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FDA Issues Draft Guidance on "Presenting Risk Information in Prescription Drug and Medical Device Promotion"

Introduction

Recently, the Food and Drug Administration issued a Draft Guidance, "Presenting Risk Information in Prescription Drug and Medical Device Promotion," that describes factors FDA intends to consider when evaluating risk information for advertisements and promotional labeling of prescription drugs, restricted medical devices,[1] and promotional labeling for all medical devices.[2] The Draft Guidance provides the industry with recommendations on how to comply with the Federal Food, Drug, and Cosmetic Act ("FDCA") and FDA's implementing regulations, as well as advises companies to use a balanced approach in presenting the benefits and the risks of a particular product. A copy of the document can be accessed here.

The Draft Guidance addresses promotion aimed at both consumers and healthcare professionals. The terms *promotional piece, promotional materials*, and *promotional communications*, as used in the Draft Guidance, refer generally to both advertising and promotional labeling, regardless of format. In addition, promotional materials include, among other things, television ads, brochures, booklets, detailing pieces, web sites, print ads, exhibits, and radio ads.

In general, but to be discussed in more detail in this Bulletin, FDA expressed concern about the presentation of information that minimizes a product's risk. Specific examples cited by the agency included visual distractions when risk information is presented, narrators who speed up their speaking pace when detailing the risks, or minimizing the presentation with phrases, such as "like all medicines, this product has side effects." FDA also noted that, for print advertisements, companies should not place unrelated headers directly over the risk information, reduce the size of the risk information relative to the positive benefit claims, or otherwise make the risk information difficult to read.

While not legally binding on FDA or the pharmaceutical or device industries, the Draft Guidance summarizes the agency's current thinking and recommendations on presenting risk information

1 A "restricted device" is a device that may be restricted to the sale, distribution, or use only with the written or oral authorization of a licensed practitioner, or in accordance with other conditions if FDA determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. 21 U.S.C. § 360j(e).

2 74 Fed. Reg. 25245 (May 27, 2009).

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How FDA Evaluates the Risk Communication in a Promotional Piece

Net Impression View

The Draft Guidance states that, when FDA evaluates risk information, it will look at the "net impression" of all the risk and benefit statements combined, as well as each individual statement of risk. Specifically, FDA will look at all the elements of the promotional piece as a whole to determine whether the piece conveys an accurate and non-misleading impression of both the benefits and risks of the promoted product. Therefore, manufacturers should focus not only on individual claims or presentations, but on the totality of the promotional message. The agency said: "a promotional communication that conveys a deceptive net impression of the product could be misleading, even if specific individual claims or presentations are not."[3]

Reasonable Consumer Standard

FDA will also evaluate claims in promotional materials from a reasonable consumer standard. The Draft Guidance states that the reasonable consumer standard that will be used to evaluate promotional materials is similar to the standard used by the Federal Trade Commission when evaluating deceptive practices under the Federal Trade Commission Act. As such, FDA will examine the practice from the perspective of a reasonable consumer acting reasonably in the circumstances. Further, if material is specifically directed to a group, FDA will examine reasonableness from the perspective of that group. In applying the reasonable consumer standard, the agency will take into account the different levels of expertise and audience. The reasonable consumer standard does not preclude multiple interpretations of a claim, so long as each interpretation is reasonable. However, if a representation conveys more than one meaning to reasonable consumers, one of which is false, FDA will consider the material to be misleading.

Factors Considered in the Review of Risk Communication

General Considerations

The Draft Guidance describes factors that FDA will consider when evaluating risk communications in promotional pieces.

- **Consistent Use of Language Appropriate for Target Audience.** Language used to communicate both benefits and risks should be comprehensible to the same audience for a piece to be considered accurate and non-misleading.

- **Use of Signals.** The Draft Guidance defines signaling as the use of "writing devices designed to emphasize aspects of a text's signature or content without altering the information in the text." FDA provides headlines and subheads as examples of commonly used signals. When reviewing promotional materials, FDA will look to see if the use of signals is consistent across benefit and risk information, so that the materials provide accurate and non-misleading impressions of a product. For example, if a piece contains a headline that signals benefit information (*e.g.*, "Drug X Provides Highly Effective Control"), some sort of headline should also signal risk information (*e.g.*, "Side Effects for Drug X"). However, the mere presence of similar signals for both benefit and risk information is not

3 Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion May 2009, at 4, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM155480.pdf.

necessarily sufficient to make a piece accurate and non-misleading. The content of the signals is also important and should not mislead or falsely emphasize or minimize the importance of benefits or risks.

- Example: The headline "Important Risk Information about Device X" is preferable to "Important Information about Device X" because the former headline indicates what type of information follows. Similarly, "Common Side Effects Seen with Drug X," is preferable to "Other Information about Drug X." Specific and clear signals are preferable because they are more effective than vague or abstract terms.

- **Framing Risk Information.** FDA is concerned about how risk information is framed, because framing can affect the presentation of risks and benefits in a promotional piece. Framing refers to how a particular piece of information is stated or conveyed, such as by emphasizing either the positive or negative aspects of the information or by presenting the information in vague versus specific terms. Risk information should be presented in the same terms or with the same degree of specificity as benefit information. For example, if a promotional piece refers to the product by name in presenting efficacy information, it should refer to the product by name in presenting risk information, rather than by referring to the product's device or drug class.

  - Example: If the benefit information refers to the brand name, "Drug X," then "Common side effects associated with Drug X" would be preferable to "Common side effects associated with [the generic name]."

  FDA warns that framing risk information in a way that minimizes the severity of a risk may cause a promotional piece to be considered false or misleading.

  - Example: If a drug's package insert contains a boxed warning about the risk of life-threatening fevers associated with its use and reports that 55 percent of patients taking the drug experience dizziness, a statement such as "Adverse events associated with drug X include fevers. Some patients experienced dizziness" misleadingly describes the risk profile of the drug by failing to convey the seriousness of the fevers and the frequency of the dizziness. Statements like "Life- threatening fevers have been reported with the use of Drug X" and "More than half of patients taking Drug X experienced dizziness" would convey the seriousness and frequency of the two risks appropriately.

- **Hierarchy of Risk Information.** FDA considers the ordering of risks within a presentation an important factor in determining the risk profile conveyed by a promotional piece, regardless of whether it is directed toward healthcare professionals or consumers. FDA recommends that the most important risk information, including relevant warnings and contraindications, be placed or stated first, especially in print materials.

  - Example: A statement in a broadcast ad that "Patients should not drink alcohol when taking Drug X. Common side effects are drowsiness and nausea" may suggest that these side effects occur only if alcohol is consumed when taking the drug. Instead, the sponsor should consider adding intervening information or changing the order of the presentation so that it is clear the side effects listed are not caused by drinking alcohol while taking the drug.

Considerations of Content

- **Quantity.** FDA considers the amount, or quantity, of information conveyed by a promotional piece in evaluating whether the content of risk presentations in a promotional piece is accurate and non-misleading. The Draft Guidance provides that the quantity of information presented can affect the net impression of the piece. FDA recommends that as the amount of benefit information conveyed increases, the amount of risk information conveyed should similarly increase. FDA warns if the benefit information is easily understood and maintained through repetition or other reinforcing techniques, and the risk information is not similarly reinforced, the net impression may not be appropriately balanced. Further, the agency recommends that manufacturers consider the space or time devoted to benefits and risks, the comprehensibility of the language used, and the information provided on benefits and risks to ensure comparable benefit and risk presentations. When determining the comparability of benefits and risks in a piece, FDA considers the following factors:
  - The number of statements about benefits and risks.
  - The completeness and depth of detail given about benefits and risks.
  - The amount of time (in both the audio and visual portions) devoted to benefits and risks in a video, audio, or broadcast communication.
  - The amount of space devoted to benefits and risks in a print communication.
  - The use of audio or visual components that enhance or distract from the presentation of risk or benefit information.

  In evaluating the net impression created by promotional communications, FDA will consider the above factors, as well as the differences in the inherent risks associated with various drugs or devices. However, simply satisfying one of the above factors will not necessarily make a promotional piece accurate and non-misleading.

- **Materiality.** Materiality is determined by the degree to which information is objectively important, relevant, or substantial to the target audience. FDA may consider a promotional piece that omits material information about a product's risks to be misleading, even if the piece devotes similar space or time to other risk and effectiveness presentations. Material facts are those facts that would influence reasonable consumers (or healthcare professionals when they are the intended audience) about a product. The Draft Guidance states that materials facts include those that influence reasonable consumers' (or healthcare professionals') understanding of the following:
  - The relevant properties of a product.
  - Whether or not the product is appropriate for them or their patients.
  - Whether or not they are willing to accept the risks or burdens associated with using or prescribing a product.

The Draft Guidance states that the most serious risks described in a product's labeling are generally material to *any* presentation of efficacy.

In determining whether or not particular information is material, FDA considers the target audience for the product. The agency will evaluate the promotion from the perspective of a reasonable member of the targeted population (*e.g.*, consumers, specific patient populations, healthcare professionals). The Draft Guidance states that communications directed to healthcare professionals should convey the most critical information they need to know about the product to help them decide whether it is appropriate for their

patients and to help enable them to safely use the product or counsel patients on the safe use of the product. Consumer-directed communications should generally convey the following:

- What is the drug's or device's use?
- Who should or should not take a drug or use a device?
- What can be expected from the product?
- What patients should ask their healthcare professionals about a drug or device?
- What patients should tell their healthcare professionals before or while taking or using a product?

FDA also looks at the package insert in determining materiality. A product's most serious or most frequently occurring risks, as listed on the insert, are likely to be material, regardless of other claims made in the piece. In addition, risk information may become material in light of specific benefit claims promoted in the piece. Further, if a piece highlights a particular benefit, the risks related to that benefit are material.

- **Comprehensiveness.** When FDA evaluates the content of a promotional piece's risk information, it assesses the quality as well as the quantity of the information. The Draft Guidance states that, because both consumers and professional audiences have come to expect that certain information will be present in promotions due to FDA oversight, missing information can have serious effects. FDA believes it is important for promotional materials to be comprehensive enough to meet these expectations. Therefore, quality and quantity of the risk information are reviewed.

Considerations of Format

FDA considers formatting factors when assessing whether a promotional piece is false or misleading. Format includes the shape, size, and general layout of all portions of a print promotional piece, as well as the general plan of organization, arrangement, and theme in non-print promotional pieces, such as videos and broadcast ads. As a general matter, the Draft Guidance states that risk and benefit information should be comparably noticeable or conspicuous in promotional pieces, and audiences should be able to read both risk and benefit information with similar ease. The Draft Guidance covers print and non-print materials separately, because formatting issues vary.

- **For Print Promotional Pieces.** The Draft Guidance lists several factors that FDA uses when evaluating print promotional materials. For instance, the Guidance addresses the following factors:
  - **Overall Location of Risk Information:** Risk information should be included in the main part of a piece.
  - **Location of Risk Information Within a Part of the Promotional Piece:** Risk information should appear as an integral part of the piece, just as benefit information does.
  - **Font Size and Style:** FDA may object to substantial differences in font size or the presentation of risk information in a difficult to read font size, regardless of the font size of benefit

information, because this may seriously reduce the ability to see or comprehend the risk information. To be comparably prominent and readable, FDA recommends that risk and benefit information be presented in type styles that are similar in the use of capitalization, serifs, the weight of the type-face, the angle of the letters, the degree of flourishes and scripting, and other typographical factors such as spacing (*e.g.*, leading and kerning).

› **Contrast:** Contrast between text and background should not highlight the benefit information more than the risk information.

› **White Space:** Background space (often called white space) between and around letters can influence the prominence and readability of text. FDA recommends that the white space for benefit information should be comparable to the white space for risk information.

- **For Non-Print Promotional Pieces.** Some print formatting issues also apply to non-print promotional pieces, such as videos, broadcast ads, and similar audio and visual pieces. However, the unique features of non-print media add complexity. As with print promotion, FDA considers factors such as location, proximity, type size, type style, and contrast when evaluating these materials. However, in non-print pieces, FDA also evaluates other formatting factors in addition to those described above to determine whether a particular piece is considered false or misleading (e.g., audio components, motion within the visual component, the juxtaposition of visual and audio components, and duration of exposure).

  › **Textual elements:** Prescription drug broadcast ads must present major product risks in the audio or audio and visual parts of the ad. The Draft Guidance states that when used to disclose risk, SUPERs (*i.e.*, superimposed texts) can pose particular problems of readability, comprehensibility, and proximity to benefit information. As such, FDA assesses the temporal location of SUPERs within a broadcast ad or video when evaluating whether it is false or misleading. In addition, FDA recommends that manufacturers keep the following factors in mind:

    · SUPERs, if used, should be reasonably visible to a person under typical viewing conditions.
    · All SUPERs should be on the screen long enough to allow the audience to read and understand their full content.
    · Graphics that distract from the presentation of risk information, including from risk-related SUPERs
    · Competition from other SUPERs (*e.g.*, presenting a SUPER related to a particular risk while unrelated SUPERs are on the screen) hampers the audience's ability to read and understand the SUPERs and could compromise the communication of risk information and make a piece misleading.

  › **Dual Mode Considerations:** Visuals in a broadcast ad should not distract the audience from the statement of a product's risks because the ad will not, as a whole, convey an accurate impression of the risks of the advertised product. A distraction could be caused by factors such as busy scenes, frequent scene changes, moving camera angles, and inherently compelling, vivid visuals. In addition, the overall tone of the ad, or of specific background visuals, can affect the comparable prominence of the risks, particularly if the tone is contrary to the risk

message.

› **Audio Considerations:** FDA considers several audio-related factors when evaluating pieces such as sound recordings, videos, or broadcast ads (*e.g.*, television, radio). These factors include:

- The qualities of speech should be similar across benefit and risk information for these components to be considered comparably prominent.
- A critical speech consideration is *pacing*. If risk information is considerably more difficult to hear and process than benefit information because it is presented at a much faster pace, the piece will not convey an accurate impression of the product.
- Markedly reducing volume or being less articulate when discussing risks compared to benefits may hinder the audience's comprehension of the risks.
- Background music should be comparable in volume and distraction potential during both benefit and risk presentations.