. The failure to treat many patients early in the course of disease leads to much avoidable suffering, higher health care costs, avoidable hospitalizations, and lost productivity for workers and employers. Notably, the critics of DTC advertising rarely, if ever, discuss the human and economic costs of under-treatment addressed by DTC advertising.

DTC advertising also serves a valuable role in educating patients about the limitations and risks associated with certain therapies. While DTC advertising cannot and should not replace the healthcare professional as the most authoritative source for obtaining information about the risks and benefits of a particular drug product, DTC advertising can encourage patients to talk to their physicians about their medical conditions and treatment options. This dialogue between a patient and physician results in better educated patients who are active in their own healthcare and generally comply with their treatment regimens. According to FDA's own surveys, a majority of doctors believe that DTC advertising prompts patients to ask better questions and generally results in better discussions about health. Kathryn J. Aiken, Ph.D., DDMAC, *The Impact of Direct-to-Consumer Prescription Drug Advertising on the Physician-Patient Relationship* (Sept. 22, 2003).

PhRMA thus commends FDA for addressing this critical health care issue. PhRMA strongly supports FDA's efforts to increase the effectiveness of DTC advertising to impart meaningful health information to patients, including risk information that is presented in a way that increases consumer comprehension and retention. PhRMA also supports efforts to streamline the regulatory requirements for DTC advertising, including the brief summary requirement. PhRMA firmly believes that when patients have access to accurate and understandable information about their medical conditions and treatment options, they can partner more effectively with their health care providers to obtain the most appropriate treatment for their individual circumstance.

### **Brief Summary Guidance**

FDA's *Brief Summary Guidance* seeks to make the risk information provided in DTC print advertisements more accessible to consumers by encouraging manufacturers (a) to present information only about the most serious and/or most common risks, and (b) to use consumer-friendly language. PhRMA strongly supports

the underlying goal of the *Brief Summary Guidance* to increase the effectiveness of risk communications to patients. PhRMA is concerned, however, that FDA's *Brief Summary Guidance* will not be effective in achieving this goal because of one major shortcoming: *it has the potential to create significant product liability issues for manufacturers using DTC advertisements.*

The brief summary requirement is mandated by the Federal Food, Drug, and Cosmetic Act (FD&C Act), which requires all prescription drug advertisements, including direct-to-consumer (DTC) advertisements, to include a "brief summary relating to side effects, contraindications, and effectiveness" 21 U.S.C. §352(n)(3). FDA regulations clarify that the "brief summary" must "disclose each specific side effect and contraindication . . . contained in required, approved, or permitted labeling for the advertised drug dosage form(s)." 21 C.F.R. §202.1(e)(3)(iii) (emphasis added). The term "side effect and contraindication" is further defined to mean "side effects, warnings, precautions, and contraindications." *Id.* Under FDA's regulations, therefore, the "brief summary" requirement is extremely broad, requiring a discussion of *all* risk information included in the FDA-approved package insert.

In order to satisfy this requirement in print advertisements, many companies reproduce the risk information from the FDA-approved professional labeling, since this already includes all relevant risk information. As a result, these "brief summaries" often are lengthy and use precise medical terminology. While this presents few problems for advertisements directed to healthcare professionals, FDA is concerned that such information included in DTC advertisements may be less accessible to consumers.

The *Brief Summary Guidance* seeks to address this problem by providing two alternative methods for making this necessarily complex medical information more accessible to consumers. First, FDA states that it will not object if companies seek to satisfy the brief summary requirement by reproducing "FDA-approved patient labeling, either in its entirety or as modified to omit less important risk information." *Brief Summary Guidance* at 3. Second, FDA states that it will not object if companies provide the risk information that would be appropriate for the FDA-approved "Highlights" section of the package insert pursuant to FDA's proposed regulation on the content and format of prescription drug labeling. See 65 Fed. Reg. 81082 (Dec. 22, 2000).<sup>1</sup>

While these alternatives would not necessarily provide information about each specific risk associated with a product, they would provide information about the product's most serious risks and less serious but most frequently occurring adverse events. Moreover, FDA encourages manufacturers to present this risk information in

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<sup>1</sup> PhRMA submitted comments on June 14, 2001, objecting to the appropriateness of including a "Highlights" section in the approved product labeling. PhRMA continues to believe that a "Highlights" section is inappropriate for the approved product labeling although, as discussed below, the concept might be useful in the brief summary context.

consumer-friendly language rather than precise medical terminology in order to enhance comprehension by lay readers.

Although PhRMA strongly supports FDA's efforts to enhance the clarity and usefulness of risk information presented in DTC communications, we are concerned that the alternatives proposed by FDA will not effectively address the problem because they entail significant product liability issues. This is because the two alternatives proposed by FDA are, in fact, framed as an exercise of FDA's enforcement discretion. For instance, rather than stating that these alternatives comply with the brief summary requirements, FDA states that it "does not intend to object" to the use of these alternatives even though the information provided would not include each specific risk mentioned in the FDA-approved professional labeling. See *Brief Summary Guidance* at 4. FDA thus appears to suggest that its alternatives do *not* meet the requirements of FDA's existing regulations to "disclose each specific side effect and contraindication," 21 C.F.R. §202.1(e)(3)(iii), but that FDA nevertheless will exercise its enforcement discretion in the interest of consumer comprehension.

While this may be an appropriate use of FDA's enforcement discretion from a regulatory standpoint, it places manufacturers in an untenable position with respect to product liability. On the one hand, FDA has offered two alternatives that appear to violate FDA's existing brief summary regulations because they fail to include all risk information contained in the approved package insert. On the other hand, FDA indicates that reproducing the risk information from the approved package insert – which clearly satisfies the regulatory requirements – may confuse consumers. *Brief Summary Guidance* at 2.

The *Brief Summary Guidance* thus creates a regulatory Catch-22 where manufacturers face potentially increased liability no matter which option they choose. If they comply with the regulations by reproducing the risk information from the approved package insert, they face criticism and potential liability risks – legitimized, in part, by FDA -- for presenting "confusing" risk information.<sup>2</sup> If they use either of the two new options described by FDA, they face increased liability for injuries resulting from side effects that are not mentioned in the streamlined brief summary document. Moreover, because such omissions technically violate FDA's regulations, manufacturers could have greater exposure to negligence claims based upon a failure to warn theory. Indeed, in many jurisdictions, the failure to comply with FDA regulations can be used as

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<sup>2</sup> We note that although FDA's draft guidance creates additional product liability risk, we do not believe such claims would be well-founded. In particular, we do not believe that the current method of risk communication is confusing, although because of its nature it may be difficult for many consumers to fully comprehend without talking to a physician. However, it is important to remember that DTC advertisements are not meant to replace a patient's physician as the primary source of information about the risks and benefits of particular therapies. They are instead intended to stimulate a more productive dialogue between patients and physicians. To the extent a patient has questions about the risk information contained in a DTC print advertisement, the patient should be encouraged to discuss those questions with his or her physician.

*prima facie* evidence that the manufacturer was negligent. See Restatement (Second) of Torts §286.

These product liability concerns thus could severely limit the ability of manufacturers to utilize FDA's proposed alternatives to provide information to consumers in the most concise and readable manner. If the guidance document fails to stimulate more accessible risk communications in DTC print advertisements, it will create increased liability risks for manufacturers with little or no countervailing public health benefit.

Despite these significant problems, PhRMA believes that FDA's proposal is extremely valuable and should be implemented. This implementation, however, should occur in a manner that benefits patients without subjecting manufacturers to potentially increased liability risks. In order to accomplish this, FDA should revise its brief summary regulations to explicitly permit these alternative presentations of risk information rather than seek to implement them through a guidance document and enforcement discretion.

Although FDA's regulations currently require disclosure of "each specific side effect and contraindication," there is nothing in the statute that requires this level of detail. The statute instead gives FDA broad authority to designate, by regulation, the contents of the brief summary. 21 U.S.C. §352(n) ("such information in brief summary relating to side effects, contraindications, and effectiveness *as shall be required in regulations . . .*") (emphasis added). FDA thus has ample authority to revise its brief summary regulations to allow manufacturers to provide streamlined, consumer-friendly risk information in DTC print advertisements rather than "each specific side effect and contraindication," as is currently required. See 21 C.F.R. §202.1(e)(3)(iii). This not only would bring the "brief summary" closer to something that truly is "brief" and a "summary," but also would avoid creating a Catch-22 situation for manufacturers.

We emphasize, however, that while this suggestion would eliminate the Catch-22 situation described above, it still might expose pharmaceutical manufacturers to meaningful product liability risks. Suits would inevitably arise based on the alleged inadequacy of the streamlined risk information and purported inconsistencies between this condensed information and the more comprehensive information contained in the approved package insert. These risks are far from speculative. Every pharmaceutical product liability case involves allegations that important information is missing or that risk or other information disclosed was not sufficiently prominent. Plaintiffs have specifically brought actions that assert liability based on product summaries that are argued to be incomplete or otherwise flawed. The best way to resolve these liability risks would be for FDA to mandate the precise contents of the brief summary for a particular product and for FDA's determination to preempt any possible tort liability based upon purported deficiencies with the brief summary.

PhRMA realizes that revising FDA's regulations may take longer than adopting an enforcement policy through issuance of a guidance document but believes that revising the regulations is the most appropriate way to achieve the desired objectives. However, in the event FDA declines to revise its brief summary regulations and instead moves forward with implementing the *Brief Summary Guidance*, the Agency should revise that guidance to clarify that it is *not* relying upon its enforcement discretion but that the two suggested alternatives instead fully satisfy the applicable regulatory requirements. For the reasons discussed above, FDA may have to modify its alternatives in order to accomplish this. For instance, FDA might recommend that companies that utilize a streamlined brief summary include in the body of their advertisements a web site address, a toll-free number, or a referral to a health care professional where interested consumers could obtain the full prescribing information. There may also be other ways to accomplish this objective. In any event, it is imperative that the alternative methods of providing the brief summary fully comply with FDA's regulations rather than just its enforcement priorities.

In addition, if FDA declines to revise its brief summary regulations, it should, at a minimum, clarify that it is appropriate for manufacturers to use the risk information from the approved package insert to satisfy the brief summary requirement. The *Brief Summary Guidance* currently contains language that appears to question the utility of this information and/or suggest that it may be potentially confusing to consumers. While PhRMA agrees that this information can be at times complex, the current regulatory requirements mandate that this option continue to be available to manufacturers.

It should also be noted that the proposed formats outlined in the *Brief Summary Guidance* do not appear to be supported by any rigorous consumer research. While the proposed formats may be shown to improve communication of risk information to consumers, PhRMA requests that FDA withhold final guidance until adequate research has been conducted to support such conclusions. FDA should develop evidence-based policy to ensure that risk information is communicated in the most beneficial and effective method possible to promote retention and comprehension of the information. To that end, PhRMA believes the best way to communicate risk information can only be determined through rigorous consumer research methods which analyze both traditional and non-traditional methods of risk communication.

Results of consumer research should support evidence-based policy and guidance, which clearly outline regulatory requirements in order to minimize the potential for subjective interpretation. For example, the options outlined in the *Brief Summary Guidance* require manufacturers to include "major precautions" related to a drug product. The requirement to include "major precautions" requires a subjective assessment by manufacturers to determine what actually constitutes a "major

precaution.” This may also result in differences of opinion among FDA reviewers responsible for interpreting this guidance. To ensure consistency across all parts of FDA, PhRMA encourages FDA to issue clear guidance that is not open to subjective rulings.

Finally, FDA has requested input on potential new approaches to providing risk information in DTC advertisements, such as bulleting risk information in a “risk box” or incorporating risk information into the body of the ad, obviating the need for disclosure of risk information in a separate part of the ad. Comment was also requested whether this approach might be appropriate for only a subset of prescription drugs. While PhRMA agrees with the Agency’s stated objectives of making labeling more consumer-friendly and accessible, any new approaches should be data-driven based upon research demonstrating increased consumer comprehension. Multiple formats should be evaluated to identify the best way to present information to consumers.

If comprehension can be demonstrated by having all risk information in the body of the ad, then this approach should be recognized by FDA as an acceptable presentation of risk information for a prescription drug advertisement. As long as increased comprehension can be demonstrated with an alternative approach, there should be no need to restrict its use to a subset of prescription drugs. In addition, such approaches should reflect the paramount importance of the physician in deciding whether a particular medication is appropriate for a particular patient. Finally, as discussed above, such approaches should carefully address the product liability implications of a change in policy regarding DTC advertisements.

### **Disease Awareness Guidance**

PhRMA strongly supports FDA’s efforts to facilitate the development and use of disease awareness communications, particularly for serious or life-threatening diseases and health conditions that are under-diagnosed or under-treated. Disease awareness advertisements, especially “help-seeking” communications directed to patients, can play a valuable role in addressing the documented patterns of under-treatment of serious medical conditions such as asthma, depression, high cholesterol, diabetes, and many others.

A study conducted by RAND Health, the nation’s largest independent health-policy research organization, and published in *The New England Journal of Medicine* in 2003 found that nearly half of all adults in the United States fail to receive recommended health care. More specifically, the study found that only 45 percent of patients with diabetes receive the care they need; only 68 percent of patients with coronary artery disease received recommended care; only 45 percent of heart attack patients received medications that could reduce their risk of death; only 54 percent of patient with colorectal cancer received recommended care; and less than 65 percent of

patients with high blood pressure received recommended care. For many of these conditions, medications are the recommended treatment option. Yet the study found that underuse of medicines occurred for several of these conditions, including asthma, cerebrovascular disease, congestive heart failure, diabetes, hip fracture, hyperlipidemia, and hypertension.

Disease awareness advertisements can play a valuable role in educating patients about relevant diseases and health conditions and prompting them to seek necessary treatment. Such advertisements can bring patients into doctors' offices and allow physicians to treat people who might otherwise go undiagnosed or untreated. Help-seeking advertisements also may help encourage patients to discuss medical problems that otherwise may not have been discussed because the disease was either thought to be too personal or that there was a stigma attached to it.

PhRMA is pleased to see FDA publicly acknowledge the value of disease awareness communications to "provide important health information to consumers and health care practitioners, and [to] encourage consumers to seek, and health care practitioners to provide, appropriate treatment." *Disease Awareness Guidance*, at 1. By clarifying the regulatory boundaries applicable to disease awareness communications, FDA will facilitate their use by industry.

PhRMA also agrees with FDA that disease awareness communications do not constitute prescription drug labeling or advertising and, as such, are outside the Agency's jurisdiction. We nevertheless are concerned that in seeking to clarify the boundaries of disease awareness communications in its *Disease Awareness Guidance*, FDA may have overstepped its own jurisdictional boundaries in certain cases. In particular, the *Disease Awareness Guidance* appears to (a) impose standards on the content of disease awareness communications even though such communications are not subject to FDA jurisdiction, and (b) transform disease awareness communications into "labeling" and/or "advertising" subject to FDA jurisdiction based upon vague criteria. We thus request that FDA revise the *Disease Awareness Guidance* to address these issues.

The *Disease Awareness Guidance* purports to define acceptable content for disease awareness communications in several sections. In lines 101 through 104, for instance, FDA states that it will treat communications as disease awareness communications if they: (1) advise consumers to "see your doctor" for possible diagnosis and/or treatment (if consumer directed); and (2) encourage awareness among physicians of the signs and symptoms of the particular disease or health condition (if physician directed). While PhRMA agrees that these statements, as a general matter, are appropriate and should be encouraged in disease awareness communications, we disagree that these statements are necessary hallmarks of a "disease awareness communication." As the draft *Guidance* itself recognizes, FDA

does not have jurisdiction over disease awareness communications that do not mention a particular drug, and this jurisdictional limitation is not affected by whether or not the communication advises consumers to "See Your Doctor" or encourages physicians to recognize the signs and symptoms of the disease. Thus, we request that FDA delete these requirements prior to finalizing the *Disease Awareness Guidance* or clearly indicate that these are merely agency suggestions.

Likewise, Section III.C is devoted entirely to providing FDA's recommendations on the content of disease awareness communications. For instance, FDA states that disease awareness communications should, among other things, be disease specific, identify the population at risk, refer consumers to qualified health care professionals for more information, and avoid encouraging self-diagnosis or self-treatment. While PhRMA agrees with these concepts in principle, we question whether it is appropriate for FDA to provide guidance on the content of communications over which it admittedly has no jurisdiction. We thus suggest that FDA delete Section III.C in its entirety or, at the very least, reiterate in Section III.C that its recommendations are non-binding and are made in an area over which FDA has no jurisdiction.

PhRMA is also concerned that the *Disease Awareness Guidance* expands FDA's jurisdiction over such communications based upon vague or inappropriate criteria defining when such communications will be considered "labeling" or advertising." For example, FDA suggests in Section III.A that it could take action against a disease awareness communication if a company is the only manufacturer of a product that treats the disease. Although FDA states that a company is not "automatically disqualified" from disseminating disease awareness communications under such circumstances, it is not clear based upon the *Disease Awareness Guidance* when such communications would be permitted. More importantly, however, as the FDA itself acknowledges, the agency has no authority over such communications. If the disease awareness communication does not mention any specific product, it is outside the scope of FDA's authority regardless of whether there is one product or multiple products available to treat the disease in question. Therefore, we request that FDA delete any suggestion that it could take enforcement action -- or even other "appropriate action (e.g., issuing a public statement or referring the matter to the FTC)" -- for these types of communications.

Finally, PhRMA agrees that disease awareness communications should be kept separate from product-focused communications, such as reminder or product claim advertisements. PhRMA further agrees that there may be limited circumstances when two communications are so closely tied together in both content and temporal/physical proximity that they could be viewed as a single communication. We do not believe, however, that these situations are common, as FDA's detailed discussion would suggest.

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While clearer ground rules would be useful for both industry and FDA in determining when two separate communications might constitute a single "combined communication," PhRMA suggests that additional research may be necessary to determine the parameters of the issue before any such rules can be formulated. After all, FDA is suggesting that advertisements which are physically and/or temporally distinct can, as a legal matter, lose their distinctiveness because of subjective associations and connections forged within a viewer's mind. We believe additional research is necessary to properly define this process. Accordingly, we recommend that FDA either delete Section IV in its entirety or limit it to a short discussion pointing out that there may be instances in which a disease awareness communication is so similar and temporally or physically proximate to a reminder ad that it will be considered "labeling" or "advertising," but that these situations are likely to be rare.

Thank you for your consideration of these comments.

Sincerely,

A handwritten signature in black ink, appearing to read "Scott M. Lassman", with a long horizontal flourish extending to the right.

Scott M. Lassman  
Assistant General Counsel