
Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs

Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

**June 2019
Electronic Submissions**

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Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs Guidance for Industry

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Contains Nonbinding Recommendations

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1 **Providing Regulatory Submissions in Electronic and Non-Electronic**
2 **Format — Promotional Labeling and Advertising Materials for**
3 **Human Prescription Drugs**
4 **Guidance for Industry¹**
5

6
7 This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on
8 this topic. It does not establish any rights for any person and is not binding on FDA or the public.² You
9 can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.
10 To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the
11 title page.
12

13
14
15 **I. INTRODUCTION**
16

17 This guidance pertains to submissions of promotional materials for human prescription drugs
18 (drugs)³ to the Food and Drug Administration (FDA or Agency) made by manufacturers,
19 packers, and distributors (firms), whether the applicant or an entity acting on behalf of the
20 applicant. Specifically, this guidance pertains to submissions made to the Office of Prescription
21 Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) and the
22 Advertising and Promotional Labeling Branch (APLB) in the Center for Biologics Evaluation
23 and Research (CBER). This guidance also explains certain aspects of electronic submission of
24 promotional materials in module 1 of the electronic common technical document (eCTD), using
25 version 3.3 or higher of the *us-regional-backbone* file.
26

¹ This guidance has been prepared by the Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) in cooperation with the Advertising and Promotional Labeling Branch (APLB) in the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration (FDA).

² This sentence does not apply to the discussion regarding the format for electronic submissions under section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

³ The recommendations in this guidance apply to biological products that are approved for marketing under section 351 of the Public Health Service Act (PHS Act) and that also meet the definition of “drug” under section 201(g) of the FD&C Act. For such products, the provisions of the FD&C Act applicable to drugs also apply, as well as the regulations implementing these provisions, except that a biological product licensed under section 351 of the PHS Act is not required to have an approved new drug application under section 505 of the FD&C Act (21 U.S.C. 355). See section 351(j) (42 U.S.C. 262(j)) of the PHS Act. Therefore, references to “drugs” in this guidance also include human biological products that fall within the definition. However, this guidance does not apply to those devices that CBER regulates as biological products under section 351 of the PHS Act. These submissions are subject to the requirements under section 745A(b) of the FD&C Act. The electronic submission requirements of section 745A(b) fall outside the scope of this guidance and are not discussed in this guidance. We note, however, that FDA issued the guidance for industry and FDA staff *eCopy Program for Medical Device Submissions* (December 2015) that implements the electronic copy provisions of section 745A(b) for medical device submissions to FDA. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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27 For the purpose of this guidance, the term *promotional materials* collectively refers to
28 promotional labeling and advertising materials, regardless of the format, manner, or medium by
29 which they are presented. Promotional materials may include, but are not limited to, television
30 advertisements (ads), brochures, booklets, detailing pieces, internet websites, print ads, exhibits,
31 sound recordings, and radio ads.

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

38
39 An exception to that framework derives from section 745A(a) of the Federal Food, Drug, and
40 Cosmetic Act (FD&C Act), wherein Congress granted authorization to FDA to require that
41 submissions under section 505(b), (i), or (j) of the FD&C Act and submissions under section
42 351(a) or (k) of the Public Health Service Act (PHS Act) be submitted in an electronic format
43 specified by FDA through guidance. Accordingly, insofar as this guidance requires that
44 submissions under section 505(b), (i), or (j) of the FD&C Act and submissions under section
45 351(a) or (k) of the PHS Act be submitted in electronic format specified by FDA, this
46 document is not subject to the usual restriction in FDA’s good guidance practice regulations that
47 guidances not establish legally enforceable responsibilities.⁴ Therefore, the portion of this
48 guidance that establishes the requirement for electronic submissions under section 745A(a) of the
49 FD&C Act has binding effect, as indicated by the use of the words *must, shall, or required*.

50
51

52 **II. BACKGROUND**

53 54 **A. Electronic Submissions to FDA Under Section 745A(a) of the Federal Food, 55 Drug, and Cosmetic Act**

56
57 Section 745A(a) of the FD&C Act, added by section 1136 of the Food and Drug Administration
58 Safety and Innovation Act (FDASIA) (Public Law 112-144), requires that submissions under
59 section 505(b), (i), or (j) of the FD&C Act and submissions under section 351(a) or (k) of the
60 PHS Act be submitted in electronic format specified by FDA beginning no earlier than 24
61 months after FDA issues a guidance specifying such electronic submission format. Certain types
62 of promotional-material-related submissions discussed in this guidance are “submissions under
63 subsection (b), (i), or (j) of section 505 of this Act or subsection (a) or (k) of section 351 of the
64 Public Health Service Act” and are, therefore, subject to the requirements of section 745A(a).
65 Specifically, this includes the following:

- 66
67 • Postmarketing submissions of promotional materials using Form FDA 2253 (required by 21
68 CFR 314.81(b)(3)(i) and 21 CFR 601.12(f)(4))
69

⁴ See 21 CFR 10.115(d).

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- 70 • Submissions of promotional materials for accelerated approval products (required by section
71 506(c)(2)(B) of the FD&C Act, 21 CFR 314.550, and 21 CFR 601.45) and other products
72 where such submissions are required for approval⁵ under section 505(b), (i), or (j) of the
73 FD&C Act
74

75 The guidance for industry *Providing Regulatory Submissions in Electronic Format —*
76 *Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act* (December
77 2014) (the 745A(a) Implementation Guidance) sets forth general information on how FDA
78 interprets and intends to implement the electronic submission requirements of section 745A(a) of
79 the FD&C Act. The 745A(a) Implementation Guidance states that it is not feasible to describe
80 and implement the electronic format(s) that would apply to all the submissions covered by
81 section 745A(a) in one guidance document. Instead, FDA will periodically issue guidances
82 specifying the electronic format for certain types of submissions. The guidance for industry
83 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical*
84 *Product Applications and Related Submissions Using the eCTD Specifications* (April 2018) (the
85 eCTD Guidance) specifies the general format for certain types of electronic submissions using
86 the eCTD, including the specifications for module 1.⁶
87

88 In addition to the more general information and implementation timeline found in those
89 guidances, this guidance provides additional information regarding the format to use for
90 electronic submission of promotional labeling and advertising materials, using the eCTD.
91 Accordingly, 24 months after the issuance of this guidance, firms will be required to submit
92 electronically all promotional submissions that fall within the scope of section 745A(a) as
93 specified in this guidance. As of that date, paper copies will no longer be accepted for such
94 submissions. Note that although only the promotional submissions discussed in sections IV.A
95 and IV.B that fall within the scope of section 745A(a) will be *required* to be submitted
96 electronically in the format specified in this guidance, firms *may* voluntarily choose to submit
97 electronically other types of promotional material submissions discussed in this guidance.⁷
98

99 This document also discusses types of promotional materials that are *not* subject to the
100 mandatory electronic submission requirement in section 745A, (i.e., all promotional materials
101 discussed in this document other than postmarketing submissions of promotional materials using

⁵ In the *Federal Register* of May 31, 2002 (67 FR 37988), FDA published final regulations (21 CFR 314.640 (subpart I) and 21 CFR 601.94 (subpart H)) under which the Agency would allow appropriate studies in animals, in certain cases, to provide substantial evidence of the effectiveness of new drug and biological products used to reduce or prevent the toxicity of chemical, biological, radiological, or nuclear substances. This rule applies when adequate and well-controlled clinical studies in humans cannot be ethically conducted and field efficacy studies are not feasible. Sponsors with products approved under these provisions are subject to similar presubmission requirements as accelerated approval products and can use the same procedures outlined in this guidance for submitting promotional materials to FDA.

⁶ The current version of the associated technical specification *The eCTD Backbone Files Specification for Module 1* provides additional information. See the FDA eCTD website at <https://www.fda.gov/ectd>.

⁷ Firms may immediately begin to submit promotional submissions electronically, whether or not the submissions fall within the scope of section 745A(a) of the FD&C Act (i.e., it is not necessary to wait until 24 months after the issuance of this guidance).

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102 Form FDA 2253 and submissions of promotional materials for accelerated approval products, as
103 discussed in sections IV.C through K of this guidance).

104

B. Promotional Labeling and Advertising

106

107 Section 201(m) of the FD&C Act defines *labeling* as “all labels and other written, printed, or
108 graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying
109 such article” (21 U.S.C. 321(m)).⁸ The U.S. Supreme Court has explained that the language
110 “accompanying such article” in the labeling definition is interpreted broadly to include materials
111 that supplement or explain an article. No physical attachment between the materials and the
112 article is necessary; rather, it is the textual relationship between the items that is significant
113 (*Kordel v. United States*, 335 U.S. 345, 350 (1948)).

114

115 FDA generally recognizes two types of labeling for drugs: (1) FDA-required labeling and
116 (2) promotional labeling. FDA-required labeling is labeling that is necessary to fulfill the
117 minimum requirements of the FD&C Act and its implementing regulations. For prescription
118 drugs, the required labeling is the labeling, drafted by the manufacturer, that is reviewed and
119 approved by FDA as part of a new drug application (NDA), an abbreviated new drug application
120 (ANDA), or a biologics license application (BLA) (21 CFR 314.50(c)(2), 314.94(a)(8), and
121 601.2(a)). Promotional labeling is generally any labeling, other than the FDA-required labeling,
122 that is devised for promotion of the product. Examples of materials that may be considered
123 promotional labeling pieces for prescription drugs are described in 21 CFR 202.1(l)(2).

124

125 The FD&C Act does not define what constitutes an *advertisement*, but FDA regulations provide
126 several examples including, but not limited to, materials “in published journals, magazines, other
127 periodicals, and newspapers and in advertisements broadcast through media such as radio,
128 television, and telephone communication systems” (21 CFR 202.1(l)(1)).

129

130

III. GENERAL CONSIDERATIONS

132

133 All submissions of promotional materials should meet a set of criteria in order to be reviewed by
134 the Agency. Firms should ensure that the following information is provided and considerations
135 are met when submitting promotional materials, regardless of the format in which the materials
136 are submitted:

137

138 • Include the appropriate NDA, ANDA, or BLA number.

139

140 • For OPDP, address submissions that require correspondences to the attention of the OPDP
141 Project Manager.

142

143 • Use the most specific material type (from Form FDA 2253) to describe the promotional
144 material that is the subject of the submission (e.g., do not use the code “promotional

⁸ See 21 CFR 1.3(a).

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- 145 labeling” when another code is available that gives a more specific description of the
146 promotional material).
- 147
- 148 • Submit different types of promotional material submissions separately (e.g., do not submit
149 materials on Form FDA 2253 per the requirement in 21 CFR 314.81(b)(3)(i)) together with
150 a voluntary request for advisory comments⁹ on launch materials).
 - 151
 - 152 • Submit promotional materials separately from other types of submissions (i.e., submissions
153 not related to promotional materials).
 - 154
 - 155 • Submit promotional materials directed to health care professionals separately from
156 submissions of promotional materials directed to consumers.
 - 157

158 Occasionally, promotional materials may be directed to both consumers and health care
159 professionals. In those circumstances, firms should identify the audience type based on the end-
160 user for the bulk of the information. For example, press releases should be submitted as
161 consumer-directed materials unless they are specifically intended for health care professionals.
162 Websites with distinct sections for health care professionals and consumers should be divided
163 into two separate submissions. If the website does not have distinct sections for each audience
164 and is not intended to be directed solely to health care professionals, firms should submit the
165 entire website as a consumer submission.

166

167 In cases where a company that holds the application collaborates with another firm to promote
168 the drug (e.g., a collaborative marketing agreement where another firm that is not the application
169 holder disseminates and submits promotional materials based on a contractual agreement with
170 the application holder), the application holder should send a general correspondence submission
171 to OPDP or APLB describing the agreement. In addition, the business relationship should be
172 indicated in subsequent submissions of promotional materials.

173
174

175 **IV. CONTENT FOR SPECIFIC TYPES OF SUBMISSIONS¹⁰**

176

177 The content of various types of submissions to the Agency relating to promotional materials is
178 described below and applies to submissions in both eCTD and non-eCTD format. Also, as
179 described in section II of this guidance, submissions described below under sections IV.A and
180 IV.B must be submitted electronically per the requirements in section 745A(a) of the FD&C Act.
181 The advertising and promotional labeling submissions described below represent the types of
182 submissions that FDA currently receives.

183

⁹ Reference in this guidance to the voluntary request for advisory comment(s) on proposed promotional materials by firms is distinct from and not to be confused with the process identified in 21 CFR 10.85.

¹⁰ Please refer to section VI of this guidance for information on how to submit promotional materials in module 1 of the eCTD using *us-regional-v3-3.dtd* or higher. Note that complaints should not be submitted using this process.

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184 **A. Promotional Materials Submitted in Fulfillment of the Postmarketing** 185 **Reporting Requirements (Form FDA 2253 Submissions)**

186
187 Under the FD&C Act and FDA's regulations implementing postmarketing reporting
188 requirements, applicants must submit specimens of mailing pieces and any other labeling or
189 advertising devised for promotion of the drug product at the time of initial dissemination of the
190 labeling and at the time of initial publication of the advertisement for a prescription drug product
191 (21 CFR 314.81(b)(3)(i) and 21 CFR 601.12(f)(4)). Each submission (also referred to as a 2253
192 submission) is required to be accompanied by a completed fillable Form FDA 2253 (Transmittal
193 of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use) and is
194 required to include a copy of the product's current professional labeling (21 CFR 314.81(b)(3)(i)
195 and 21 CFR 601.12(f)(4)).¹¹

196
197 The following provides details on submitting promotional materials in fulfillment of
198 postmarketing reporting requirements. OPDP and APLB have different procedures, so firms
199 should pay careful attention to the following information.

200
201 Firms are required to include the following:

- 202
- 203 • Form FDA 2253: Transmittal of Advertisements and Promotional Labeling for Drugs and
204 Biologics for Human Use. (For OPDP submissions, submit this form with *final* promotional
205 materials only.) Firms must use the most current version of the fillable Form FDA 2253.^{12,13}
206
 - 207 - On Form FDA 2253, Box 14 titled "For CBER Products Only":
 - 208 ○ OPDP: Do NOT check the "Draft" or "Final" boxes.
 - 209 ○ APLB: Check the "Final" box only for Final postmarketing submissions.
 - 210
 - 211 - For cases where promotional materials mention multiple products, note the lead
212 application number on Form FDA 2253 and include an attachment that identifies the
213 other referenced products (e.g., application type and number, trade name, established
214 name).
 - 215
 - 216 • Promotional material(s).
 - 217
 - 218 • Current product labeling.
 - 219

¹¹ For more information, see the draft guidance for industry *Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics* (January 2014). When final, this guidance will represent FDA's current thinking on this topic.

¹² The most current version of Form FDA 2253 can be found on the OPDP web page at <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090142.htm>.

¹³ Do not include Form FDA 356h for submissions to OPDP or APLB.

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220 Firms are also encouraged, but not required, to submit annotated versions of the promotional
221 material(s) cross-referenced to the product labeling and references, if applicable.
222

223 Professional and consumer materials should be submitted separately and should not include a
224 cover letter or correspondence. For 2253 submissions to OPDP, if a drug has multiple approved
225 indications that are covered by different reviewers in OPDP,¹⁴ firms should submit (when
226 possible) promotional materials that only promote one indication separately from promotional
227 materials that promote only another indication. In such cases, firms may choose to communicate
228 the indication being promoted in the promotional materials in the Comments section of Form
229 FDA 2253.
230

B. Presubmission of Promotional Materials for Accelerated Approval Products

233 Applicants whose drug products are approved under the accelerated approval framework (section
234 506(c) of the FD&C Act, 21 CFR 314 (subpart H), and 21 CFR 601 (subpart E)) and applicants
235 with other products where such submissions are required for approval must submit promotional
236 materials to OPDP and APLB as required under section 506(c)(2)(B) of the FD&C Act, 21 CFR
237 314.550, and 21 CFR 601.45. Under section 506(c)(2)(B) of the FD&C Act, FDA may grant
238 accelerated approval of a drug product on the condition, among others, that the sponsor submit
239 copies of all promotional materials related to the product during the preapproval review period
240 and, following approval and for such period thereafter as the Agency determines to be
241 appropriate, at least 30 days before dissemination of the materials. Additionally, there may be
242 other situations when the Secretary of Health and Human Services¹⁵ may establish
243 presubmission conditions on promotional materials similar to those in place for accelerated
244 approval products (e.g., section 564(e)(4)(A) of the FD&C Act). In such situations, like the drug
245 products approved under the accelerated approval framework, sponsors will be required to use
246 the format for electronic submission outlined in section VI of this guidance, no earlier than 24
247 months after publication of this guidance.
248

249 According to 21 CFR 314.550 and 21 CFR 601.45, unless otherwise informed by the Agency,
250 applicants being considered for accelerated approval must submit to the Agency, during the
251 preapproval review period, copies of all promotional materials, including both promotional
252 labeling and ads, intended for dissemination or publication within 120 days following marketing
253 approval (launch). Under the same regulatory provisions, after 120 days following marketing
254 approval, unless otherwise informed by the Agency, the applicant must submit promotional
255 materials at least 30 days before the intended time of initial dissemination of the labeling or
256 initial publication of the advertisement (non-launch).
257

¹⁴ For information about OPDP reviewer assignments based on therapeutic area, refer to
<https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm154886.htm>.

¹⁵ The authority for this provision has been delegated to FDA.

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258 The submission should include the following:

259

- 260 • Correspondence stating that it is a presubmission of promotional material(s) for an
261 accelerated approval product (Please refer to section VI.E of this guidance for additional
262 details on what to include in the correspondence.)
263
- 264 • A clean version of the draft promotional material(s) that does not include annotations to the
265 label or references
266
- 267 • An annotated copy of the proposed promotional material that clearly identifies the source of
268 support for each claim (e.g., specific page and lines of the FDA-approved full prescribing
269 information (PI) or specific page and column/paragraph from other references)
270
- 271 • The most current FDA-approved PI and, if applicable, the FDA-approved patient labeling or
272 Medication Guide with annotations cross-referenced to the proposed promotional material
273
- 274 • If applicable, annotated references to support product claims not contained in the PI, cross-
275 referenced to the proposed promotional material
276
- 277 • If applicable, annotated references to support disease or epidemiology information, cross-
278 referenced to the proposed promotional material
279

280 For draft promotional materials submitted to APLB under 21 CFR 601.45, use Form FDA 2253
281 with line 14 checked as “Draft.” Do *not* use Form FDA 2253 for submissions of draft
282 promotional materials for accelerated approval products to OPDP under 21 CFR 314.550 or
283 21 CFR 601.45.

284

C. Promotional Materials Submitted Voluntarily for Advisory Comments

285

286
287 Section 21 CFR 202.1(j)(4) provides firms with a voluntary opportunity to submit promotional
288 materials to FDA for advisory comment before the dissemination or publication of those
289 promotional materials. Firms may request advisory comments on draft promotional materials
290 and receive comments in writing from the Agency. Because this process is intended to provide
291 input before dissemination or publication, if the Agency learns that the materials submitted or
292 that substantially similar claims or presentations have been disseminated or published—
293 including after submission for comments—the Agency will generally not review the materials
294 under the voluntary advisory comment process.

295

1. Requests for Comments on Draft Promotional Materials Other Than DTC TV Ads Under 21 CFR 202.1(j)(4)

296

297
298
299 Launch materials are draft promotional materials that are voluntarily submitted by a firm to
300 OPDP or APLB during the launch phase (i.e., the first 120 days that an FDA-approved product,
301 indication, delivery system, formulation, dosage form, dosing regimen, strength, or route of
302 administration is marketed to the public) for review and comment before dissemination or
303 publication.

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304
305 Requesting comments on promotional materials before launch is encouraged. Review of core
306 launch materials is a high priority for Agency reviewers. Core launch materials generally
307 include the following:¹⁶

- 308
- 309 • One comprehensive promotional labeling piece directed toward professionals (e.g., sales aid,
310 visual aid, detail aid, or exhibit panel (if there is a major conference within the launch
311 phase)), limited to 12 or fewer pages
- 312
- 313 • One advertisement directed toward professionals (e.g., journal ad), limited to 4 or fewer
314 pages, not including the PI or brief summary
- 315
- 316 • One comprehensive direct-to-consumer (DTC) labeling piece (e.g., patient brochure), limited
317 to 12 or fewer pages
- 318
- 319 • One DTC advertisement (e.g., magazine ad), limited to 4 or fewer pages, not including the
320 brief summary
- 321
- 322 • A professional and/or DTC product website (limited to 12 printed legible pages each) or
323 electronic sales aid if it is a derivative (i.e., contains similar claims and/or presentations) of a
324 comprehensive labeling piece that is also submitted for voluntary advisory comment
- 325

326 Launch materials other than those listed above (e.g., slide kits and materials longer than the page
327 limits listed above) are considered non-core launch materials. Non-core launch materials are a
328 lower priority than core launch materials. The Agency recommends that firms apply the
329 Agency's comments on the core materials to non-core materials.

330
331 Non-launch materials consist of draft promotional materials that a firm voluntarily submits to
332 OPDP or APLB for review and comment before their first use in the public domain but after the
333 launch phase (i.e., after the first 120 days that an FDA-approved product, indication, delivery
334 system, formulation, dosage form, dosing regimen, strength, or route of administration is
335 marketed to the public).

336
337 In general, the submission should include the following:

- 338
- 339 • Correspondence stating that it is a voluntary request for advisory comments (Please refer to
340 section VI.E of this guidance for additional details on what to include in the
341 correspondence.)¹⁷
- 342

¹⁶ FDA may determine that the materials submitted do not meet the definition of core materials if they exceed content or page limitations.

¹⁷ For draft promotional materials submitted voluntarily to APLB for advisory comment, please use the fillable Form FDA 2253 with the box in line 14 checked as "Draft." Please do *not* use Form FDA 2253 for submissions of draft promotional material submitted voluntarily to OPDP.

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- 343 • A clean version of the draft promotional material(s) that does not include annotations to the
344 label or references
345
- 346 • An annotated copy of the proposed promotional material(s) that clearly identifies the source
347 of support for each claim (e.g., specific page and lines of the PI or specific page and
348 column/paragraph from other references)
349
- 350 • The most current FDA-approved PI and, if applicable, the FDA-approved patient labeling or
351 Medication Guide with annotations cross-referenced to the proposed promotional material
352
- 353 • If applicable, annotated references to support product claims not contained in the PI, cross-
354 referenced to the promotional material
355
- 356 • If applicable, annotated references to support disease or epidemiology information, cross-
357 referenced to the promotional material
358

359 The following are recommendations for voluntarily submitting draft promotional materials—
360 other than TV ads—for advisory comments:
361

- 362 • Draft promotional materials submitted for comment should be consolidated together into one
363 submission for each intended audience (i.e., one submission with professional materials and
364 one submission with consumer materials).
365
- 366 • It is also suggested that draft core launch materials be consolidated into a single submission
367 for each intended audience rather than sending the materials piecemeal in several
368 submissions over the course of a few days or weeks.
369
- 370 • In cases when the firm intends to submit professional and consumer launch core materials at
371 around the same time, it is suggested that both submissions be sent on the same day.
372
- 373 • Likewise, it is suggested that draft non-core launch promotional materials be consolidated
374 into single submissions for each intended audience to the extent possible.
375
- 376 • Submissions of draft DTC TV ads should not be included in submissions with other types of
377 materials. (See section VI of this guidance for information on how to submit.)
378

2. *Requests for Comments on Proposed DTC TV Ads Under 21 CFR 202.1(j)(4)*

381 The submission should include the following:
382

- 383 • Correspondence stating it is a voluntary request for advisory comments on a proposed TV ad
384 (Please refer to section VI.E of this guidance for additional details on what to include in the
385 correspondence.)
386

Contains Nonbinding Recommendations

- 387 • A clean version of the storyboard of the proposed TV ad that does not include annotations to
388 the label or references
389
- 390 • An annotated version of the storyboard of the proposed TV ad that clearly identifies the
391 source of support for each claim (e.g., specific page and lines of the PI or specific page and
392 column/paragraph from other references)
393
- 394 • The most current FDA-approved PI and, if applicable, the FDA-approved patient labeling or
395 Medication Guide with annotations cross-referenced to the storyboard
396
- 397 • Other appropriate documentation if any of the following apply:
398
- 399 – Annotated references to support product claims not contained in the PI, cross-referenced
400 to the storyboard
401
 - 402 – If the advertisement identifies a person as an actual patient (e.g., a spokesperson) or
403 actual health care professional, a signed statement by that person verifying that he or she
404 has in fact used or prescribed the drug product for the advertised indication and is not
405 merely an actor or model
406
 - 407 – Verification, in the form of a signed statement by the translator, that an official
408 translation of a foreign-language TV ad is accurate
409
 - 410 – Annotated references to support disease or epidemiology information, cross-referenced to
411 the storyboard
412
 - 413 – Optionally, submissions for advisory review may include a video or animatic of the
414 proposed TV ad (if included, the video or animatic should be in an acceptable file
415 format¹⁸)
416

417 Materials unrelated to a proposed TV ad being voluntarily submitted for advisory comment
418 should not be included in the review package. However, more than one TV ad proposal for a
419 particular indication for a product may be submitted in the same submission.
420

D. Resubmissions¹⁹

421
422

423 After FDA has responded to a voluntary request for advisory comments or has commented on an
424 accelerated approval presubmission, firms may revise and resubmit draft materials.
425

426 In general, the resubmission should include the following:

¹⁸ The document on *Specifications for File Format Types Using eCTD Specifications* is in the eCTD Submission Standards on the FDA eCTD website at <https://www.fda.gov/ectd>.

¹⁹ Please note that resubmissions are not to be used for submissions under Form FDA 2253, “Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use.”

Contains Nonbinding Recommendations

- 427
- 428 • Correspondence stating that it is a voluntary request for advisory comments on a revised
429 submission (Please refer to section VI.E of this guidance for additional details on what to
430 include in the correspondence.)
- 431
- 432 • A clean version of the draft promotional material(s) that does not include annotations to the
433 label or references
- 434
- 435 • An annotated copy of the proposed promotional material that clearly identifies the source of
436 support for each claim (e.g., specific page and lines of the PI or specific page and
437 column/paragraph from other references)
- 438
- 439 • The most current FDA-approved PI and, if applicable, the FDA-approved patient labeling or
440 Medication Guide with annotations cross-referenced to the proposed promotional material
- 441
- 442 • If applicable, annotated references to support disease or epidemiology information, cross-
443 referenced to the proposed promotional material
- 444
- 445 • If applicable, annotated references to support product claims not contained in the PI, cross-
446 referenced to the proposed promotional material

E. General Correspondence

447

448

449

450 General correspondence includes any correspondence submitted to FDA that may or may not
451 reference a specific drug product application and that does not fall into one of the other
452 categories (e.g., 2253 submission, voluntary request for advisory comments). Please note that
453 complaints should not be submitted under the category of “general correspondence.”

454

455 Examples of types of correspondence to submit under this category include the following:

456

- 457 • Letters in which a firm informs OPDP or APLB of an error that occurred in its promotional
458 material(s) or activities for its drug product(s)
- 459
- 460 • Safety update letters in which a firm informs OPDP or APLB that it will promptly revise all
461 of its promotional materials for a particular drug(s), to be consistent with new safety
462 information added to the product labeling²⁰
- 463
- 464 • General responses to comments from FDA provided in response to advice (voluntary request
465 for comments or general) when no revised materials are included and there is no further

²⁰ This type of correspondence is not necessary if the firm notifies FDA in another correspondence (e.g., a presubmission for accelerated approval products) that it intends to comply with 21 CFR 314.70(a)(4) or 21 CFR 601.12(a)(4). If this type of correspondence is submitted, the recommended subject line is “General Correspondence – Intent to Comply.”

Contains Nonbinding Recommendations

466 voluntary request from the firm to FDA for advisory comments (include the Marketing &
467 Advertising (MA) number)²¹

- 468
- 469 • Notifications from a firm to FDA that it plans to disseminate or publish promotional
470 materials for accelerated approval products previously submitted as required under 21 CFR
471 314.550 or 601.45 before receipt of comments by FDA (e.g., after 30 days for a non-launch
472 presubmission or after application approval for a launch submission)²²
 - 473
 - 474 • Notifications from a firm regarding agreements with other companies for the promotion of
475 the product
 - 476
 - 477 • Notifications from a firm regarding a change in promotional labeling and advertising contact
478 information
 - 479

480 The submission should include the following:

- 481
- 482 • Correspondence stating that it is a general correspondence (Please refer to section VI.E of
483 this guidance for additional details on what to include in the correspondence.)
 - 484

F. Amendments (Submission of Previously Missing or Rejected Materials)

485

486

487 If a previous voluntary request for advisory comments, a presubmission for accelerated approval
488 product, or a 2253 submission to FDA is missing one or more of the promotional materials listed
489 in the correspondence or on Form FDA 2253, these materials should be submitted as
490 amendments. Amendments may also be submitted if an incorrect document file was included
491 with a submission in eCTD format.

492

493 For voluntary requests for advisory comments, the submission should include the following:

- 494
- 495 • Correspondence stating that it is an amendment that includes accompanying materials that
496 were previously missing (Please refer to section VI.E of this guidance for additional details
497 on what to include in the correspondence.)
 - 498
 - 499 • Promotional material(s) or the correct document that was omitted from a previous submission
500 to FDA
 - 501

²¹ The MA number is the tracking number that CDER uses to identify a submission. CBER uses the *CBER secondary number*. When the term *MA number* is used in this guidance, it refers to both the MA number and CBER secondary number, as applicable.

²² Please also refer to section IV.H of this guidance regarding withdrawal requests. If a firm plans to disseminate or publish promotional materials for accelerated approval products submitted as required under 21 CFR 314.550 or 601.45 without waiting for comments from FDA, the firm should notify OPDP or APLB in a general correspondence submission. If a firm decides that it does not intend to disseminate or publish promotional materials for accelerated approval products, the firm should notify OPDP or APLB in a withdrawal request submission.

Contains Nonbinding Recommendations

- 502 • Annotated copy of the promotional materials that were omitted from a previous submission
503 to FDA
504
- 505 • The most current FDA-approved PI and, if applicable, the FDA-approved patient labeling or
506 Medication Guide with annotations cross-referenced to the proposed promotional material
507
- 508 • If applicable, annotated references to support disease or epidemiology information, cross-
509 referenced to the proposed promotional material that was previously omitted from a
510 submission to FDA
511
- 512 • If applicable, annotated references to support product claims not contained in the PI, cross-
513 referenced to the proposed promotional material that was previously omitted from a
514 submission to FDA
515

516 If an incorrect document was included or if FDA notifies a firm that promotional materials are
517 missing from a previous 2253 submission that was submitted in paper or non-eCTD format, the
518 firm should resubmit the entire 2253 submission rather than submitting an amendment. If part of
519 a non-eCTD 2253 submission is rejected (e.g., a video does not play), the entire 2253 submission
520 should be resubmitted.
521

522 If the 2253 submission was in eCTD format, the firm should submit an amendment and include
523 the following:
524

- 525 • Correspondence stating that it is an amendment that includes accompanying promotional
526 materials that were previously missing or rejected (Please refer to section VI.E of this
527 guidance for additional details on what to include in the correspondence.)
528
- 529 • Promotional materials that were missing or rejected from a previous submission to FDA
530 (firm does not need to resubmit the entire 2253 submission)
531

532 *Example:* A firm voluntarily submits a request for advisory comments on launch
533 promotional materials, using the eCTD. The correspondence file states that three
534 promotional materials are included in the submission along with annotated copies and
535 references. However, upon receipt, FDA notes that the actual submission only includes two
536 promotional materials with annotated copies and references. FDA notifies the firm that one
537 promotional material is missing from the submission and provides the MA number. The firm
538 should then submit the missing promotional material and the annotated copy and references
539 as an amendment, using the eCTD. The subject line of the correspondence should note that
540 the submission is an amendment and include the MA number.
541

G. Withdrawal Requests

542 A firm may request to withdraw a previous submission to FDA. No materials are submitted with
543 such a request.
544
545
546

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547 Because submission of promotional materials for accelerated approval products is required under
548 21 CFR 314.550 and 601.45, firms should only use a withdrawal request for such materials if the
549 firm does not plan to disseminate or publish the promotional materials.²³

550

551 The submission should include the following:

552

- 553 • Correspondence stating that it is a withdrawal request (Please refer to section VI.E of this
554 guidance for additional details about what to include in the correspondence.)

555

556 *Example 1:* A firm voluntarily submits draft promotional materials for advisory review for
557 its product (not approved under the accelerated approval regulations at 21 CFR 314.510 or
558 601.41) and later decides to disseminate the promotional materials without waiting for FDA
559 comments. The firm should notify FDA of its intent to withdraw the request for comments.
560 The subject line of the correspondence should note that the submission is a withdrawal
561 request and include the date of the request or MA number.

562

563 *Example 2:* A firm voluntarily submits draft promotional materials for advisory review for
564 its product (not approved under the accelerated approval regulations at 21 CFR 314.510 or
565 601.41) and later decides not to disseminate the promotional material. The firm should
566 notify FDA of its intent to withdraw the request for comments. The subject line of the
567 correspondence should note that the submission is a withdrawal request and include the date
568 of the request or MA number.

569

570 *Example 3:* A firm submits draft non-launch promotional materials for its product approved
571 under the accelerated approval regulations at 21 CFR 314.510 or 601.41 and, two weeks
572 later, decides that it does not intend to disseminate the promotional material. The firm
573 should notify FDA of its intent to withdraw the submission. The subject line of the
574 correspondence should note that the submission is a withdrawal request and include the date
575 of the submission or MA number.

576

577 *Example 4:* A firm submits final promotional material under cover of Form FDA 2253 in
578 fulfillment of the postmarketing reporting requirements and subsequently decides that it will
579 never disseminate the promotional material. The firm should immediately notify FDA of its
580 intent to withdraw the 2253 submission by submitting a correspondence. The subject line of
581 the correspondence should note that the submission is a withdrawal request and include the
582 date of the submission or MA number. Please refer to section VI.E of this guidance for
583 additional details about what to include in the correspondence.

584

²³ Please also refer to section IV.F of this guidance regarding general correspondence. If a firm plans to disseminate or publish promotional materials for accelerated approval products submitted as required under 21 CFR 314.550 or 601.45 without waiting for comments from FDA, the firm should notify OPDP or APLB in a general correspondence submission. If a firm decides that it does not intend to disseminate or publish promotional materials for accelerated approval products, the firm should notify OPDP or APLB in a withdrawal request submission.

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585 **H. Response to Untitled Letter or Warning Letter**

586
587 A response to an untitled letter or a warning letter is a correspondence type that includes a firm's
588 initial response or additional correspondence pertaining to an untitled letter or warning letter
589 from FDA regarding promotion.

590
591 The submission should include the following:

- 592
- 593 • Correspondence stating that it is a response to an untitled letter or warning letter — This
594 response may include the firm's initial or subsequent responses. (Please refer to section VI.E
595 of this guidance for additional details on what to include in the correspondence.)
596
 - 597 • Corrective piece(s), if applicable
598

599 **I. Response to Information Request**

600
601 FDA may issue a letter of inquiry to firms when investigating potentially violative activity. The
602 firm's response to a letter of inquiry is considered a *response to an information request*. FDA
603 will notify the firm when a response should be considered a response to an information request.
604 The correspondence should state that it is a response to an information request. The
605 correspondence should include the firm's response to the questions and issues raised in FDA's
606 letter of inquiry, including any materials FDA has requested. (Please refer to section VI.E of this
607 guidance for additional details on what to include in the correspondence.)
608

609 **J. Reference Document**

610
611 Reference documents are annotated materials that were missing from a previous submission to
612 FDA. Promotional materials that were entirely omitted from a previous submission should not
613 be included in this type of submission. (Please refer to section IV.G of this guidance if
614 promotional materials were entirely omitted from a previous submission.)
615

616 The submission should include the following:

- 617
- 618 • Correspondence stating that it is a reference document submission and the specific
619 information regarding what is in the submission (i.e., annotated references, annotated
620 promotional materials, and/or annotated labeling) — (Please refer to section VI.E of this
621 guidance for additional details on what to include in the correspondence.)
622
 - 623 • Annotated references, annotated promotional materials, and/or annotated labeling
624

625 *Example:* A firm voluntarily submits a request for advisory comments for non-launch
626 materials that includes two clean copies of promotional materials. However, the submission
627 does not include annotated copies of the promotional materials or annotated references. FDA
628 notifies the firm and provides the MA number. The firm should submit the missing materials
629 as a reference document. The subject line of the correspondence should note that it is a
630 reference document submission and include the MA number.

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K. Complaints

Please note that complaints about prescription drug promotion are not accepted in eCTD format and should be submitted as either paper copies or in an electronic non-eCTD format.²⁴ Please submit complaints regarding professional and consumer materials separately. A duplicate copy of the submission should be provided. Please do not include Form FDA 2253 or Form FDA 356h.²⁵

The submission should include the following:

- Correspondence stating that it is a complaint — Please include the drug, manufacturer, and specific regulatory concerns in the correspondence. In addition, the correspondence should include the name, title, address, phone, fax, and email of the person that the Agency should contact about issues related to the submission.
- Supporting information or documentation, if available.

V. FORMAT FOR SUBMISSION OF PROMOTIONAL MATERIALS IN PAPER COPY

Paper copies of all promotional submission types will be accepted until 24 months following publication of this guidance. When paper copy materials are submitted, sponsors are encouraged, but not required, to include one non-eCTD copy of the contents of the submission on a CD and include a statement in the cover letter verifying that the contents of the CD match the contents of the paper submission. Please refer to tables 1 and 2 to determine the number of copies to submit for each submission type.²⁶ Beginning 24 months after this guidance publishes, paper copies will no longer be accepted for postmarketing submissions made under 21 CFR 314.81(b)(3)(i) or 21 CFR 601.12(f)(4) (see table 2) or for presubmissions of promotional materials for accelerated approval or other products where such submissions are required for approval under section 745A(a) of the FD&C Act (see table 1). (See section VI of this guidance for further discussion.)

²⁴ If applicable, an electronic copy of a TV or radio ad in an acceptable file format (e.g., a CD containing a .wmv or .wma file) may be included with a complaint.

²⁵ FDA Form 356h is titled “Application to Market a New or Abbreviated New Drug or Biologic for Human Use.”

²⁶ Note that once a firm submits an application-related document in eCTD format including, but not limited to, the types of documents described in this guidance, paper copies related to that application should no longer be submitted unless specifically requested by the Agency.

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665 Please note that complaints are not accepted in the eCTD and should only be submitted as paper
 666 copies. If any submission is submitted electronically in eCTD format, paper copies should not
 667 also be submitted, unless specifically requested.²⁷
 668

669 **Table 1: Number of Paper Copies for Various Submission Types Based on Recipient**

Type of Submission	Number of Paper Copies	
	If Recipient is OPDP	If Recipient is APLB
Voluntary advisory submission (not a TV ad)	3	2
Voluntary advisory submission of a TV ad	10*	2*
Presubmission of promotional materials for accelerated approval products	3	2
Resubmission	3	2
General correspondence	2	2
Amendment	3	2
Withdrawal request	2	2
Response to notice of violation or warning letter	2	2
Response to information request	2	2
Reference document	3	2
Complaint	2	2

670
 671
 672 **Table 2: Number of Paper Copies of Promotional Materials to Submit in Fulfillment of the**
 673 **Postmarketing Reporting Requirements (2253 Submissions)***

2253 Submissions	Number of Paper Copies
If the promotional material(s) mentions a single product	2
If the promotional material(s) mentions multiple products	3

674 * The number of copies is the same for OPDP and APLB. Note that beginning 24 months after publication of this
 675 guidance, under section 745A(a) of the FD&C Act, firms will no longer be able to submit these promotional
 676 materials in paper copy.
 677

678 OPDP and APLB will continue to accept promotional materials submitted in fulfillment of the
 679 postmarketing reporting requirements (2253 submissions) in electronic, non-eCTD, format (e.g.,
 680 CDs) until 24 months after publication of this guidance. Such submissions do not require

²⁷ FDA may request paper copies of a submission if upon receipt of the electronic representation of the promotional material it appears to be inadequate to allow FDA to conduct a proper review (e.g., a unique promotional material that requires physical manipulation in the hands of the reviewer). In such cases, FDA will notify the firm of the need to submit in paper and the number of copies requested.

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681 inclusion of a paper copy of the entire submission, except that a signed paper copy of Form FDA
682 2253 must be included to allow for processing. Please follow the recommendations in table 2 for
683 the number of copies to submit.

684

685 **A. Submitting Paper Copy Promotional Materials to OPDP**

686

687 Please send paper copies to the following address:

688

689 **Office of Prescription Drug Promotion**

690 Food and Drug Administration

691 5901-B Ammendale Road

692 Beltsville, MD 20705-1266

693

694 For time-sensitive materials, please confirm receipt of the submission with a phone call to the
695 OPDP project manager at 301-796-1200 or by email at CDER-OPDP-RPM@fda.hhs.gov.

696

697 OPDP suggests applying an “OPDP” sticker or other prominent directional notation to the
698 exterior of packages submitted to OPDP to help avoid misdirection of promotional materials. If
699 it is not possible to add this notation to the exterior of the package, OPDP recommends adding a
700 prominent directional notation (e.g., sticker, rubber stamp) to the cover letter itself.

701

702 **B. Submitting Paper Copy Promotional Materials to APLB**

703

704 Please send paper copies to the following address:

705

706 **Advertising and Promotional Labeling Branch, HFM-602**

707 Food and Drug Administration

708 Center for Biologics Evaluation and Research

709 Document Control Center

710 10903 New Hampshire Ave.

711 WO71 – G112

712 Silver Spring, MD 20993-0002

713

714 Any questions for APLB may also be addressed to APLB by phone at 240-402-9158.

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717 **VI. FORMAT FOR SUBMISSION OF PROMOTIONAL MATERIALS** 718 **ELECTRONICALLY**²⁸

719
720 This section provides information on specific aspects of how to submit promotional labeling and
721 advertising materials to FDA electronically in eCTD format.²⁹ As discussed in section II of this
722 guidance, there are two types of submissions related to promotional materials that are
723 “submissions under subsection (b), (i), or (j) of section 505 of [the FD&C] Act or subsection (a)
724 or (k) of section 351 of the Public Health Service Act” and are, therefore, subject to the
725 mandatory electronic submission requirement in section 745A(a) of the FD&C Act.

726
727 The two types of submissions are as follows:

- 728
- 729 1. Postmarketing submissions of promotional materials using Form FDA 2253 (required by
730 21 CFR 314.81(b)(3)(i) and 21 CFR 601.12(f)(4))
 - 731 2. Submissions of promotional materials for accelerated approval products (required by
732 section 506(c)(2)(B) of the FD&C Act, 21 CFR 314.550, or 21 CFR 601.45) and other
733 products where such submissions are required for approval
734

735
736 This guidance, along with the eCTD Guidance, specifies the electronic format for these
737 submission types. Therefore, beginning no earlier than 24 months after publication of this
738 guidance, firms will be *required* to submit these types of submissions electronically. As of that
739 date, paper copies will no longer be accepted for such submissions.

740
741 Although the other types of submissions related to promotional materials discussed in this
742 guidance are not subject to the mandatory electronic submission requirement in section 745A(a)
743 of the FD&C Act,³⁰ firms may—and are strongly encouraged to—make such submissions
744 electronically. However, paper copies will still be accepted for submission types that do not fall
745 under section 745A(a). We note that if firms do choose voluntarily to submit other materials
746 electronically, CDER is currently only able to accept them in eCTD format using *us-regional-v3-*
747 *3.dtd*.³¹ Once a firm submits an application-related document in eCTD format, including, but not
748 limited to, the types of documents described in this guidance, paper copies related to that
749 application should no longer be submitted unless specifically requested by the Agency.
750

²⁸ Insofar as section VI of this guidance establishes the requirement for electronic submissions under section 745A(a) of the FD&C Act, it has binding effect.

²⁹ The eCTD module 1 specifications discussed in this section can be located in the eCTD Submission Standards on the FDA eCTD website at <https://www.fda.gov/ectd>.

³⁰ Table 1 (with the exception of presubmissions of promotional materials for accelerated approval products) provides a list of the types of submissions that are not subject to the mandatory electronic submission requirement in section 745A(a) of the FD&C Act.

³¹ CBER is able to accept eCTD submissions using previous versions of the *us-regional-backbone* file until 24 months after publication of this guidance.

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751 In some cases, the company that holds the application for a drug collaborates with another
752 company to promote the drug. If the company handling promotion of the drug wants to submit
753 promotional materials to OPDP or APLB using the eCTD, the company should work with the
754 application holder to ensure that both companies are using the same version of the *us-regional-*
755 *backbone* file. If the submission is for OPDP, both companies will need to use the same version
756 (for example, *us-regional-v3-3.dtd*). In addition, both companies should work together to come
757 up with a system for generating sequence numbers in order to avoid the use of duplicate
758 sequence numbers that will result in a rejection of one of the submissions. For example, a
759 company could choose to assign a block of numbers to a particular vendor (e.g., start
760 promotional submissions with sequence 5000).

761
762 Please note that the eCTD format accommodates a wide range of applications and related
763 submission types other than submissions of promotional materials. Therefore, a specific
764 submission may not use all of the possible section-heading elements in each module. The
765 following sections describe specific procedures for submitting promotional labeling and
766 advertising to FDA in eCTD format, including submissions made under section 745A(a) of the
767 FD&C Act.

A. Submission-Description Element

768
769
770 The *submission-description* element is an optional field. FDA recommends including the
771 *submission-description* element to provide a high-level description of the purpose of the
772 submission and to help differentiate similar types of submissions. If used, the *submission-*
773 *description* element should include the description of the type of submission and materials, the
774 date of the submission,³² and the MA number (if the MA number has been provided in a
775 previous communication with FDA).

776
777
778 The following are examples of helpful submission descriptions:

- 779
- 780 • Request for comments on professional launch website, print ad, and sales aid 20140501
 - 781 • Withdrawal request 20140405 for print ad MA61 submitted on 20140115
 - 782 • Response to untitled letter 20140301 MA456
 - 783 • Reference documents for professional launch print ad 20140302 MA31
 - 784 • Consumer 2253 submission 20140915

B. Submission-Type and Submission-Sub-Type

785
786
787 For all promotional materials submitted to FDA via the eCTD (including promotional materials
788 submitted in fulfillment of the postmarketing reporting requirements), use the *submission-type*
789 “Promotional Labeling Advertising.” If promotional materials are submitted in the eCTD
790 without specifying “Promotional Labeling Advertising” as the *submission-type*, the submission
791 may not be appropriately routed to OPDP or APLB and, as a result, there may be a rejection or
792 delay in processing and responding to the submission.
793
794

³² The date format to be used is yyyyymmdd (four-digit year, two-digit month, and two-digit day).

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795 The attribute *submission-sub-type* is used to further clarify the purpose of the submission. The
796 following are the current valid *submission-sub-type* codes for the *submission-type* “Promotional
797 Labeling Advertising”:
798

- 799 • *Original* — Use this *submission-sub-type* for all promotional materials submitted in
800 fulfillment of the postmarketing reporting requirements (2253 submissions) and for materials
801 that do not have a submission history with FDA. This includes original promotional
802 materials such as voluntary requests for advisory comments on launch materials or non-
803 launch materials, and presubmission of promotional materials for accelerated approval
804 products. Also use this code for responses to untitled letters, warning letters, and information
805 requests and for other general correspondence if no submission history with FDA exists for
806 the materials.
807
- 808 • *Resubmission* — Use this *submission-sub-type* for voluntary requests for advisory comments
809 and presubmissions of revised promotional materials that were previously submitted as an
810 “original” submission. Do not use this *submission-sub-type* for any 2253 submissions.
811
- 812 • *Amendment* — Use this *submission-sub-type* for a submission that contains additional
813 supportive material to augment information previously submitted, e.g., the submission of
814 promotional material that was previously missing or rejected, withdrawal requests, and
815 submissions of annotated references. In addition, use this *submission-sub-type* for responses
816 to untitled letters, warning letters, and information requests and for general correspondence if
817 there was an original submission to FDA in eCTD format.
818

819 Table 3 summarizes the submission process and the *submission-sub-type* code for new
820 submissions. The submission history is defined by the format through which the original
821 submission was made. For example, if a 2253 submission was received in paper format (or on a
822 CD in non-eCTD format), the entire submission is considered to be “paper,” and all subsequent
823 submissions related to the original 2253 submission (amendments, withdrawal requests, etc.)
824 made prior to the 24 months after publication of this guidance should be made in paper format.
825 FDA will work with firms to determine the appropriate format for subsequent submissions made
826 after 24 months of publication of this guidance to a 2253 submission originally received in paper
827 format. If a submission is received in eCTD format, all subsequent submissions related to the
828 submission should be made in eCTD format.
829

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830 **Table 3: Submission Process and Coding**

Submission History	Action	Code for <i>Submission-Sub-Type</i>
Has no prior FDA submission history	Submit to the eCTD with the same <i>submission-id</i> as the sequence number	<ul style="list-style-type: none"> • “Original”
All promotional materials submitted in fulfillment of the postmarketing reporting requirements (2253 submissions)	Submit to the eCTD with the same <i>submission-id</i> as the sequence number	<ul style="list-style-type: none"> • “Original”
Already has an associated eCTD promotional submission	Submit to the eCTD with the same <i>submission-id</i> as the original promotional submission	<ul style="list-style-type: none"> • “Resubmission” for resubmissions • “Amendment” for amendments; withdrawal requests; reference documents; responses to untitled letters, warning letters, and information requests; and general correspondence
Has a paper-copy submission history only	Do not submit to the eCTD*	<ul style="list-style-type: none"> • Resubmissions: Submit using paper-copy process* • Amendments; withdrawal requests; reference documents; responses to untitled letters, warning letters, and information requests; and general correspondences: Submit using paper copy process.

831 * FDA will work with firms to determine the appropriate format for subsequent submissions made after 24 months
832 of publication of this guidance to a 2253 submission originally received in paper format. If a submission is received
833 in eCTD format, all subsequent submissions related to the submission should be made in eCTD format.
834

835 **C. Form Element**
836

837 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
838 use *form-type* Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for
839 Drugs and Biologics for Human Use) and submit this form in section 1.1. For cases where
840 promotional material(s) mention multiple products,³³ include the attachment listing the other
841 referenced products as a separate leaf title with Form FDA 2253 in section 1.1.³⁴ Do not include
842 Form FDA 356h for submissions to OPDP or APLB.
843

³³ Please refer to section VI.J of this guidance regarding submitting promotional materials that reference more than one application.

³⁴ Please refer to section VI.K of this guidance for a detailed description of leaf titles.

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844 **D. Promotional Audience Type**

845
846 When providing information in module 1.15, reference the leaves at the lowest heading elements.
847 For example, the *m-1-15-promotional-material* heading element needs an attribute of
848 *promotional-material-audience-type*. When a leaf is referenced in any subsection of
849 module 1.15, provide the attribute as a coded value from its corresponding attribute list
850 (*promotional-material-audience-type.xml*).

851
852 The current valid codes for *promotional-material-audience-type* are as follows:

- 853
- 854 • *Consumer* — for promotional materials directed to consumers
- 855 • *Professional* — for promotional materials directed to health care professionals
- 856

857 **E. Correspondence Related to Promotional Materials (Section 1.15.1)**

858
859 Submit the correspondence relating to promotional materials as an individual portable document
860 format (PDF) file in the appropriate subsection of 1.15.1. Firms will need to submit a
861 correspondence for all submission types listed in section 1.15.1. A separate cover letter should
862 not be submitted in section 1.2. Please note that firms should not submit a correspondence or a
863 cover letter with 2253 submissions.³⁵ In some cases, the correspondence may be the actual
864 response and the only file necessary for the submission (e.g., response to untitled letter, response
865 to an Agency communication, or a general correspondence). Correspondence submitted to
866 section 1.15.1 should include the following:

- 867
- 868 • Subject line describing the reason for the submission, the NDA/ANDA/BLA number, the
869 proprietary name/established name (dosage form), and the name of the TV ads (if applicable)
- 870

871 Examples of acceptable descriptions to be included in the subject line include the following:

- 872
- 873 – Request for Comments on Launch Materials
- 874 – Request for Comments on Non-Launch Materials
- 875 – Presubmission of Launch Promotional Materials for Accelerated Approval Product
- 876 – Presubmission of Non-Launch Promotional Materials for Accelerated Approval Product
- 877 – Response to Untitled Letter
- 878 – Response to Warning Letter
- 879 – Response to Information Request
- 880 – Amendment
- 881 – Withdrawal Request
- 882 – Submission of Annotated References
- 883 – General Correspondence
- 884

³⁵ If, however, a firm is withdrawing a Form FDA 2253 submission, the firm must submit a correspondence withdrawing the submission in section 1.15.1.9.

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885 The body of the correspondence should include the following information:
886

- 887 • Regulatory description of the submission.
888
- 889 • Statement that the submission is virus free, with a description of the software (name, version,
890 and company) used to check the files for viruses.
891
- 892 • A list of all promotional materials included in the submission, with the material type,
893 material ID, and description for each item listed.
894
- 895 • A concise description of use of the promotional material(s), if applicable.³⁶
896
- 897 • Whether the submission is for a launch or non-launch.
898
- 899 • If the submission is for a launch, whether the promotional materials are core or non-core.
900
- 901 • Whether the submission is subject to the regulations in 21 CFR 314.550 or 21 CFR 601.45.
902
- 903 • Whether the submission is a TV ad.
904
- 905 • If the submission is the initial response to an untitled letter or warning letter, a list of all
906 promotional materials (with the 2253 submission date) for the drug product(s) that contain
907 violations similar to those described in the letter.
908
- 909 • Whether the submission contains health-care-professional-directed materials or consumer-
910 directed materials.
911
- 912 • Where applicable, whether the Agency has previously commented on the promotional
913 material(s); the comment date; and the Marketing, Advertising and Communications
914 Management Information System (MACMIS) number, MA number, or CBER secondary
915 number.
916
- 917 • The name, title, address, phone, fax, and email of the individual the Agency should contact
918 about issues related to the submission. If there are separate regulatory and technical points of
919 contact, please include this information for both individuals.
920

³⁶ Please refer to section VII.C of this guidance for additional details.

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921 F. Materials (Section 1.15.2)³⁷

922

923 1. Attributes

924

925 Submit promotional labeling and advertising materials as individual files in an approved file
926 format in section 1.15.2.³⁸ When providing information in a subsection of module 1.15.2
927 materials, three attributes are needed: *promotional-material-doc-type*, *promotional-material-*
928 *type*, and *material-id*. An optional attribute, *issue-date*, should only be provided when the
929 *promotional-material-doc-type* is a promotional 2253 submission.³⁹ The attribute *promotional-*
930 *material-doc-type* indicates the purpose of the promotional submission and needs to be provided
931 with the *m1-15-2-materials* heading element. Provide the attributes as coded values from their
932 corresponding attribute list (*promotional-material-doc-type.xml*). Table 4 shows the current
933 valid codes for *promotional-material-doc-type*.

934

935 **Table 4: Promotional Material Document Types and Descriptions**

Promotional Material Document Type	Description
Promotional 2253	Form and materials required from submitter at initial dissemination of labeling as well as initial publication of an advertisement
Request for Advisory Launch	Voluntary submission of launch promotional materials for FDA review and comment sent before dissemination or publication
Request for Advisory Non-Launch	Voluntary submission of non-launch promotional materials for FDA review and comment sent before dissemination or publication
Presubmission Accelerated Launch	Promotional materials intended to be used in the first 120 days after approval that are submitted to FDA before dissemination or publication as required by 21 CFR 314.550 and 601.45
Presubmission Accelerated Non-Launch	Promotional materials intended to be used after the 120-day postapproval period that are submitted to FDA before dissemination or publication as required by 21 CFR 314.550 and 601.45

936

937 The attribute *promotional-material-type* indicates the type of media/delivery method of the
938 promotional material and should be provided with the *m-1-15-2-1 material* heading element.

³⁷ If including multiple promotional materials in one submission, please refer to section VI.I of this guidance. If submitting promotional materials that reference more than one application, see section VI.J of this guidance.

³⁸ The *Specifications for File Format Types Using eCTD Specifications* is in the eCTD Submission Standards on the FDA eCTD website at <https://www.fda.gov/ectd>.

³⁹ The date format to be used is *yyyymmdd* (four-digit year, two-digit month, and two-digit day).

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939 Provide the attributes as coded values from their corresponding attribute list (promotional-
940 material-type.xml).⁴⁰

941
942 The *material-id* attribute may consist of letters, numbers, or both, and should not exceed
943 30 characters. The *issue-date* attribute, if applicable, should follow the date format as
944 yyyyymmdd (four-digit year, two-digit month, and two-digit day).

945 2. *Clean Version of Materials Submitted (Section 1.15.2.1.1)*

946
947 For draft promotional materials submitted (1) voluntarily for advisory comment, or (2) under 21
948 CFR 314.550 or 601.45, submit clean versions of the promotional materials (i.e., versions not
949 including annotations to the label or references) in section 1.15.2.1.1.

950
951 Clean versions of corrective pieces should also be submitted in section 1.15.2.1.1, using the
952 eCTD “replace” operation.

953
954 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
955 clean final versions of the promotional materials without any annotations must be submitted in
956 section 1.15.2.1.1.

957 3. *Annotated Version of Promotional Materials (Section 1.15.2.1.2)*

958
959 For draft promotional materials submitted (1) voluntarily for advisory comment, or (2) under 21
960 CFR 314.550 or 601.45, submit annotated versions of the promotional materials (i.e., versions
961 that are cross-referenced to the product labeling and, if applicable, references) in section
962 1.15.2.1.2.

963
964 Annotated versions of corrective pieces should also be submitted in section 1.15.2.1.2, using the
965 eCTD “replace” operation.

966
967 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
968 firms may choose to submit annotated versions of the promotional materials in section 1.15.2.1.2
969 that are cross-referenced to the product labeling and, if applicable, references. References
970 improve the efficiency of review.

971
972 Firms should highlight and annotate the materials with a cross-reference to the product labeling
973 or references. When product labeling or other references are used to support a claim or
974 presentation in proposed promotional materials, hypertext links should be provided in the
975 annotated promotional material to the specific page that contains the supporting information.

976
977
978

⁴⁰ The current codes for *promotional-material-type*, as well as the codes for other attributes, are located in the eCTD Submission Standards, on the FDA eCTD website at <https://www.fda.gov/ectd>.

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979 **G. Product Labeling (Section 1.14.6 and Section 1.15.2.1.3)**

980 981 *1. Product Labeling Accompanying Form FDA 2253 Submissions (Section 1.14.6)*

982
983 Form FDA 2253 specifies that the most current product labeling accompany the submission.
984 Firms must submit the most current product labeling, as required in 21 CFR 314.81(b)(3)(i), to
985 section 1.14.6. For promotional labeling pieces, this is the PI that accompanies the promotional
986 materials. The required format for the PI is PDF.⁴¹

987 988 *2. Annotated Product Labeling (Section 1.15.2.1.3)*

989
990 For draft promotional materials submitted (1) voluntarily for advisory comment, or (2) under 21
991 CFR 314.550 or 601.45, include the annotated product labeling in section 1.15.2.1.3.⁴² Firms
992 should highlight and annotate, with a cross-reference to the promotional materials, the sections
993 of the product labeling that are referred to in the promotional materials. When product labeling
994 is used to support a claim or presentation in proposed promotional materials, hypertext links
995 should be provided to the specific page that contains the supporting information.

996
997 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
998 firms may choose to provide the annotated product labeling with hypertext links.⁴³

999 1000 **H. Annotated References (Section 1.15.2.1.4)**

1001
1002 If references are provided, submit each reference as an individual PDF file and place it in
1003 section 1.15.2.1.4. Firms should highlight and annotate, with a cross-reference to the
1004 promotional materials, the sections of the full reference that are referred to in the promotional
1005 materials. When a reference is used to support a claim or presentation in proposed promotional
1006 materials, firms should provide, in the annotated promotional material, hypertext links to the
1007 specific page of the reference that contains the supporting information.

1008
1009 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
1010 firms may choose to provide references with hypertext links. References improve the efficiency
1011 of review.

1012

⁴¹ Firms may choose to submit the current product labeling with each 2253 submission. Alternatively, once product labeling is submitted to section 1.14.6 with a 2253 submission, firms may cross-reference the current product labeling within the XML backbone. If firms choose to reference the current product labeling within the XML backbone, they should ensure that the version of the product labeling that is referenced is correct and that the leaf title is revised with each 2253 submission to be informative for Agency reviewers (e.g., include the date of submission). Refer to section VI.K of this guidance for recommendations regarding leaf titles.

⁴² Even if the submission does not include annotations to the label or a part of the label, firms should still include the entire label in section 1.15.2.1.3.

⁴³ Annotated labeling submitted in fulfillment of the postmarketing reporting requirements must be included as a PDF file in section 1.15.2.1.3. The current product labeling must still be submitted in section 1.14.6.

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1013 **I. Including Multiple Promotional Materials in One Submission**

1014
1015 For draft promotional materials voluntarily submitted for advisory comment or submitted as
1016 required under 21 CFR 314.550 or 601.45, if multiple promotional materials are included in one
1017 submission, each of these materials is to be submitted with its own clean version, annotated
1018 version, annotated labeling, and annotated references.

1019
1020 The following example shows how to submit multiple promotional materials in one submission
1021 in section 1.15 for advisory comments:
1022

1.15 Promotional material (Professional)

1.15.1 Correspondence relating to promotional materials

1.15.1.1 Request for advisory comments on launch materials

Request for professional launch advisory for sales aid and print ad 20140501

1.15.2 Materials (Request for Advisory Launch)

1.15.2.1 Material (Sales Aid)(65NO35482)

1.15.2.1.1 Clean version

Sales aid 65NO35482 Considerations for treatment 20140501 CLEAN

1.15.2.1.2 Annotated version

Sales aid 65NO35482 Considerations for treatment 20140501 ANNOTATED

1.15.2.1.3 Annotated labeling version

PI annotated to sales aid

1.15.2.1.4 Annotated references

Reference 1 Smith et al. for sales aid

1.15.2.1 Material (Print Ad)(77UY6788)

1.15.2.1.1 Clean version

Print ad 77UY6788 A new option 20140501 CLEAN

1.15.2.1.2 Annotated version

Print ad 77UY6788 A new option 20140501 ANNOTATED

1.15.2.1.3 Annotated labeling version

PI annotated to print ad

1.15.2.1.4 Annotated references

Reference 1 Murray et al. for print ad

Reference 2 Shoon et al. for print ad

1023
1024 For promotional materials submitted in fulfillment of the postmarketing reporting requirements,
1025 if multiple promotional materials are included in one submission, submit clean versions of each
1026 promotional material in section 1.15.2.1.1.
1027

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1028 The following example shows how to submit multiple promotional materials in one submission
1029 in section 1.15:
1030

<p>1.1 Forms Form FDA 2253: Transmittal of Advertisements and Promotional Labeling for Drugs And Biologics for Human Use Form FDA 2253 Professional website and print ad 20140105</p> <p>1.14 Labeling 1.14.6 Product labeling for 2253 submissions Drug X PI Rev20131205</p> <p>1.15 Promotional material (Professional) 1.15.2 Materials (Promotional 2253) 1.15.2.1 Material (www-website)(68443439)(20140105) 1.15.2.1.1 Clean version Website 68443439 Challenges to treatment 20140105 CLEAN</p> <p>1.15.2.1 Material (Print Ad)(3945730)(20140105) 1.15.2.1.1 Clean version Print ad 3945730 A new treatment 20140105 CLEAN</p>

1031
1032 **J. Submission of Promotional Materials Referencing More Than One**
1033 **Application (Grouped Submissions)**
1034

1035 Firms are encouraged to submit promotional materials that promote more than one product (i.e.,
1036 a multiple-product submission) as a grouped submission.⁴⁴ However, only one application type
1037 can be used in a grouped submission. Therefore, should a promotional material apply to more
1038 than one application type (e.g., a BLA and NDA), submit the promotional material as a separate
1039 submission for each application type (i.e., there would be two separate submissions—one for the
1040 BLA application and one for the NDA application).

1041
1042 **K. Leaf Titles**
1043

1044 Appropriately named leaf titles allow FDA reviewers to navigate through submissions and
1045 distinguish one submission from another in the eCTD viewer. A leaf title should include the MA
1046 number if it has been provided in a previous communication with FDA.

1047
1048 The format of the leaf title for the actual form for Form FDA 2253 submissions (placed in
1049 section 1.1) should be informative for Agency reviewers. For example, the leaf title “Form FDA
1050 2253 Consumer print ad 20140105” is more informative and searchable than a leaf title of
1051 “2253Form.” Although both examples identify the submission by type, in the first example the
1052 Agency reviewer will know the audience for the promotional material (consumer), the material
1053 type code, and the date of the submission—all without having to open the file itself.
1054

⁴⁴ For instructions on assembling grouped submissions, please see *The eCTD Backbone Files Specification for Module 1*, located in the eCTD Submission Standards on the FDA eCTD website at <https://www.fda.gov/ectd>.

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1055 In addition, the leaf title for the correspondence related to promotional materials (placed in
1056 section 1.15.1) should help the Agency reviewer identify the incoming submission by type. A
1057 leaf title of “Response to untitled letter 20140105 MA37” is more informative than a leaf title of
1058 “Response to untitled letter,” because the former example identifies the type of correspondence,
1059 the letter date of the submission, and the MA number.

1060
1061 Leaf titles for each promotional material (placed in section 1.15.2) should also be informative.
1062 For example, a health-care-professional-directed sales aid with the leaf title “Sales Aid
1063 65NO35482 Considerations for treatment 20140102” is more informative than the leaf title
1064 “promotional material.pdf.” When displayed in the eCTD viewer, the first example immediately
1065 identifies the material type code, the material identifying number of the piece (if applicable), a
1066 description of the piece, and the date of the submission. All of this information is useful to the
1067 Agency reviewer, even though there may be some redundancy between information in the leaf
1068 title and the materials attributes discussed previously in section VI.F of this guidance.

L. Use of Operator Attributes

1070
1071
1072 When using life cycle operations, use the operator attributes as follows:

- 1073
1074 • For resubmissions, use the “replace” operator attribute to replace the previously submitted
1075 files with the resubmission’s updated files. If a firm is only resubmitting part of the original
1076 submission, the operator for the correspondence file should be “new.”
1077
- 1078 • For withdrawals, submit the withdrawal request and use the “delete” operator attribute on all
1079 leaves that are affected by the withdrawal request. The operator for the correspondence file
1080 should be “new.”
1081
- 1082 • For promotional materials submitted in fulfillment of the postmarketing reporting
1083 requirements (2253 submissions), if a material previously submitted under cover of Form
1084 FDA 2253 is revised, use the “replace” operator attribute to replace the previously submitted
1085 files with the revised materials. (The *submission-sub-type* should be “Original,” as indicated
1086 in table 3 of this guidance.)
1087

VII. PRESENTATION ISSUES

1088
1089
1090
1091 Because electronic images may not adequately convey the net impression of the promotional
1092 material or the details of the intended promotional message within the piece, firms should follow
1093 the guidelines in this section to facilitate review by the Agency.

A. General Presentation Considerations

1094
1095
1096
1097 In general, the presentation considerations below encompass the appearance, layout, format, and
1098 visible impression of promotional materials submitted for all promotional submission types and
1099 audiences. Optimally, Agency reviewers should be able to use or view each promotional
1100 material submitted to the Agency in the same manner as the end-user audience. In instances

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1101 when this is not possible, firms are to submit electronic promotional materials in a manner for
1102 which the net impression is clear and legible; likewise for the individual representations in each
1103 promotional material.

1104
1105 Provide each promotional material submitted to the Agency in electronic format as an individual
1106 file in an approved file format. If the current list of approved file formats does not allow the firm
1107 to submit a fully functional piece, the submission must provide the ability to view all interactive
1108 selection options as still images with annotations or notes that clearly describe the functionality
1109 of the piece.

1110
1111 Please note that promotional materials submitted with Form FDA 2253 to OPDP must include a
1112 representation of the actual piece that is disseminated rather than solely a proof or galley copy of
1113 the promotional material.⁴⁵ However, a proof or galley copy of the promotional material may
1114 also accompany the actual piece as part of the submission in order to demonstrate layout or size
1115 presentation elements. Please refer to section VII.K of this guidance for additional details on
1116 providing the size or dimensions of materials. Proof or galley copies of the promotional material
1117 should be submitted within section 1.15.2.1.2 of module 1.

1118 1119 **B. Visibility of Text and Images**

1120
1121 Promotional materials should present clear and legible text and images regardless of the format
1122 (electronic and/or physical media). Although the Agency recognizes that electronic images and
1123 text may require magnification on computer screens during the review process, the majority of
1124 images and text within each electronic file should not require excessive magnification in order to
1125 obtain the net impression of the piece or an understanding of the individual claims.

1126 1127 **C. Concise Description of Use**

1128
1129 Each promotional material should include a concise description of use. The description may
1130 include, but should not be limited to, the purpose of the piece, setting of use for the piece, and/or
1131 an explanation of additional materials that will be used in conjunction with the piece. The
1132 concise description of use may be presented on Form FDA 2253 under “Comments,” as a
1133 comment on the electronic version of the promotional material, as a comment on an optional
1134 proof or galley piece, and/or within the correspondence of a voluntary request for comments. A
1135 concise description of use is particularly important in situations where additional context is
1136 necessary, such as the following:

- 1137
- 1138 • The purpose of the promotional material is not self-evident after looking at an image of the
1139 piece or reading its title (e.g., a journal ad may be designed with an appearance similar to a
1140 booth panel).
 - 1141 • The promotional material is designed for use only in conjunction with other specific
1142 promotional materials.
- 1143

⁴⁵ Proof or galley copies are samples or preliminary versions of promotional material created for review and/or proofreading by the firm.

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1144

1145 • The promotional material is designed for use in a very specific setting.

1146

1147 • The promotional material (with the same material ID number) is designed for multiple uses
1148 in different and unique settings.

1149

1150 Concise descriptions of use may include, but should not be limited to, language such as:

1151

1152 • Booth panel A will be used only in conjunction with booth panels B, C, and D.

1153 • For use as a journal ad and a physician leave-behind.

1154 • Item 1 of 5 of kit.

1155 • For one-time use during [Conference Title, Month/Year].

1156

D. Layout Indicators

1157

1158

1159 Firms should submit promotional materials with clear and legible indicators for navigating
1160 through each promotional material, as applicable. Indicators describing location and navigation
1161 elements in the piece should be presented on each electronic page or image and should not
1162 obstruct the image of the promotional materials. Indicators may include, but should not be
1163 limited to, the following:

1164

1165 • Front cover, back cover, inside front cover, inside back cover

1166 • Bottom of piece or page, top of piece or page

1167 • Front of piece, back of piece

1168 • Page numbers

1169 • Inserts

1170 • Pockets and pocket content

1171 • Tabs or section dividers

1172 • Folds

1173 • Blank pages or panels

1174 • Annotations to references

1175 • Actual size

1176 • Clarifying the PI position

1177

1178 Indicators may be presented as symbols or text. A key should be provided (e.g., along the
1179 margin of the piece) if symbols are presented as indicators within a submission.

1180

E. Websites, Electronic Interactive Programs, and Electronic Detail Aids

1181

1182

1183 Electronic promotional material submissions including, but not limited to, websites, electronic
1184 interactive programs, and electronic detail aids should clearly display and communicate how the
1185 promotional material will look and convey messages to the end user. Preferably, the submission
1186 should allow FDA reviewers to view and interact with the piece in the same manner as the end
1187 user. For example, static electronic images may not adequately convey how complex interactive
1188 promotional materials convey promotional messages. Such promotional submissions may also

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1189 be accompanied by a video showing manipulation of the promotional program or application.
1190 Also see the eCTD Technical Conformance Guide for additional considerations related to
1191 submitting websites and other electronic promotional materials in the eCTD.⁴⁶
1192

1193 In general, to comply with the postmarketing requirement for promotional materials in 21 CFR
1194 314.81(b)(3)(i), a firm must submit its entire product website at the time of first use. If the firm
1195 then updates one page or section of the website, the firm need only submit the updated page or
1196 section with a cross-reference to the original submission of the website noted on Form FDA
1197 2253, including the date of the original submission. If the website is substantially revised, the
1198 firm must submit the revised website in its entirety.^{47,48}
1199

F. Materials Requiring Physical Manipulation by the End User

1200
1201
1202 Promotional materials requiring physical manipulation by the end user to obtain the net
1203 impression of the promotional message (and/or the details of the promotional message) should be
1204 submitted in a format that allows the Agency to view all aspects of the promotional material. For
1205 example, the electronic submission of a lenticular refrigerator magnet may display one image if
1206 tilted left and an alternate image if tilted right. Representations for both images should be
1207 submitted in this case.
1208

G. Three-Dimensional Promotional Materials

1209
1210
1211 Electronic submission of three-dimensional promotional objects should provide sufficient detail
1212 to allow FDA to view the promotional material from all possible views. In addition, images
1213 should provide adequate information to allow Agency reviewers to determine the size of the
1214 object (e.g., point size, dimensions). In rare situations, it may not be possible to accurately
1215 represent the promotional material in an electronic format. In these situations, the best possible
1216 electronic image should be submitted electronically, and a courtesy copy of the promotional
1217 material can also be sent for the reviewer. The courtesy copy of the promotional material should
1218 be submitted as a general correspondence and should include a reference to the electronic
1219 submission and sequence number.
1220

⁴⁶ The eCTD Technical Conformance Guide is available on the FDA eCTD website at <https://www.fda.gov/ectd>.

⁴⁷ If submitted in eCTD format, an updated page or section of a website should be submitted with the *submission-sub-type* of “Original” and the operator attribute “new.” If a website is substantially revised, the *submission-sub-type* should be “Original” and the “replace” operator attribute should be used to replace the previously submitted files with the revised website. Please refer to section VI.L of this guidance for more information about the use of operator attributes.

⁴⁸ For more information regarding fulfilling regulatory requirements for postmarketing submissions of interactive promotional media, see the draft guidance *Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics*. When final, this guidance will represent FDA’s current thinking on this topic.

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1221 **H. Multi-Page Spreads**⁴⁹

1222
1223 Promotional materials that include text or images that span more than one page or for which the
1224 promotional message may be interpreted as spanning more than one page (e.g., a two- or three-
1225 page brochure spread) should include a clear image or representation of the entire spread within
1226 a single view. All possible spreads of a given promotional material should be presented. In
1227 addition, electronic images of print materials and electronic materials should be presented in a
1228 manner and sequence as they would appear to the end user.

1230 **I. Kits**

1231
1232 Electronic submission of kits should clearly indicate the components of the kit. Components of
1233 the kit that are not intended for distribution apart from the kit should be labeled as such. The
1234 accompanying Form FDA 2253 must include the material ID number or identifier for the kit, as
1235 well as the material ID number or identifier for each individual component of the kit.

1237 **J. Dimensions**

1238
1239 All images of physical materials should include dimensions. Acceptable methods to identify
1240 dimensions include, but are not limited to, photographs of materials placed next to rulers,
1241 annotations on PDF images, or prominent PDF bookmarks identifying the dimensions of a
1242 piece.⁵⁰ Images of three-dimensional pieces should be identified as such in the descriptions and
1243 should provide information adequate to determine height, width, and depth dimensions.

1244
1245 Dimensions should be presented with standard units of measure.

1247 **K. Examples of Appropriately Submitted Promotional Materials**

1248
1249 Although not exhaustive, the following examples illustrate appropriate electronic submissions of
1250 promotional materials in terms of presentation issues:

1251
1252 *Example 1:* A firm creates a website for a new product that includes links and videos — As
1253 part of its postmarketing requirements, the firm must submit an electronic version of the
1254 product website under cover of Form FDA 2253. The firm consults the *eCTD Technical*
1255 *Conformance Guide* and the *Specifications for File Format Types Using eCTD Specifications*
1256 for additional considerations regarding submitting websites in acceptable formats.⁵¹ The
1257 submission should allow the FDA reviewer to click on links within the website and view

⁴⁹ In this guidance, the term *spread* is used to refer to adjacent pages of promotional material with related matter or connecting elements extending across the fold.

⁵⁰ For additional details regarding the submission of PDF documents in eCTD format, please see the Portable Document Format (PDF) Technical Specifications Document available at <https://www.fda.gov/ectd>.

⁵¹ The *eCTD Technical Conformance Guide* is available on the FDA eCTD website at <https://www.fda.gov/ectd>. The *Specifications for File Format Types Using eCTD Specifications* is in the eCTD Submission Standards on the FDA eCTD website at <https://www.fda.gov/ectd>.

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1258 videos or other animations as an end user will experience while using the site.⁵² If the firm is
1259 unable to provide active links within the electronic submission, the firm should provide
1260 electronic images of each web page in conjunction with videos.

1261

1262 *Example 2:* A firm is disseminating an electronic version of a promotional labeling piece
1263 containing a health-care-professional-directed quiz. As part of its postmarketing
1264 requirements, the firm should submit an electronic working version of the quiz under cover
1265 of Form FDA 2253. If the firm is unable to provide a working version of the quiz, the
1266 submission must include images that convey the results of selecting correct answers as well
1267 as the images resulting from incorrect answers.

1268

1269 *Example 3:* A firm voluntarily submits, for comments, an electronic image of a promotional
1270 mug that displays a product logo, a frequently used tagline, and a graphic that appears on the
1271 mug when hot liquid is added. The submission should include images of the front, back,
1272 inside, bottom, and sides of the mug, regardless of whether any particular view contains a
1273 promotional claim or representation. In addition, the submission should also include images
1274 of the mug when hot liquid is added, along with an explanation of when the images appear.
1275 Such a submission would benefit from layout indicators such as “front,” “back,” and
1276 “intentionally left blank,” in addition to measurement indicators.

1277

1278 *Example 4:* A firm voluntarily submits, for comments, an electronic image of a trifold
1279 branded print brochure. The firm should present, in the following order, images of (1) the
1280 front cover of the brochure, (2) all possible two-page spreads when the brochure is partially
1281 opened, (3) the single three-page spread when the brochure is completely opened, and (4) the
1282 back cover of the brochure. Such a submission would benefit from layout indicators such as
1283 “front panel,” “rear panel,” “2-panel spread,” and “3-panel spread,” in addition to
1284 measurement indicators.

1285

1286 *Example 5:* A firm is developing a kit that includes consumer-directed promotional materials
1287 that are exclusive to the kit to be submitted for voluntary comments — For each piece of
1288 material included in the kit, the firm should provide a concise description for use. For
1289 example, a promotional material that is intended only for distribution within the kit would
1290 include the following description: “Intended for distribution in consumer-directed sample kit
1291 only.”

1292

1293 *Example 6:* A firm is developing a Form FDA 2253 submission for an electronic banner
1294 used within an exhibit booth. The firm should submit a working version of the banner.
1295 However, if a working version of the banner cannot be submitted, the firm should submit a
1296 video of the banner in conjunction with screen shots. This is preferable to a submission
1297 consisting only of static screen shots. For example, the submission should include a video of
1298 the banner along with screen shots that convey how the message will scroll, the time lapse
1299 for the complete scroll of the message, and any variation in the rate that the message is
1300 scrolled across a screen.

1301

⁵² A fully functional website should be submitted in an accessible format whenever possible. Firms should not send links to websites—even if they are password-protected.

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1302 *Example 7:* A firm is developing a Form FDA 2253 submission for a consumer-directed
1303 branded video game that is embedded within a standard website. If a working version of the
1304 game cannot be submitted using an acceptable file format, the firm should submit a video of
1305 the game being played in addition to electronic still images of the game. If the game will
1306 also be available to consumers within a conference exhibit setting, the firm should include a
1307 concise description of use disclosing this additional unique setting.

1308
1309

VIII. PAPERWORK REDUCTION ACT OF 1995

1310

1311 This guidance contains information collection provisions that are subject to review by the Office
1312 of Management and Budget (OMB) under the Paperwork Reduction Act of 1995
1313 (44 U.S.C. 3501-3520).

1314

1315 The time required to complete this information collection is estimated to average the following:

1316

- 1317 • 51 hours for promotional labeling voluntarily submitted for comments, including
1318 resubmissions and amendments
- 1319 • 3 hours for general correspondence submitted to FDA
- 1320 • 3 hours for requests to withdraw a previous submission to FDA
- 1321 • 13 hours for responses to untitled or warning letters
- 1322 • 13 hours for responses to information requests
- 1323 • 13 hours for reference documents
- 1324 • 13 hours for complaints submitted to OPDP

1325

1326 These estimates include the time to review instructions, search existing data sources, gather the
1327 data needed, and complete and review the information collection. Send comments regarding this
1328 burden estimate or suggestions for reducing this burden to:

1329

1330 Office of Prescription Drug Promotion, Center for Drug Evaluation and Research, Food
1331 and Drug Administration, 10903 New Hampshire Avenue, Bldg. 51, Rm. 3374, Silver
1332 Spring, MD 20993-0002

1333

1334 This guidance also refers to previously approved collections of information found in FDA
1335 regulations and collections of information that are currently under OMB review. The collections
1336 of information in 21 CFR 202.1, including voluntary requests for advisory comments,
1337 resubmissions, and amendments for advertisements, have been approved under OMB control
1338 number 0910-0686; the collections of information in 21 CFR 601.45 (presubmission of
1339 promotional materials for accelerated approval products under part 601) have been approved
1340 under OMB control number 0910-0338; the collections of information for Form FDA 2253 and
1341 the presubmission of promotional materials for accelerated approval products under 21 CFR part
1342 314 have been approved under OMB control number 0910-0001.

1343

1344 An Agency may not conduct or sponsor, and a person is not required to respond to, a collection
1345 of information unless it displays a currently valid OMB control number. The OMB control
1346 number for this information collection is 0910-0870 (expires 05/31/2022).

1347