
Orange Book

Questions and Answers

Guidance for Industry

DRAFT GUIDANCE

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

**May 2020
Generics**

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Questions and Answers

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*Additional copies are available from:
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Center for Drug Evaluation and Research
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<https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

**U.S. Department of Health and Human Services
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TABLE OF CONTENTS

I.	INTRODUCTION.....	1
II.	BACKGROUND	1
III.	QUESTIONS AND ANSWERS.....	3
A.	General Inquiries About the Content and Format of the Orange Book.....	3
B.	Petitioned ANDAs	6
C.	The Movement of Drug Products Between the Active and Discontinued Sections of the Orange Book	6
D.	Patent Listings.....	8
1.	<i>Listing Patents</i>	<i>8</i>
2.	<i>Patent Listing Disputes</i>	<i>11</i>

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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

I. INTRODUCTION

This guidance is intended to assist interested parties (including prospective drug product applicants, drug product applicants, and approved application holders) in utilizing the *Approved Drug Products With Therapeutic Equivalence Evaluations* publication (the Orange Book).² This guidance provides answers to commonly asked questions that we have received from these interested parties regarding the Orange Book.³

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

II. BACKGROUND

The Orange Book identifies (1) drug products approved by FDA under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and (2) patent and exclusivity information related to approved drug products. In particular, the main criteria for the inclusion of a drug product in the Orange Book are that the drug product is the subject of an approved application and that FDA has not

¹ This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research at the Food and Drug Administration.

² The Orange Book is available at <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>.

³ This guidance generally does not include topics addressed in the Orange Book Preface, the Frequently Asked Questions on The Orange Book, and the Frequently Asked Questions on Patents and Exclusivity web pages, which are available at <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm>, <https://www.fda.gov/Drugs/InformationOnDrugs/ucm114166.htm>, and <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079031.htm>, respectively.

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36 determined the drug product to have been withdrawn from sale for safety or effectiveness
37 reasons.⁴

38

39 The Orange Book is composed of four main parts:

40

41 (1) The Prescription Drug Product List, which is a list of approved marketed prescription
42 drug products with therapeutic equivalence evaluations (which along with the OTC Drug
43 Product List is referred to as the “Active Section”);

44

45 (2) The OTC Drug Product List, which is a list of marketed over-the-counter (OTC) drug
46 products that have been approved in new drug application (NDAs) or abbreviated new
47 drug applications (ANDAs) (which along with the Prescription Drug Product List is
48 referred to as the “Active Section”);

49

50 (3) The Drug Products with Approval under Section 505 of the FD&C Act Administered by
51 the Center for Biologics Evaluation and Research List; and

52

53 (4) The Discontinued Drug Product List, which is a cumulative list of approved drug
54 products that have never been marketed, are for exportation (e.g., only marketed outside
55 the United States), are for military use, are not commercially distributed by a United
56 States federal or state government entity, have been discontinued from marketing and
57 FDA has not determined that they were withdrawn from sale for reasons of safety or
58 effectiveness, or have had their approvals withdrawn for reasons other than safety or
59 effectiveness subsequent to being discontinued from marketing (commonly referred to as
60 the “Discontinued Section”).

61

62 The Orange Book contains additional information, including three appendices and two addenda
63 related to patents and exclusivity. The Orange Book website also has a number of additional
64 resources that can assist stakeholders with using the Orange Book and related questions.⁵

65

66 In addition, the Orange Book contains therapeutic equivalence⁶ evaluations for approved
67 multisource prescription drug products, which are reflected for drug products in the Active
68 Section.⁷ These evaluations have been prepared to serve as public information and advice to

⁴ See 21 CFR 314.161.

⁵ Available at the Orange Book homepage at <https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm>.

⁶ Approved drug products are therapeutic equivalents if they are pharmaceutical equivalents for which bioequivalence has been demonstrated, and they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling (21 CFR 314.3(b)).

⁷ We note that those products with approved applications that are *single-source* (i.e., there is only one approved product available for that active ingredient, dosage form, route of administration, and strength) are also included in the Orange Book, but no therapeutic equivalence code is included with such products.

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69 state health agencies, prescribers, and pharmacists to promote public education on drug product
70 selection and to foster containment of health care costs.⁸

71
72 The coding system for therapeutic equivalence evaluations is designed (1) to allow users to
73 determine quickly whether the Agency has determined that a particular approved drug product
74 (e.g., a particular strength, dosage form, and route of administration of an approved drug) is
75 therapeutically equivalent to other pharmaceutically equivalent⁹ drug products and (2) to provide
76 additional information to users on the basis of FDA's evaluations; the first item (i.e., therapeutic
77 equivalence) is reflected in the first letter of the therapeutic equivalence code, and the second
78 item (i.e., additional information) is reflected in the second letter of the code.

79
80 As noted in the Introduction, this guidance provides answers to questions that have been received
81 by the FDA staff that publishes and manages the Orange Book. The questions and answers in
82 this guidance cover the following topics:

- 83
- 84 • General inquiries about the content and format of the Orange Book
- 85
- 86 • Petitioned ANDAs
- 87
- 88 • The movement of drug products between the Active and Discontinued Sections of the
- 89 Orange Book
- 90
- 91 • Patent listings
- 92
- 93

94 **III. QUESTIONS AND ANSWERS**

95 **A. General Inquiries About the Content and Format of the Orange Book**

96 **Q1. Which applications are not listed in the Orange Book?**

- 97
- 98 **A1.** The Orange Book does not include: (1) approved drug products that were discontinued
99 either before the first edition in October 1980 or discontinued between 1980 and 1987,
100 prior to the identification of discontinued products; (2) drug products that have a tentative
101
102

⁸ Therapeutic equivalence evaluations in the Orange Book are not official FDA actions affecting the legal status of products under the FD&C Act. See, e.g., 45 FR 72582 at 72597 (October 31, 1980).

⁹ Pharmaceutical equivalents are drug products in identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient, *i.e.*, the same salt or ester of the same therapeutic moiety, or, in the case of modified-release dosage forms that require a reservoir or overage or such forms as prefilled syringes where the residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; do not necessarily contain the same inactive ingredients; and meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates (21 CFR 314.3(b)). They may differ in characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time, and, within certain limits, labeling (Orange Book Preface at vii).

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103 approval;¹⁰ (3) drug products marketed before 1962 for which a Drug Efficacy Study
104 Implementation review has not been completed; (4) biological products licensed by FDA
105 under the Public Health Service Act (42 U.S.C. 262);¹¹ (5) marketed drug products that
106 are not the subject of an approved NDA or ANDA (e.g., under OTC monograph); and (6)
107 drug products compounded by a pharmacy pursuant to section 503A of the FD&C Act
108 and drug products compounded by an outsourcing facility pursuant to section 503B of the
109 FD&C Act. Approved drug products are removed from the Orange Book when, for
110 example, an approval is withdrawn under section 505(e) or 505(j)(6) of the FD&C Act,¹²
111 when FDA has determined that the drug product was withdrawn from sale for reasons of
112 safety or effectiveness,¹³ or when the status of an approval is converted from final
113 approval to tentative approval.

115 **Q2. Can I access the current data files for the Orange Book? How are data provided?**

116
117 A2. Yes. The Orange Book Data Files¹⁴ contain current Orange Book data for approved drug
118 products and unexpired patent and exclusivity data, which are updated monthly. They
119 are available in a compressed ZIP file under “Additional Resources.”

121 **Q3. Is it possible to obtain previous editions of the Orange Book or an Orange Book Data File?**

122
123
124 A3. Requests for previous editions of the Orange Book or an Orange Book Data File should
125 be made under the Freedom of Information Act. Requests should be submitted either
126 online via <https://www.accessdata.fda.gov/scripts/foi/FOIRequest/index.cfm> or in writing
127 to FDA’s Freedom of Information Staff at the following address:

128
129 Food and Drug Administration

¹⁰ 21 CFR 314.3(b). *Tentative approval* is notification that an NDA or ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year period of orphan exclusivity for a listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter, or that a 505(b)(2) application or ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved until the conditions in § 314.107(b)(1)(iii), (b)(3), or (c) are met; because there is a period of exclusivity for the listed drug under § 314.108; because there is a period of exclusivity for the listed drug under section 505A of the Federal Food, Drug, and Cosmetic Act; because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act; or because a court order pursuant to 35 U.S.C. 271(e)(4)(A) orders that the NDA or ANDA may be approved no earlier than the date specified. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval letter after any necessary additional review of the NDA or ANDA.

¹¹ See the *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations* available at <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm>.

¹² See section 505(e) and 505(j)(6) of the FD&C Act.

¹³ 21 CFR 314.161.

¹⁴ Available at the Orange Book homepage at <https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm>.

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130 Division of Freedom of Information
131 Office of the Executive Secretariat, OC
132 5630 Fishers Ln., Rm. 1035
133 Rockville, MD 20857.¹⁵
134

135 **Q4. For daily updates to the Orange Book (e.g., posting of newly submitted or revised**
136 **patent information or newly approved generic drug products), is there a specific**
137 **time of the day when the electronic Orange Book is updated?**
138

139 A4. Updates to the electronic Orange Book are generally posted in the afternoon, Eastern
140 Time.
141

142 **Q5. When are newly approved NDA drug products listed in the Orange Book?**
143

144 A5. Newly approved NDA drug products will generally appear in the Active Section of the
145 Orange Book in the month following their approval, and will remain there, unless the
146 NDA holder notifies FDA that the drug product will not be available for sale within 180
147 days of approval.¹⁶ If the NDA holder notifies FDA that it does not intend to market
148 upon approval, the NDA drug product will, in the month following such approval, appear
149 in the Discontinued Section. The monthly cumulative supplement of the Orange Book is
150 generally updated at the end of the second full week of each month.
151

152 **Q6. Are the marketing reports required under section 506I of the FD&C Act available**
153 **to the public?**¹⁷
154

155 A6. No. Consistent with section 506I(f) of the FD&C Act, FDA will not publish copies of
156 marketing reports submitted to the Agency, but will update the Orange Book, as
157 appropriate, as the reports are reviewed and processed.
158

¹⁵ Recommendations on submitting a Freedom of Information Act request are provided on FDA's How to Make a FOIA Request web page, available at <https://www.fda.gov/RegulatoryInformation/FOI/HowtoMakeaFOIARequest/default.htm>.

¹⁶ See section 506I(b) of the FD&C Act. If an NDA holder intends to market the drug product within 180 days of approval, no such notification should be submitted to the Agency.

¹⁷ The FDA Reauthorization Act of 2017, Public Law 115-52 (Aug. 18, 2017) (FDARA) added section 506I to the FD&C Act, which imposes certain reporting requirements on NDA and ANDA holders regarding the marketing status of approved drug products. Specifically, the three required marketing status notifications set forth in section 506I of the FD&C Act include the following: notifications of the withdrawal of approved drugs from sale, notifications of approved drugs not being available for sale, and one-time reports on the marketing status of approved drugs.

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159 B. Petitioned ANDAs

160

161 **Q7. A petitioned ANDA¹⁸ drug product is listed in the Orange Book without a**
162 **therapeutic equivalence code. What is its reference listed drug (RLD)¹⁹? Should a**
163 **therapeutic equivalence code be assigned to that ANDA?**

164

165 A7. For a petitioned ANDA, the RLD should be the listed drug referenced in the approved
166 suitability petition.²⁰ The first petitioned ANDA approved will not be pharmaceutically
167 equivalent to the RLD and thus no therapeutic equivalence code would be assigned to it.
168 However, after the first petitioned ANDA is approved, FDA generally will assign
169 therapeutic equivalence codes to all ANDAs that contain the same petitioned differences
170 (i.e., in dosage form, route of administration, strength, or active ingredient (in a drug
171 product with more than one active ingredient)) as the first petitioned ANDA.

172

173 C. The Movement of Drug Products Between the Active and Discontinued 174 Sections of the Orange Book

175

176 **Q8. Are only those drug products for which approval of the application has been**
177 **withdrawn (i.e., the approval of the drug product application has been withdrawn**
178 **by FDA) considered *withdrawn from sale* by FDA?**

179

180 A8. No. A drug product considered withdrawn from sale is not limited to the withdrawal of
181 approval of a drug product application. The Agency has previously indicated that
182 withdrawal from sale is not limited to a permanent withdrawal of a product but can
183 include drug products for which “any decision to discontinue marketing”²¹ has been
184 made. In particular, FDA previously explained its interpretation that a drug is considered
185 to have been “withdrawn from sale” for purposes of section 505(j)(5) and 505(j)(6)(C) of the
186 FD&C Act if:

187

188 the applicant has ceased its own distribution of the drug, whether or not it has
189 ordered recall of previously distributed lots of the drug. A routine, temporary
190 interruption in the supply of a drug product would not be considered a
191 withdrawal from sale, however, unless triggered by safety or effectiveness
192 concerns.²²

¹⁸ A *petitioned ANDA* is a type of ANDA for a proposed drug product that differs from the RLD in its dosage form, route of administration, strength, or active ingredient (in a product with more than one active ingredient) and for which FDA has determined, in response to a suitability petition submitted under section 505(j)(2)(C) of the FD&C Act, that clinical studies are not necessary to establish the safety and effectiveness of that proposed drug product. See also, proposed rule Abbreviated New Drug Applications and 505(b)(2) Applications 80 FR 6802 at 6806 (February 6, 2015).

¹⁹ Reference listed drug is the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA (21 CFR 314.3(b)).

²⁰ 21 CFR 314.94(a)(3)(i).

²¹ See the final rule Abbreviated New Drug Applications Regulations 57 FR 17950 at 17956 (April 28, 1992).

²² See the proposed rule Abbreviated New Drug Application Regulations 54 FR 28872 at 28907 (July 10, 1989).

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Likewise, FDA has considered a drug product to have been withdrawn from sale if the NDA or ANDA holder has notified FDA that the drug product is not being marketed.

Q9. How should an NDA or ANDA holder notify FDA, under section 506I of the FD&C Act, that a drug product is or will be withdrawn from sale?

- A9. The NDA or ANDA holder should submit a notification of withdrawal from sale in a letter to the applicable NDA or ANDA file through the electronic submissions gateway.²³ The notification should prominently identify the submission as an “ADMINISTRATIVE CHANGE / NOT AVAILABLE FOR SALE.”²⁴

NDA and ANDA holders are required to provide a written notification to FDA 180 days prior to withdrawing an approved drug product from sale.²⁵ If it is not practicable to submit the notification 180 days before withdrawing the drug product from sale, that submission should be made “as soon as practicable, but not later than the date of withdrawal” from sale.^{26,27}

Q10. How and when should an NDA or ANDA holder request that an application be moved from the Discontinued Section of the Orange Book to the Active Section?

- A10. Prior to requesting that an application be moved from the Discontinued Section to the Active Section, the application holder should determine whether the submission of a supplement under 21 CFR 314.70 or 314.97 is required prior to or at the time of introduction of the drug product into the marketplace.

If a prior approval supplement under 21 CFR 314.70(b) is required:

- The application holder should notify the Orange Book 1-2 months prior to the approval of the supplement that the application holder is seeking market entry or re-entry via submission to the application file identified as an “ADMINISTRATIVE CHANGE / NOTIFICATION OF COMMERCIAL MARKETING.”
- The Orange Book will move the product from the Discontinued Section to the Active Section upon approval of the supplement in the subsequent monthly cumulative supplement.

²³ The electronic submissions gateway is available at <https://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/>. Questions related to electronic submissions should be emailed to the CDER Electronic Submission (ESUB) Team at esub@fda.hhs.gov.

²⁴ See draft guidance for industry *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format*. When final, this guidance will represent FDA’s current thinking on this topic.

²⁵ Section 506I(a) of the FD&C Act.

²⁶ Id.

²⁷ This notification addresses only the requirement in section 506I(a) of the FD&C Act; additional notifications may be required when a drug product is withdrawn from sale, for example, under section 506C(a) of the FD&C Act.

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- 229 If a Changes Being Effected supplement under 21 CFR 314.70(c) is required:
230
- 231 • The application holder should determine the anticipated launch date, which is
232 generally the date the drug product is put into the marketplace for distribution.
 - 233 • The application holder should notify the Orange Book that the application holder
234 is seeking market entry or re-entry approximately 1 – 2 months before the
235 anticipated launch date via submission to the application file identified as an
236 “ADMINISTRATIVE CHANGE / NOTIFICATION OF COMMERCIAL
237 MARKETING.”
 - 238 • The Orange Book will move the product from the Discontinued Section to the
239 Active Section upon the anticipated launch date in the subsequent monthly
240 cumulative supplement.

241 **Q11. When will a move of a drug product to or from the Discontinued Section be**
242 **reflected in the Orange Book?**
243

244 A11. A move to or from the Discontinued Section will generally be reflected in a future
245 Orange Book monthly cumulative supplement update. The monthly electronic Orange Book is
246 generally updated by the end of the following month’s second work week (e.g., November’s
247 edition of the electronic Orange Book will be updated by the end of the second full work week in
248 December).²⁸
249

250 **D. Patent Listings**

251 *1. Listing Patents*
252
253

254 **Q13. How does an NDA holder ensure that Form FDA 3542 (Patent Information**
255 **Submitted Upon and After Approval of an NDA or Supplement)²⁹ is timely filed?**
256

257 A13. An NDA holder must submit information for each patent that claims the drug or method
258 of using the drug and for which a claim of patent infringement could reasonably be
259 asserted against a person engaged in the unlicensed manufacture, use, or sale of the drug
260 product.³⁰ The NDA holder must submit this patent information to the NDA on a Form
261 FDA 3542.³¹ FDA publishes this patent information in the Orange Book. For a patent to
262 be considered timely filed, a Form FDA 3542 must be submitted to the NDA within 30
263 days after the date of approval of the NDA or supplement or within 30 days of issuance
264 of a patent for each patent that claims the drug substance (active ingredient), drug product

²⁸ We note that there may be user fee implications associated with moves to and from the Discontinued Section. See the guidance for industry *Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017*.

²⁹ The Form FDA 3542 is available at <https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm048345.pdf>.

³⁰ See section 505(b)(1) and 505(c)(2) of the FD&C Act; see also 21 CFR 314.53(b)(1).

³¹ 21 CFR 314.53(c)(2)(ii).

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265 (formulation or composition), and/or approved method of using the approved drug
266 product.³²

267
268 With respect to any errors or omissions that FDA identifies in a Form FDA 3542, 21 CFR
269 314.53(c)(2)(ii) provides:

270
271 If the applicant submits the required patent information within the 30 days, but
272 we notify an applicant that a declaration form is incomplete or shows that the
273 patent is not eligible for listing, the applicant must submit an acceptable
274 declaration form within 15 days of FDA notification to be considered timely
275 filed.

276
277 Under the terms of the regulation, to be considered timely filed as of the date of the
278 original submission of patent information, the NDA holder must submit an acceptable
279 Form FDA 3542 within 15 days of FDA's original notification.³³ NDA holders should
280 carefully read the instructions to Form FDA 3542 in correcting such deficiencies.

281
282 **Q14. How does an NDA holder ensure that an amendment to the description of an**
283 **approved method of use claimed by the patent is timely filed?**

284
285 A14. An NDA holder's amendment to the description of an approved method(s) of use (MOU)
286 claimed by the patent will be considered timely filed if it is submitted within 30 days of
287 (1) patent issuance, (2) approval of a corresponding change to the drug product labeling,
288 or (3) a decision by the U.S. Patent and Trademark Office or a Federal court that is
289 specific to the patent and alters the construction of a method-of-use claim(s) of the
290 patent.³⁴ Outside of these circumstances, and except as provided in the patent listing
291 dispute regulations,³⁵ an amendment to the description of the approved MOU claimed by
292 the patent will not be considered timely filed.³⁶

293
294 **Q15. How can an NDA holder submit a reissued patent to the Orange Book for listing?**

295
296 A15. An NDA holder is required to request that the original patent be removed from the
297 Orange Book³⁷ once a patent is reissued because, upon patent reissuance, the original

³² 21 CFR 314.53(c)(1) and 21 CFR 314.53(c)(2)(ii) and 21 CFR 314.53(d)(3).

³³ 21 CFR 314.53(c)(2)(ii).

³⁴ 21 CFR 314.94(a)(12)(vi) and 21 CFR 314.50(i)(4). For a decision by the U.S. Patent and Trademark Office or a Federal court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, the amendment must contain a copy of that decision. 21 CFR 314.94(a)(12)(vi) and 21 CFR 314.50(i)(4).

³⁵ See 21 CFR 314.53(f)(1).

³⁶ 21 CFR 314.94(a)(12)(vi) and 21 CFR 314.50(i)(4).

³⁷ 21 CFR 314.53(f)(2)(i).

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298 patent is surrendered and ceases to have legal effect.³⁸ Consistent with our regulations
299 for any request to withdraw a patent from the Orange Book, the original patent will
300 remain listed in the Orange Book until FDA determines that no first applicant is eligible
301 for 180-day exclusivity based on a paragraph IV certification to that patent or after the
302 180-day exclusivity period of a first applicant based on that patent has expired or has
303 been extinguished or relinquished.³⁹
304

305 **Q16. How does FDA receive and process a request from an NDA holder for removal of a**
306 **patent from the Orange Book?**
307

308 A16. If an NDA holder determines that a patent or patent claim no longer meets the statutory
309 requirements for listing (e.g., if a court finds a listed patent invalid or unenforceable,
310 from which no appeal has been or can be taken), the NDA holder must promptly notify
311 FDA to amend or withdraw the patent information and request that the patent information
312 be removed from the Orange Book.⁴⁰ If the NDA holder is required by court order to
313 amend patent information or withdraw a patent from the Orange Book, the NDA holder
314 must submit an amendment to its NDA that includes a copy of the order within 14 days
315 of the date of order entry.⁴¹ As described above, FDA will remove a patent from the
316 Orange Book if there is no first applicant eligible for 180-day exclusivity based on a
317 paragraph IV certification to that patent or after the expiration, extinguishment, or
318 relinquishment of any 180-day exclusivity period for a first applicant.⁴²
319

320 An NDA holder may submit a withdrawal of a patent and request for removal of the
321 patent from the Orange Book by letter to the NDA file.⁴³ The letter must contain the
322 NDA number, each product to which the request applies, and the patent number.⁴⁴ A
323 Form FDA 3542 is not required to be submitted for this request, but the NDA holder
324 should clearly and prominently identify that it is seeking patent withdrawal and removal
325 from the Orange Book under 21 CFR 314.53(f)(2)(iv).
326

327 **Q17. An NDA holder has requested that a patent be removed from the Orange Book.**
328 **The patent remains in the Orange Book with a *delist request* flag. When will the**
329 **patent be removed?**
330

³⁸ See final rule Abbreviated New Drug Applications and 505(b)(2) Applications, 81 FR 69580 at 69601 (October 6, 2016) referencing 37 CFR 1.178(a).

³⁹ 21 CFR 314.53(f)(2)(i).

⁴⁰ Id.

⁴¹ Id.

⁴² Id.

⁴³ 21 CFR 314.53(f)(2)(iv).

⁴⁴ Id.

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331 A17. A patent may remain listed for a certain period even if the NDA holder requests that it be
332 removed because a first applicant may retain eligibility for 180-day exclusivity based on
333 a paragraph IV certification to this patent.⁴⁵

334
335 Until the patent is removed from the Orange Book — after any associated 180-day
336 exclusivity has expired or has been extinguished or relinquished — ANDA applicants
337 must submit or maintain appropriate certifications to the patent notwithstanding the NDA
338 holder’s request to remove the patent.⁴⁶ Applicants submitting a section 505(b)(2)
339 application are not required to certify to a patent when the delist request flag is set to *Y* in
340 the Orange Book.⁴⁷

341
342 2. *Patent Listing Disputes*

344 **Q18. Can a patent listing be disputed?**

345
346 A18. Yes. 21 CFR 314.53(f)(1) outlines a process through which a person other than the NDA
347 holder can dispute the accuracy or relevance of patent information published in the
348 Orange Book, as well as the process for the relevant NDA holder to respond to such
349 disputes. If any person either “disputes the accuracy or relevance of patent information
350 submitted to the Agency” and published by the Agency in the Orange Book or “believes
351 that an NDA holder has failed to submit required patent information, that person must
352 first notify the Agency in a written or electronic communication titled ‘314.53(f) Patent
353 Listing Dispute.’”⁴⁸ The patent listing dispute may be sent to the Orange Book Staff at
354 orangebook@fda.hhs.gov.⁴⁹

355
356 The patent listing dispute “must include a statement of dispute that describes the specific
357 grounds for disagreement regarding the accuracy or relevance of patent information,”
358 which FDA will send to the applicable NDA holder.⁵⁰ 21 CFR 314.53(f)(1) states:

359
360 For a dispute regarding the accuracy or relevance of patent information regarding
361 an approved method of using the drug product, this statement of dispute must be
362 only a narrative description (no more than 250 words) of the person’s
363 interpretation of the scope of the patent. This statement of dispute must only
364 contain information for which the person consents to disclosure because FDA
365 will send the text of the statement to the applicable NDA holder without review
366 or redaction.

⁴⁵ 21 CFR 314.53(f)(2)(i).

⁴⁶ 21 CFR 314.94(a)(12)(viii)(B).

⁴⁷ 21 CFR 314.50(i)(6)(ii) (“A 505(b)(2) applicant is not required to provide or maintain a certification to a patent or patent information that remains listed only for purposes of a first applicant’s 180-day exclusivity for its ANDA”).

⁴⁸ 21 CFR 314.53(f)(1).

⁴⁹ Alternatively, the patent listing dispute may be submitted to the following address: Office of Generic Drugs, Central Document Room, 5901B Ammendale Road, Beltsville, MD 20705.

⁵⁰ 21 CFR 314.53(f)(1).

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367
368 FDA will forward the dispute to the NDA holder as described in the regulation.
369

370 **Q19. How does FDA provide notification of whether a patent listing dispute has been**
371 **submitted?**

372
373 A19. For all patent listing disputes, FDA promptly posts information to a Patent Listing
374 Dispute List website⁵¹ indicating whether (1) a patent listing dispute has been submitted
375 to FDA and (2) the NDA holder has timely responded to the patent listing dispute.⁵² The
376 Patent Listing Dispute List contains relevant drug product information and information
377 on the disputed patent. This list is cumulative in nature and is organized by the drug
378 product established name and patent number(s).

⁵¹ The Orange Book Patent Listing Dispute List website is available at <https://www.fda.gov/Drugs/InformationOnDrugs/ucm559235.htm>.

⁵² See 21 CFR 314.53(f)(1)(iii).