
Medical Product Communications That Are Consistent With the FDA-Required Labeling — Questions and Answers

Guidance for Industry

DRAFT GUIDANCE

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Office of the Commissioner (OC)**

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Consistent With the FDA-Required Labeling — Questions and Answers
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3 **FDA-Required Labeling — Questions and Answers**
4 **Guidance for Industry¹**
5

6
7 This draft guidance, when finalized, will represent the current thinking of the Food and Drug
8 Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not
9 binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the
10 applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible
11 for this guidance as listed on the title page.
12

13
14
15 **I. INTRODUCTION**
16

17 This guidance provides information for firms² about how FDA evaluates firms' medical product³
18 communications, including promotional materials, that present information that is not contained
19 in the FDA-required labeling for the product but that may be consistent with the FDA-required
20 labeling for the product. As used in this guidance and further explained below, information that
21 is *consistent with the FDA-required labeling* is limited to information about the approved or
22 cleared⁴ uses of a product. The term *FDA-required labeling* as used in this guidance includes
23 the labeling reviewed and approved by FDA as part of the medical product marketing application
24 review process.⁵ For products not subject to premarket approval, but instead subject to
25 premarket notification requirements or exempt from premarket review, the term *FDA-required*
26 *labeling* also includes the labeling relied on to provide adequate directions for use and other
27 information required to appear on the label or in labeling.

¹ This guidance has been prepared by the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health, the Center for Veterinary Medicine, and the Office of the Commissioner at the Food and Drug Administration.

² The term *firms* refers to medical product manufacturers, packers, and distributors and their representatives.

³ The term *medical product(s)* refers to drugs and medical devices for humans, including those that are licensed as biological products, and animal drugs. See Q.1/A.1 in section III of this guidance.

⁴ For ease of reference, when *approval* and *clearance* (and similar terms) are used in discussing devices, the terms refer to FDA permitting the marketing of a device via the premarket approval, 510(k), *de novo* classification, or Humanitarian Device Exemption (HDE) pathway and to devices that are exempt from premarket notification.

⁵ Such labeling may include, for example, the FDA-approved prescribing information for a human drug (including a drug that is licensed as a biological product), including FDA-approved patient labeling, if any, that, under 21 CFR 201.100(d), must accompany any labeling distributed by or on behalf of the manufacturer, packer, or distributor of the drug; the FDA-approved prescribing information for an animal drug; or the labeling approved during the premarket approval process for a device.

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28
29 FDA has received a number of questions concerning this topic. As a result, FDA is providing
30 guidance in a question and answer format, addressing frequently asked questions.

31
32 In general, FDA’s guidance documents do not establish legally enforceable responsibilities.
33 Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only
34 as recommendations, unless specific regulatory or statutory requirements are cited. The use of
35 the word *should* in Agency guidances means that something is suggested or recommended, but
36 not required.

37
38

39 **II. BACKGROUND**

40

41 FDA determines whether a medical product is safe and effective for use under the conditions
42 prescribed, recommended, or suggested in the proposed labeling submitted to FDA with the
43 product’s marketing application or submission (and for devices, also during the classification
44 process).⁶ In making this determination, FDA evaluates whether the conditions of use in the
45 proposed labeling are supported by the required levels and types of evidence of safety and
46 effectiveness and whether the benefits of using the product under those specific conditions of use
47 outweigh the risks of the product. After FDA approves or clears a medical product, the FDA-
48 required labeling sets forth the conditions of use under which the product has been shown to
49 meet the relevant standard for marketing, and it provides directions and information on how to
50 use the product safely and effectively under those conditions.

51

52 The FDA-required labeling is the primary tool that FDA uses to communicate the essential
53 information needed for the safe and effective use of the product, and firms have an obligation to
54 update their FDA-required labeling as needed to ensure it is not false or misleading. The FDA-
55 required labeling is subject to content requirements and limitations to help ensure it effectively
56 communicates information. It is not intended to be an exhaustive summary of all that is known
57 about a product for its approved or cleared uses.

58

59 Medical product firms have told FDA that they are interested in communicating, including in
60 their promotional materials, data and information about the approved/cleared uses of their
61 products that are not contained in their products’ FDA-required labeling. We also recognize that
62 firms have questions about how FDA determines when communications that contain data and
63 information that are not in the FDA-required labeling are consistent with the FDA-required
64 labeling, and how such communications are viewed by FDA.

65

66 The purpose of this guidance is to provide clarity for firms regarding FDA’s thinking when
67 examining the consistency of a firm’s communications about a medical product with that

⁶ See, e.g., sections 505(d)(1), (2), (4) and (5); 512(d)(1)(A), (B), (D) and (E); 513(a)(2)(B); and 515(d)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The determination of whether a human or animal drug is not a new drug because it is generally recognized as safe and effective likewise turns on conditions prescribed, recommended, or suggested in its labeling. See sections 201(p) and (v) of the FD&C Act.

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68 product's own FDA-required labeling.⁷ As is explained in the questions and answers in
69 section III, firms' communications of information that is not contained in their product's FDA-
70 required labeling but that are determined to be consistent with the FDA-required labeling are not
71 alone considered evidence of a new intended use.

72
73 Because a communication that is consistent with a product's FDA-required labeling could
74 nonetheless misbrand the product and subject a firm to enforcement action if the representations
75 or suggestions made in the communication are false or misleading in any particular, this
76 guidance also provides general (but not comprehensive) recommendations for conveying
77 information that is consistent with the FDA-required labeling in a truthful and non-misleading
78 way, as well as examples to illustrate these concepts. These general recommendations are
79 specific to communications that are consistent with the FDA-required labeling; communication
80 of information that is not consistent with the FDA-required labeling is outside the scope of these
81 recommendations.

82
83

III. QUESTIONS AND ANSWERS

84

85 ***Q.1. What FDA-regulated products fall within the scope of this guidance?***

86

87
88 A.1. This guidance applies to drugs and devices for humans, including those that are
89 licensed as biological products, and animal drugs (collectively, *medical products*).

90

91 ***Q.2. How does FDA determine whether a firm's communication about a medical***
92 ***product is consistent with the FDA-required labeling for that product?***

93

94 A.2. FDA determines whether the representations or suggestions in a communication
95 about a product are consistent with the product's FDA-required labeling by
96 considering the three factors below. If a communication fails to satisfy any one of
97 these factors, it is not considered consistent with the FDA-required labeling. FDA
98 recognizes that there is overlap in these factors and expects that communications that
99 are not consistent with the FDA-required labeling may fail to satisfy multiple factors.

100

101 **Factor 1:** How the information in the communication compares to the information
102 about those conditions of use in the FDA-required labeling identified in the bullets
103 below⁸ — If the answer to any of the following questions is yes, that indicates the
104 communication is not consistent with the FDA-required labeling:

105

⁷ This guidance does not address considerations relating to the approval of generic drugs and biosimilar products involving the submission of information to show that the condition(s) of use in the labeling proposed for the proposed generic or biosimilar product have been previously approved for the reference product. See sections 505(j)(2)(A)(i) and 512(n)(1) of the FD&C Act; section 351(k)(2)(A)(i)(III) of the Public Health Service Act (PHS Act).

⁸ This guidance is not intended to provide a definitive FDA interpretation of *conditions of use* for all circumstances.

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- 106 • **Indication** – Do the representations/suggestions about the product in the
107 communication relate to a different indication than the one(s) reflected in the
108 product’s FDA-required labeling?
- 109 • **Patient Population** – Is the patient population represented or suggested in the
110 communication outside the approved/cleared patient population reflected in
111 the FDA-required labeling?
- 112 • **Limitations and Directions for Handling/Use** – Do the
113 representations/suggestions in the communication conflict with the use
114 limitations or directions for handling, preparing, and/or using the product
115 reflected in the FDA-required labeling?
- 116 • **Dosing/Administration** – Do the representations/suggestions about the
117 product conflict with the recommended dosage or use regimen, route of
118 administration, or strength(s) (if applicable) set forth in the FDA-required
119 labeling?

120 Factor 2: Whether the representations/suggestions in the communication increase the
121 potential for harm to health relative to the information reflected in the FDA-required
122 labeling —

123
124 When reviewing a medical product’s marketing application or submission (and in the
125 device classification process), FDA weighs the benefits and risks of a medical
126 product for the conditions of use prescribed, recommended, or suggested in the
127 product’s labeling and determines whether the benefits of using the product under
128 those conditions of use outweigh the potential or probable risks of the product. Under
129 certain circumstances, FDA may also consider additional risks and potential harms in
130 determining whether a product meets the relevant standard for marketing. For
131 example, FDA may assess the risks of abuse or misuse of certain products, the
132 potential for harm to the health of humans from certain animal drug uses, or the
133 potential for harm to health from secondary exposure to certain medical products. If
134 a communication alters the benefit-risk profile of a product in a way that may result
135 in increased harm to health, this indicates that the communication is not consistent
136 with the FDA-required labeling.⁹

137
138 Factor 3: Whether the directions for use in the FDA-required labeling enable the
139 product to be safely and effectively used under the conditions represented/suggested

⁹ For example, if a firm’s communication claims that its drug has superior effectiveness compared to another drug for treating a particular disease or condition, but its drug is reserved for third-line use due to severe risks associated with its use while the comparator drug is approved for first-line use as a result of its more favorable overall benefit-risk profile, such a communication has the potential to increase harm to the health of patients by suggesting use in a broader patient population (e.g., all patients with the disease/condition instead of just patients for whom first- and second-line therapies are not suitable) than the drug’s benefit-risk profile justifies. This communication could also fail on other factors, but this example is provided to illustrate how factor 2 is applied.

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140 in the communication — If the answer is no, that indicates the communication is not
141 consistent with the FDA-required labeling.

142
143 ***Q.3. Does FDA view firm communications that are consistent with the FDA-required***
144 ***labeling, alone, as providing evidence of a new intended use?***

145
146 A.3. No. If a firm’s communication is consistent with the FDA-required labeling, that
147 communication alone is not viewed by FDA as providing evidence of a new intended
148 use. In addition, FDA does not view a communication that is consistent with the
149 FDA-required labeling as failing to comply with the Federal Food, Drug, and
150 Cosmetic Act’s (FD&C Act) requirement that a medical product’s labeling bear
151 adequate directions for use (see section 502(f) of the FD&C Act) based solely on the
152 fact that it presents data and information that are not reflected in the product’s FDA-
153 required labeling.

154
155 Firms also must ensure their communications satisfy other applicable requirements
156 (see Q.6/A.6 and Q.7/A.7).

157
158 ***Q.4. What are examples of the kinds of information that could be consistent with the***
159 ***FDA-required labeling for a product?***

160
161 A.4. Below are examples of some general types of information that could be consistent
162 with the FDA-required labeling. Note that these examples are provided for
163 illustrative purposes only and are not intended to be comprehensive or restrictive.
164 Furthermore, not all representations or suggestions about a product that relate to the
165 general categories described in this answer will be consistent with the FDA-required
166 labeling for the specific product. That determination is fact-specific and is made by
167 evaluating the particular representations or suggestions being made in a
168 communication using the factors outlined in Q.2/A.2.

169
170 In addition, device firms should consider these examples in conjunction with the
171 Agency’s existing regulations, guidances, and policies, for example, regarding when a
172 special control may trigger certain labeling requirements for a specific device type or
173 when a modification to the indications for use of a device would trigger the need for a
174 new premarket submission. If the information that a firm wants to communicate
175 represents such a modification to the indications for use of the device, it would not be
176 considered consistent with the FDA-required labeling.

177
178 Also, as is further discussed in Q.6/A.6, if the representations or suggestions in a
179 firm’s communication are false or misleading, the communication would misbrand
180 the product and could subject the firm to enforcement action regardless of whether
181 the communication is consistent with the FDA-required labeling.

182
183 Examples of some types of information that could be consistent with the FDA-
184 required labeling include the following:

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- Information based on a comparison of the safety or efficacy of a medical product for its approved/cleared indication to another medical product approved/cleared for the same indication (e.g., a firm’s communication provides information from a head-to-head study indicating that its drug that is approved to treat high blood pressure in adults has superior efficacy to another drug that is also approved to treat high blood pressure in adults)
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- Information that provides additional context about the adverse reactions associated with the approved/cleared uses of the product reflected in the product’s FDA-required labeling (e.g., the FDA-required labeling for a product identifies nausea as a potential adverse reaction and further indicates the product can be taken with or without food. A firm’s communication about the product provides information about how taking a product with food might reduce nausea)¹⁰
- 198
- 199
- 200
- 201
- 202
- 203
- Information about the onset of action of the product for its approved/cleared indication and dosing/use regimen (e.g., the FDA-required labeling for a product approved/cleared to treat major depressive disorder does not contain information about onset of action prior to the point in time designated as the study’s endpoint, and a firm’s communication provides information indicating that the product shows an effect relative to the control at 2 weeks)
- 204
- 205
- 206
- 207
- Information about the long-term safety and/or efficacy of products that are approved/cleared for chronic use (e.g., a firm provides postmarketing information for its product, which was approved/cleared for chronic use based on 24-week study data, regarding persistent safety and/or efficacy over 18 months)
- 208
- 209
- 210
- 211
- 212
- 213
- Information about the effects or use of a product in specific patient subgroups that are included in its approved/cleared patient population (e.g., a firm’s communication provides information on the number of female patients that were studied in its pivotal clinical trials and the treatment effects in that patient group, or, in the case of a diagnostic product, the diagnostic performance in that patient group)

¹⁰ In June 2014, FDA issued a draft guidance entitled *Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products — Recommended Practices* (Risk Information Draft Guidance), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm400104.pdf>. That draft guidance relates to “information that becomes available after a drug is marketed that rebuts or mitigates information about a risk already identified in the approved labeling or otherwise refines risk information in the approved labeling in a way that does not indicate greater seriousness of the risk” (Risk Information Draft Guidance, page 3 (footnote omitted)). To the extent there is overlap between the Risk Information Draft Guidance and this draft guidance, FDA recommends that firms consider the recommendations in both draft guidances. When final, these guidances will represent FDA’s current thinking on these topics. Please check the FDA guidance Web page at <http://www.fda.gov/RegulatoryInformation/Guidances/default.htm> for the most current version of a guidance.

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- 214 • Information concerning the effects of a product that comes directly from the
215 patient (i.e., patient-reported outcomes) when the product is used for its FDA-
216 approved/cleared indication in its approved/cleared patient population (e.g., a
217 firm’s communication provides information concerning patient
218 compliance/adherence, or a firm’s communication provides information about
219 patients’ perceptions of the product’s effect on their basic activities of daily
220 living)
- 221 • Information concerning product convenience (e.g., a firm’s communication for its
222 drug product, which is indicated for the treatment and prevention of ectoparasites
223 in dogs, provides information about the convenient dosing schedule of the product
224 for pet owners based on its long duration of effect)
- 225 • Information that provides additional context about the mechanism of action
226 described in the FDA-required labeling (e.g., the FDA-required labeling for a
227 drug product indicates it exerts its effects by binding to a certain receptor, and a
228 firm’s communication provides additional information about the product’s
229 selectivity for that receptor)
- 230 ***Q.5. What are examples of the kinds of information that are not considered consistent***
231 ***with the FDA-required labeling for a product?***
232
- 233 A.5. Examples of some general types of information that are not considered consistent
234 with the FDA-required labeling include the following. As with the examples
235 provided in Q.4/A.4, note that these examples are provided for illustrative purposes
236 only and are not intended to be comprehensive.
237
- 238 • Information about the use of a product to treat or diagnose a different disease or
239 condition than the product is approved/cleared to treat or diagnose (e.g., a product
240 is approved/cleared to treat cardiovascular disease, and a firm’s communication
241 provides information about using the product to treat diabetes)
- 242 • Information about the use of a product to treat or diagnose patients who are not
243 included in the product’s approved/cleared patient population (e.g., a device is
244 cleared for use in individuals with cystic fibrosis (CF) for diagnosing a specific
245 CF gene mutation and a firm’s communication provides information about using
246 the device in individuals who do not have CF to determine if they are carriers of
247 the CF gene; an animal drug is approved only for use in feedlot cattle, and a
248 firm’s communication provides information about using the product in veal or
249 dairy cattle)
- 250 • Information about the use of a product to treat a different stage, severity, or
251 manifestation of a disease than the product is approved/cleared to treat (e.g., a
252 product is approved/cleared only to treat severe asthma, and a firm’s
253 communication provides information about using the product to treat patients with
254 mild asthma)

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- Information about the use of a product as monotherapy when it is only approved/cleared for use in conjunction with one or more other products or therapeutic modalities (e.g., the FDA-required labeling for a product indicates it is for use as an adjunct to surgery and radiation, and a firm’s communication provides information about using the product to treat patients who are not undergoing surgery and radiation)
 - Information about using a product through a different route of administration or in a different tissue type than the product is approved/cleared for (e.g., a product is approved only for intramuscular injection, and a firm’s communication indicates the product can be injected intravenously)
 - Information about the use of a different strength, dosage, or use regimen than the approved/cleared strength, dosage, or use regimen (e.g., the FDA-required labeling for a drug indicates it should be taken twice a day 12 hours apart, and a firm’s communication represents that the product can instead be taken once a day, with both doses being taken together in the morning)
 - Information about the use of a product in a different dosage form than what is set forth in the FDA-required labeling (e.g., the product’s approved dosage form is a capsule, and a firm’s communication provides information about use of the product as an oral solution)

276 ***Q.6. What evidentiary support should a firm have for its communications that are***

277 ***consistent with the FDA-required labeling?***

278

279 A.6. Communications that lack appropriate evidentiary support are likely to be false or

280 misleading and can cause patient harm. Under the FD&C Act and implementing

281 regulations, labeling and FDA-regulated advertising materials are required to be

282 truthful and non-misleading, which includes revealing facts that are material about the

283 product being promoted, including information about the risks of the product.¹¹ To

284 be truthful and non-misleading, representations or suggestions made by firms about

285 their products need to be grounded in fact and science and presented with appropriate

286 context. Any data, studies, or analyses relied on should be scientifically appropriate

287 and statistically sound to support the representations or suggestions made in the

288 communication. In addition, the evidence should be accurately characterized in the

289 communication, including limitations of the strength of the evidence and the

290 conclusions that can be drawn from it (see Q.8/A.8). However, firms should note that

291 if a communication relies on a study that is inadequate to support the representations

292 or suggestions it presents, disclosure of the material limitations of that study does not

293 correct the misleading message conveyed by the communication.

294

¹¹ See, e.g., sections 201(n), 502(a), 502(n), 502(q), and 502(r) of the FD&C Act; 21 CFR 202.1(e)(5).

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295 The safety and effectiveness of the drug or device under the conditions of use in the
296 FDA-required labeling have already been established by appropriate evidence during
297 the premarket review process (and/or through the device classification process).
298 Therefore, FDA would not consider representations or suggestions in a
299 communication that is consistent with the FDA-required labeling to be false or
300 misleading based only on the lack of evidence sufficient to satisfy the applicable
301 approval/clearance standard. Nevertheless, the communication could be false or
302 misleading for other reasons. Accordingly, the representations or suggestions should
303 be supported and presented as described in this guidance.

304
305 For example, certain analyses of pivotal trial data may provide information that
306 elaborates on the data reflected in the product's FDA-required labeling and could
307 improve understanding of a product (e.g., information from separate analyses of the
308 individual components of a composite endpoint that was successfully used as the
309 primary endpoint and that are derived from appropriate statistical tests¹² and pre-
310 specified in the statistical analysis plan). However, if the pivotal trial was, for
311 example, not adequately powered to determine treatment effect on the individual
312 components of the composite endpoint and/or type 1 error (false positive rate) was
313 not controlled for these analyses, these analyses would generally not support
314 conclusions about a treatment effect of the product on the individual components of
315 the composite endpoint. In such a case, representing or suggesting that the data
316 support such efficacy conclusions, either directly (e.g., by claiming the product has
317 demonstrated efficacy on the individual components) or indirectly (e.g., by presenting
318 p-values, which would imply a statistically rigorous conclusion where one does not
319 exist), would be false or misleading.

320
321 ***Q.7. What other considerations apply to communications that are consistent with the***
322 ***FDA-required labeling?***

323
324 ***A.7.*** In addition to the standards for scientific substantiation addressed in Q.6/A.6, firms
325 should ensure their FDA-regulated promotional materials otherwise satisfy the
326 applicable requirements of the FD&C Act and FDA's implementing regulations.

327
328 Nothing in this draft guidance is intended to change a firm's existing obligations
329 under the FD&C Act, the Public Health Service Act (PHS Act), or FDA's
330 implementing regulations to update its FDA-required labeling to ensure that the

¹² See, e.g., FDA's guidance *E9 Statistical Principles for Clinical Trials* (September 1998), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073137.pdf>; FDA's guidance *Design Considerations for Pivotal Clinical Investigations for Medical Devices* (November 2013), available at <http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm373750.htm>; and FDA's guidance *Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests* (March 2007), available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071148.htm>.

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331 labeling is not false or misleading or for other reasons.¹³ In addition, as outlined in
332 Q.4/A.4, this draft guidance is not intended to change the Agency’s existing
333 regulations, guidances, and policies regarding when a modification to the indications
334 for use of a device would trigger the need for a new premarket submission.
335

336 ***Q.8. What does FDA recommend that firms consider when developing communications***
337 ***that are consistent with the FDA-required labeling to help ensure that the***
338 ***presentation of this information does not render the communication false or***
339 ***misleading?***
340

341 **A.8.** The way a firm presents information that is consistent with the FDA-required labeling
342 (including the express and implied claims made and the overall impression created by
343 the communication as a whole) affects how the information is understood. The
344 following are some high-level recommendations for firms to consider when
345 developing their presentations of information that is consistent with the FDA-required
346 labeling to help ensure the presentations do not mislead the applicable audience(s):
347

- 348 • Any study results or other data and information that are relied upon to support a
349 firm’s communication should be accurately represented in the communications.
350 Moreover, material aspects of study design and methodology for any studies
351 relied on should be clearly and prominently disclosed in firms’ communications
352 to allow audiences to accurately interpret the information (e.g., type of study,
353 study objectives, product dosage/use regimens, controls used, patient population
354 studied), and material limitations related to the study design, methodology, and
355 results should also be disclosed in a clear and prominent manner.
- 356 • The communication should accurately characterize and contextualize the relevant
357 information about the product, including by disclosing unfavorable or inconsistent
358 findings. For example, if a firm presents efficacy results from a postmarketing
359 study of its product that evaluated the effect of the product on two different
360 endpoints, such as overall survival and progression-free survival, and the product
361 failed to demonstrate an effect on one of these two endpoints, the firm should
362 disclose this in the communication, rather than selectively presenting only the
363 positive efficacy results.
- 364 • For communications that present data or information that is not in the FDA-
365 required labeling, but where the FDA-required labeling contains other data or
366 information related to what is being represented/suggested in the communication,
367 the communication should also include the data or information from the FDA-

¹³ See, e.g., 21 CFR 201.56(a)(2) (“[approved] labeling must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading”); 21 CFR 314.70 and 601.12 (concerning supplements and other changes to an approved application, including labeling); 21 CFR 514.8(c) (concerning supplements and other changes to an approved application for a new animal drug, including labeling); 21 CFR 814.39 (concerning supplements to an approved premarket approval application (PMA), including labeling); and 21 CFR 814.108 (concerning supplements to an approved HDE application, including labeling).

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368 required labeling to provide the audience with appropriate context. For example,
369 if a communication provides postmarketing information about the types and rates
370 of occurrence of adverse events that have been observed in practice, the
371 communication should also include information from the FDA-required labeling
372 about the types and rates of occurrence of adverse reactions observed in clinical
373 trials to provide context.

374 The considerations described above are not intended to be a comprehensive summary
375 of everything a firm should factor into its analysis of whether its presentations are
376 truthful and non-misleading. FDA recommends that, before disseminating a
377 communication regarding a medical product, firms should have qualified medical,
378 legal, and regulatory personnel carefully review the communication to ensure it is not
379 false or misleading.
380

381 ***Q.9. What are some examples of communications that are consistent with the FDA-***
382 ***required labeling and with the recommendations in this guidance?***
383

384 A.9. Below are two examples of communications FDA would consider to be consistent
385 with the FDA-required labeling and the recommendations in Q.6/A.6 and Q.8/A.8.
386

387 ***Example 1:*** Product B is an Immune Globulin Intravenous (Human), 10% liquid
388 indicated for the treatment of primary humoral immunodeficiency (PI) and chronic
389 immune thrombocytopenic purpura (IPT). Product B's firm develops promotional
390 materials which communicate that clearance of Product B is comparable in males and
391 females taking it to treat PI and IPT. These materials cite to the pharmacokinetic
392 information obtained from the pivotal study of the product.
393

394 *Is this consistent with the FDA-required labeling?* Yes. This claim about the product
395 is within the scope of the uses approved by FDA, as the FDA-required labeling
396 reflects that the product is indicated for use in both males and females to treat PI and
397 IPT, and does not contain any limitations or directions or other special considerations
398 related to the gender of patients using the product. The representation about similar
399 clearance of the product in males and females is not expected to increase the potential
400 for harm to patients, and the directions in the FDA-required labeling enable the
401 product to be safely and effectively used to treat PI and IPT regardless of gender.
402 This would be an example of a communication that FDA would consider to be
403 consistent with the FDA-required labeling.
404

405 *Is this truthful and non-misleading?* Yes, assuming the clearance information from
406 the pivotal study is accurately reported in the firm's promotional materials and the
407 material aspects of the underlying study design and methodology are disclosed,
408 including any material limitations of the information. As indicated in Q.7/A.7, the
409 firm should also ensure the rest of the information in the promotional materials is
410 truthful and non-misleading and satisfies any other applicable requirements.
411

412 ***Example 2:*** An implantable device is approved for use as an adjunctive therapy for
413 reducing symptoms of a chronic disease that are not adequately controlled by

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414 medication. The device is clinician/patient-controlled based on the disease state and
415 symptoms. The directions for use do not prescribe a specific use schedule. In the
416 clinical study that supported the device's premarket approval application (PMA),
417 approximately half of the patients using the device reported severe headaches, but
418 many patients tolerate this risk because of the benefits of amelioration of symptoms
419 associated with their chronic illness.

420
421 The firm enrolled patients with the implanted device in a postmarketing registry,
422 which was designed to better identify and quantify rare adverse events and evaluate
423 the longer-term effectiveness of the therapy. In addition to clinical visits for follow-
424 up, patients used a diary to record device use, symptoms, and adverse events. Data
425 from the registry suggest that patients who use the device more frequently and for
426 shorter periods of time (such use is consistent with the approved labeling) have a
427 reduced incidence of severe headaches associated with use of the device compared to
428 that reported in the PMA-approved labeling.

429
430 The device firm develops promotional materials to communicate this information;
431 these materials also outline specific information regarding the registry, including the
432 number of patients enrolled in the registry, patient population, outcome measures, and
433 a summary of the device use, as well as symptoms and adverse events reported in the
434 patient diaries. The proposed communications clearly disclose that the trends related
435 to the diary information are descriptive, not statistically powered, and not pre-
436 specified, meaning the relationship between the use patterns described and the
437 reduced incidence of severe headaches is only hypothesized and that no conclusions
438 can be drawn from the data. They also disclose the data from the premarket clinical
439 study along with the registry data to provide context.

440
441 *Is this consistent with the FDA-required labeling?* Yes. These representations about
442 the use of the product are within the scope of the uses approved by FDA, as the
443 product is being used for its approved indication in its approved patient population
444 and in a manner that comports with the directions for use in the FDA-required
445 labeling. These representations are not expected to increase the potential for harm to
446 patients relative to the information reflected in the FDA-required labeling. The
447 directions for use in the FDA-required labeling enable the product to be safely and
448 effectively used under the conditions represented in the communication. While the
449 communication provides supplementary information about use of the device in a
450 specific manner, the information provided is consistent with the directions for use in
451 the labeling, which do not prescribe a specific use schedule, and the information does
452 not otherwise alter or compromise the directions for use in the FDA-required
453 labeling. A firm's communication of this information would be considered consistent
454 with the FDA-required labeling.

455
456 *Is this truthful and non-misleading?* If the data and information are being accurately
457 reported in the firm's promotional materials and the material aspects of the
458 underlying study design and methodology are disclosed in the materials, including
459 material limitations of the information, FDA would consider this to be truthful and

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460 non-misleading. Provided the rest of the information in the promotional materials is
461 truthful and non-misleading, this is an example of a communication that FDA would
462 also consider to be consistent with the recommendations in Q.6/A.6 and Q.8/A.8.

463
464 ***Q.10. What are examples of communications FDA would consider to be inconsistent with***
465 ***the FDA-required labeling or inconsistent with the recommendations in this***
466 ***guidance?***

467
468 A.10. Below are two examples. The first example illustrates a communication that FDA
469 would consider to be inconsistent with the FDA-required labeling, and the second
470 example illustrates a communication that FDA would consider to be inconsistent with
471 the recommendations in Q.6/A.6 and Q.8/A.8.

472
473 ***Example 1:*** A drug is indicated for the treatment of bovine respiratory disease (BRD)
474 associated with certain susceptible bacteria in beef and non-lactating dairy cattle. The
475 firm develops promotional materials to communicate information about the use of the
476 drug to prevent BRD if used 5 days before shipment of cattle.

477
478 *Is this consistent with the FDA-required labeling?* No. These representations about
479 the use of the product are not within the scope of the uses approved by FDA.
480 Treatment of BRD and prevention of BRD are distinct indications, and this drug is
481 not approved for prevention of BRD. The benefit/risk profile of the product for the
482 unapproved disease prevention indication could be materially different than for the
483 approved treatment indication, and the FDA-required labeling for treatment of BRD
484 does not provide directions for using the product for disease prevention. The
485 administration of the drug to cattle 5 days before shipment to prevent BRD could
486 increase the potential for harm to health (including harm to the health of cattle and of
487 humans) from resistant bacteria originating from treated cattle. FDA considers
488 appropriate risk factors, including considerations of animal and public health, in
489 determining whether an animal drug product is safe and effective under particular
490 conditions of use.

491
492 ***Example 2:*** Drug A is approved for the long-term, maintenance treatment of asthma
493 patients 12 years of age and older. The safety and efficacy of Drug A for this
494 indication was evaluated versus placebo treatment in a randomized, double-blind
495 study. The study also included an active comparator (Drug B), approved for the same
496 indication and with a comparable risk profile, which was similarly evaluated versus
497 placebo. The study was not designed to test the non-inferiority or superiority of Drug
498 A directly against Drug B (i.e., the Drug B arm was included for assay sensitivity).
499 Drug A and Drug B demonstrated statistically significant improvements versus
500 placebo in the co-primary efficacy endpoints, but Drug A's results showed a
501 numerically greater improvement versus placebo than those for Drug B. Based on
502 this study, Drug A's firm develops promotional materials to communicate that Drug
503 A is clinically superior to Drug B for the long-term, maintenance treatment of asthma
504 patients 12 years of age and older.

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506
507 *Is this consistent with the FDA-required labeling?* Yes. The information the firm
508 proposes to present is within the scope of the uses approved by FDA for Drug A. The
509 communication relates to the indicated use of Drug A in the approved patient
510 population at the same dosing strength and frequency recommended in the FDA-
511 required labeling. The information is not expected to increase the potential for harm
512 to the health of patients relative to the information reflected in the FDA-required
513 labeling — both Drug A and Drug B are approved for the same indication and patient
514 population and have similar risk profiles. Furthermore, the directions in the FDA-
515 required labeling enable Drug A to be safely and effectively used under the
516 conditions presented in the communication. This communication could be considered
517 consistent with the FDA-required labeling.

518
519 *Is this truthful and non-misleading?* No. The communication is misleading because
520 it makes a claim of superior effectiveness for Drug A versus Drug B based on a study
521 that was not designed to evaluate superiority or non-inferiority of Drug A to Drug B.
522 Thus, the communication would not be consistent with the recommendations in
523 Q.6/A.6 and Q.8/A.8.

524
525 If the firm wishes to present data and information from this study, it should do so in a
526 truthful and non-misleading way. For example, the firm could describe the study
527 design and objectives, including the material limitations of both, and include
528 prominent contextual information that the study was not designed to provide
529 comparative efficacy data and should not be interpreted as providing evidence of
530 superiority or non-inferiority of Drug A to Drug B. The communication should not
531 contain representations or suggestions that are not supported by appropriate evidence,
532 such as any representation or suggestion of Drug A's superior effectiveness over
533 Drug B.

534
535 ***Q.11. What are the Agency's policies for communication of information that is not***
536 ***consistent with the FDA-required labeling (i.e., information about unapproved uses***
537 ***of approved/cleared medical products)?***

538
539 A.11. FDA has issued a draft guidance describing its thinking on how firms can respond to
540 unsolicited requests for unapproved use information related to their FDA-approved
541 prescription drugs and FDA-approved or cleared devices.¹⁴ In addition, FDA has
542

¹⁴ FDA's draft guidance *Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices Practices* (December 2011), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM285145.pdf>. When final, this guidance will represent FDA's current thinking on this topic.

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543 provided separate guidances describing recommended practices for the dissemination
544 by firms of scientific and medical publications discussing unapproved uses of
545 approved drugs or approved or cleared devices.^{15,16}
546
547
548
549

¹⁵ FDA's guidance *Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publication on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices* (January 2009), available at <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm>.

¹⁶ FDA's revised draft guidance *Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices* (February 2014), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm387652.pdf>. When final, this guidance will represent FDA's current thinking on this topic.