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# Guidance for Industry

## Labeling OTC Human Drug Products

### Questions and Answers

#### *DRAFT GUIDANCE*

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For questions on the content of the draft document, contact Cazemiro R. Martin or Gerald M. Rachanow at 301-827-2222.

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

**OTC  
January 2005**

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# Guidance for Industry

## Labeling OTC Human Drug Products Questions and Answers

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

**OTC  
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# Guidance for Industry<sup>1</sup>

## Labeling OTC Human Drug Products — Questions and Answers

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

### I. INTRODUCTION

This guidance is intended to assist manufacturers, packers, and distributors of over-the-counter (OTC) drug products who have questions about the standardized labeling content and format requirements in § 201.66 (21 CFR 201.66). The examples in this guidance illustrate various format and content features of the labeling requirements and show how OTC drug monograph labeling information can be converted to the OTC "Drug Facts" format. This is one of a series of guidances intended to facilitate compliance with the labeling requirements in § 201.66.

### II. BACKGROUND

In the *Federal Register* of March 17, 1999 (64 FR 13254), the Food and Drug Administration (FDA) published a final rule (21 CFR 201.66) establishing standardized content and format for the labeling of OTC drug products (Drug Facts labeling). The Drug Facts labeling for OTC drug products is intended to make it easier for consumers to read and understand OTC drug product labeling and use OTC drug products safely and effectively. The Drug Facts labeling regulation in § 201.66 covers all OTC drug and drug-cosmetic products, whether marketed under a new drug marketing application (NDA), abbreviated new drug application (ANDA), or OTC drug monograph (or product not yet the subject of a final OTC drug monograph).<sup>2</sup>

The regulation is divided into two main parts: (1) Content requirements (i.e., headings, subheadings, and the order in which certain information must be listed) and (2) format

<sup>1</sup>This guidance has been prepared by the Division of Over-the-Counter (OTC) Drug Products in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA).

<sup>2</sup> The text of § 201.66 can be found at the FDA Division of Dockets Management Internet site located at <http://www.fda.gov/cder/otc/label/label-fr-reg.htm>.

39 requirements (i.e., graphic specifications). This guidance primarily discusses questions received  
40 from manufacturers, packers, and distributors relating to these requirements, which are set forth in  
41 § 201.66 (c) and (d), respectively.

42  
43  
44

### III. CONTENT LABELING REQUIREMENTS

45  
46 The following questions and answers address the OTC labeling requirements in § 201.66. Tables in  
47 Appendix A of this draft guidance list the specific section-by-section requirements in § 201.66(c)  
48 and (d) as well as the expectations for implementing the requirements in the regulation. Please refer  
49 to these tables for details on specific requirements.

50

51 **Question 1:** *What labeling information do the regulations require for all OTC drug products?*

52

53 **Answer 1:** Section 201.66 requires that all OTC drug product labeling contain the following  
54 information about the product. This information must be organized according to the  
55 following headings and must be presented in the following order:

- 56 1. Title ("Drug Facts" or "Drug Facts (continued)")
- 57 2. Active ingredients
- 58 3. Purpose
- 59 4. Use(s)
- 60 5. Warnings
- 61 6. Directions
- 62 7. Other information
- 63 8. Inactive ingredients
- 64 9. Questions (optional) ("Questions?" or "Questions or comments?")

65

66 This information must appear on the outside container or wrapper of the retail  
67 package, or the immediate container label if there is no outside container or wrapper.  
68 (If the Drug Facts information appears on the outside container or wrapper of the  
69 retail package, its use on the immediate container is optional. See Appendix A.)

70

71 **Question 2:** *Why must the title "Drug Facts (continued)" appear on each subsequent panel in  
72 which the Drug Facts appear?*

73

74 **Answer 2:** The title "Drug Facts" must appear on the first panel and the title "Drug Facts  
75 (continued)" must appear on each subsequent panel to ensure that the person reading  
76 the labeling can follow through to the end of the labeling (§ 201.66(c)(1)).

77

78 **Question 3:** *What indications can be included in the Use(s) section if the product is a drug and  
79 cosmetic product?*

80

81 **Answer 3:** For drug-cosmetic products, only the drug-related indications can be included in the  
82 *Use(s)* section.

83

84 **Question 4:** *Is there a required order for listing subject specific warnings?*

85  
86 **Answer 4:** Section 201.66(c) requires that warnings in paragraph (c)(5) appear in the order  
87 listed.  
88

89 **Question 5:** *What information must appear under the Warnings subheading "Do not use"?  
90 Can I convert the text of existing warnings in final OTC monographs or approved  
91 applications to the bulleted statement format under this subheading?*  
92

93 **Answer 5:** The "Do not use" subheading (§ 201.66(c)(5)(iii)) is reserved for (1) products that  
94 should not be used unless a previous diagnosis has been made by a doctor or (2)  
95 products that should not be used under any circumstances by certain consumers,  
96 regardless of whether a doctor or health professional is consulted.  
97

98 Manufacturers can convert existing formats to the Drug Facts labeling format. For  
99 example, the current warning "Do not use this product unless a diagnosis of asthma  
100 has been made by a doctor" can be placed under the subheading "Do not use" and  
101 shortened to read "unless a diagnosis of asthma has been made by a doctor." (i.e.,  
102 "Do not use unless a diagnosis of asthma has been made by a doctor")  
103

104 **Question 6:** *How could I convert a lengthy warning under the subheading "Ask a doctor  
105 before use if you have" into the bulleted text format?*  
106

107 **Answer 6:** Here is an example: The warning for oral and topical antitussives states: "Do not  
108 take this product for persistent or chronic cough such as occurs with smoking,  
109 asthma, or emphysema, or if cough is accompanied by excessive phlegm (mucus)  
110 unless directed by a doctor." Under this subheading, this warning can be converted  
111 into bulleted statements as follows:

- 112 ● cough that occurs with too much phlegm (mucus)
- 113 ● chronic cough that lasts as occurs with smoking, asthma, chronic bronchitis, or  
114 emphysema  
115

116 **Question 7:** *How could I convert the OTC antihistamine drug product warning "Do not take  
117 this product if you are taking sedatives or tranquilizers without first consulting  
118 your doctor" into bulleted text ?*  
119

120 **Answer 7:** This warning could appear as follows:  
121 "Ask a doctor or pharmacist before use if you are taking sedatives or  
122 tranquilizers," or

- 123
- 124 "Ask a doctor or pharmacist before use if you are taking ● sedatives  
125 ● tranquilizers"  
126

127 **Question 8:** *What information must appear under the subheading "When using this product"?  
128 How could I convert text of existing required warnings to bulleted text format  
129 under this subheading?*  
130

131 **Answer 8:** This subheading must be used for all side effects that consumers may experience. It  
132 identifies substances (e.g., alcohol) or activities (e.g., operating machinery, driving a  
133 car) that should be avoided while using the product. This subheading must also  
134 include warnings for drugs in dispensers pressurized by gaseous propellants. Such  
135 information would appear in bulleted text format as follows:

- 136
- 137 ● may cause drowsiness [or may appear as: ● drowsiness may occur]
- 138 ● alcohol, sedatives, and tranquilizers may increase the drowsiness effect  
139 [or may appear as: ● alcohol, sedatives, and tranquilizers may increase drowsiness]
- 140 ● do not puncture or incinerate; contents under pressure.
- 141

142 **Question 9:** *What information must appear under the subheading "Stop use and ask a doctor*  
143 *if"?*

144

145 **Answer 9:** You must include under the "Stop use..." subheading any signs of toxicity or other  
146 reactions that would require a consumer to immediately stop using the product. For  
147 example, the bulleted statement "you get nervous, dizzy, or sleepless" would appear  
148 in this section.

149

150 **Question 10:** *Where must I put warnings required in an applicable OTC drug monograph, in*  
151 *other OTC drug regulations, or in an approved drug application that do not*  
152 *otherwise fit under the Warning heading or subheadings?*

153

154 **Answer 10:** Such warnings must be placed in the Drug Facts *Warning* section. For example,  
155 chlorofluorocarbons (CFC) warnings, required in certain approved drug applications,  
156 must be put in the *Warnings* section. The warning would appear as follows:  
157 "Contains CFC-[insert number] and CFC-[insert number], substances that harm  
158 public health and the environment by destroying ozone in the upper atmosphere"  
159 (§ 201.320).

160

161 **Question 11:** *Where must pregnancy information and related warnings be placed?*

162

163 **Answer 11:** When applicable, these types of warnings must also be placed in the second to last  
164 subsection of the *Warnings* section. Warnings may include one or more of the  
165 following:

- 166
- 167 ● The pregnancy/breast-feeding warning
- 168 ● The third trimester warning for products containing aspirin or carbaspirin  
169 calcium.
- 170 ● The third trimester warning in approved drug applications for products containing  
171 ketoprofen, naproxen sodium, or ibuprofen (if not intended exclusively for use in  
172 children).
- 173

174 **Question 12:** *Should all OTC drug product labeling include the "Keep out of reach of children"*  
175 *and the accidental overdose/ingestion warnings?*

176

177 **Answer 12:** In most cases, these warnings are required for OTC drug products and therefore must be  
178 included in the Drug Facts box. In a few very special instances, the “Keep out of reach  
179 of children” warning may be omitted. (See lipstick with a sunscreen in  
180 § 352.52(f)(1)(vi).) The accidental overdose/ingestion warning may also be omitted in  
181 some instances, as specified in an applicable OTC drug monograph or approved new  
182 drug application.  
183

184 **Question 13:** *Do I have to present information under Directions in a table format?*  
185

186 **Answer 13:** Depending on the product, the directions can appear completely in a table, as a  
187 number of bulleted statements, or as a combination of a table and bulleted  
188 statements. For example, a table format must be used when dosage directions are  
189 provided for three or more age groups or populations (§ 201.66(d)(9)). Dosage  
190 directions provided for one or two age groups or populations can be presented using  
191 bulleted statements. However, a table format can be used for two age groups or  
192 populations if it helps make the presentation of the information clearer and easier to  
193 read.  
194

195 Under this heading, information other than age groups should appear as bulleted  
196 statements. For example:

- shake well
- drink a full glass (8 oz) of liquid with each dose
- do not use more than directed

adults and children 12 years and older	2 tablets every 6 hours
children 6 -12 years	1 tablet every 6 hours
children under 6 years	ask a doctor

201

202

203

204 **Question 14:** *What information must be included under the heading Other information?*  
205

206 **Answer 14:** This section must include information that is not included under the other headings  
207 or subheadings, but is required or is made optional under an OTC drug monograph,  
208 other OTC drug regulation, or approved drug application.  
209

210 If applicable, the first bulleted statement under this heading must include calcium,  
211 magnesium, potassium, and sodium to read as follows: “each (insert appropriate  
212 dosage unit) contains: [in bold type] (insert name(s) of ingredient(s) and quantity of  
213 each ingredient)” (§§ 201.70, 201.71, 201.72, 201.64, respectively. See also  
214 § 201.66(c)(7)(i)).  
215

216 If applicable, phenylalanine/aspartame content shall appear as the next item as  
217 follows: “Phenylketonurics: Contains Phenylalanine (insert quantity) mg per (insert  
218 appropriate dosage unit).” This statement must be listed as the first bulleted



219 statement under this heading or the second bulleted statement if Ca, Mg, Na, or K is  
220 (are) present. For example:

221  
222 **Other information**

- 223 ● **each tablet contains:** calcium 10 mg, magnesium 10 mg, and sodium 15 mg
- 224 ● Phenylketonurics: Contains Phenylalanine 10 mg per tablet
- 225 ● [insert storage conditions] if applicable
- 226 ● [insert tamper-evident statement]

227  
228 **Question 15:** *Where must the tamper-evident statement appear in my OTC product labeling?*

229  
230 **Answer 15:** The tamper-evident statement must be prominently placed on the drug product  
231 package to alert consumers about the product's tamper-evident features (21 CFR  
232 211.132). The tamper-evident statement describes the tamper-evident feature of the  
233 product package and advises consumers that, if the feature is breached or missing  
234 when the product is purchased, tampering may have occurred. Tamper-evident  
235 packaging with an appropriate labeling statement will be more likely to protect  
236 consumers because the consumer will be in a better position to detect tampering  
237 when he or she has knowledge that a tamper-evident feature has been incorporated  
238 into the product design. The Agency allows flexibility in the placement of this  
239 statement on the package and does not require that it be included within the Drug  
240 Facts section. However, if included in this section, the statement must appear under  
241 the heading "**Other information**" (see 21 CFR 201.66(c)(7)).

242  
243 The Agency also noted in the final rule preamble for the Drug Facts regulation that  
244 many products are now marketed with "peel back" or "fold out" labels affixed to the  
245 product package and that these labels could be used to accommodate all of the FDA  
246 required information in the Drug Facts section (64 FR 13254 at 13268; March 17,  
247 1999). These types of labels were not in use at the time the tamper-evident  
248 requirements became effective. Recently, interested parties have inquired whether  
249 the tamper-evident statement may be included in a Drug Facts section that appears in  
250 such "peel back" or "fold out" labels. We believe that the goals of the tamper  
251 evident statement would likely not be achieved if the statement only appears in a  
252 "peel back" or "fold out" label and is not clearly visible without peeling back or  
253 folding out the label.

254  
255 It is important that the consumer view the tamper-evident statement before purchase  
256 and use of the product so that he or she will be better aware of the tamper-evident  
257 features and any signs of tampering. Once the consumer opens the tamper-evident  
258 package, the tamper-evident features have been breached. If the consumer has failed  
259 to examine these features before opening, then the consumer will likely not know if  
260 there were any signs of tampering. A tamper-evident statement inside a "peel back"  
261 or "fold out" label that is not visible on the outside of the package is unlikely to be  
262 viewed before breach of the tamper evident feature. The consumer may not be aware  
263 to peel back or unfold this label to view the tamper-evident statement before opening  
264 the package. Thus, we recommend that the statement not appear within the Drug

265 Facts box in a "peel back" or "fold out" label if the statement would not be clearly  
266 visible without peeling back or folding out the label. We recommend instead in these  
267 circumstances that the tamper evident statement be outside the Drug Facts box in  
268 another part of the label where the statement is clearly visible without further  
269 manipulation of that label.  
270

271 **Question 16:** *Do I have to list the inactive ingredients in my OTC drug product labeling in*  
272 *alphabetical order?*  
273

274 **Answer 16:** It depends.  
275

276 For OTC drug products that are not also cosmetic products, the established name of  
277 each inactive ingredient must be listed in alphabetical order (§ 201.66(c)(8)). For  
278 example, the *Inactive ingredients* section would appear as follows:  
279

280 **Inactive ingredients** colloidal silicon dioxide, FD&C blue #1 lake,  
281 hydroxypropyl methylcellulose, lactose, magnesium stearate, polyethylene  
282 glycol, povidone, propylene glycol, titanium dioxide  
283

284 For an OTC product that is a drug-cosmetic product, the inactive ingredients must be  
285 listed in descending order of predominance in the product formulation  
286 (§§ 201.66(c)(8) and 701.3(a)). For example, the *Inactive ingredients* section would  
287 appear as follows:  
288

289 **Inactive ingredients** water, sorbitan isostearate, sorbitol,  
290 triethanolamine, stearic acid, barium sulfate, benzyl alcohol,  
291 dimethicone, methylparaben, aloe extract, carbomer, disodium EDTA  
292

293 **Question 17:** *Do I have to include a Questions section in the Drug Facts box or similar*  
294 *enclosure?*  
295

296 **Answer 17:** No. Although this heading and subsequent information is not required, the Agency  
297 encourages all manufacturers, distributors, and repackers to include a telephone  
298 number in this section. The telephone number of a source to answer questions about  
299 the product would be included in this section.  
300

301 Although not permitted to appear in or otherwise interrupt the required Drug Facts  
302 labeling information, brand names or product attributes can appear in the telephone  
303 number and/or in the Web site address, if used. However, if the telephone number  
304 appears as letters of the brand name or product attribute, FDA recommends that the  
305 manufacturer should also include the numerical representation of the telephone  
306 number in this section.  
307  
308

309 **IV. FORMAT LABELING REQUIREMENTS<sup>4</sup>**

310

311 **Question 18:** *How must the content labeling requirements be presented within the Drug Facts*  
312 *box or similar enclosure?*

313

314 **Answer 18:** All features of the Drug Facts box or similar enclosure and the required content  
315 information must be presented according to graphic specifications, which are listed in  
316 Appendix A (Table 2) of this draft guidance document (see also §§ 201.66(c) and (d)).

317

318 **Question 19:** *Can I use bold type for any information I consider needs greater prominence?*

319

320 **Answer 19:** FDA recommends that you avoid using bold type in the immediate area where  
321 existing regulations require specific text be in bold type.

322

323 **Question 20:** *How should fractions be expressed within the Drug Facts box?*

324

325 **Answer 20:** Fractions (e.g., 1/2) can be expressed in mathematical notation or text format (i.e.,  
326 one-half). The text must be in the same single, clear, easy-to-read type style and  
327 type size used for the other text included in the Drug Facts box. If expressed in  
328 mathematical notation, each component of the numerical notation must be no smaller  
329 than 6-point type.

330

331 **Question 21:** *How should I arrange additional text related to a single bulleted statement?*

332

333 **Answer 21:** FDA recommends that additional text be formatted as indented subbulleted  
334 statements. For example:

335

*Uses*

336

• temporarily relieves pain and itching due to:

337

• insect bites • minor skin irritations

338

• dries the oozing and weeping of:

339

• poison ivy • poison oak • poison sumac

340

341 **Question 22:** *Can I begin a bulleted statement on the same line as a heading or subheading?*

342

343 **Answer 22:** Yes. However, no bulleted statement or text can appear on the same line as the  
344 *Warning* heading.

345

346 **Question 23:** *Should bulleted statements be left justified when using the standard labeling*  
347 *format?*

348

349 **Answer 23:** Yes. The first bulleted statement on each horizontal line of text must be left  
350 justified, except if the bulleted statement appears on the same line of an appropriate  
351 heading or subheading (§ 201.66(d)(4)). Any bulleted statements that do not fit  
352 entirely on a multi-bulleted line should begin left justified on the following line.

---

<sup>4</sup> See Appendix A (Table 2) of this draft guidance for specific format labeling requirements in § 201.66(d).

353 (Note: no bulleted statement or text can appear on the same line as the *Warning*  
354 heading.)

355  
356 For example:

- 357 **Ask a doctor before use if you have**  
358 ● heart disease ● glaucoma ● high blood pressure  
359 ● thyroid disease ● diabetes  
360 ● trouble urinating due to an enlarged prostate gland  
361 ● a breathing problem such as emphysema or chronic bronchitis  
362

363 **Question 24:** *Should bulleted statements be aligned with the bulleted statements on the previous*  
364 *line when using the modified labeling format?*

365  
366 **Answer 24:** No. Using this format, bulleted statements do not need to be aligned and can  
367 continue to the next line of text (§ 201.66(d)(10)(iv)). For example:

- 368  
369 **Ask a doctor before use if you have** ● heart disease ● glaucoma  
370 ● high blood pressure ● thyroid disease ● diabetes ● trouble urinating due to  
371 an enlarged prostate gland ● a breathing problem such as emphysema or chronic  
372 bronchitis  
373

374 **Question 25:** *Where can I find guidance on the use of a column format as part of the new OTC*  
375 *labeling requirements?*

376  
377 **Answer 25:** A guidance document entitled *Labeling OTC Human Drug Products Using a*  
378 *Column Format* is available on the CDER Internet site at  
379 <http://www.fda.gov/cder/guidance/index.htm>. A written request for a copy can be  
380 submitted to the Division of Drug Information (HFD-240), Center for Drug  
381 Evaluation and Research, FDA, 5600 Fishers Lane, Rockville, MD 20857.  
382

383 **Question 26:** *How can I obtain copies of other FDA labeling guidance relating to the new OTC*  
384 *labeling requirements?*

385  
386 **Answer 26:** Copies of the guidances are available on the Internet at [http://www.fda.gov/cder/](http://www.fda.gov/cder/guidance/index.htm)  
387 [guidance/index.htm](http://www.fda.gov/cder/guidance/index.htm), or send a written request for single copies to the Division of  
388 Drug Information (see address above).  
389

390 **Question 27:** *How must I list ingredients under the heading Active ingredients?*

391  
392 **Answer 27:** The ingredients must be listed in alphabetical order.  
393

394 **Question 28:** *How should I list under the heading Purpose ingredients with the same*  
395 *pharmacological action?*  
396

397 **Answer 28:** When more than one active ingredient has the same purpose, the information can be  
398 presented in a manner that readily associates each active ingredient with its purpose  
399 (by using brackets, dot leaders, or other graphical features). For example:  
400

	<b>Active ingredients</b>	<b>Purpose</b>
401	Homosalate 6% }	
402	Oxybenzone 3% }	Sunscreen
403	Padimate O 2% }	
404		
405		

406 **Question 29:** *How should I list inactive ingredients that may or may not be contained in my*  
407 *product?*  
408

409 **Answer 29:** These ingredients should be listed in alphabetical order along with those ingredients  
410 that are contained in your product. FDA recommends that you place an asterisk next  
411 to those ingredients that, depending on the source, may or may not be contained in  
412 the product (e.g., acacia\*, dextrose\*, sucrose, xanthum gum\*). The asterisk should  
413 be referenced at the bottom or end of the inactive ingredient section in the Drug  
414 Facts box, with the notation “\* contains one or more of these ingredients” (if more  
415 than one ingredient may or may not be in the product), or “\* may contain this  
416 ingredient” (if only one ingredient may or may not be in the product), whichever is  
417 appropriate.  
418

419 FDA recommends that for product labeling using the standard labeling format as  
420 described in §§ 201.66(d)(1) through (d)(9), the statement (“\* contains one or more  
421 of these ingredients,” or “\* may contain this ingredient,” whichever is appropriate)  
422 should be left justified at the end of the inactive ingredient section. The type size of  
423 these statements must be at least 6-point type. For product labeling that uses the  
424 modified format as described in § 201.66(d)(10), the asterisk statement could appear  
425 on the same line as the last listed inactive ingredient if separated from the last listed  
426 ingredient by at least two square "ems"<sup>3</sup>.  
427

428 Listing too many alternative ingredients could be misleading and may cause  
429 consumer confusion. To avoid such confusion, sponsors may wish to consider using  
430 a second set of labels for products with a lengthy list of different inactive  
431 ingredients.  
432

433 Additionally, to provide consumers with the opportunity to learn if an ingredient is  
434 in the lot number of the product, the Agency recommends that the optional  
435 information in § 201.66(c)(9) (*Questions?* or *Questions or comments?* followed by  
436 the telephone number of a source to answer questions about the product) be included  
437 in labeling.  
438

439 Sponsors are also reminded to follow all applicable current good manufacturing  
440 practice regulations Part 211 for finished pharmaceuticals so that manufacturers

---

<sup>3</sup> Two square "ems" are two squares of the size of the letter "M." (See 21 CFR 201.66(d)(4).)

441 maintain appropriate records showing which lot numbers of the product contain  
442 which inactive ingredients.

443

444 **Question 30:** *Can I use a pictogram or graphical image such as the Universal Product Code*  
445 *(UPC) symbol within the Drug Facts box?*

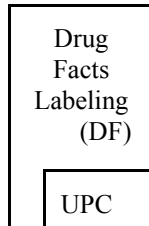
446  
447 **Answer 30:** No. The only pictogram that may be included within the Drug Facts information is a  
448 telephone or telephone receiver before the Questions heading. Pictograms and graphical  
449 images such as the Universal Product Code (UPC) symbol cannot appear in, or in any  
450 way interrupt, the information required in the Drug Facts labeling (§ 201.66(d)(7)).  
451 They can appear outside the Drug Facts box. The following examples illustrate how the  
452 UPC code can be placed in relation to the Drug Facts Box.

453

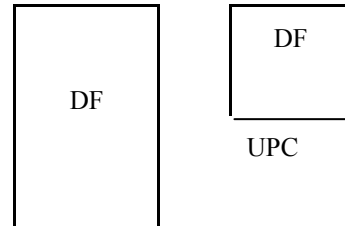
454

455

**Illustration 1.**



**Illustration 2.** (showing second panel)



456

457

458 **Question 31:** *When can I use the modified labeling format?*

459

460 **Answer 31:** When the required Drug Facts content information printed in the standardized format  
461 plus any other FDA required information for drug or drug-cosmetic products, other  
462 than information required to appear on the principal display panel, requires more  
463 than 60 percent of the total surface area available to bear labeling.

464

465 **Question 32:** *What is the difference between the standard and modified labeling formats?*

466

467 **Answer 32:** The following table illustrates the differences between the two labeling formats.

468  
469  
470  
471**Table 1. Standard Versus Modified Labeling Format**

<b>Labeling Element</b>	<b>Standard Format</b>	<b>Modified Format</b>
Drug Facts Box	Set off by barline	Barline may be omitted if color contrast used to set off from the rest of the labeling
Drug Facts	Larger than largest type size used in Drug Facts box or similar enclosure	Larger than largest type size used in Drug Facts box or similar enclosure
Drug Facts (continued)	No smaller than 8-point type	No smaller than 7-point type
Headings	≥8-point or greater type, or 2-point type greater than point size of text	≥7-point or greater type, or 1-point type greater than point size of text
Subheadings	No smaller than 6-point type	No smaller than 6-point type
Bulleted text	No smaller than 6-point type	No smaller than 6-point type
Leading	Minimum 0.5 point	Less than 0.5 point may be used, provided the ascenders and descenders do not touch
Bullets	Minimum 5-point type Vertical alignment	Minimum 5-point type No alignment required

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**Question 33:** *What other labeling requirements may be applicable in addition to the standardized content and format requirements in § 201.66?*

**Answer 33:** Additional labeling requirements in Part 201 that may be applicable are summarized as follows:

**Table 2. Additional Labeling Requirements**

<b>Paragraph</b>	<b>Description of Paragraph</b>
§ 201.1	Name and place of business of manufacturer, packer, or distributor
§ 201.17	Location of expiration dates
§ 201.18	Control numbers
§ 201.60	Principal display panel
§ 201.61	Statement of identity <ul style="list-style-type: none"> <li>• Established name of drug</li> <li>• Statement of general pharmacological category(ies) or the principal intended actions</li> <li>• Bold type</li> <li>• Size related to the most prominent printed matter</li> </ul>
§ 201.62	Declaration of net quantity of contents
§ 201.20	Declaration of the presence of FD&C Yellow No. 5 and/or FD&C Yellow No. 6
§ 211.132(c)	Tamper-evident labeling

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482 **Question 34:** *When must my product comply with the new OTC labeling requirements?*

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484 **Answer 34:** The date by which your product must comply with the new labeling requirements  
485 depends on its current marketing status. See Appendix A (Table 3) of this guidance  
486 to determine the date of implementation of the "Drug Facts" requirements.  
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488 **V. EXEMPTION AND DEFERRALS**

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490 **Question 35:** *Are there any exemptions or deferrals to the Drug Facts labeling requirements?*

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492 **Answer 35:** Section 201.66(e) provides that FDA on its own initiative or in response to written  
493 request from any manufacturer, packer, or distributor, may exempt or defer, based on the  
494 particular circumstances presented, one or more specific requirements set forth in §  
495 201.66(a) through (d), on the basis that the requirement is inapplicable, impracticable, or  
496 contrary to public health or safety. FDA points out that exemption and deferral requests  
497 shall: (1) Document why a particular requirement is inapplicable, impracticable, or is  
498 contrary to public health or safety; and (2) include a representation of the proposed  
499 labeling, including any outserts, panel extensions, or other graphical or packaging  
500 techniques intended to be used with the product. FDA reviews each exemption and  
501 deferral request submitted and, based on the data submitted, makes a determination  
502 whether to grant or deny such requests.  
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504 If you have questions on whether a particular FDA requirement applies to your drug or drug-  
505 cosmetic product, please contact:

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507 Office of Compliance (HFD-310)  
508 Center for Drug Evaluation and Research  
509 Food and Drug Administration  
510 5600 Fishers Lane  
511 Rockville, MD 20857  
512 301-827-8958 or 301-827-8959

513 Division of OTC Drug Products (HFD-560)  
514 Center for Drug Evaluation and Research  
515 Food and Drug Administration  
516 5600 Fishers Lane  
517 Rockville, MD 20857  
518 301-827-2222

519 Office of Cosmetics and Colors (HFS-105)  
520 Center for Food Safety and Applied Nutrition  
521 Food and Drug Administration  
522 200 C St., SW.  
523 Washington, DC 20204  
524 202-205-4061



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## APPENDIX A: SUMMARY

Table 1. Labeling Content: § 201.66(c)(1) Through (c)(9)

Paragraph	Description of Paragraph	Comments
(c)(1)	<b>Drug Facts, Drug Facts (continued)</b>	Title to be used is <b>Drug Facts</b> (on subsequent panels use “ <b>Drug Facts (continued)</b> ”)
(c)(2)	<b>Active ingredient</b> (established name, strength/concentration)	For drug-cosmetic products, the drug ingredients are considered the active ingredients, and the cosmetic ingredients are considered the inactive ingredients.
(c)(3)	<b>Purpose(s)</b>	If there is no statement of identity or no applicable OTC drug monograph, the ingredient purpose is stated based on its general pharmacological category(ies), or the principal intended action(s) of the drug. See 21 CFR 201.66(b)(2), (b)(8), (c)(8); and 21 CFR 701.3(a) and (f).
(c)(4)	<b>Use(s)</b>	The use(s) is/are the specific indication(s) or approved use(s) for the drug product. For drug-cosmetic products, the use in the <b>Drug Facts</b> labeling is attributed only to the drug component.
(c)(5)	<b>Warning(s)</b>	Warning(s) information appears in a specific order, under the heading <b>Warnings</b> , as applicable. Most warnings follow specific subheadings, as described below in (c)(5)(i) through (c)(5)(x).
(c)(5)(i)	<b>For external/rectal/ vaginal use only</b>	Appears in bold type. In some instances (e.g., lip protectant drug products), the <b>external use only</b> warning may be omitted.
(c)(5)(ii)	All applicable warnings	Appear with subheadings highlighted in bold type.
(c)(5)(ii)(A)	<b>Reye’s syndrome warning</b>	When this warning is required, it is the first warning of the warnings listed in paragraphs (c)(5)(ii)(A) through (c)(5)(ii)(G) to appear in this location in the <b>Warnings</b> labeling.
(c)(5)(ii)(B)	Allergic reaction warnings	Subheading <b>Allergy alert</b> is used.
(c)(5)(ii)(C)	<b>Flammability warning</b> , with appropriate signal word	The appropriate flammability signal word in an approved drug application or OTC drug monograph is used.
(c)(5)(ii)(D)	Water soluble gum warning, <b>Choking</b>	The subheading <b>Choking</b> is used.
(c)(5)(ii)(E)	<b>Alcohol warning</b>	Subheading <b>Alcohol warning</b> is used.
(c)(5)(ii)(F)	<b>Sore throat warning</b>	Subheading <b>Sore throat warning</b> is used.
(c)(5)(ii)(G)	<b>Dosage warning</b>	The warnings in 21 CFR 201.307(b)(2)(i) or (b)(2)(ii) for drug products containing sodium phosphates. The subheading <b>Dosage warning</b> is used to introduce this information.
(c)(5)(iii)	<b>Do not use</b>	Subheading used for all absolute contraindications and involve several different types of situations.

Paragraph	Description of Paragraph	Comments
(c)(5)(iv)	<b>Ask a doctor before use if you have</b>	Subheading is used for certain preexisting conditions.
(c)(5)(v)	<b>Ask a doctor or pharmacist before use if you are</b>	Subheading used for all drug-drug and drug-food interactions.
(c)(5)(vi)	<b>When using this product</b>	Subheading used for all side effects that the consumer may experience; identifies substances or activities that should be avoided while using the product.
(c)(5)(vii)	<b>Stop use and ask a doctor if</b>	Subheading used for any signs of toxicity or other adverse reactions that would necessitate immediately discontinuing use of product.
(c)(5)(viii)	Any required warnings	Location used to include any other required warnings that do not fit within sections 201.66(c)(5)(i) through (c)(5)(vii), (c)(5)(ix), and (c)(5)(x).
(c)(5)(ix)	<b>The pregnancy/breast feeding warning</b>	General warning and other related warnings.
(c)(5)(x)	<b>Keep out of reach of children</b>	General warning and accidental <b>overdose/ingestion</b> warning in 21 CFR 330.1(g).
(c)(6)	<b>Directions</b>	Described in an applicable OTC drug monograph or approved drug application.
(c)(7)	<b>Other information</b> and additional information not included in (c)(2) – (c)(6), (c)(8), (c)(9) of this section, e.g., storage conditions.	Subheading used for additional information that is not included under the other subheadings, but which is required or is made optional under an OTC drug monograph(s), other OTC drug regulation(s), or approved drug application.
(c)(7)(i)	certain ingredients (e.g. Na)	See 21 CFR 201.64(b), 201.70(b), 201.71(b), and 201.72(b)
(c)(7)(ii)	Phenylalanine	See 21 CFR 201.21(b)
(c)(7)(iii)	additional information	For example: storage conditions, tamper-evident statement
(c)(8)	<b>Inactive ingredients</b>	List of each inactive ingredient, using its established name
(c)(9)	<b>Questions? (or Questions or Comments?)</b>	Optional heading used to provide a telephone number of a source to answer questions about the product.

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**Table 2 Labeling Format: 21 CFR 201.66(d)(1) through (d)(9)**

Paragraph	Description of Paragraph
(d)(1)	Drug Facts: first letter of words uppercase
“	Headings, subheadings: first letter of first word uppercase
“	Left justification
(d)(2)	Drug Facts type size greater than largest type size used in Drug Facts labeling
“	Heading 8 pt or 2 point sizes greater than text point size

Paragraph	Description of Paragraph
“	Type size $\geq 6$ pt size for information in Drug Facts
“	Subheadings $\geq 6$ point type size
“	Drug Facts (continued) type size no smaller than 8-point type
(d)(3)	Letters do not touch
“	$\geq .5$ pt leading (space between lines)
“	No more than 39 characters per inch
“	Bold Italic headings and title
“	Bold subheading except the phrase “(continued)”
“	Contrasting dark color for title and heading
(d)(4)	Bullet: solid circle or square 5 pt type, same shape and color, left justified or separated from heading or subheading by at least two square “ems”
“	Bullet on same lines: end of statement separated from bulleted statement by two “ems”
“	Bullet on same lines: additional bulleted statement does not continue on next line
“	Vertical alignment of bulleted statements
(d)(5)	Appear on more than one panel
“	Visual graphic signals continuation
(d)(6)	Left justification of information required by (c)(2)
“	Right justification of information required by (c)(3)
“	Alphabetical order of active ingredients
“	Information required by (c)(4), (c)(6) - (c)(9) may start on same line as required headings
“	None of information required in (c)(5) shall appear on same line as Warnings
(d)(7)	Graphical images should not interrupt the heading, subheading and information. Hyphens should not be used except to punctuate compound words.
(d)(8)	Enclosed box using barline
“	Horizontal barline separates headings listed in (c)(2) - (c)(9)
“	Horizontal hairline precedes heading immediately after the title “Drug Facts”
“	Horizontal hairline follows the title “Drug Facts (continued)”
“	Horizontal hairline extending within 2 spaces on either side of the Drug Facts box shall immediately follow the title and precede the subheadings set forth in (c)(5) [except (c)(5) (ii) A – G]
(d)(9)	Directions in table format when dosage instructions are provided for three or more age groups or populations
“	Horizontal barline preceding the next heading may end the table

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538**Table 3. Implementation Chart**

<b>Products</b>	<b>Time periods*</b>
<b>Subject to NDA/ANDA:</b>	
<i>Single</i> entity products approved before May 16, 1999.	By May 16, 2002 (or by May 16, 2003, if annual sales of the product are less than \$25,000).
<i>Single</i> entity products approved on or after May 16, 1999.	Immediately upon approval of the application.
<i>Combination</i> products approved before May 16, 1999.	By May 16, 2002 (or by May 16, 2003, if annual sales of the product are less than \$25,000).
<i>Combination</i> products approved on or after May 16, 1999.	Immediately upon approval of the application.
<b>Subject to OTC Drug Monograph(s):</b>	
<i>Single</i> entity products finalized before May 16, 1999.	By May 16, 2002 (or by May 16, 2003, if annual sales of the product are less than \$25,000).
<i>Single</i> entity products finalized on or after May 16, 1999.	Within the period specified in the final monograph. However, if a monograph has not been finalized as of May 16, 2002, then the product must comply as of the first major labeling revision after May 16, 2002, or May 16, 2005, whichever occurs first.
<i>Combination</i> products in which all applicable monographs were finalized before May 16, 1999.	By May 16, 2002 (or by May 16, 2003, if annual sales of the product are less than \$25,000).
<i>Combination</i> products in which at least one applicable monograph was finalized before May 16, 1999, and at least one applicable monograph is finalized on or after May 16, 1999.	Within the period specified in the last applicable monograph to be finalized, or by May 16, 2002 (or by May 16, 2003, if annual sales of the product are less than \$25,000), whichever occurs first, unless the last applicable monograph to be finalized specifies a later date.
<i>Combination</i> products in which all applicable monographs are finalized on or after May 16, 1999.	Within the period specified in the last applicable monograph to be finalized. However, if the last monograph is not finalized as of May 16, 2002, then the product must comply as of the first major labeling revision after May 16, 2002, or by May 16, 2005, whichever occurs first.
<i>All other single entity and combination</i> OTC drug products (e.g., products in the OTC drug review that are not yet the subject of proposed OTC drug monographs).	If a monograph has not been finalized as of May 16, 2002, then the product must comply as of the first major labeling revision after May 16, 2002, or by May 16, 2005, whichever occurs first.

539 \* Time delayed until further notice for OTC drug products that contain no more than two doses of  
540 an OTC drug product and, because of their limited total surface area available to bear labeling,  
541 qualify for the labeling modifications set forth in § 201.66(d)(10).  
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