FDA Issues Draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion

How to Convey the Good, Bad and Ugly

By Alan G. Minsk, Jennifer S. Blakely and Meredith M. Burris
Recently, the US Food and Drug Administration (FDA) issued Draft Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion, which describes factors FDA intends to consider when evaluating risk information for advertisements and promotional labeling of prescription drugs and restricted medical devices, and promotional labeling for all medical devices. The draft guidance provides recommendations on how to comply with FDA’s requirements to ensure the presentation of truthful product information, and advises companies to use a balanced approach in conveying the benefits and the risks of a particular product. While not legally binding on FDA or the pharmaceutical or device industries, the draft guidance summarizes the agency’s current thinking and recommendations on presenting risk information.

The draft guidance addresses promotion aimed at both consumers and healthcare professionals. The terms “promotional piece,” “promotional materials,” and “promotional communications,” as used in the draft guidance, refer generally to both advertising and promotional labeling, regardless of format. Promotional materials include print, television and radio advertisements, brochures, booklets, detailing pieces, websites and exhibits.

In particular, FDA expressed concern about presentation of information that minimizes a product’s risks. Specific examples cited by the agency include using visual distractions during presentation of risk information, speeding up the pace of narration when detailing risks and downplaying concerns with statements such as, “Like all medicines, this product has side effects.” FDA also noted that in 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.

How FDA Evaluates 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The draft guidance states that when FDA evaluates risk information, it will look at the “net impression” of all the risk and benefit statements combined, as well as each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. In other words, FDA will look at all the elements of the promotional piece as a whole to determine whether the piece conveys an accurate and nonmisleading impression of both the promoted product’s benefits and risks. Therefore, manufacturers should focus not only on individual claims or presentations, but also on the totality of the promotional message. The draft guidance states, “A promotional communication that conveys a deceptive net impression of the product could be misleading, even if specific individual claims or presentations are not.”

Reasonable Consumer Standard
FDA will also evaluate claims in promotional materials against a reasonable consumer standard similar to the standard used by the Federal Trade Commission when evaluating deceptive practices under the Federal Trade Commission Act. This means FDA will examine claims from the perspective of a reasonable consumer acting reasonably in the circumstances. Further, if material is directed to a specific 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 types of audience (e.g., doctors vs. consumers). 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 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 nonmisleading.
- Use of signals—The draft guidance defines “signals” as “writing devices designed to emphasize aspects of a text’s structure or content without altering the information in the text.” FDA provides 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 nonmisleading 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 necessarily sufficient to make a piece accurate and nonmisleading. The content of the signals is also important and should not mislead...
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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 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 or by presenting the information in vague vs. 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 when presenting efficacy information, it should refer to the product by name when 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% 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 such as, “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: The statement in a broadcast advertisement, “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 quantity of information conveyed by a promotional piece in evaluating whether the content of risk presentations is accurate and non-misleading. The draft guidance indicates 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 that 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 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 nonmisleading.

- 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 influence reasonable consumers (or healthcare professionals when they are the intended audience) about the following aspects of a product:
  - relevant properties of the product
  - whether the product is appropriate for them or their patients
  - whether 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:
  - the drug or device’s use
  - who should or should not take the drug or use the device
  - what can be expected from the product
  - what patients should ask their healthcare professionals about the drug or device
  - what patients should tell their healthcare professionals before or while taking or using the 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 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 nonprint pieces, such as videos and broadcast advertisements. As a general matter, 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 nonprint materials separately, because formatting issues vary.

- Print Promotional Pieces—The draft guidance lists several factors FDA reviews when evaluating print promotional materials:
  - 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, risk and benefit information should 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 be comparable to the white space for risk information.

Nonprint Promotional Pieces—Some print formatting issues also apply to nonprint promotional pieces, such as videos, broadcast advertisements and similar audio and visual pieces. However, the unique features of nonprint 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 nonprint pieces, FDA evaluates other formatting factors (e.g., audio components, motion within the visual component, the juxtaposition of visual and audio components and duration of exposure) in addition to those described above to determine whether a particular piece is considered false or misleading.

Textual elements—Prescription drug broadcast advertisements must present major product risks and around letters.
parts of the advertisement. 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 advertisement 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 (e.g., busy scenes, frequent scene changes, vivid and compelling visuals and moving camera angles) can misleadingly minimize the risks of the product being promoted by detracting from the audience’s comprehension of the risk presentation.
- 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.

**Audio considerations**—FDA considers several audio-related factors when evaluating pieces such as sound recording, videos and broadcast advertisements (e.g., television, radio):

- 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.

**Conclusion**

FDA’s draft guidance is a must-read for regulated industry to better understand what the agency expects relating to the presentation of risk information in product promotion. While the draft guidance is not legally binding, compliance with recommendations offered (which are similar to concerns raised in enforcement letters) should help companies minimize the risk of disseminating false or misleading product information, which could lead to enforcement action.

**References**

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).

**Authors**

Alan G. Minsk is a partner and leader of the Food and Drug Practice Team of Arnall Golden Gregory LLP. He also serves on the Board of Editors for Regulatory Focus. Minsk can be reached at alan.minsk@agg.com. Jennifer S. Blakely is an associate in the Life Sciences Practice Group and Healthcare Practice Group of Arnall Golden Gregory LLP. She can be reached at Jennifer.blakely@agg.com. Meredith M. Burris is an associate at Arnall Golden Gregory LLP. She can be reached at Meredith.burris@agg.com.