
Guidance for Industry Presenting Risk Information in Prescription Drug and Medical Device Promotion

DRAFT GUIDANCE

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Guidance for Industry Presenting Risk Information in Prescription Drug and Medical Device Promotion

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Guidance for Industry

Presenting Risk Information in Prescription Drug and Medical Device Promotion

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This draft guidance, when finalized, will represent the Food and Drug Administration’s (FDA’s) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This draft guidance describes factors FDA considers when evaluating advertisements (ads) and promotional labeling for prescription drugs,¹ ads for restricted medical devices,² and promotional labeling for all medical devices for their compliance with the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act) and relevant regulations.³ The draft guidance discusses factors that are relevant to the disclosure of risk information and provides numerous examples to illustrate FDA’s thinking on these factors. This guidance responds to stakeholder requests for specific guidance on how FDA evaluates prescription drug and medical device promotional pieces to determine whether they adequately present risk information. The recommendations contained in this draft guidance apply to promotional materials directed to both consumers and healthcare professionals.

¹ This draft guidance does not address over-the-counter (OTC) drug promotional labeling, which FDA also regulates. FDA encourages all manufacturers to ensure that their promotional labeling is truthful and non-misleading. FDA recognizes that the marketing status of animal drugs may vary, depending upon the intended species. For example, several anthelmintics on the market are available only by prescription for dogs and cats, yet very similar products are available OTC for horses and food animals. OTC drugs intended for food animals, in particular, may carry significant risks that may affect not only the intended food animal, but also other animal species and humans. OTC promotional labeling for animal drugs should convey the serious risks associated with use of the products, especially those affecting the public health.

² Devices may become restricted, either by regulation issued under section 520(e) of the Act (21 U.S.C. 360j(e)), or by order approving an application for premarket approval (PMA), pursuant to section 515(d)(1)(B)(ii) (21 U.S.C. 360e(d)(1)(B)(ii)).

³ This draft guidance also does not apply to those *reminder* promotions (labeling or advertising that calls attention to the name of a drug or device but does not include indications, dosage recommendations, or other information) that are exempted by regulation from the requirements under the FD&C Act for the disclosure of risk information. See 21 CFR 200.200, 201.100(f), 201.105(d)(2), 202.1(e)(2)(i), 801.109(d). But see 21 U.S.C. 352(r) (requiring certain risk information in all restricted device advertisements).

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29 Although this draft guidance focuses on the presentation of risk information in prescription drug and
30 medical device promotion, the factors relating to effective communication outlined below are also
31 applicable to the presentation of benefit information in promotion. Indeed, when FDA evaluates
32 promotional pieces for compliance with the Act and relevant regulations, it determines whether claims
33 about both risk and benefit of the product are accurate and non-misleading, and it also looks at whether
34 risks and benefits are presented in a comparably prominent manner. Thus, considerations involving the
35 content and format of benefit information are an inherent part of FDA's evaluation of risk presentations in
36 promotional pieces. FDA recommends that companies take the factors outlined in this document into
37 account when developing both risk and benefit presentations in their promotional pieces, as the public
38 health is best served when risk and effectiveness information about drug and device products is clearly
39 and accurately communicated.

40

41 FDA's guidance documents, including this draft guidance, do not establish legally enforceable
42 responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed
43 only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the
44 word *should* in Agency guidances means that something is suggested or recommended, but not required.

45

46

47 **II. BACKGROUND**

48

49 The regulation of prescription drug and medical device promotion to healthcare professionals and
50 consumers is a broad and complex topic.⁴ This document addresses one key aspect of this topic – the
51 presentation of risk information. FDA believes it is critically important to disclose risk information in
52 prescription drug and medical device promotion appropriately and effectively to healthcare professionals
53 and consumers.⁵ This information helps consumers know whether drugs or devices may be appropriate
54 for them as well as what they should tell their healthcare professionals about before taking or using or
55 while taking or using a product. It also lets consumers know what risks they might experience and what
56 steps they need to take for safety reasons (e.g., no driving) because of taking or using a product.
57 Appropriate risk disclosures help healthcare professionals by giving them some of the information they
58 need to know about the product that will enable them to safely use or prescribe it. Recently published
59 industry guidelines encourage manufacturers to develop prescription medicine promotion that is

⁴ Although beyond the scope of this document, the complexity of the topic can be demonstrated by past studies that have shown potential positive and negative effects of direct-to-consumer (DTC) advertising for prescription drugs. For example, FDA research suggests that DTC advertising seems to increase awareness of conditions and treatments, to motivate questions for the healthcare provider, and to help patients ask better questions. Yet this research also suggests that almost half of physicians feel some pressure to prescribe as a result of DTC advertising, and patients and physicians report a belief that these ads overstate the drug product's efficacy and do not present a fair balance of benefit and risk information. For the complete study results, see 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, November 19, 2004, available at: <http://www.fda.gov/cder/ddmac/Final%20Report/FRfinal111904.pdf>.

⁵ Effectively disclosing risk information also requires a consideration of whether an advertisement or promotional material over warns. For example, a drug advertisement that includes a listing of side effects that are not included in the drug's approved labeling may lead to under-emphasis of the most important and serious risks. FDA takes care to ensure that important risk information is included in the drug's approved labeling, and sponsors have an obligation to update their labeling with appropriate new safety information. 21 CFR 201.57(c)(6); 201.80(e). Nothing in this guidance should be construed as recommending that the sponsor of a drug include in advertising or promotional materials risk information not in the product's approved labeling or appropriate for inclusion in the labeling. See 73 Fed. Reg. 2848, 2851 (January 16, 2008).

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60 “designed to achieve a balanced presentation of both the benefits and the risks associated with the
61 advertised” product.⁶

62
63 However, omission or minimization of risk information is the most frequent violation of the regulations
64 cited in advertising and promotion enforcement letters sent to sponsors, and illustrative research in one of
65 the areas this guidance covers, direct-to-consumer prescription drug advertising, has shown that 60
66 percent of patients believe ads directed at them do not provide enough information about risks, 60 percent
67 of physicians believe that patients have little or no understanding from these ads about what the possible
68 risks and negative effects of the products are, and 72 percent of physicians believe that patients have little
69 or no understanding from these ads about who should not use the product.⁷

70
71 FDA is issuing this draft guidance to aid sponsors in effectively communicating risk information in their
72 promotion to both healthcare professionals and consumers. This draft guidance describes how FDA
73 reviews prescription drug and medical device promotional pieces to determine whether they adequately
74 present risk information. The document begins with some background information, including a brief
75 overview of legal requirements and a discussion of policy considerations related to drug and device
76 promotional materials. The draft guidance then describes factors FDA considers when reviewing risk
77 communication in promotional materials. Because the principles within this guidance are based on
78 universal concepts of communication and understanding of risk information, the guidance will address
79 promotion aimed at both lay consumer and healthcare professional audiences.

80

81 **A. LEGAL OVERVIEW**

82

83 Under the FD&C Act and FDA's implementing regulations, promotional pieces (such as promotional
84 labeling for drugs and devices and advertisements for prescription drugs and restricted devices) making
85 claims about a product are deemed misleading if they fail to disclose certain information about the
86 product's risks.⁸ Generally, to comply with the FD&C Act and FDA's implementing regulations, such
87 promotional pieces:⁹

88

89 — Cannot be false or misleading in any particular¹⁰

90

91 — Must reveal material facts about the product being promoted, including facts about the
consequences that can result from use of the product as suggested in the promotional piece¹¹

⁶ PhRMA, PhRMA Guiding Principles Direct to Consumer Advertisements About Prescription Medicines, Principle 11, November 2005, available at: <http://www.phrma.org/files/DTCGuidingprinciples.pdf>.

⁷ 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, November 19, 2004, available at: <http://www.fda.gov/cder/ddmac/Final%20Report/FRfinal111904.pdf>.

⁸ The relevant statutory provisions and regulations are discussed in more detail in the Attachment to this guidance.

⁹ The terms *promotional piece*, *promotional materials*, and *promotional communications* are used in this guidance to refer generally to both advertising and promotional labeling, regardless of format. Promotional materials include, among others, television ads, brochures, booklets, detailing pieces, internet web sites, print ads, exhibits, and sound recordings or radio ads. As noted in the introduction, this guidance applies to all types of promotion for prescription drugs, advertisements for restricted devices and promotional labeling for all devices.

¹⁰ Drugs and devices are misbranded under the Act if their labeling is false or misleading in any particular (21 U.S.C. 352(a)). Similarly, prescription drugs and restricted devices are misbranded if their advertising is false or misleading in any particular (21 U.S.C. 352(n) & (q)(1); 21 CFR 202.1(e)(5)(i)).

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92 and
93 — Should present information about effectiveness and information about risk in a balanced
94 manner¹²

95
96 This draft guidance document describes factors FDA considers when evaluating risk disclosure in
97 prescription drug and medical device promotional materials to determine whether these materials comply
98 with the statutory and regulatory requirements. The draft guidance also makes recommendations about
99 how manufacturers can develop the content and format of promotional communications to comply with
100 these requirements. The examples and recommendations provided are intended to provide guidance and
101 illustrate possible approaches; manufacturers are free to use alternative approaches if these approaches
102 satisfy the requirements of the statute and regulations. Unless otherwise specified in this draft guidance,
103 the principles set forth below apply to all promotional pieces, regardless of the medium used or the target
104 audience.

106 **B. POLICY OVERVIEW**

107
108 Section III of this guidance highlights several factors, including those related to content and format, that
109 FDA uses to evaluate the risk communication in a promotional piece. We recommend that manufacturers
110 consider these factors when trying to achieve effective risk communication. It is important to emphasize
111 that when FDA evaluates the risk communication in a promotional piece, FDA looks not just at specific
112 risk-related statements, but at the *net impression* – i.e., the message communicated by all elements of the
113 piece as a whole. The purpose of the evaluation is to determine whether the piece *as a whole* conveys an
114 accurate and non-misleading impression of the benefits and risks of the promoted product. Manufacturers
115 should therefore focus not just on individual claims or presentations, but on the promotional piece as a
116 whole.¹³ A promotional communication that conveys a deceptive net impression of the product could be
117 misleading, even if specific individual claims or presentations are not misleading.

118
119 FDA’s consideration of the net impression of risk information is based on well-developed social science
120 principles supported by decades of scientific research¹⁴ and is consistent with the approach of other
121 agencies and organizations. For example, the Federal Trade Commission (FTC) uses the interpretation of
122 the net impression of the piece to determine whether a promotional piece is likely to mislead a
123 consumer.¹⁵ Pharmaceutical industry members have also conducted social science research showing that,
124 when evaluating a promotional piece, the net impression conveyed by the piece as a whole is an important
125 element to consider, independent of individual statements within the piece.

¹¹ 21 U.S.C. 321(n); 21 CFR 1.21 & 202.1(e)(5)(iii).

¹² See 21 CFR 202.1(e)(5)(ii).

¹³ Manufacturers should note that, although this guidance focuses on risk disclosures in promotional pieces, any claims in a promotional piece that are misleading, whether risk-related or not, can cause the product being promoted to become misbranded (21 U.S.C. 352(a), (n) & (q)(1); 21 CFR 202.1(e)(5)(i)).

¹⁴ For reviews of this field, see Kimble, G.A. (1985) The psychology of learning enters its second century. In Hammonds, B.L. (Ed.), *Psychology and learning*. Washington, DC: American Psychological Association (pp. 5-47) and Mayer, R.E. (2003) Memory and information processes. In Reynolds, W.M., & Miller, G.E. (Eds.), *Handbook of Psychology: Educational Psychology*, 7. New York: John Wiley & Sons, Inc. (pp. 47-57).

¹⁵ See Federal Trade Commission, FTC Policy Statement on Deception, (Oct. 14, 1983), appended to *FTC v. Cliffdale Associates, Inc., et al.*, 103 F.T.C. 110, 170 (1984) (hereinafter “FTC Policy Statement on Deception” with page references to 103 F.T.C. 110).

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Section III of the guidance contains examples of how various aspects of content and format can contribute to a misleading net impression in promotional pieces. The following two examples also illustrate this.

Example 1: A broadcast television ad for a cholesterol-lowering drug contains a factually accurate audio risk statement that discloses the drug’s major side effects and contraindications. This audio presentation is accompanied by quick scene changes showing comforting visual images of patients benefiting from the drug. It is also accompanied by loud, upbeat music. In this case, the audio disclosure may not adequately communicate risks because of the accompanying discordant visuals and distracting music.

Example 2: A one-page prescription drug ad for an arthritis drug, run in a medical journal, prominently presents the following headline claims in large bolded font and with abundant surrounding white space:

- **Benefits! DrugX is proven safe and effective for the relief of arthritis pain and stiffness,**
- **Difference! DrugX’s unique gel formulation is convenient and easy to use, and**
- **Reason to Believe! Drug X is the most frequently prescribed arthritis drug in the United States**

The bottom of the page contains an inconspicuous statement in small, non-bolded font and without surrounding white space: “Like all arthritis medications, Drug X has been associated with a risk of serious infection.” The emphasis on benefit information in this piece – in terms of the way the information is formatted and framed – overwhelms the risk information and may cause readers to receive an erroneous impression that the drug is safer than it has proven to be, even though the statements themselves may be factually accurate.

Using the factors explained in Part III of this draft guidance, trained professionals at FDA with expertise in areas including communication, drug information, medicine and law, apply these factors and evaluate claims in promotional pieces from the perspective of a reasonable consumer. As FDA has stated,¹⁶ the agency believes that the reasonable consumer standard is the appropriate standard to use in determining whether a claim in the labeling of a dietary supplement or conventional food is misleading. The agency confirms that the reasonable consumer standard will be used to evaluate communications covered by this guidance document. The *reasonable consumer standard* used by FDA in evaluating promotional materials is similar to the FTC standard:

[W]e examine the practice from the perspective of a consumer acting reasonably in the circumstances. If the representation or practice affects or is directed primarily to a particular group, the Commission examines reasonableness from the perspective of that group.¹⁷

¹⁶ Guidance for Industry: Qualified Health Claims in the Labeling of Conventional Foods and Dietary Supplements (Dec. 2002) (replaced by Guidance for Industry and FDA: Interim Procedures for Qualified Health Claims in the Labeling of Conventional Food and Human Dietary Supplements (July 2003)); see 70 Fed. Reg. 824 (Jan. 5, 2005) (noting that, although the Guidance for Industry on Qualified Health Claims in Labeling of Conventional Foods and Dietary Supplements (Dec. 2002) “has been ‘replaced’ by subsequent guidance, the agency has not abandoned the position in the 2002 guidance regarding reasonable consumer standard”).

¹⁷ See FTC Policy Statement on Deception at 170.

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166 This standard does not preclude multiple interpretations of a claim, as long as they are reasonable. As the
167 FTC’s Policy Statement provides:

168
169 To be considered reasonable, the interpretation or reaction does not have to be the only
170 one. When a seller’s representation conveys more than one meaning to reasonable
171 consumers, one of which is false, the seller is liable for the misleading interpretation.¹⁸
172

173 In applying the reasonable consumer standard, FDA, like FTC, takes into account the different levels of
174 expertise of lay consumers and healthcare professionals. Due to their training and experience, healthcare
175 professionals develop a level of knowledge related to scientific concepts and medical conditions and
176 products that lay consumers do not possess. FDA takes this difference in knowledge and experience into
177 account when assessing promotional materials directed at healthcare professionals versus those directed at
178 lay audiences. However, research has shown that experts (in this case, healthcare professionals) are
179 subject to the same cognitive biases and processing limitations as non-experts.¹⁹
180

181 Cognitive science research has demonstrated that all people, regardless of expertise, are only able to think
182 through and process a limited amount of information at one time.²⁰ However, our ability to process
183 information can be greatly improved by considering and controlling for the factors that affect attention
184 and comprehension. This guidance discusses those factors, how we apply them to our review of
185 promotional materials, and what manufacturers can do to ensure that their materials comply with the
186 regulations.
187

188

189 **III. FACTORS CONSIDERED IN THE REVIEW OF RISK COMMUNICATION**

190
191 FDA relies on a vast scientific body of knowledge regarding human cognition in assessing which factors
192 to consider in evaluating promotional pieces and making regulatory decisions about the presentation of
193 risk information. The following sections highlight factors that FDA considers when determining whether
194 risk information is communicated in a fashion consistent with the regulations.
195

¹⁸ *Id.* at 177.

¹⁹ Although physicians generally do not believe that they are influenced by advertising, (Spiller & Wymer, 2001), research has shown that physicians are influenced by promotional activities (e.g., advertising: Avorn et al., 1982; sales representatives: Gonul et al., 2001). Avorn, J., Chen, M. & Hartley, R. (1982) Scientific versus commercial sources of influence on the prescribing behavior of physicians. *American Journal of Medicine*, 73, 4-8. Gonul, F.F., Carter, F., Petrova, E., & Srinivasan, K. (2001) Promotion of prescription drugs and its impact on physicians’ choice behavior. *Journal of Marketing*, 65, 79-90. Spiller, L.D., & Wymer, W.W. (2001) Physicians’ perceptions and uses of commercial drug information sources: An examination of pharmaceutical marketing to physicians. *Health Marketing Quarterly*, 19, 91-106.

²⁰ See, e.g., Lavie, N. (2001) Capacity limits in selective attention: Behavioral evidence and implications for neural activity. In Braun, J., Koch, C., et al. (Eds.), *Visual attention and cortical circuits*. Cambridge, MA: The MIT Press (pp. 49-68); Miller, G.A. (1994) The magical number seven, plus or minus two: Some limits on our capacity for processing information. Reprinted in Gutfreund, H., & Toulouse, G. (Eds.), *Biology and computation: A physicist’s choice*. River Edge, NJ: World Scientific Publishing Co. (pp. 207-233); Shapiro, K. (Ed.) (2001) *The limits of attention: Temporal constraints in human information processing*. London: Oxford University Press.

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196 A. GENERAL CONSIDERATIONS

197
198 This section explores some important factors that relate to both the content and the format of a
199 promotional piece. FDA will consider the use of language and signals and how information is framed and
200 ordered.

201 202 1. Consistent Use of Language Appropriate for Target Audience

203
204 Both language used to communicate benefits and language used to communicate risks should be
205 comprehensible to the same audience for a piece to be considered accurate and non-misleading. Thus,
206 promotional materials directed to professionals can reasonably describe benefits and risks in medical
207 language, but promotional materials directed to consumers should convey benefits and risks in language
208 understandable to consumers.²¹

209
210 *Example 3:* A consumer-directed ad for a drug that presents benefit claims in consumer friendly
211 language should mention a risk of “fainting,” not “syncope.”

212
213 With respect to consumer-directed materials, FDA encourages manufacturers to present both benefit and
214 risk information in clear, understandable, and non-technical language for consumer audiences.²²

215 216 2. Use of Signals

217
218 Signaling is an important component of information communication.²³ In written materials, *signaling* has
219 been defined as the use of “writing devices designed to emphasize aspects of a text’s structure or content
220 without altering the information in the text.”²⁴ Headlines and subheads are examples of commonly used
221 signals.²⁵ Depending on the circumstance, “accurate information in the text may not remedy a false
222 headline [or signal] because reasonable consumers may only glance at the headline” and skip the

²¹ See Root, J., & Stableford, S. (1999) Easy-to-read consumer communications: A missing link in Medicaid managed care. *Journal of Health Politics, Policy, & Law*, 24, 1-26.

²² Although not a true measure of “understandability,” text reading level, often expressed as “grade level,” is one way to assess text difficulty. Text that scores at a higher grade level (e.g., 12th grade) is considered more complex than text scoring at a lower grade level (e.g., 8th grade). Several validated reading level measures are available to provide an approximate measure of text complexity. See, e.g., Kincaid, J.P., Fishburne, R., Rogers, R.L., Chissom, B.S. (1975) *Derivation of New Readability Formulas (Automated Reliability Index, Fog Count, and Flesch Reading Ease Formula) for Navy Enlisted Personnel*. Research Branch Report 8-75. Memphis: Naval Air Station; McLaughlin, G.H. (1969) SMOG grading: A new readability formula. *Journal of Reading*, 12, 639-646; Mosenthal, P.B. (1998) A new measure of assessing document complexity: The PMOSE/IKIRSCH document readability formula. *Journal of Adolescent and Adult Literacy*, 41, 620-638. We encourage manufacturers to test text comprehensibility as well.

²³ Loman, N.L., & Mayer, R.E. (1983) Signaling techniques that increase the understandability of expository prose. *Journal of Educational Psychology*, 75, 402-412; Meyer, B.J.F. (2003) Text coherence and readability. *Topics in Language Disorders*, 23, 204-224; Spyridakis, J.H., & Standal, T.C. (1987) Signals in expository prose: Effects on reading comprehension. *Reading Research Quarterly*, 22, 285-298.

²⁴ Lorch, R.F., Lorch, E.P., & Inman, W.E. (1993) Effects of signaling structure on text recall. *Journal of Educational Psychology*, 85, 281-290, p. 281.

²⁵ Hyona, J., & Lorch, R.F. (2004) Effects of topic headings on text processing: Evidence from adult readers’ eye fixation patterns. *Learning and Instruction*, 14, 131-152.

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223 remainder of the text.²⁶ Signals are also used in broadcast situations, such as when an announcer draws
224 attention to different items of information, when a word on the screen identifies a new topic, or when
225 headlines emphasize some messages but not others.

226
227 When reviewing promotional materials, FDA looks to see if the use of signals is consistent across benefit
228 and risk information, so that the materials provide accurate and non-misleading impressions of a drug or
229 device.

230
231 *Example 4:* If a piece contains headlines that signal benefit information, (e.g., “Drug X Provides
232 Highly Effective Control”), some sort of headline should also signal risk information (e.g., “Side
233 Effects for Drug X”).

234
235 However, the mere presence of similar signals for both benefit and risk information is not necessarily
236 sufficient to make a piece accurate and non-misleading. The content of the signals is also important.
237 Certain headlines may *frame* (see next section) subsequent risk information in ways that emphasize or
238 minimize its importance.

239
240 *Example 5:* The headline “Important Risk Information about Device X” is preferable to
241 “Important Information about Device X” because the former headline indicates what type of
242 information follows. Similarly, “Common Side Effects Seen with Drug X,” is preferable to
243 “Other Information about Drug X.” Specific and clear signals are preferable because they are
244 more effective than vague or abstract terms.

245
246 Presenting risk information with no signal, or beginning the presentation of risk information with
247 unrelated information (e.g. presenting risk information in a paragraph that begins with information on
248 indication or dosing) can also minimize the risks of the product and mislead the audience. For example,
249 the headlines in the following example convey additional benefit information, potentially misleading the
250 audience about the overall risk-benefit profile of the product.

251
252 *Example 6:* Placing risk information under headlines such as “Now Approved for Epilepsy” or
253 “Safe Enough for Children Under 5” minimizes the risk information that follows, particularly if
254 individuals only look at the headlines. Instead, headlines preceding risk presentations should
255 signal that a risk presentation follows, for example, “Important Risk Information About Drug X.”

256
257 In videos, broadcast ads, and other promotional pieces with audio components, a change of announcer or
258 a statement in the audio portion of the piece to signal to the audience that risk information follows can aid
259 effective communication. However, manufacturers should consider comparable voice characteristics, as
260 discussed in Section III.C.2. Risk information may also be signaled graphically or visually. Similar to
261 print pieces, specific and straightforward audio signals are most likely to adequately convey risk
262 information.

263
264 **3. Framing Risk Information**

265
266 FDA evaluates how risk information is framed because framing can affect the presentation of risks and
267 benefits in a promotional piece. Framing commonly refers to how a particular piece of information is
268 stated or conveyed, such as by emphasizing either the positive or negative aspects of the information or
269 by presenting the information in vague versus specific terms. Research consistently shows that framing

²⁶ FTC Policy Statement on Deception at 182.

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270 the same information in different ways can change the way audience members respond to that
271 information.²⁷ Thus, the way information is phrased can significantly influence the message the audience
272 receives from a promotional piece.

273
274 Framing risk information in non-specific terms can undermine the effective communication of that
275 information to the audience. Risk information should be presented in the same terms or with the same
276 degree of specificity as benefit information. For example, if a promotional piece refers to the product by
277 name in presenting efficacy information, it should refer to the product by name in presenting risk
278 information, rather than by referring to the product's device or drug class.

279
280 *Example 7:* If the benefit information refers to the brand name, “Drug X,” then “Common side
281 effects associated with Drug X” would be preferable to “Common side effects associated with
282 [the generic name].”

283
284 Moreover, within the risk information presentation, phrases such as “*Like all medicines*, Drug X has some
285 side effects,” may have the effect of minimizing the risks that follow. Framing risk information in a way
286 that minimizes the severity of a risk event may also cause a promotional piece to be considered false or
287 misleading.

288
289 *Example 8:* If a drug's package insert contains a boxed warning about the risk of life-threatening
290 fevers associated with its use and reports that 55 percent of patients taking the drug experience
291 dizziness, a statement such as “Adverse events associated with drug X include fevers. Some
292 patients experienced dizziness” misleadingly describes the risk profile of the drug by failing to
293 convey the seriousness of the fevers and the frequency of the dizziness. Statements like “Life-
294 threatening fevers have been reported with the use of Drug X” and “More than half of patients
295 taking Drug X experienced dizziness” would convey the seriousness and frequency of the two
296 risks appropriately.

297
298 In addition, the risks conveyed in the piece should be framed in a way that accurately reflects their nature.

299
300 *Example 9:* A statement such as “continuation of therapy may necessitate certain monitoring” is
301 too vague for a product that requires monthly blood tests to check for liver damage. This
302 statement fails to convey the risk of liver damage and also misleadingly suggests that routine
303 monitoring may *not* be necessary for some patients. A statement like “Monthly blood tests
304 should be performed to check for liver damage” would accurately convey the type of monitoring
305 needed and the risk involved.

306 307 4. Hierarchy of Risk Information

308
309 FDA considers the ordering of risks within a presentation an important factor in determining the risk
310 profile conveyed by a piece, regardless of whether it is directed toward healthcare professionals or

²⁷ See Armstrong, K., Schwartz, J.S., Fitzgerald, G., Putt, M., & Ubel, P.A. (2002) Effect of framing as gain versus loss on understanding and hypothetical treatment choices: survival and mortality curves. *Medical Decision Making*, 22, 76-83; Dunegan, K.J. (1993) Framing, cognitive modes, and imagery theory: Toward an understanding of a glass half full. *Journal of Applied Psychology*, 78, 491-503; Rothman, A.J., & Salovey, P. (1997) Shaping perceptions to motivate healthy behavior: The role of message framing. *Psychological Bulletin*, 121, 3-19; Smith, S.M., & Petty, R.E. (1996) Message framing and persuasion: A message processing analysis. *Personality and Social Psychology Bulletin*, 22, 257-268; Tversky, A., & Kahneman, D. (1981) The framing of decisions and the psychology of choice. *Science*, 211, 453-458.

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311 consumers. As discussed in Section III.B.2 (below) and reflected in the format of the package insert for
312 prescription drugs and medical devices, risks associated with a specific product are assigned a hierarchy
313 of importance.

314
315 Memory research consistently shows that, in an experimental setting, when people process an entire list or
316 text, they are better able to recall items at the beginning and the end than items in the middle.²⁸
317 Consequently, in a broadcast ad, where viewers do not have the opportunity to control the speed at which
318 information is presented to help them to process it, the beginning or end, or both, should be reserved for
319 the most important risk information. On the other hand, when reading a print promotional piece under
320 normal circumstances, readers may lose interest toward the end of a lengthy paragraph, and it is not likely
321 that the information at the end will be as well-comprehended as the information at the beginning. If a
322 product's most important risks are located in the middle of a list of less important risks, the important
323 risks may not be effectively communicated. FDA therefore recommends that the most important risk
324 information, including relevant warnings and contraindications, be placed or stated first, especially in
325 print materials. As discussed in Section III.C.1 (below), manufacturers should also note, however, that
326 risk information should not just be presented in one location in a piece, but should, like benefit
327 information, appear as an integral part of the piece.

328
329 FDA also considers the order in which risk information is presented to determine whether this ordering
330 suggests that certain risks apply only to certain populations or only under certain conditions when this is
331 not the case.

332
333 *Example 10:* A statement in a broadcast ad that “Patients should not drink alcohol when taking
334 Drug X. Common side effects are drowsiness and nausea” may suggest that these side effects
335 occur only if alcohol is consumed when taking the drug. Instead, the sponsor should consider
336 adding intervening information or changing the order of the presentation so that it is clear the side
337 effects listed are not caused by drinking alcohol while taking the drug.

B. CONSIDERATIONS OF CONTENT

338
339
340 This section discusses how FDA evaluates the content of risk presentations in determining whether a
341 promotional piece is accurate and non-misleading.

1. Quantity

342
343
344 One content factor FDA considers is the amount or quantity of information conveyed by a promotional
345 piece. For example, a 30-second broadcast ad is likely to present less information than a 60-second
346 broadcast ad. As the amount of benefit information conveyed increases, the amount of risk information
347 conveyed should similarly increase.

348
349
350 The quantity of information presented can affect the net impression of the piece. The amount of
351 information presented is one component that, together with choice of words, color, graphics, voiceover,
352 and other aspects of the piece, can affect *cognitive load*, the mental effort required to understand the
353

²⁸ See Botvinik, M.M., & Plaut, D.C. (2006) Short-term memory for serial order: A recurrent neural network model. *Psychological Review*, 113, 201-233; Capitani, E.; della Sala, S.; Logie, R.H.; & Spinnier, H. (1992) Recency, primacy, and memory: Reappraising and standardizing the serial position curve. *Cortex*, 28, 315-342; Murdock, B.B. (1962) The serial position effect of free recall. *Journal of Experimental Psychology*, 64, 482-488.

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354 various components of information in the piece.²⁹ If the benefit information is easily understood and
355 maintained through repetition or other reinforcing techniques, and the risk information is not similarly
356 reinforced, the net impression may not be appropriately balanced.

357
358 To ensure comparable benefit and risk presentations, manufacturers should consider the space or time
359 devoted to benefits and risks, the comprehensibility of the language used, and the information provided
360 on benefits and risks. FDA will look to see that promotional communications allot sufficient time and
361 space to convey the important benefits and risks of the product being promoted to ensure that, *as a whole*,
362 the communication provides an accurate and non-misleading impression of the product.

363
364 A promotional piece with several paragraphs of information regarding benefits differs from a piece
365 consisting mainly of one-line benefit claims. The treatment of risk information in each piece should be
366 comparable to the treatment of benefit information, including how it is conveyed.

367
368 Promotional pieces do not have to convey an identical number of benefits and risks, and a given drug or
369 device may have few or many risks.³⁰ FDA considers these factors when determining the comparability
370 of benefits and risks in a piece:

- 371
- 372 — The number of statements about benefits and risks
 - 373 — The completeness and depth of detail given about benefits and risks
 - 374 — The amount of time (in both the audio and visual portions) devoted to benefits and risks in a
375 video, audio, or broadcast communication
 - 376 — The amount of space devoted to benefits and risks in a print communication
 - 377 — The use of audio or visual components that enhance or distract from the presentation of risk
378 or benefit information
- 379

380 As stated in the Background and discussed above, FDA evaluates the net impression created by
381 promotional communications. This evaluation includes considering the above factors as well as the
382 differences in the inherent risks associated with various drugs or devices. Simply satisfying one of the
383 above factors (e.g., devoting the same amount of time or space to risk and benefit information) will not
384 necessarily make a promotional piece accurate and non-misleading. Furthermore, certain important risk
385 information should be in all promotional pieces regardless of their length (*see* Section III.B.2 below).

386 387 2. *Materiality and Comprehensiveness*

388
389 Generally speaking, *materiality* is determined by the degree to which information is objectively
390 important, relevant, or substantial to the target audience. A promotional piece that omits material
391 information about a product's risks could be considered misleading even if the piece devotes similar
392 space or time to risk and effectiveness presentations.³¹

²⁹ See Mayer, R.E., & Moreno, R. (2003) Nine ways to reduce cognitive load in multimedia learning. *Educational Psychologist*, 38, 43-52; Pass, F., Renkl, A., & Sweller, J. (2004) Cognitive load theory: Instructional implications of the interaction between information structures and cognitive architecture. *Instructional Science*, 32, 1-8.

³⁰ 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.

³¹ 21 U.S.C. 321(n); see also 21 CFR 1.21 & 202.1(e)(5)(iii). Please see the Attachment to this document for a full description of the relevant requirements.

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393
394 *Material facts* are those that would influence reasonable consumers (or healthcare professionals when
395 they are the intended audience) about a product. Material facts include those that influence such people’s
396 understanding of the following:

- 397
398 — The relevant properties of a product
399 — Whether or not the product is appropriate for them or their patients
400 — Whether or not they are willing to accept the risks or burdens associated with using or
401 prescribing a product
402

403 Some drug and device risks are material regardless of the amount or type of benefit claims in a piece.
404 The most serious risks set forth in a product’s labeling are generally material to *any* presentation of
405 efficacy. A promotional piece that communicates a product’s benefits should similarly communicate the
406 most serious risks involved in using the product. Similarly, the most frequently occurring risks would
407 usually be material to consumers and healthcare professionals in promotion, particularly if a product is
408 only associated with a small number of more serious risks, because of the likelihood that they will affect
409 patients taking the drug or using the device.

- 410
411 • Consideration of Target Audience

412
413 FDA considers the target audience of a promotional piece to be critical in determining what risk
414 information is material. FDA evaluates the promotion from the perspective of a reasonable member of
415 the targeted population (e.g., consumers, specific patient populations, healthcare professionals). As is
416 explored in more detail below (e.g., Examples 11 and 13), different information can be material to
417 different audiences. For example, in a piece promoting use of a product in a selected class of patients,
418 risks especially applicable to that selected class of patients are material (see “The Nature of Benefit
419 Claims,” below).³²

420
421 Generally speaking, communications directed to healthcare professionals should convey the most critical
422 information they need to know about the product to help them decide whether it is appropriate for their
423 patients and to help enable them to safely use the product or counsel patients on the safe use of the
424 product. Consumer-directed communications should generally convey the following:

- 425
426 — What the drug or device is used for
427 — Who should or should not take a drug or use a device
428 — What can be expected from a drug or device
429 — What patients should ask their healthcare professionals about a drug or device
430 — What patients should tell their healthcare professionals about before or while taking a drug or
431 using a device
432

433 *Example 11:* A drug’s package insert includes a warning for healthcare professionals about dosing
434 adjustments in patients with kidney disease. This information is material for healthcare professionals,
435 both because of the seriousness indicated by its warning status and because of its relevance to safe
436 prescribing. However, although this information is important to the safe use of the drug and should
437 be considered by prescribers, it is not material to consumers, although the reasons for such care in
438 dosing (e.g., the consequences of inappropriate dosing) could be.
439

³² See 21 CFR 202.1(e)(7)(x).

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440 • Importance of Package Insert

441
442 In determining the materiality of the risks associated with a drug or device, FDA refers to the product's
443 package insert. FDA is more likely to consider as important or material a product's most serious or most
444 frequently occurring risks than a product's less serious or less commonly occurring risks.³³ FDA
445 characterizes the risks associated with a specific product along a hierarchy of importance reflected by
446 placement in a risk-related section of the product's package insert – traditionally, the Contraindications,
447 Warnings or Hazards, Precautions, Adverse Reactions or Side Effects sections, as well as the
448 Overdosage, and Drug Abuse and Dependence sections in the case of prescription drugs – and in the use
449 of various means to emphasize certain risks, such as boxed warnings and bolded statements. For labeling
450 that complies with the new formatting requirements in the recently finalized Physician Labeling Rule for
451 prescription drugs,³⁴ the risk-related sections include Boxed Warning, Contraindications, Warnings and
452 Precautions, Adverse Reactions, Drug Interactions, Use in Specific Populations, Drug Abuse &
453 Dependence, and Overdosage.

454
455 For prescription drug physician labeling that follows the new requirements, the risks included in the
456 *Highlights* section of labeling are the most important risks associated with the drug. For other labeling,
457 contraindications and warnings or hazards are considered to contain the most serious and material risk
458 information associated with a drug or device and convey information that must be understood before the
459 product is prescribed or used. Contraindications and boxed warnings are generally considered the most
460 important. Precautions also convey important risk information that can help healthcare professionals and
461 patients use a drug or device more safely. These include ways to avoid adverse effects and information
462 about important differences in individual response and, for drugs, about interactions with other drugs or
463 food. Risks conveyed only in the adverse events or side effects section are generally less serious or less
464 well-documented than those in the preceding three categories. They are often the most commonly
465 experienced risks associated with a product, however, and they therefore may constitute important
466 information for both healthcare professionals and consumers.

467
468 • The Nature of Benefit Claims

469
470 Promotional pieces should reveal risk information that is material in light of the specific benefit claims
471 made in the piece.

472
473 *Example 12:* If a piece claims convenience because the promoted drug is dosed once-weekly,
474 information about risks directly related to the regimen's convenience is material. Such risk
475 information might include, for example, that inflammatory reactions such as swelling have been
476 reported at the application site for a topical product, or that patients must restrict their activities
477 for some time after taking an oral medication because of a risk of fainting.

³³ As indicated above, the most serious risks set forth in a product's labeling are generally material to any presentation of efficacy. Frequently occurring, less serious risks (e.g., those reflected in Adverse Reactions) can be material, particularly for a product that is not associated with serious risks, but these less serious risks may not be material for a product that has many serious risks that need to be disclosed in promotion, or whose most frequently occurring risks occur at a very low rate. In general, FDA believes that exhaustive lists of minor risks distract from and make it difficult to comprehend and retain information on the more important risks. To this end, we have issued a draft guidance for prescription drugs entitled *Brief Summary Disclosing Risk Information in Consumer-Directed Print Advertisements*, which suggests approaches to communicating less, but better, information in consumer brief summaries. Once finalized, this guidance will represent the Agency's thinking on this topic.

³⁴ See 71 Fed. Reg. 3922 (Jan. 24, 2006). The rule became effective June 30, 2006.

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478
479 Similarly, as stated above, for promotional pieces that promote a product's benefits in a selected class of
480 patients, the significant risks applicable to that class of patients are material.³⁵

481
482 *Example 13:* If a Web site for a product approved to treat high blood pressure presents
483 information about a product's benefits in postmenopausal women, any risks specific to
484 postmenopausal women are particularly material.

- 485
486 • Accuracy and Comprehensiveness of Risk Information

487
488 When it evaluates the content of a promotional piece's risk information, FDA assesses the quality as well
489 as the quantity of the information. Both consumer and professional audiences expect that certain
490 information will be present in promotions for prescription drugs and medical devices. This expectation
491 results from schemas,³⁶ or mental frameworks, about these promotional pieces that have developed from
492 previous exposures (i.e., preconceived expectations based on past experience). Consumers have
493 preconceived ideas about the amount of scrutiny these ads undergo. Many believe FDA exercises tight
494 regulatory control over the content of these ads and to some extent, believe that all ads have been pre-
495 reviewed prior to airing.³⁷ As a result, consumers are likely to expect that the most relevant risks have
496 been included in the ad. Because people expect to see risk information, there is no reason for them to
497 imagine that the product has important risks that have been omitted. Instead, the audience is likely to
498 believe that all significant risks are included, especially if some risks are included. This missing risk
499 information can have serious effects; it may cause consumers to fail to inform their healthcare
500 professionals of important considerations, and healthcare professionals to prescribe inappropriately or
501 even dangerously.

502
503 *Example 14:* A product is associated with the rare but serious risk of a heart attack. FDA is likely
504 to consider an ad misleading if it devotes a certain amount of time or space to the presentation of
505 claims about the product's efficacy in treating migraines and then devotes a similar amount of
506 time or space to describing only the frequently occurring, least serious adverse events, or only
507 one of several significant risks.

508
509 Even though a similar *quantity* of risk and benefit information may be conveyed, a promotional piece that
510 presents information on the benefits of the product but then communicates only its least serious risks, or
511 an inadequate set of its serious risks, will not have conveyed an accurate understanding of the product's
512 relevant properties.

513 514 C. CONSIDERATIONS OF FORMAT

515
516 FDA also considers formatting factors when assessing whether a piece is false or misleading. *Format*
517 includes the shape, size, and general layout of all portions of a print promotional piece, as well as the

³⁵ See 21 CFR 202.1(e)(7)(x).

³⁶ See Kardash, C.A.M., Royer, J.M., & Greene, B.A. (1988) Effects of schemata on both encoding and retrieval of information from prose. *Journal of Educational Psychology*, 80, 324-329; Smith, E.E., & Swinney, D.A. (1992) The role of schemas in reading text: A real-time examination. *Discourse Processes*, 15, 303-316.

³⁷ See, e.g., 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, November 19, 2004, available at: <http://www.fda.gov/cder/ddmac/Final%20Report/FRfinal111904.pdf>; Prevention Magazine (2004) 5th Annual Survey: Consumer Reaction to DTC Advertising of Prescription Medicines. Emmaus, PA: Rodale.

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518 general plan of organization, arrangement, and theme in non-print promotional pieces such as videos and
519 broadcast ads.

520
521 To process information, a person must first pay attention to it. Several factors contribute to whether
522 people will pay attention to information. These factors also may help or hinder people's understanding of
523 information once it has drawn their attention. When evaluating whether a promotional piece
524 appropriately communicates risk information, FDA considers several formatting factors.³⁸ Because these
525 factors apply to information processing in general, prescription drug and medical device manufacturers
526 should keep them in mind when developing promotional pieces.

527
528 As a general matter, risk and benefit information should be comparably noticeable or conspicuous in
529 promotional pieces, and audiences should be able to read both risk and benefit information with similar
530 ease (e.g., comparably legible and understandable; *see* Section III.A.1 above).³⁹ Manufacturers should
531 note that any one of the following formatting factors could make a piece false or misleading and that each
532 factor could interact with others to increase this problem or to create a false or misleading impression
533 when there might not be one if a factor were considered in isolation.

534 535 *1. Print Promotion*

536
537 The layout of a print promotional piece (generally, its plan, design, or arrangement) influences readers'
538 ability to pay attention to and process specific features of the piece.⁴⁰ FDA considers the following
539 selected aspects of the layout of a print promotional piece when assessing the comparable prominence and
540 readability of risk and efficacy information. This is not an exhaustive list; other issues, such as language
541 comprehension and the risk hierarchy, are covered in other sections.

542 543 • Overall Location of Risk Information

544
545 For a piece to be accurate and non-misleading, risk information should be included in the main part of a
546 piece. If the omission of risk information in any part of a piece makes that part of the piece false or
547 misleading, the problem cannot be corrected simply by including the risk information in a separate part of
548 the piece.⁴¹ To be comparably prominent to benefit information, risk information should generally appear
549 in the same parts of the piece as the benefits.

³⁸ See, e.g., 21 CFR 202.1(e)(7)(viii) for a list of implementing factors FDA takes into consideration when evaluating the balance between benefit and risk information in an ad. *See generally* 21 CFR 202.1(e)(6)-(7).

³⁹ See 21 U.S.C. § 352(c).

⁴⁰ See Adams, A.S., & Edworthy, J. (1995) Quantifying and predicting the effects of basic text display variables on the perceived urgency of warning labels: Tradeoffs involving font size, border weight, and color. *Ergonomics*, 38, 2221-2237; Brundage, M., Feldman-Stewart, D., Leis, A., Bezjak, A., Degner, L., Velji, K., et al. (2005) Communicating quality of life information to cancer patients: A study of six presentation formats. *Journal of Clinical Oncology*, 23, 6949-6956; Frantz, J.P. (1993) Effect of location and presentation format on attention to and compliance with product warnings and instructions. *Journal of Safety Research*, 24, 131-154; Morrow, D., Leirer, V., Altieri, P. (1995) List formats improve medication instructions for older adults. *Educational Gerontology*, 21, 151-166; Niemela, M., & Saariluoma, P. (2003) Layout attributes and recall. *Behaviour and Information Technology*, 22, 353-363; Wogalter, M.S., & Vigilante, W.J., Jr. (2003) Effects of label format on knowledge acquisition and perceived readability by younger and older adults. *Ergonomics*, 46, 327-344.

⁴¹ See 21 CFR 202.1(e)(3)(i). The prescription drug regulations allow the presentation of risk information in a particular part of a promotional piece to be concise if it is supplemented by a prominent reference on each page to the presence and location of a more complete discussion of such information elsewhere in the piece. *Id.* However,

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550

551 Complete separation of benefit and risk information (e.g., presenting several pages of benefits before any
552 risks) is one example of a lack of appropriate prominence.⁴² FDA will also look to see that risk
553 information is not placed in such a way as to interfere with readers' perceptions of the relative importance
554 or utility of the information.

555

556 • Location of Risk Information within a Part of the Promotional Piece

557

558 In addition to appearing with or near benefit presentations, risk information should appear as an integral
559 part of the piece, just as benefit information does. For example, a prescription drug ad should not present
560 risks only on a brief summary page.

561

562 *Example 15:* A product's logo and a tagline are often used to signal the end of a piece. Readers
563 may assume that any risk information placed below the logo and tagline is there only for liability
564 purposes or to fulfill a regulatory requirement and is unrelated to the main message, especially if
565 the information is presented in small type or otherwise lacking in emphasis.

566

567 *Example 16:* A seven-page sales aid devotes the first six pages to effectiveness claims, which are
568 prominently presented with colorful graphics, abundant white space, and large, colorful headers.
569 Three of these pages also include a footnote referring readers to "Important Information on page
570 7." The seventh page summarizes some risk information from the PI in single-spaced paragraph
571 format without headers or other presentation elements to emphasize to the reader that it is
572 important risk information. Such a presentation creates problems regarding the adequate
573 presentation of risk. The important risk information about the drug should instead be integrated
574 into the piece and presented with similar prominence to the effectiveness claims.

575

576 Similarly, problems can arise when parts of a print promotional piece appear so unrelated that the risks do
577 not look to be part of the piece.

578

579 *Example 17:* Risk information is placed in a thin column along the side of an ad in a different font
580 and color scheme, so that the visuals and benefit information form a complete whole, separate
581 from the risk information. This is not likely to be considered an adequate presentation of risk
582 information.

583

584 • Font Size and Style

585

586 Font size and type style are format factors that can affect the prominence and readability of information.⁴³
587 FDA does not object to a presentation on the basis of minor differences in font size alone, depending on

although the regulations allow for the "concise" presentation of such information, the nature and importance of this information should be accurately conveyed. For example, if a drug contains a boxed warning with information on the risk of elevations in potassium levels that can lead to life-threatening complications in some patients, a statement in a part of a promotional piece that "Drug X may increase your potassium levels; see Prescribing Information (PI) for more information" is not likely to convey to consumers or healthcare professionals the magnitude (i.e., life-threatening nature) of the risk.

⁴² 21 CFR 202.1(e)(3)(i); see also 21 U.S.C. 321(n), 21 CFR 202.1(e)(5)(iii).

⁴³ Adams, A.S., & Edworthy, J. (1995) Quantifying and predicting the effects of basic text display variables on the perceived urgency of warning labels: Tradeoffs involving font size, border weight, and color. *Ergonomics*, 38, 2221-2237; Arditi, A., & Cho, J. (2005) Serifs and font legibility. *Vision Research*, 45, 2926-2933; Baker, S.

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588 other factors used to achieve emphasis (e.g., bolded lettering, bullets). However, FDA may object to
589 substantial differences in font size or the presentation of risk information in a difficult to read font size,
590 irrespective of the font size of benefit information, because this may seriously reduce the ability to see or
591 comprehend the risk information.

592
593 Even with identical risk and benefit font sizes, differences in type styles can render some information
594 easier to read than other information.⁴⁴ To be comparably prominent and readable, FDA recommends that
595 risk and benefit information be presented in type styles that are similar in the use of capitalization, serifs,
596 the weight of the type-face, the angle of the letters, the degree of flourishes and scripting, and other
597 typographical factors such as spacing (e.g., leading and kerning).⁴⁵

- 598
599 • Contrast

600
601 Contrast between text and background should not highlight the benefit information more than the risk
602 information.

603
604 *Example 18:* If benefit information in a piece is presented in white letters on a black background,
605 risk information should be presented with similar contrast. If the piece presents risk information
606 in a way that would make it difficult to discern (e.g., using white letters on a light gray
607 background or gray letters on a black background), the presentation may be considered false or
608 misleading.

609
610 Even if the background is a color designed to attract attention, the contrast influences the prominence of
611 the words once attention has been gained. In fact, printing words in some attention-grabbing colors (e.g.,
612 red) may make the words difficult to read.⁴⁶ Similarly, the placement of risk information over pictures or

(2006). Provision of effective information. *British Dental Journal*, 201, 100; Sheedy, J.E., Subbaram, M.V., Zimmerman, A.B., & Hayes, J.R. (2005) Text legibility and the letter superiority effect. *Human Factors*, 47, 797-815; Tantillo, J., Di Lorenzo-Aiss, J., & Mathisen, R.E. (1995) Quantifying perceived differences in type styles: An exploratory study. *Psychology and Marketing*, 12, 447-457; Wogalter, M.S., & Vigilante, W.J. (2003) Effects of label format on knowledge acquisition and perceived readability by younger and older adults. *Ergonomics*, 46, 327-344.

⁴⁴ English, E. (1944) A study of the readability of four newspaper headline types. *Journalism Quarterly*, 21, 217-229; Mansfield, J.S., Legge, G.E., & Bane, M.C. (1996) Psychophysics of reading. XV: Font effects in normal and low vision. *Investigative Ophthalmology and Visual Science*, 37, 1492-1501; Sheedy, J.E., Subbaram, M.V., Zimmerman, A.B., & Hayes, J.R. (2005) Text legibility and the letter superiority effect. *Human Factors*, 47, 797-815; Tantillo, J., Di Lorenzo-Aiss, J., & Mathisen, R.E. (1995) Quantifying perceived differences in type styles: An exploratory study. *Psychology and Marketing*, 12, 447-457.

⁴⁵ See Arditi, A., & Cho, J. (2005) Serifs and font legibility. *Vision Research*, 45, 2926-2933; Baker, S. (2006) Provision of effective information. *British Dental Journal*, 201, 100; Moriarty, S.E., & Scheiner, E.C. (1984) A study of close-set text type. *Journal of Applied Psychology*, 69, 700-702; Paterson, D.G., & Tinker, M.A. (1947) Influence of leading upon readability of newspaper type. *Journal of Applied Psychology*, 31, 160-163; Smither, J.A., & Braun, C.C. (1994) Readability of prescription drug labels by older and younger adults. *Journal of Clinical Psychology in Medical Settings*, 1, 149-159; Tinker, M.A., & Paterson, D.G. (1946) Effect of line width and leading on readability of newspaper type. *Journalism Quarterly*, 23, 307-309.

⁴⁶ See Pearson, R., & van Schaik, P. (2003) The effect of spatial layout and link colour in web pages on performance in a visual search task and an interactive search task. *International Journal of Human-Computer Studies*, 59, 327-353; but see Adams, A.S., & Edworthy, J. (1995) Quantifying and predicting the effects of basic text display variables on the perceived urgency of warning labels: Tradeoffs involving font size, border weight, and color. *Ergonomics*, 38, 2221-2237.

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613 other visual elements with multiple colors can cause this information or portions of this information to
614 lack prominence and be difficult to read.⁴⁷ Furthermore, a print piece that superimposes risk information
615 over a visual image could compromise the accuracy of the piece as a whole by drawing attention away
616 from the risk information.⁴⁸

617

- 618 • White Space

619

620 Background space (often called *white space*) between and around letters can influence the prominence
621 and readability of text.⁴⁹ Presenting benefit information in multiple paragraphs with double spaces
622 between each paragraph, while presenting risk information in one block paragraph without spacing or
623 indentation could reduce the comparability of the risk and benefit presentations. Moreover, if a
624 promotional piece uses headings, bullets, and other attention-getting symbols to emphasize product
625 benefits, FDA recommends that it use similar techniques to present product risks.⁵⁰

626

627 2. *Non-Print Promotion*

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629 Some print formatting issues also apply to non-print promotion such as videos, broadcast ads, and similar
630 audio and visual pieces. However, the unique features of non-print media add complexity. As with print,
631 FDA considers factors such as location, proximity, type size, type style, and contrast when evaluating
632 these materials. These factors are especially important with regard to text that is superimposed on other
633 images in videos or broadcast ads (SUPERS) and other visual components, such as graphics, within the
634 scene. In non-print pieces, FDA also evaluates other formatting factors in addition to those described
635 above to determine whether a particular piece is considered false or misleading (e.g., audio components,
636 motion within the visual component, the juxtaposition of visual and audio components, and duration of
637 exposure).

638

- 639 • Textual Elements

640

641 Prescription drug broadcast ads must present major product risks in the audio or audio and visual parts of
642 the ad.⁵¹ Thus, broadcast ads and videos often use SUPERS and other text to present risk-related
643 qualifying information. When used to disclose risk, SUPERS can pose particular problems of readability,
644 comprehensibility, and proximity to benefit information. For example, the FTC, which requires that

⁴⁷ See, e.g., Hillstrom, A.P., & Chai, Y. (2006) Factors that guide or disrupt attentive visual processing. *Computers in Human Behavior*, 22, 648-656; Petty, R.E., Wells, G.L., & Brock, T.C. (1976) Distraction can enhance or reduce yielding to propaganda: Thought disruption versus effort justification. *Journal of Personality and Social Psychology*, 34, 874-884; Zimbardo, P.G., Snyder, M., Thomas, J., Gold, A., & Gurwitz, S. (1970) Modifying the impact of persuasive communications with external distraction. *Journal of Personality and Social Psychology*, 16, 669-680.

⁴⁸ See Shiffrin, R.M., & Schneider, W. (1977) Controlled and automatic human information processing II: Perceptual learning, automatic attending, and a general theory. *Psychological Review*, 84, 127-190.

⁴⁹ Adams, A.S., & Edworthy, J. (1995) Quantifying and predicting the effects of basic text display variables on the perceived urgency of warning labels: Tradeoffs involving font size, border weight, and color. *Ergonomics*, 38, 2221-2237; Pracejus, J.W., Olsen, G.D., & O'Guinn, T.C. (2006) How nothing became something: White space, rhetoric, history, and meaning. *Journal of Consumer Research*, 33, 82-90.

⁵⁰ See Luckiesh, M., & Moss, F.K. (1940) Boldness as a factor in type-design and typography. *Journal of Applied Psychology*, 24, 170-183.

⁵¹ 21 CFR 202.1(e)(1).

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645 “[q]ualifying disclosures...be legible and understandable,” recognizes that, “in many circumstances
646 reasonable consumers do not read the entirety of an ad or are directed away from the importance of the
647 qualifying phrase by acts or statements of the seller.”⁵² FDA has similar concerns.

648
649 FDA assesses the temporal location of SUPERS within a broadcast ad or video when evaluating whether
650 it is false or misleading. If claims must be qualified to avoid misleading the audience, we recommend
651 that the qualifier be vocalized, presented through visual images, or placed in a prominent SUPER that
652 runs **concurrently** with the claim.⁵³ If SUPERS do not appear close enough to the claim or risk
653 information requiring qualification, a misleading impression of the product may result.⁵⁴ In addition, if
654 qualifying information is complex and requires more than one line of text, we recommend that
655 manufacturers use other means to convey this information.

656
657 Other issues FDA considers important that manufacturers should keep in mind include the following:
658

- 659 — SUPERS, if used, should be reasonably visible to a person under typical viewing conditions.
 - 660 — All SUPERS should be on screen long enough to allow the audience to read and understand their
661 full content.
 - 662 — Graphics that distract from the presentation of risk information, including from risk-related
663 SUPERS (e.g., busy scenes, frequent scene changes, vivid and compelling visuals⁵⁵ and moving
664 camera angles) can misleadingly minimize the risks of the product being promoted by detracting
665 from the audience’s comprehension of the risk presentation.
 - 666 — Competition from other SUPERS (e.g., presenting a SUPER related to a particular risk while
667 unrelated SUPERS are on the screen) hampers the audience’s ability to read and understand the
668 SUPERS and could compromise the communication of risk information and make a piece
669 misleading.⁵⁶
 - 670 — Factors such as font size, type style, and capitalization can also affect the readability of
671 SUPERS.⁵⁷ Words presented in all upper case letters are more difficult to read than words
672 presented in upper and lower case letters.⁵⁸
- 673

⁵² FTC Policy Statement on Deception at 183.

⁵³ See 21 CFR 202.1(e)(3)(i).

⁵⁴ Manrai, L.A., Manrai, A.K., & Murray, N. (1994) Comprehension of info-aid supers in television advertising for social ideas: Implications for public policy. *Journal of Business Research*, 30, 75-84.

⁵⁵ Vivid visual images are those images, pictures or other visual stimuli that are emotionally or cognitively interesting, attention-getting, compelling, provoking, or personal in a sensory, temporal or spatial manner (after Nisbett, R., and Ross, L. (1980) *Human Inference: Strategies and Shortcomings of Social Judgment*. Englewood Cliffs, NJ: Prentice-Hall). Background music can also be distracting (Furnham, A., & Strbac, L. (2002). Music is as distracting as noise: The differential distraction of background music and noise on the cognitive test performance of introverts and extraverts. *Ergonomics*, 45, 203-217).

⁵⁶ See, e.g., Mackie, D.M., & Worth, L.T. (1989) Processing deficits and the mediation of positive affect in persuasion. *Journal of Personality and Social Psychology*, 57, 27-40; Manrai, L.A., Manrai, A.K., & Murray, N. (1994) Comprehension of info-aid supers in television advertising for social ideas: Implications for public policy. *Journal of Business Research*, 30, 75-84.

⁵⁷ Baker, S. (2006) Provision of effective information. *British Dental Journal*, 201, 100; Manrai, L.A., Manrai, A.K., & Murray, N. (1994) Comprehension of info-aid supers in television advertising for social ideas: Implications for public policy. *Journal of Business Research*, 30, 75-84.

⁵⁸ Paterson, D.G., & Tinker, M.A. (1941) Caps vs. lower-case in headlines. *Editor & Publisher*, 74, 51.

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674 • Contrast

675

676 Contrast is an important visual factor⁵⁹ that FDA considers when evaluating television ads and videos.⁶⁰

677 As in print pieces, risk disclosures presented in SUPERS should be in a font color that reasonably
678 contrasts with the background visuals. Because important non-benefit information is often conveyed by
679 SUPERS, any obstacle to the prominence and readability of this information, and thus to the audience’s
680 understanding of SUPERS, may result in a misleading risk presentation.

681

682 • Dual Mode Considerations

683

684 The interplay of visual and audio components in pieces such as television ads and videos introduces
685 unique factors FDA must consider when evaluating the adequacy of risk disclosure. The issues raised
686 above in Textual Elements about distracting visuals apply not only to the SUPER presentation but also to
687 the audio presentation of risks.⁶¹ If visuals in a broadcast ad distract the audience from the statement of a
688 product’s risks, the ad will not, as a whole, convey an accurate impression of the risks of the advertised
689 product. This distraction could be caused by factors including busy scenes, frequent scene changes,
690 moving camera angles, and even inherently compelling, vivid visuals. In addition, the overall tone of the
691 ad or of specific background visuals can affect the comparable prominence of the risks, particularly if the
692 tone is contrary to the risk message.

693

694 *Example 20:* A video or broadcast ad depicts a joyous or exhilarating moment, contains images of
695 people enjoying the benefits of the product, or includes otherwise compelling or distracting non-
696 risk related images while major risks are communicated in a voiceover. The inconsistent tone or
697 images may be too distracting for the audience to listen to or process the risks, causing the video
698 or broadcast ad to communicate a false or misleading net impression of the product.

699

700 • Audio Considerations

701

702 FDA considers several audio-related factors when evaluating pieces such as sound recordings, videos, or
703 broadcast ads, including television, radio, and telephone communications.

704

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

714

⁵⁹ Mitzner, T.L., & Rogers, W.A. (2006) Reading in the dark: Effects of age and contrast on reading speed and comprehension. *Human Factors*, 48, 229-240.

⁶⁰ Seibert, W.F., Kasten, D.F., & Potter, J.R. (1959) A study of factors influencing the legibility of televised characters. *Journal of the Society of Motion Picture & Television Engineers*, 68, 467-472.

⁶¹ See, e.g., Regan, D.T., & Cheng, J.B. (1973) Distraction and attitude change: A resolution. *Journal of Experimental Social Psychology*, 9, 138-147.

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IV. CONCLUSION

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The FDA’s regulation of prescription drug and medical device promotion to healthcare professionals and consumers is a broad and complex topic. A vast scientific body of knowledge is available regarding human cognition, and FDA relies on this knowledge when evaluating promotional pieces and making regulatory decisions about the presentation of benefit and risk information. The Agency hopes that by discussing the most relevant factors and by providing specific examples, manufacturers will gain a better understanding of what they should consider as they develop the content and format of their promotional communications.

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It is important to re-emphasize that, in addition to specific risk-related claims, FDA also considers the net impression conveyed by all the elements of a piece. For this reason, manufacturers should focus not just on individual claims or presentations, but on the messages conveyed by the promotional piece as a whole.

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ATTACHMENT: STATUTORY AND REGULATORY REQUIREMENTS FOR LABELING AND ADVERTISING

FDA regulates the manufacture, sale, and distribution of drugs and devices in the United States under the authority of the Federal Food, Drug, and Cosmetic Act (the Act). This authority includes oversight of labeling for all drugs and devices and of advertising for prescription drugs and restricted devices. 21 U.S.C. 352(a), (n), (q), & (r). In regulating the labeling and advertising of drugs and devices, FDA attends to the First Amendment.

The Act defines label to mean “a display of written, printed, or graphic matter upon the immediate container of any article” 21 U.S.C. 321(k). According to FDA regulations (21 CFR 1.3(b)): “Label means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.” The Act defines labeling to mean “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.” 21 U.S.C. 321(m). Similarly, FDA regulations (21 CFR 1.3(a)) provide that labeling includes “all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.”

According to *Kordel v. United States*, 335 U.S. 345, 350 (1948), the language “accompanying such article” in the “labeling” definition includes materials that supplement or explain an article, “in the manner that a committee report of the Congress accompanies a bill. No physical attachment one to the other is necessary. It is the textual relationship that is significant.” FDA’s prescription drug advertising regulations (21 CFR 202.1(l)(2)) thus provide as examples of labeling a wide variety of written, printed, or graphic matter that bears a textual relationship with a product.

FDA generally recognizes two types of labeling for drugs and devices: FDA-required labeling and promotional labeling. Much FDA-required labeling is subject to FDA review and approval. For example, after drafting by the manufacturer, required labeling is reviewed and approved by FDA as part of the new drug application (NDA), new animal drug application (NADA), biologics license application (BLA) or premarket approval application (PMA) review (21 CFR 314.50(c)(2), 514.1(b)(3), 601.2(a), and 814.20(b)(10)).

For devices that are not subject to premarket approval, but instead are subject to premarket notification requirements or are exempt from premarket review, there is no agency review or approval of labeling, but such devices remain subject to all of the requirements of applicable labeling regulations, including those for adequate directions for use. For a prescription drug or prescription device to be exempted from the Act’s requirement of adequate directions for use (21 U.S.C. 352(f)(1)), its FDA-required labeling must contain, among other information, information addressing product hazards and other risk information, as specified in FDA regulations.⁶²

Promotional labeling is generally any labeling other than the FDA-required labeling that is devised for promotion of the product. Promotional labeling may include items such as “brochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar

⁶² 21 CFR 201.100(d)(1), (3), 201.105(c)(1), & 801.109(d).

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775 pieces of printed, audio, or visual matter”⁶³ The Act specifies that a drug or device shall be deemed
776 to be misbranded if its labeling is false or misleading in any particular. 21 U.S.C. 352(a). The Act further
777 specifies that labeling or advertising may be considered misleading if it fails to reveal material facts about
778 the product being promoted, including facts about the consequences that can result from use of the
779 product as suggested in a promotional piece. 21 U.S.C. 321(n). In addition, the Act specifies that a drug
780 or device will be deemed to be misbranded if any word, statement, or other information required under
781 the Act to appear on the label or labeling is not “prominently placed thereon with such conspicuousness
782 (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to
783 render it likely to be read and understood by the ordinary individual under customary conditions of
784 purchase and use.” 21 U.S.C. 352(c).

785
786 Advertising⁶⁴ for prescription drugs and restricted devices is also subject to requirements under the Act
787 for the disclosure of risk and other information. Under section 502(n) of the Act (21 U.S.C. 352(n)) and
788 FDA’s implementing regulations (21 CFR Part 202), an ad for a prescription drug must include, in
789 addition to the product’s established name and quantitative composition, a “true statement” of information
790 in brief summary “relating to side effects, contraindications and effectiveness” of the product with respect
791 to the use or uses that the message promotes.⁶⁵ Advertisements for restricted devices must include “a
792 brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and
793 contraindications” 21 U.S.C. 352(r)(2). For prescription drug advertisements, FDA’s implementing
794 regulations specify that, among other things, the statutory requirement of a “true statement” is not
795 satisfied if an ad for a prescription drug product is false or misleading with respect to side effects,
796 contraindications or effectiveness or if it fails to reveal material facts about “consequences that may result
797 from the use of the drug as recommended or suggested in the advertisement.” 21 CFR 202.1(e)(5).
798 Similarly, the Act also specifies that restricted device advertisements must not be false or misleading (21
799 U.S.C. 352(q)(1)) and must reveal facts that are material about the product being advertised, including
800 facts about the consequences that can result from use of the product as suggested in an ad. 21 U.S.C.
801 321(n).

802
803 The prescription drug regulations also specify that ads must present a fair balance between information
804 relating to risks and benefits, which is achieved when the treatment of risk and benefit information in a
805 promotional piece is comparably thorough and complete throughout the piece. 21 CFR 202.1(e)(5)(ii).
806 These regulations also provide illustrations of the factors FDA considers in determining whether
807 promotional pieces comply with the above requirements relating to risk disclosure. Specifically, these
808 regulations identify twenty types of advertising communications that FDA considers “false, lacking in fair
809 balance, or otherwise misleading.” 21 CFR 202.1(e)(6). These include, for example, representations or
810 suggestions that a drug is more effective or safer than has been demonstrated by substantial evidence or
811 substantial clinical experience, the use of pictures or graphics in a way that is misleading, and the
812 presentation of risk information “by means of a general term for a group” rather than disclosing specific

⁶³ See, e.g., 21 CFR 202.1(1)(2).

⁶⁴ The act does not define “advertising” or “advertisement.” According to FDA regulations (21 CFR 202.1(1)(1)), “Advertisements subject to section 502(n) of the act include advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems.”

⁶⁵ According to 21 CFR 202.1(e)(3)(iii), the information in brief summary relating to side effects and contraindications 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 added).

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813 risks. 21 CFR 202.1(e)(6)(i), (xviii), & (xx). Representing or suggesting that a drug product is “safer
814 than has been demonstrated by substantial evidence or substantial clinical experience” means obscuring
815 or failing to include the most serious risk information set forth in the drug's FDA-approved labeling, and
816 does not refer to a failure to include risk information that is not set forth in the drug's FDA-approved
817 labeling.

818

819 In addition, these regulations identify thirteen additional types of advertising communications that “may
820 be false, lacking in fair balance, or otherwise misleading.” 21 CFR 202.1(e)(7). These include, for
821 example, advertising communications that fail to “present information relating to side effects and
822 contraindications with a prominence and readability reasonably comparable with the presentation of
823 information relating to effectiveness of the drug.” 21 CFR 202.1(e)(7)(viii).

824

825 Although the regulations discussed above were promulgated in the context of prescription drug
826 advertising, the guidance they provide on what FDA considers false or misleading in promotion has
827 broader applicability. For example, promotional pieces that fail to present a balanced view of the risks
828 and benefits of a product are generally considered to be false or misleading and also generally fail to
829 reveal material facts about the product being promoted. Because both labeling pieces for drugs and
830 devices, and advertising pieces for prescription drugs and restricted devices, are considered to misbrand a
831 product if they are false or misleading or fail to reveal material facts,⁶⁶ drug and device manufacturers
832 should take into account the guidance provided by these regulations when developing promotional
833 labeling and advertising pieces for their products.

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⁶⁶ 21 U.S.C. 352(a), (n), (q)(1) & 321(n); 21 CFR 202.1(e)(5).