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

Re: Draft Guidance for Industry on Presenting Risk Information in Prescription Drug and Medical Device Promotion (Docket No. FDA-2008-D-0253)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is pleased to submit these comments in response to FDA's draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion (the "draft guidance") issued in May 2009. PhRMA represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA companies are leading the way in the search for new cures. PhRMA members alone invested an estimated $50.3 billion in 2008 in discovering and developing new medicines. Industry-wide research and investment reached a record $65.2 billion in 2008. PhRMA's member companies are the source of nearly all new drugs discovered and marketed throughout the world.

PhRMA welcomes FDA's efforts, through the Division of Drug Marketing, Advertising, and Communications ("DDMAC"), to provide formal advice regarding the presentation of risk information—and by extension the presentation of benefit information—in promotional materials. PhRMA and its member companies believe that FDA's guidance is helpful in our continuing efforts to help ensure that information about prescription drugs is communicated in a clear and accurate manner and that healthcare professionals and consumers receive information from numerous sources to assist them in determining whether a particular treatment is appropriate. PhRMA's *Guiding Principles on Direct to Consumer Advertisements About Prescription Medicines*, which are cited in the draft guidance, demonstrate the commitment of our members to truthful, scientifically accurate communications with healthcare professionals and patients. These principles are based on the premise that direct-to-consumer (DTC) advertising should educate consumers and encourage informed conversation about health, disease, and treatment options between patients and their healthcare providers. Of course, promotional materials about medicines can never replace the essential dialogue between patients and their physicians.

PhRMA respectfully offers the following comments on the draft guidance.

I. General Comments

A. Consistency with FTC Guidance

PhRMA supports FDA's statement that promotional claims should be evaluated from the perspective of the reasonable consumer. The Federal Trade Commission ("FTC") has also taken this approach, explaining that "[w]hen representations or sales practices are targeted to a specific audience, the Commission determines the effect of the practice on a reasonable member of that group." PhRMA supports FDA's conclusion that under the "reasonable consumer" standard, the Agency will consider the "reasonable consumer" to be "a reasonable member of the targeted population (e.g., consumers, specific patient populations, healthcare professionals.)."[1] We suggest that, in its review of specific promotional pieces, FDA consider ways to employ empirical evidence while attempting to avoid unnecessary bias (e.g., professional or lay panels as appropriate) to help determine whether materials are truthful and not misleading prior to issuing warning or advisory correspondence.

The FTC has also stated that it "will evaluate the entire advertisement, transaction, or course of dealing in determining how reasonable consumers are likely to respond." PhRMA supports FDA's decision to adopt a similar and consistent policy of evaluating a promotional piece as a whole, as the Agency makes a determination regarding whether risk information is appropriately presented.

B. Application to Internet Promotion

The draft guidance makes clear that it is intended to apply to all promotional materials, including promotional information provided on the Internet.[2] Recent DDMAC letters have also addressed promotional claims made in various online formats, such as web pages, sponsored links on search engines, banner ads, and YouTube videos. These letters have applied "traditional" interpretations of rules regarding drug advertising and promotion without apparent consideration of the fact that Internet promotion can be fundamentally different from print and broadcast promotion.

For example, DDMAC's recent communications regarding sponsored search results focused only on the contents of the sponsored search result, with no consideration of the fact that users would almost certainly view the hyperlinked sponsored web page, which presumably would contain the necessary fair balance. PhRMA believes that FDA should acknowledge that search engine users generally enter queries into search engines with the expectation and intent that they will be directed to, and will view, a page to which the sponsored search result hyperlinks. In addition, promotional web sites are typically linked together to form what may be interpreted as a collective promotional piece.

The FTC has recognized that the "Internet combines aspects of print, television, and radio advertising in an interactive environment, and while it presents a new and fast-paced experience for consumers, it also raises interesting — and occasionally complex — questions

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[1] Draft guidance at 12.
[2] *See* draft guidance at 3 n.9, 4.

about the applicability of laws that were developed long before 'dot com' became a household phrase."[3] In a 2000 staff paper, the FTC explained that it would "continue to evaluate online advertising, using traditional criteria, while recognizing the uniqueness of the new medium." The paper provided guidelines for presenting the necessary disclosures that "prevent an [Internet] ad from being misleading."[4] One approach discussed in the paper is the use of clear and conspicuous hyperlinks for providing disclosures, such as those used in sponsored links on search engines. The FTC stated that web sites "are interactive and have a certain depth—with multiple pages linked together and pop-up screens, for example—that may affect how proximity [of disclosures] is evaluated."[5] Especially relevant to risk communication for pharmaceuticals, the FTC's staff paper concludes that "[h]yperlinked disclosures may be particularly useful if the disclosure is lengthy."[6]

PhRMA requests that FDA provide guidance that is consistent with the FTC's recognition that unique considerations apply to Internet promotion. We request FDA's further guidance on the application of its existing regulations to Internet-specific promotional activities. Specifically, in evaluating whether risk information is likely to be clear and conspicuous in online promotional materials, FDA should consider the placement of the risk information in a promotional piece and its proximity to the relevant claim—including clearly labeled hyperlinked disclosures; the prominence of the information; whether items in other parts of the piece distract attention from the risk information; whether the piece is so lengthy that the information needs to be repeated; and whether the language of the disclosure is understandable to the intended audience.[7] PhRMA also notes, and requests that FDA acknowledge, that not all activities regarding prescription medicines on the Internet are promotional, and not all websites maintained by or on behalf of a manufacturer qualify as promotional labeling or advertising within the meaning of the FDCA. It would be helpful if FDA would clearly indicate the types of web sites and Internet activities that are not considered promotional labeling or advertising.

C. Quantity of Risk Information

In several places, the draft guidance discusses the quantity of information presented in a promotional piece and suggests that the amount of risk information should increase as the amount of benefit information increases. Yet the overall risk-benefit profile of each drug is unique to that drug, and the "fair balance" for each drug is similarly unique. FDA should acknowledge in the final guidance that: (1) each product has a distinct benefit-risk profile, and (2) given the unique characteristics of a product, there is not necessarily a requirement for there to be a linear relationship between the length of a promotional piece and the time or space devoted to risk information and benefit information. FDA supports this concept in footnote 30 of its draft guidance, in which the Agency provides the following example:

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[3] FTC, Dot Com Disclosures: Information About Online Advertising 3 (2000), *available at* http://www.ftc.gov/bcp/edu/pubs/business/ecommerce/bus41.pdf.
[4] *Id.* at 17.
[5] *Id.* at 6.
[6] *Id.* at 8.
[7] FTC's staff paper sets forth a number of specific best practices for ensuring that these disclosures are clear and conspicuous, along with accompanying examples.

> If the drug or device being promoted is associated with a minimal number of risks, and *all* of these risks are conveyed in a format that is comparably prominent to the presentation of benefit information, then the risk presentation in such an ad or promotional labeling piece would be considered accurate, non-misleading and balanced even if the ad presented several more benefit than risk claims.[8]

Thus, as FDA acknowledges, a fair and meaningful presentation of a drug's risks can be achieved in many cases without devoting precisely equal time to risks and benefits.

In addition, the draft guidance uses the word "comparable" when discussing the prominence of risk information. FDA's regulations, however, use the term "reasonably comparable."[9] FDA's guidance should be consistent with its regulations, and therefore should use the term "reasonably comparable."

D. Presentation of Risk Information in Patient Materials

PhRMA is concerned that the draft guidance may perpetuate an unresolved tension between a consumer-friendly approach to risk communication in DTC materials that provides appropriate risk information, on the one hand, and a requirement that all adverse events be disclosed in an advertisement, on the other. Specifically, the draft guidance states that consideration of the target audience is critical in determining which risk information is material and that promotional materials should convey benefits and risks in language understandable to consumers.[10] But the draft guidance also cites the requirement in 21 C.F.R. § 202.1(e)(3)(iii) that the brief summary must disclose "*each specific side effect and contraindication* (which include side effects, warnings, precautions, and contraindications and include any such information under such headings as cautions, special considerations, important notes, etc. . . .) contained in required, approved, or permitted labeling for the advertised drug dosage form(s)" (emphasis in draft guidance). PhRMA requests that FDA provide affirmative guidance on how patient-directed promotional pieces can comply with the brief summary requirement while still providing risk information in consumer-friendly language. Such guidance would be consistent with FDA's 2004 draft guidance on the brief summary requirement in which the Agency stated:

> FDA-approved professional labeling has often included all possible adverse events, including those that are unlikely to be drug related.
>
> Although this approach complies with the brief summary requirement, FDA believes it is less than optimal for consumer-directed print advertisements because many consumers do not have the technical background to understand this information.[11]

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[8] Draft guidance at 11, n.30.
[9] *See* 21 C.F.R. § 202.1(e)(7)(viii).
[10] Draft guidance at 12.
[11] FDA, Draft Guidance for Industry: Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements 2 (2004).

PhRMA requests that FDA make clear that the options set forth in its 2004 draft guidance for complying with the brief summary requirement in DTC advertising remain acceptable. FDA should provide guidance on how patient-directed promotional pieces can comply with the statutory and regulatory requirements for the disclosure of risk information, while still providing such information in language that is understandable to consumers.

In addition, FDA should consider issuing separate guidances for patient-directed and physician-directed promotion, respectively, and developing a glossary of acceptable consumer-friendly risk presentation terms that would help manufacturers use appropriate patient-friendly language.

E. Use of Examples

The draft guidance is enhanced through the use of examples to illustrate the various factors that should be considered in evaluating the presentation of risk information. PhRMA is concerned, however, that several of the examples provided are prescriptive or definitive in tone, which may not be appropriate for a guidance document. For example, Example 8 explains that a promotional statement "misleadingly describes the risk profile of a drug." PhRMA suggests revising such language to make clear that such a statement "*may* misleadingly describe the risk profile of a drug." In addition, we request that FDA review all conclusions in the draft guidance to make sure that they are compliant with FDA's good guidance practices.[12]

We understand that many of the examples employed by FDA in the draft guidance are based on actual promotional pieces that were the subject of correspondence from DDMAC. In addition to seeing the actual piece, DDMAC was aware of the larger context in which the piece was used—for example, who the intended audience was, whether the drug raised any special safety considerations, and whether the Agency had been in previous contact with the company. This larger context directly informed the Agency's correspondence regarding the piece. But readers of the draft guidance are in most cases unaware of these other factors and cannot fully understand why DDMAC reached the conclusion it did. PhRMA believes that the examples cannot therefore stand on their own as establishing best practices. We suggest that the draft guidance be revised to reflect that the issues discussed in the examples are only discrete parts of a larger discussion regarding whether a given piece would have provided adequate risk information.

Further, PhRMA is concerned that several of the recommendations provided in the examples are not accompanied by citations to FDA's detailed prescription drug regulations on labeling and advertising to support the conclusions reached:

- Examples 3, 4, 5, 6, 7, 8, 9, 10, 14, 15, 16, 17, and 18 do not contain citation to FDA's legal authorities. We believe that FDA should provide such a connection to the existing regulatory requirements.

- In footnote 41, FDA appears to establish a requirement beyond the cited requirement in 21 C.F.R. § 202.1(e)(3)(i) to provide a "concise" presentation of risk information

[12] *See* 21 C.F.R. § 10.115

where there is a prominent reference to more complete risk information in a prescription drug advertisement.

- FDA's guidance at lines 315-327 (concerning order of risk information and placement) does not contain citation to FDA's comprehensive regulations in this area.

PhRMA requests that FDA review these sections to ensure that the Agency's guidance is consistent with its advertising and labeling regulations.

F. Use of Highlights Section of Labeling to Satisfy Fair Balance Requirement

FDA should state in the guidance that inclusion of the information in the "Highlights" section of a drug's labeling would satisfy the "fair balance" requirement for promotional labeling and advertising directed toward healthcare professionals. FDA's advertising regulations require inclusion of "a fair balance between information relating to side effects and contraindications and information relating to effectiveness of the drug…."[13] FDA has stated that the Highlights section of labeling – summarized in 21 C.F.R. § 201.57(a) – contains, among other things a "summary of the most clinically significant" warnings and precautions.[14] In adopting the Highlights section, FDA determined that the "preference for highlighting the most important information that is part of a larger body of information is consistent with good risk communication practices and with well-established cognitive principles. The Agency employed these principles in designing Highlights."[15] Because the Highlights section necessarily contains an FDA-approved summary of the "most clinically significant" warnings and precautions, inclusion of the Highlights in a promotional piece should satisfy the Agency's fair balance requirement.

G. Research Relating to Direct-to-Consumer (DTC) Advertising

PhRMA appreciates that FDA cited PhRMA's *Guiding Principles on Direct to Consumer Advertisements About Prescription Medicines*, which demonstrates the commitment of our members to providing truthful and accurate information about medicines to benefit patients. We note that FDA cited an older version of the PhRMA Principles (2005), and that the current version was revised in 2008[16] to include the following principle, which, among others, are relevant to FDA's guidance:

> DTC television and print advertising should be designed to achieve a balanced presentation of both the benefits and the risks associated with the advertised prescription medicine. Specifically, risks and safety information, including the substance of relevant boxed warnings, should be presented with reasonably comparable prominence to the benefit information, in a clear, conspicuous and neutral manner, and without distraction from the content. In addition, DTC television advertisements should support responsible patient education by directing patients to health care

[13] *See* 21 C.F.R. § 202.1(e)(5)(ii).
[14] 21 C.F.R. § 201.57(a)(10).
[15] 71 Fed. Reg. 3922, 3931 (Jan. 24, 2006).

> professionals as well as to print advertisements and/or websites where additional benefit and risk information is available.[17]

PhRMA is concerned that FDA included an incomplete summary of a study on DTC advertising (Aikin et al.) that FDA admits is "beyond the scope of this document."[18] These data, from a 2004 study, are now out of date, as they preceded the adoption of the PhRMA Guiding Principles. Because the preferences expressed in the study do not reflect views on current DTC advertisements, and because FDA admits that the data are "beyond the scope" of the draft guidance, FDA should remove references to the study. If FDA seeks data based on more current DTC advertisements and consumer views, FDA could cite the most recent research conducted by *Prevention* magazine and made available to FDA.[19] In that study, 76% of respondents stated that DTC advertising of medicines allows them to be more involved in their healthcare, and 78% of respondents who had watched DTC advertising on television responded that the risk information presented was very or somewhat useful.[20]

The statistics provided by FDA in the draft guidance from the study by Aikin et al. are one-sided and fail to include other results of the same study that demonstrate the benefits of DTC advertising – especially in fostering increased communication between patients and their physicians.[21] If FDA decides to retain this description of the research, the Agency should describe the research in an evenhanded manner by including the following results from the study:

Physician Views About DTC Advertising

- "With regard to general benefits of DTC advertising, 72 percent of physicians agreed that DTC advertising increases awareness of possible treatments, and 44 percent of physicians believed that it facilitates earlier awareness of health conditions."[22]

- "About a third of physicians thought that DTC advertising increases the likelihood of proper medication usage, and a third believed it helps patients maintain their treatment over time."[23]

Impact on Doctor-Patient Interactions

- "Overall, 73 percent of physicians indicated that their patient in this encounter asked thoughtful questions because of the DTC exposure."[24]

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[16] PhRMA, PhRMA Guiding Principles: Direct to Consumer Advertisements About Prescription Medicines (2008).
[17] Id. at 7 (Guiding Principle #14).
[18] Draft guidance at 2, n.4 (citing K. Aikin, J. Swasy & A. Braman, Patient and Physician Attitudes and Behaviors Associated With DTC Promotion of Prescription Drugs – Summary of FDA Survey Research Results, Final Report (2004)).
[19] *See* Rodale, Inc., Consumer Reaction to DTC Advertising of Prescription Drugs (12th ed. 2009).
[20] *Id.*
[21] *See* draft guidance at 2 - 3 (n. 4 and lines 63-69).
[22] K. Aikin, J. Swasy & A. Braman, Patient and Physician Attitudes and Behaviors Associated With DTC Promotion of Prescription Drugs – Summary of FDA Survey Research Results, Final Report, at 7 (2004).
[23] *Id.* at 7.
[24] *Id.* at 5.

- "Forty-one percent of physicians reported that DTC exposure led to benefits, whereas 18 percent reported that the exposure led to problems."[25]

Patient Experience with DTC Advertising

- "Seventy-three percent (73%) of patients agreed that the ads do not minimize the role of the physician in product decisions."[26]

- "Forty-three percent (43%) felt the ads help them have better discussions with their doctor (a decline from 62%)."[27]

PhRMA appreciates that FDA has relied upon a significant amount of empirical research in developing its draft guidance. We are concerned that FDA has not provided any citation or evidence to justify the following assumption, which appears to minimize the importance of healthcare professionals in assessing their patients' conditions and explaining benefits and risks of medicines to patients:

> Because people expect to see risk information [in advertisements], there is no reason for them to imagine that the product has important risks that have been omitted. Instead, the audience is likely to believe that all significant risks are included, especially if some risks are included. This missing risk information can have serious effects; it may cause consumers to fail to inform their healthcare professionals of important considerations, and healthcare professionals to prescribe inappropriately or even dangerously.[28]

PhRMA requests that FDA provide a citation to support the assertion. PhRMA members take the obligation to provide important risk information in advertising extremely seriously. However, a DTC advertisement cannot be expected to replace a serious patient examination and conversation with a healthcare professional. Instead, DTC advertisements should be expected to start – not foreclose – a substantive conversation prior to any prescription. Indeed, the benefits of DTC advertising in starting conversations with healthcare professionals have been demonstrated in numerous studies, including the Aiken et al. study relied upon by FDA.[29]

H. First Amendment Considerations

PhRMA appreciates FDA's summary of the statutory and regulatory requirements for labeling and advertising including the acknowledgment that "[i]n regulating the labeling and advertising of drugs and devices, FDA attends to the First Amendment."[30] Given the importance

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[25] *Id.* at 4.
[26] *Id.*
[27] *Id.* at 4.
[28] Draft guidance at 14.
[29] *See* Aikin et al., supra, at 4 ("Forty-three percent (43%) felt the ads help them have better discussions with their doctor … . Seventy-three percent (73%) of patients agreed that the ads do not minimize the role of the physician in product decisions."); Rodale, Inc., *supra* (finding that 76% of consumers surveyed felt that DTC advertisements "allow people to be more involved in their health care.").
[30] Draft guidance at 22.

of health communication to healthcare professionals and patients, we think that FDA's legal summary would benefit from a deeper discussion of FDA's views of its First Amendment obligations in reviewing communications between pharmaceutical companies and healthcare professionals and patients.

Where the communications at issue are commercial speech, FDA has a clear, public policy interest in regulating speech that is false, misleading, or proposes an otherwise unlawful activity.[31] FDA's actions, however, affect the First Amendment interests of patients as well as manufacturers. Any limitations on these communications should therefore be undertaken with great care. In making determinations about whether promotion is false or misleading—particularly in new situations, such as the Internet—FDA should be mindful of the fact that any vagueness or uncertainty with respect to the governing legal standards could have a chilling effect on speech. On the other hand, overly prescriptive regulation of promotional material could run afoul of the First Amendment. Regulations that effectively ban truthful, non-misleading commercial speech about a lawful product "hinder consumer choice [and] impede debate over central issues of public policy" and, therefore, "rarely survive constitutional review."[32] As such, to impose a limitation on speech, FDA must demonstrate that "the harms it recites are real and that its restriction will in fact alleviate them to a material degree."[33]

PhRMA therefore requests that FDA provide additional information about how it "attends to the First Amendment" and specifically how it balances the competing interests discussed above. Specifically, we request guidance and transparency on how FDA performs analyses to determine that specific promotional materials may be false or misleading. PhRMA also requests that FDA provide guidance on how manufacturers may provide substantiation regarding specific claims that may be questioned by DDMAC staff on initial review. Given the potential impact on commercial speech, we believe that FDA should allow for timely sponsor dialog with DDMAC management and/or the Office of Chief Counsel when there are questions regarding DDMAC staff review.

H. Advertising and Promotional Labeling

In footnote 9, FDA discusses both advertising and promotional labeling, and states that the draft guidance applies to both. Of course, both the FDCA and FDA's regulations distinguish between advertising and labeling, creating separate obligations for each. FDA should acknowledge that advertising and promotional labeling are distinct and entail different statutory

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[31] *See Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n*, 447 U.S. 557, 563 (1980) ("[T]here can be no constitutional objection to the suppression of commercial messages that do not accurately inform the public about lawful activity"); *Virginia Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 772 (1976) (The government may rightfully ensure "that the stream of commercial information flow[s] cleanly as well as freely.").

[32] *44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503, 504 (1996). *See also Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81, 85 (D.D.C. 1999) ("FDA may not restrict speech based [simply] on its perception that the speech could, may, or might mislead.").

[33] *Edenfeld v. Fane*, 507 U.S. 761, 770-71 (1993).

and regulatory requirements and should clarify the instances in the guidance in which its recommendations apply to advertising, labeling, or both.

Following are PhRMA's comments on the specific examples and analysis provided by FDA in the guidance.

II. Comments Regarding Specific Examples

A. Examples 4-6

Examples 4-6 relate to the use of signals in promotional pieces. Of course, PhRMA supports balanced discussions of benefit and risk in promotional communication about prescription medicines. We are concerned that FDA's examples suggest that a piece must contain particular headlines discussed in the examples in order to be balanced. FDA should acknowledge that fair balance can be achieved in any number of ways. There are numerous ways to call attention to particular risks, and a piece that does not contain headlines such as "Important Safety Information" could be considered balanced. We therefore suggest that FDA revise these examples to reflect that the use of headlines or signals is one of many mechanisms to achieve fair balance.

In addition, FDA states, "In videos, broadcast ads, and other promotional pieces with audio components, a change of announcer or a statement in the audio portion of the piece to signal to the audience that risk information follows can aid effective communication. However, manufacturers should consider comparable voice characteristics … Risk information may also be signaled graphically or visually. Similar to print pieces, specific and straightforward audio signals are most likely to adequately convey risk information." It is unclear what is meant by "audio signals," and we request that FDA provide an example.

B. Example 7

Example 7 concerns specificity in risk presentation. PhRMA is concerned that lines 284-287 suggest that using verbatim language from FDA-approved Prescribing Information (which may include phrases such as "like all medicines") in promotional labeling that contains a general statement about side effects should not be used in presenting the risk information. We request that FDA revise the guidance to clarify that using FDA-approved language from the Prescribing Information to present risk information would not be considered false or misleading. We also note that FDA itself has used the phrase "like all medicines" in describing the side effects of certain treatments,[34] and we note that FDA has provided no empirical evidence to support the claim in the draft guidance that use of the phrase "may have the effect of minimizing the risks that follow."[35]

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[34] *See* FDA, High Blood Pressure--Medicines to Help You, *available at* http://www.fda.gov/ForConsumers/ByAudience/ForWomen/ucm118594.htm (stating "Like all medicines, high blood pressure medicines can sometimes cause side effects").

[35] Draft guidance at 9.

C. Example 16

Example 16 concerns the location of risk information in a multi-page promotional piece. PhRMA believes that it should be clarified. We understand that many multi-page promotional pieces place all of the safety information on one page with repeated cross references to the safety information. We do not understand whether this example is meant to suggest that such a practice is not recommended or simply that the page with the safety information should contain the same "colorful graphics, abundant white space, and large, colorful headers" as the pages containing the benefit information. We think clarifying this example is particularly important, given that FDA's regulations allow for a manufacturer to provide a "concise" presentation of risk information where there is a prominent reference to more complete risk information in a prescription drug advertisement.[36]

D. Example 18

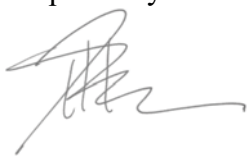
With regard to Example 18, FDA states, "In fact, printing words in some attention-grabbing colors (e.g., red) may make the words difficult to read."[37] We believe that layout, including colors, should be considered as part of the "net impression" of a promotional piece. Many factors, including white space and other format or layout options, should determine what colors would be appropriate for each promotional piece.

FDA also states, "Factors such as font size, type style, and capitalization can also affect the readability of SUPERs. Words presented in all upper case letters are more difficult to read than words presented in upper and lower case letters."[38] Consistent with FDA's analysis in other parts of the draft guidance, we believe that font styles should be assessed in conjunction with the white space and other format and layout options – determined based on the "net impression" rather than just one style. We suggest that FDA state that words in uppercase letters "may be more difficult to read…."

Conclusion

PhRMA looks forward to a continued dialogue with FDA about the important risk communication issues raised in the draft guidance. Please do not hesitate to contact me if you would like to discuss any of PhRMA's comments further.

Respectfully submitted,



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[36] *See* 21 C.F.R. § 202.1(e)(3)(i).
[37] Draft guidance at 17 (footnote omitted).
[38] *Id.* at 19 (footnote omitted).