

---

# Guidance for Industry ANDA Submissions — Content and Format of Abbreviated New Drug Applications

## *DRAFT GUIDANCE*

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Elizabeth Giaquinto 240-402-7930 or (CBER) Office of Communication, Outreach, and Development, 800-835-4709 or 240-402-7800.

**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 2014  
Generics**

---

# Guidance for Industry ANDA Submissions — Content and Format of Abbreviated New Drug Applications

*Additional copies are available from:  
Office of Communications  
Division of Drug Information, WO51, Room 2201  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Ave., Silver Spring, MD 20993  
Phone: 301-796-3400; Fax: 301-847-8714  
druginfo@fda.hhs.gov*

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

*and/or*

*Office of Communication, Outreach and Development  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Ave., WO 71, Room 3128  
Silver Spring, MD 20993  
Phone: 800-835-4709 or 240-402-7800  
ocod@fda.hhs.gov*

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

**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 2014  
Generics**

*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

**TABLE OF CONTENTS**

<b>I.</b>	<b>INTRODUCTION.....</b>	<b>1</b>
<b>II.</b>	<b>BACKGROUND .....</b>	<b>2</b>
<b>A.</b>	<b>Module 1 – Administrative Information.....</b>	<b>4</b>
	1. <i>Forms and Cover Letter.....</i>	4
	2. <i>Administrative Information.....</i>	4
	3. <i>References.....</i>	6
	4. <i>Other Correspondence.....</i>	6
	5. <i>Labeling .....</i>	8
<b>B.</b>	<b>Module 2 – CTD Summaries.....</b>	<b>10</b>
	1. <i>Quality Overall Summary.....</i>	10
	2. <i>Clinical Summary .....</i>	10
<b>C.</b>	<b>Module 3 – Quality.....</b>	<b>11</b>
	1. <i>Drug Substance.....</i>	11
	2. <i>Drug Product.....</i>	13
	3. <i>Appendices.....</i>	19
	4. <i>Regional Information.....</i>	20
	5. <i>Literature References.....</i>	20
<b>D.</b>	<b>Module 4 – Nonclinical Study Reports.....</b>	<b>20</b>
<b>E.</b>	<b>Module 5 – Clinical Study Reports.....</b>	<b>21</b>
	1. <i>Complete Study Data .....</i>	21
	2. <i>Literature References.....</i>	23
	<b>APPENDIX A: REFERENCED GUIDANCES .....</b>	<b>24</b>
	<b>APPENDIX B: COVER LETTER TEMPLATE.....</b>	<b>27</b>

*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

1 **Guidance for Industry<sup>1</sup>**  
2 **ANDA Submissions — Content and Format of Abbreviated New**  
3 **Drug Applications**  
4

5  
6 This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current  
7 thinking on this topic. It does not create or confer any rights for or on any person and does not operate to  
8 bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of  
9 the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA  
10 staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call  
11 the appropriate number listed on the title page of this guidance.  
12

13  
14  
15  
16 **I. INTRODUCTION**  
17

18 This guidance is intended to assist applicants in preparing abbreviated new drug applications  
19 (ANDAs) for submission to the Food and Drug Administration (FDA) under section 505(j) of the  
20 Federal Food, Drug and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(j)). This guidance details  
21 the information to be provided in each section of the Common Technical Document (CTD)  
22 format for human pharmaceutical product applications and identifies supporting guidance  
23 documents and recommendations issued by FDA to assist in preparing the submission. This  
24 guidance does not address the fee structure or payment of obligations under the Generic Drug  
25 User Fee Amendments (GDUFA)<sup>2</sup> and does not address the submission and assessment of drug  
26 master files (DMFs), amendments to original ANDAs, and changes being effected or prior  
27 approval supplements.  
28

29 This guidance identifies the information an applicant should include to ensure that a complete,  
30 high-quality application is submitted to FDA. FDA has previously published guidance on the  
31 filing process, including the refuse-to-accept standards, which should be reviewed thoroughly to  
32 avoid common deficiencies found in ANDA submissions (Ref. 1).  
33

34 FDA's guidance documents, including this guidance, do not establish legally enforceable  
35 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should  
36 be viewed only as recommendations, unless specific regulatory or statutory requirements are  
37 cited. The use of the word *should* in Agency guidances means that something is suggested or  
38 recommended, but not required.  
39  
40

---

<sup>1</sup> This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration in cooperation with the Center for Biologics Evaluation and Research.

<sup>2</sup> Information on fees and industry obligations is available at <http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

### **41 II. BACKGROUND**

42  
43 Procedures for ANDAs submissions are set forth in FDA’s regulations in part 314 (21 CFR part  
44 314). An ANDA is usually<sup>3</sup> submitted for a drug product that is the same as an already approved  
45 drug or listed drug. A *listed drug* is defined in § 314.3(b) as a new drug product that has an  
46 effective approval under section 505(c) of the FD&C Act for safety and effectiveness or under  
47 section 505(j) of the FD&C Act, which has not been withdrawn or suspended under section  
48 505(e)(1) through (e)(5) or (j)(5) of the FD&C Act, and which has not been withdrawn from sale  
49 for what FDA has determined are reasons of safety or effectiveness (§ 314.161). An applicant  
50 submits an ANDA based on a listed drug, and the previously approved drug product on which the  
51 ANDA relies is officially known as the *reference listed drug* (RLD). A reference listed drug (RLD)  
52 is defined as the listed drug identified by FDA as the drug product upon which an applicant relies  
53 in seeking approval of its abbreviated application (§ 314.3(b)). FDA lists approved drugs that  
54 may be referenced in an ANDA in the *Approved Drug Products with Therapeutic Equivalence*  
55 *Evaluations* (the Orange Book).<sup>4</sup> The Orange Book is updated by a monthly cumulative  
56 supplement.

57  
58 On July 9, 2012, GDUFA was signed into law by the President to speed the delivery of safe and  
59 effective generic drugs to the public and reduce costs to industry. Under GDUFA, FDA agreed  
60 to meet certain obligations as laid out in the GDUFA Commitment Letter.<sup>5</sup> Among these  
61 obligations is FDA’s commitment to performance metrics for the review of new ANDAs that are  
62 submitted electronically following the electronic CTD (eCTD) format. For example, FDA has  
63 committed to review and act<sup>6</sup> on 90 percent of original ANDA submissions within 10 months  
64 from the date of submission in Year 5 of the program, which begins on October 1, 2016.

65  
66 To meet these performance goals, FDA is issuing this guidance to assist ANDA applicants in  
67 improving the quality of submissions, to increase the number of original ANDAs acknowledged  
68 for receipt upon initial submission, and to decrease the number of review cycles. FDA is  
69 committed to providing comprehensive assistance in the early stages of the application process  
70 so that an original ANDA will contain all information necessary for FDA to complete its review  
71 in one review cycle.

### **72 73 74 III. CTD FORMAT**

75  
76 The CTD format was developed by the International Conference on Harmonisation (ICH) in an  
77 attempt to streamline the variability of submission requirements among Japan, the European  
78 Union, and the United States. The CTD collects quality, safety, and efficacy information into a  
79 common format that has been adopted by ICH regulatory authorities. As previously stated, only

---

<sup>3</sup> An ANDA may be submitted for certain changes in drug product that differ from the RLD in accordance with section 505(j)(2)(C) of the FD&C Act and § 314.93.

<sup>4</sup> Available at <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>.

<sup>5</sup> See GDUFA Program Performance Goals and Procedures available at <http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf>.

<sup>6</sup> As defined in the Commitment Letter, an action on a submission includes issuance of a complete response, an approval letter, a tentative approval letter, or a refuse-to-accept action.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

80 ANDA submissions made electronically following the eCTD format on the date of submission  
81 will be subject to the review metric goals described in the GDUFA Commitment Letter.<sup>7</sup>  
82

83 Section 745A(a) of the FD&C Act, added by section 1136 of the Food and Drug Administration  
84 Safety and Innovation Act (FDASIA) (Pub. L. 112-144), requires that submissions under section  
85 505(b), (i), or (j) of the FD&C Act and section 351(a) or (k) of the Public Health Service Act (42  
86 U.S.C. 262(a) or (k)) be submitted in electronic format specified by FDA, beginning no earlier  
87 than 24 months after FDA issues a final guidance specifying an electronic submission format.  
88 When finalized, the guidance for industry *Providing Regulatory Submissions in Electronic*  
89 *Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using*  
90 *the eCTD Specifications* (Ref. 2) will implement the electronic submission requirements of  
91 section 745A(a) of the FD&C Act by requiring the eCTD format for ANDA submissions,  
92 among other submission types.  
93

94 Applicants are reminded that any record in electronic form submitted to FDA under requirements  
95 of the FD&C Act are subject to the provisions of 21 CFR part 11 (part 11) unless exempted. Part  
96 11 regulations were issued in 1997 to provide criteria for acceptance of electronic records,  
97 electronic signature and handwritten signatures executed to electronic records as equivalent to  
98 paper records and handwritten signatures on paper (Ref. 3).  
99

100 FDA has issued several guidance documents specific to the CTD and eCTD submissions.<sup>8</sup> The  
101 information contained in these guidances focuses on the technical aspects of filing a CTD  
102 application and should be reviewed thoroughly prior to submitting an ANDA. This guidance  
103 addresses the content of the CTD for an original ANDA.  
104

105 The CTD is comprised of the following modules:

- 106
- 107 • Module 1:<sup>9</sup> Administrative information;
- 108 • Module 2: CTD Summaries;
- 109 • Module 3: Quality;
- 110 • Module 4: Nonclinical study reports; and
- 111 • Module 5: Clinical study reports.  
112

113 The sections that follow in this guidance detail the information to be submitted in the applicable  
114 Modules, sections, and subsections.

---

<sup>7</sup> See Commitment Letter at 7.

<sup>8</sup> See the Drugs guidance Web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> and electronic submissions Web page at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/default.htm>. See the Biologics Web page at <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm163685.htm>.

<sup>9</sup> Module 1 contains administrative information and is not considered part of the “common” application. Each regulatory authority that accepts the CTD uses its own Module 1. The information described for Module 1 in this guidance applies only to ANDAs submitted to the U.S. FDA. Modules 2 through 5 of the CTD are common for all regions.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

115  
116  
117  
118  
119  
120  
121  
122  
123  
124  
125  
126  
127  
128  
129  
130  
131  
132  
133  
134  
135  
136  
137  
138  
139  
140  
141  
142

### **A. Module 1 – Administrative Information**

#### ***1. Forms and Cover Letter***

Section 1.1 of the ANDA submission contains several forms.<sup>10</sup>

**1.1.2** Contains the completed, signed Application Form FDA 356h (§ 314.94(a)(1)).<sup>11</sup> Applicants should provide complete contact information, including phone and fax numbers, for the agent stationed at each facility listed in the 356h form, along with detailed descriptions of the type of testing performed at each, where applicable. Applicants will be notified of failure to complete facility and testing information. Failure to provide the requested information in a timely fashion will result in the application being refused for receipt (Ref. 1). Applicants may use continuation pages, as necessary.

**1.1.2** Also contains copy of the GDUFA user fee cover sheet (FDA Form 3794).<sup>12</sup>

**1.2** Contains a cover letter. A suggested cover letter template is attached to this guidance at Appendix B.

**1.2.1** Contains the completed, signed Form FDA 3674, Certification of Compliance Under 42 U.S.C. 282(j)(5)(B) with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. 282(j)).

#### ***2. Administrative Information***

**1.3.1.2** Contains a U.S. agent letter of appointment, if applicable. The U.S. agent letter of appointment is a separate document submitted in addition to the U.S. agent’s signature on Form 356h, if applicable. If the applicant does not reside or have a place of business in the United

---

<sup>10</sup> FDA Forms listed in this section and other parts of this guidance are available at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.

<sup>11</sup> For original (initial) applications, Field 29 should include complete information on the locations of all manufacturing, packaging, and control sites for both drug substance and drug product. For each site, include the establishment name, address, registration (FEI) number, Master File (MF); Drug Master File (DMF) or Biologic Master File (BMF) number (for facilities used under a MF), and establishment DUNS number. Indicate whether the establishment is new to the application (new establishments will have, by default, a “pending” status). If the establishment is not new, indicate its current status (e.g., active, inactive, or withdrawn) in the appropriate box. Also provide the name, address, phone number, fax number and email address for the contact at the site. In the section “Manufacturing Steps, and/ or Type of Testing,” provide a brief description of the specific manufacturing steps and/or type of testing (e.g., final dosage form, stability testing) conducted at the site (i.e., describe the type(s) of assays or testing completed). Also, indicate whether the site is ready for inspection so that FDA can evaluate whether the site is able to reliably perform intended operation(s) at a commercial scale. Regarding readiness for commercial manufacturing, refer to Compliance Program Guidance Manual 7346.832. If the establishment is not ready for inspection at the time of submission of Form 356h, indicate when it will be ready. Instructions for completing FDA Form 356h are available at <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm321897.pdf>.

<sup>12</sup> All applicants submitting original ANDAs, with the exception of positron emission tomography drugs (section 744B(l) of the FD&C Act), are required to pay the generic drug user fee. See Generic Drug User Fee Cover Sheet and Payment Information available at <http://www.fda.gov/forindustry/userfees/genericdruguserfees/ucm322629.htm>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

143 States, an agent that resides or maintains a place of business in the United States must  
144 countersign the application (§ 314.50(a)(5)).

145  
146 **1.3.2** Contains the field copy certification (§ 314.94(d)(5)). The applicant will certify that the  
147 field copy submitted to the appropriate district office is a true copy of the technical section  
148 contained in the archival and review copies of the ANDA.

149  
150 **1.3.3** Contains the debarment certification required under the Generic Drug Enforcement Act of  
151 1992 (section 306(k) and 306(a) and (b) of the FD&C Act (21 U.S.C. 335a(k) and 335(a) and  
152 (b))). The applicant must certify that it did not and will not use the services of any debarred  
153 persons in connection with the application. The applicant must also list all convictions described  
154 in the FD&C Act (section 306(k) and 306(a) and (b)). The applicant may use the following  
155 language from section 306(k)(1) for the certification required for section 1.3.3:<sup>13</sup>

156  
157 *(Name of Applicant)* hereby certifies that it did not and will not use in any capacity the  
158 services of any person debarred under section 306 of the Federal Food, Drug, and  
159 Cosmetic Act in connection with this application.

160  
161 (See also Ref. 4.)

162  
163 **1.3.4** Contains financial certification for any clinical investigator who has no disclosable  
164 financial interests in, or arrangements with, any applicant of the covered clinical study (FDA  
165 Form 3454) or disclosure statement for each clinical investigator who, or whose spouse or  
166 dependent child, had disclosable financial interests in and/or arrangements with any sponsor of  
167 the covered clinical study (FDA Form 3455) (21 CFR part 54 and § 54.2(e)).

168  
169 **1.3.5** Contains patent information and certification. Applicants are required to list each patent  
170 issued by the U.S. Patent and Trademark Office that claims the drug substance, drug product, or  
171 that claims a use of the RLD that is cited by the ANDA (§ 314.94(a)(12)). FDA recommends  
172 that when providing patent information, applicants include the expiration date for each patent,  
173 whether the RLD is protected by any pediatric exclusivity, and when that pediatric exclusivity  
174 will expire. For each patent listed, the applicant must certify to one of the following paragraphs  
175 (§ 314.94(a)(12)(i)(A)(1) through (4)):

- 176  
177
- That the patent information has not been submitted to FDA (Paragraph I certification)
  - That the patent information has expired (Paragraph II certification)
  - The date on which the patent will expire (Paragraph III certification)
  - That the patent is invalid, unenforceable, or will not be infringed by the manufacture,  
181 use, or sale of the drug product for which the ANDA is submitted (Paragraph IV  
182 certification)
- 183

184 If the RLD is covered by a patent claiming a method of using the listed drug and the labeling for  
185 the drug product for which the applicant is seeking approval does not include any indications that

---

<sup>13</sup> Qualifying phrases, such as “to the best of our knowledge,” should be avoided.



## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

186 are covered by the use patent, the applicant must also submit a statement explaining that the  
187 method of use patent does not claim any of the proposed indications (§ 314.94(a)(12)(iii)).  
188

189 Applicants submitting a Paragraph IV certification will provide the following language from  
190 § 314.94(a)(12)(i)(A)(4):  
191

192 I, *(name of applicant)*, certify that Patent No. \_\_\_\_\_ *(is invalid, unenforceable, or*  
193 *will not be infringed by the manufacture, use, or sale of) (name of proposed drug*  
194 *product)* for which this application is submitted.  
195

196 Applicants submitting a Paragraph IV certification must also certify that they will provide notice  
197 to the owner of the patent(s) and the holder of the approved application that lists the patent(s)  
198 that is/are being challenged (§ 314.94(a)(12)(i)(A)(4)). The process for notice is provided in  
199 section 505(j)(2)(B) of the FD&C Act and § 314.95.<sup>14</sup>  
200

201 Applicants should also submit an exclusivity statement regarding their marketing intentions.  
202 This statement is relevant when the generic applicant intends to remove or *carve out* any  
203 protected indication(s) from the labeling in order to gain market entry prior to a use's expiry.  
204

### *3. References*

205  
206  
207 **1.4.2** Contains the statement of right of reference for each and every DMF referenced in the  
208 application. Applicants should submit the letter of authorization (LOA) provided to the applicant  
209 by the DMF holder which gives authorization to rely on the information in the DMF (§  
210 314.420(d)).<sup>15</sup>  
211

### *4. Other Correspondence*

212  
213  
214 **1.12.4** Contains a statement that a request for a proprietary name has been made, if applicable.  
215 An ANDA applicant requesting a proprietary name should submit that request when the ANDA  
216 is submitted to ensure an acceptable name is available at the time of approval. When requesting  
217 a proprietary name, a separate electronic submission should be made and identified as a  
218 **“REQUEST FOR PROPRIETARY NAME REVIEW”** (Ref. 5).  
219

220 **1.12.11** Must contain the basis for submission, which is the reference to the RLD  
221 (§ 314.94(a)(3)). Applicants should review the guidance for industry *Variations in Drug*  
222 *Products that May Be Included in a Single ANDA* (Ref. 6) to determine whether one or more  
223 ANDAs should be submitted for variations of a specific drug product dosage form. The  
224 applicant should provide: (1) the name of the RLD; (2) the NDA or ANDA number of the RLD;  
225 and (3) the holder of the application for the RLD.

---

<sup>14</sup> Notice is to be provided only **after** the applicant has received a formal correspondence from FDA stating that the ANDA has been acknowledged for receipt.

<sup>15</sup> More information on DMFs and the list of received DMFs is available at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/default.htm>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

226  
227 For an ANDA based on an approved petition under § 10.30 (21 CFR 10.30) or § 314.93, this  
228 section must contain the FDA docket number and a copy of FDA’s correspondence approving  
229 the suitability petition (§ 314.94(a)(3)(iii)). If the generic drug differs from the RLD in strength,  
230 route of administration, dosage form, or single active ingredient in a combination drug product,  
231 applicants must first submit a suitability petition to FDA’s Division of Dockets Management to  
232 obtain permission to file their ANDA (§ 314.93; § 10.20 (21 CFR 10.20), § 10.30). The  
233 applicant must submit the suitability petition in accordance with the requirements of §§ 10.20  
234 and 10.30 (§ 314.93(c)). The suitability petition must be approved before the ANDA is  
235 submitted (§ 314.93(b)). The information to be included in the suitability petition is listed at  
236 § 314.93(d). FDA will review the suitability petition to determine whether the requested change  
237 from the listed drug will have an impact on the safety and effectiveness of the generic product  
238 and if any applicable requirements of the Pediatric Research Equity Act (PREA) may be waived  
239 (Ref. 7). After a suitability petition is approved for a change to a drug product, any applicant  
240 may refer to that petition as the basis of submission for an ANDA. Once an application based on  
241 a suitability petition is approved, the suitability petition may no longer be relied upon as a basis  
242 of submission. The approved drug product will become the RLD for the basis of submission.  
243

244 When an applicant wants FDA to designate a second RLD, the request is made through a citizen  
245 petition submitted to FDA’s Division of Dockets Management in accordance with §§ 10.20 and  
246 10.30. An applicant may submit the application only after the citizen petition has been granted.  
247

248 If an applicant refers to a listed drug that has been voluntarily withdrawn from sale in the United  
249 States, the applicant must submit a citizen petition under § 10.25(a) (21 CFR 10.25(a)) and  
250 § 10.30 to FDA’s Division of Dockets Management requesting FDA to determine whether the  
251 listed drug was withdrawn for reasons of safety or effectiveness (§ 314.122) (often referred to as  
252 a relisting petition). A relisting petition may be submitted concurrently with the ANDA.  
253 However, approval of the ANDA will be dependent on FDA’s response to the petition.  
254

255 **1.12.12** Contains information demonstrating that the generic product is the *same* as the RLD  
256 (section 505(j)(2)(A) of the FD&C Act and § 314.94). *Same* means that the generic product has  
257 the same active ingredient(s), dosage form, strength, route of administration, and conditions of  
258 use as the RLD (§ 314.92(a)(1)). To demonstrate the comparison to the RLD, applicants  
259 provide:

- 260 (1) a statement that the conditions of use for the generic product have been previously  
261 approved for the RLD (§ 314.94(a)(4));
- 262 (2) information to show that the active ingredient(s) is the same as the RLD (§ 314.94(a)(5));
- 263 (3) information to show that the route of administration, dosage form and strength are the  
264 same as those of the RLD (§ 314.94(a) (6)); and
- 265 (4) as applicable, information to indicate the strength of the generic drug product used in the  
266 in vivo bioequivalence studies (fasting and fed) to demonstrate bioequivalence of the  
267 generic drug product to the RLD.

268  
269 Applicants must also identify and characterize the inactive ingredients and demonstrate that the  
270 inactive ingredients do not affect the safety or efficacy of the proposed drug product

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

271 (§ 314.94(a)(9)(ii)). This means that any differences in the identity or amount of an inactive  
272 ingredient between the proposed product and the RLD product must be identified and  
273 demonstrated as having no effect on safety or efficacy. Given that the nature of the data and  
274 information necessary to demonstrate safety and efficacy can vary by product, applicants should  
275 submit a controlled correspondence to GenericDrugs@fda.hhs.gov, consult the FDA  
276 Bioequivalence Recommendations for Specific Products Web site for current product-specific  
277 data recommendations and the Biopharmaceutics guidances Web site, or contact the appropriate  
278 CBER review division prior to submission of the application.

279  
280 FDA recommends that an applicant submit within the original application all strengths that the  
281 applicant intends to market. However, note that applicants are not able to submit a new  
282 pharmacy bulk strength in an amendment (see Ref. 6 for more exceptions).

283  
284 **1.12.14** Contains the environmental assessment (EA) (21 CFR 25.20), environmental impact  
285 statement (EIS) (21 CFR 25.22), or claim of categorical exclusion under 21 CFR 25.30 or 21  
286 CFR 25.31 and the justification for the exclusion. Failure to provide the EA or statement for  
287 categorical exclusion is sufficient grounds to refuse to receive the application (§ 314.101(d)(4))  
288 (Ref. 8).

289  
290 **1.12.15** Contains a request to waive the requirement to submit evidence measuring in vivo  
291 bioavailability (BA) or demonstrating in vivo bioequivalence (BE) of the generic product  
292 (known as a biowaiver), if applicable (21 CFR 320.22). The data necessary to support a waiver  
293 request vary by product. For this reason, applicants should submit a controlled correspondence  
294 to GenericDrugs@fda.hhs.gov, consult the FDA Bioequivalence Recommendations for Specific  
295 Products Web site for current product-specific data recommendations and the Biopharmaceutics  
296 guidances Web site, or contact the appropriate CBER review division prior to submission of the  
297 application.

### *5. Labeling*

298  
299  
300  
301 **1.14.1** Contains labeling for the generic product submitted in text-based Portable Document  
302 Format (PDF),<sup>16</sup> Microsoft Word, and Structured Product Labeling (SPL) formats  
303 (§ 314.94(a)(8)(ii) and Ref. 9). If the application is for a pharmacy bulk package product,  
304 applicants should complete and submit the Pharmacy Bulk Package Sterility Assurance Table to  
305 address sterility assurance of the drug product associated with the labeling and microbiological  
306 study data that may be submitted in the application.<sup>17</sup>

307  
308 **1.14.1.1** Contains the draft label and labeling for each strength and container including  
309 package size. Applicants should ensure that label and labeling design do not contribute to  
310 medication error (Ref. 9). Confirm if the container closure is child resistant (CRC).

311

---

<sup>16</sup> For all PDF submissions, FDA requests that applicants submit text-based PDF files, not image-based PDF files

<sup>17</sup> See the ANDA Forms and Submission Requirements page on the FDA Web site available at  
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm120955.htm>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

312 **1.14.1.2** Contains side-by-side labeling comparison of container(s) and carton(s) with the  
313 RLD for each strength and package size. All differences should be highlighted and  
314 annotated. Applicants should indicate the RLD version used for the side-by-side  
315 comparison.

316  
317 **1.14.1.3** Contains the prescribing and patient information in text-based PDF, Microsoft  
318 WORD and SPL formats. Applicants should identify the RLD version used for the side by  
319 side comparison.

320  
321 **1.14.1.4** Contains Pharmacy Bulk Package Sterility Assurance Table, if applicable.

322  
323 **1.14.1.5** Contains labeling history.

324  
325 Applicants are encouraged to review and use the Labeling Question-Based Review (QbR) model  
326 when developing labels and labeling.<sup>18</sup> Responses to the QbR should be provided in section  
327 1.14.1.5, as applicable.

328  
329 **1.14.3** Contains the RLD labeling and a comparison of that labeling to the draft labeling for the  
330 generic product. Applicants must submit side-by-side labeling comparison(s) with all  
331 differences highlighted and annotated (§ 314.94(a)(8)(iv)). Applicants should also submit the  
332 RLD package insert, Medication Guide, one container label, and one outer carton, if applicable,  
333 for each strength and package size listed in the application (§ 314.94(a)(8)(i)). Applicants are  
334 reminded to use the most recent RLD labeling available at the Drugs@FDA Web site.

335  
336 **1.14.3.1** Contains side-by-side labeling (professional insert, patient insert and Medication  
337 Guide) comparison. All differences are highlighted and annotated. In addition, applicants  
338 should state that a sufficient number of patient inserts will be included in each package  
339 size. Applicants should confirm that Medication Guides will be distributed in accordance  
340 with 21 CFR 208.24.

341  
342 **1.14.3.3** Contains the RLD professional and patient inserts, Medication Guide, one (1)  
343 RLD container label, and one (1) RLD outer carton label for each strength and package  
344 size, if applicable.

345  
346 **1.16.1** Contains the risk management plan (section 505-1 of the FD&C Act (21 U.S.C. 355-1))  
347 for products that require tools to minimize risks while preserving benefits.

348  
349 **1.16.2** Contains the risk evaluation and mitigation strategy (REMS) and all supporting  
350 documents, if the RLD has a REMS (Ref. 10). A REMS for an ANDA must have the same  
351 Medication Guide and patient package insert as does the RLD (section 505-1(i)(1)(A) of the  
352 FD&C Act). In addition, if applicable, a REMS for an ANDA must use a single, shared system  
353 of elements to assure safe use, unless FDA waives the requirement under 505-1(i)(1)(B).  
354 However, an ANDA REMS does not include a timetable for submission of assessments of the  
355 REMS and does not include a communication plan (Ref. 10).

---

<sup>18</sup> Id.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

356  
357  
358  
359  
360  
361  
362  
363  
364  
365  
366  
367  
368  
369  
370  
371  
372  
373  
374  
375  
376  
377  
378  
379  
380  
381  
382  
383  
384  
385  
386  
387  
388  
389  
390

### **B. Module 2 – CTD Summaries**

#### *1. Quality Overall Summary*

**2.3** Contains the Quality Overall Summary (QOS), which provides an overview of the chemistry, manufacturing, and controls (CMC) section of the application (§ 314.50(c)(2)(iv)). The QOS summarizes what is known about the drug substance (the active pharmaceutical ingredient (API)) in section **2.3.S** and the drug product in section **2.3.P**. Applicants should provide separate information on each drug substance contained in the product in section 2.3.S. All information provided in the summary needs to be accurate and supported by information, data, or justification included in Module 3 or other parts of the application (Ref. 11).

Applicants should use the Question-Based Review (QbR) model when writing their summaries. FDA introduced the QbR initiative in 2005 as a tool for the review of the CMC — Drug Substance and Drug Product Quality — sections of the ANDA<sup>19</sup> and updated the QbR model to include additional CMC questions from microbiology in 2011. The QbR model assists applicants in developing their QOS by providing specific questions that, when answered, ensure adequate information is submitted for FDA review. FDA has posted the QbR-QOS outlines designed for simple dosage form products (solution or immediate-release solid oral dosage forms)<sup>20</sup> and for sterility assurance of products terminally sterilized by moist heat.<sup>21, 22</sup> FDA has also developed example QOS summaries for controlled-release capsules<sup>23</sup> and immediate-release tablets.<sup>24</sup> Additionally, FDA recommends that applicants refer to the QbR Frequently Asked Questions and the QbR for Sterility Assurance of Terminally Sterilized Products: Frequently Asked Questions for further guidance on completing the QOS, including page limits.<sup>25</sup>

FDA recommends that the QOS be submitted in MS Word and text-based PDF file. If the applicant provides a scanned PDF copy of the QOS, FDA requests that the applicant also submit the QOS in Microsoft Word.

#### *2. Clinical Summary*

**2.7** Contains the submission of summary data critical to the determination of bioequivalence (21 CFR 320.21(b) and 21 CFR 320.24(b)). FDA has developed model summary tables to assist applicants in summarizing these data.<sup>26, 27</sup> The tables provide a format for applicants to

---

<sup>19</sup> Id.

<sup>20</sup> Id.

<sup>21</sup> Id.

<sup>22</sup> Portions of the QbR for terminally sterilized products may also directly apply to sterile drug products that are aseptically filled. Specifically, the P.1, P.2, P.5, P.8, Appendices A.2, and Regional Information components of Module 2.3.P would also apply to sterile products that are aseptically filled.

<sup>23</sup> Supra note 17.

<sup>24</sup> Id.

<sup>25</sup> Id.

<sup>26</sup> See id. for the Model Bioequivalence Summary Data Tables.

<sup>27</sup> FDA has also developed summary tables for clinical endpoint bioequivalence studies. Id.

## Contains Nonbinding Recommendations

Draft — Not for Implementation

391 summarize various aspects of the BE submission such as the design and outcome of in vivo and  
392 in vitro BE studies as well as the results of in vitro dissolution testing. These model tables are  
393 available on the FDA ANDA Forms and Submission Requirements Web site.<sup>28</sup> In addition,  
394 applicants should submit summary tables for all studies conducted, whether they are passing or  
395 failed studies (Ref. 12).

396

397 **2.7** Contains the completed tables in Microsoft Word and text-based PDF file.

398

399 **2.7.1.1** Contains summary reports and/or data for in vivo BE studies with clinical endpoints or  
400 skin irritation/sensitization/adhesion studies.<sup>29</sup>

401

### 402 **C. Module 3 – Quality**

403

404 Module 3 contains all of the CMC information necessary to support the application  
405 (§ 314.94(a)(9)(i)), including the information supporting and verifying what was summarized in  
406 Module 2.3. The specific placement of product quality microbiology information in Module 3 is  
407 listed in CDER’s Manual of Policies and Procedures (MAPP) 5040.1 *Product Quality*  
408 *Microbiology Information in the Common Technical Document*<sup>30</sup> (see also Ref. 13 and Ref. 14).  
409 Any analytical procedure submitted in the summaries of Module 2 should be described in  
410 sufficient detail to allow an analyst to reproduce the conditions and obtain results comparable to  
411 what is stated in the application (Ref. 15). FDA recommends that applicants submit a table of  
412 contents for Module 3.

413

414 It is recommended that applicants review the following guidances for industry to assist in the  
415 preparation of Module 3: *ANDAs: Impurities in Drug Products* (Ref. 16), *ANDAs: Impurities in*  
416 *Drug Substances* (Ref. 17), and *ANDAs: Stability Testing of Drug Substances and Products* (Ref.  
417 18).<sup>31</sup>

418

#### 419 *1. Drug Substance*

420

421 Section 3.2.S contains the CMC information specific to the drug substance(s) (§ 314.50(d)(1)(i)).  
422 For a drug product containing more than one drug substance, the information requested for part  
423 “S” should be provided in its entirety for each drug substance. To assist in preparing data for the  
424 drug substance section, applicants should review the guidance for industry *Guideline for*

---

<sup>28</sup> Applicants should periodically refer to the Web site as the Agency may update existing tables or expand the number of tables to address additional study types as well as waiver requests.

<sup>29</sup> See the FDA Data Standards Resources Web Site for current FDA data standards catalog available at <http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>.

<sup>30</sup> See the CDER Manual of Policies and Procedures page of the FDA Web site available at <http://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/default.htm>.

<sup>31</sup> FDA further recommends that applicants review the following guidances for industry, as applicable: *Genotoxic and Carcinogenic Impurities in Drug Substances and Products: Recommended Approaches* (Ref. 19); *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (Ref. 20); *Size of Beads in Drug Products Labeled for Sprinkle* (Ref. 21); *Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules* (Ref. 22); *ANDAs: Stability Testing of Drug Substances and Products Questions and Answers* (Ref. 23) and *ANDA Submissions — Refuse-to-Receive Standards* (Ref. 1).

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

425 *Submitting Supporting Documentation in Drug Applications for the Manufacture of Drug*  
426 *Substances* (Ref. 24).

427  
428 **3.2.S.1** Contains general information about the drug substance including: (1) the nomenclature,  
429 (2) the structure, and (3) general properties. Section 3.2.S.1 should not include any references to  
430 the DMF.

431  
432 **3.2.S.2** Contains information related to each drug substance manufacturer including:  
433 (1) the name and full address of the facility(ies);  
434 (2) contact information for an agent at the facility (phone, fax numbers and email address);  
435 (3) function or responsibility;  
436 (4) the Type II DMF number for the API; and  
437 (5) the Central File Number (CFN), Facility Establishment Identifier (FEI) or Data Universal  
438 Numbering System (DUNS) numbers, if known.

439 The applicant should also provide current good manufacturing practice (cGMP) and/or  
440 Debarment Certification of the facility that matches the information provided in FDA Form  
441 356h. Subsections 3.2.S.2.2 through 3.2.S.2.6 may refer to the DMF. If there is no DMF  
442 referenced in the application, detailed information should be provided in these subsections (Ref.  
443 24). For a sterile substance for use in a sterile drug product, section 3.2.S.2.2 will include the  
444 sterilization process and any in-process controls and section 3.2.S.2.5 will contain the validation  
445 of sterilization processes for the drug substance.

446  
447 **3.2.S.3** Contains characterization information for the API. FDA recommends that applicants  
448 complete the Summary Tables for the Listing and Characterization of Impurities and Justification  
449 of Limits in Drug Substance.<sup>32</sup>

450  
451 **3.2.S.4** Contains all information about the control of the drug substance.

452  
453 **3.2.S.4.1** Contains the drug substance specifications. These specifications include the  
454 tests, acceptance criteria, and references to methods in tabular form. If the application  
455 contains a sterile substance for use in a sterile drug product, this section will also contain  
456 the microbiological specification for the drug substance.

457  
458 **3.2.S.4.2** Contains the description of analytical procedures (compendial and/or in-house).  
459 If the application contains a sterile substance for use in a sterile drug product, this section  
460 will also contain the microbiological analytical procedures used to test the drug  
461 substance.

462  
463 **3.2.S.4.3** Contains the validation of analytical procedures including:  
464 (1) full validation reports for in-house methods and their equivalence to United States  
465 Pharmacopeia (USP) procedures if available for the drug substance;  
466 (2) verification of USP <1226> or DMF procedures, when referenced;

---

<sup>32</sup> Supra note 17.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 467 (3) legible spectra and chromatograms for reference standards and test samples; and  
468 (4) Sample Statement(s) of Availability and identification of the drug substance,  
469 along with associated lot numbers (Ref. 15).<sup>33</sup>

470 If the application contains sterile substance for use in a sterile drug product, this section  
471 will also contain the validation of the microbiological analytical procedures used to test  
472 the drug substance.

473  
474 **3.2.S.4.4** Contains the batch analysis including the Certificates of Analysis (COAs) from  
475 both the drug substance manufacturer (s) and drug product manufacturer for the batches  
476 used to produce the exhibit batch(es) of the drug product.

477  
478 **3.2.S.4.5** Contains the justification of the specifications including, but not limited to,  
479 references to compendia (e.g., USP, European Pharmacopeia (EP), and the Japanese  
480 Pharmacopeia (JP)), ICH, and/or RLD analysis. FDA recommends that applicants  
481 complete the Summary Tables for the Listing and Characterization of Impurities and  
482 Justification of Limits in Drug Substance.<sup>34</sup>

483  
484 **3.2.S.5** Contains information about the reference standards or materials. Appropriate  
485 certification, characterization, and qualification information should be provided for the reference  
486 standards of the drug substance and impurities. Reference to the DMF alone is inadequate.

487  
488 **3.2.S.6** Contains information about the container closure systems (Ref. 25). If the application  
489 contains a sterile substance for use in a sterile drug product, this section will also contain a  
490 description of the container closure system used for the drug substance and the validation of the  
491 container closure integrity.

492  
493 **3.2.S.7** Contains stability data including the retest date or expiration date of the API.  
494 Information provided should include the retest date or expiration date of the API at both the drug  
495 product manufacturing site and the drug substance manufacturing site (Refs. 18 and 23).

### 496 497 **2. Drug Product**

498  
499 Section 3.2.P contains detailed information known about the drug product (§ 314.50(d)(1)(ii)).  
500 During the development of the application, applicants should review the guidances for industry  
501 *Q8(R2) Pharmaceutical Development* (Ref. 26) and *Submission Documentation for Sterilization*  
502 *Process Validation in Applications for Human and Veterinary Drug Products* (Ref. 13) and the  
503 product-specific CMC guidances for industry (e.g., metered dose inhalers, nasal spray) as  
504 applicable. A drug product supplied with a reconstitution diluent should include a separate  
505 Module 3.2.P with the diluent information.

506

---

<sup>33</sup> Method validation/verification reports for all analytical methods are to be provided in section 3.2.S.4.3.

<sup>34</sup> Supra note 17.



## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 507 **3.2.P.1** Contains the description and composition of the drug product. For each strength,<sup>35</sup>  
508 provide:
- 509 (1) the quantitative composition and function of each component in the drug product; include  
510 solvents and processing aids that are used during manufacture, as applicable;
  - 511 (2) information related to the physical description of the product (tablet size, scoring) and  
512 comparison to the RLD (Refs. 20 and 22);
  - 513 (3) the quality standards (e.g., USP, National Formulary (NF)) of components; composition  
514 of colors, flavors,<sup>36</sup> and imprinting ink, if applicable;
  - 515 (4) amounts of inactive ingredients that are appropriate per the Inactive Ingredient  
516 Database<sup>37</sup> (per dose or unit dose) and justification (FDA recommends that applicants  
517 provide the justification in a tabular format);
  - 518 (5) conversion from percentage to milligram (mg)/dose values for all components, as  
519 applicable;
  - 520 (6) identification and justification of any formulation overages or overfills that appear in the  
521 final product;
  - 522 (7) daily elemental iron calculation or statement of adherence to 21 CFR 73.1200;<sup>38</sup>
  - 523 (8) if the RLD is packaged with a specific diluent, demonstration that the diluent is  
524 qualitatively and quantitatively the same (Q/Q same) as that packaged with the RLD;
  - 525 (9) a calculation of the amount of phenylalanine (mg per dosage unit) for products that  
526 contain aspartame (21 CFR 201.21);
  - 527 (10) for OTC products that contain potassium calcium, magnesium, and/or sodium: the  
528 calculation for potassium, calcium, magnesium and/or sodium content of a single  
529 maximum recommended dose;
  - 530 (11) a calculation of absolute alcohol in terms of percent volume (v/v) for products that  
531 contain alcohol (21 CFR 201.10(d)(2)); and
  - 532 (12) for antibiotics that contain sodium: the calculation for sodium content (per  
533 tablet/capsule, per unit dose).

534 For sterile products, this section will contain a description of the primary container closure  
535 system information for each configuration.

536  
537 For drug products containing inactive ingredient changes permitted in accordance with  
538 § 314.94(a)(9)(iii)-(v), applicants must also identify and characterize the differences and provide  
539 information that demonstrates the change(s) does/do not affect the safety or efficacy of the drug  
540 product. This means that any differences in the identity or amount of an inactive ingredient  
541 between the proposed product and the RLD product must be identified and demonstrated as

---

<sup>35</sup> One 3.2.P section should encompass all strengths. ICH guidance documents indicate that the information for all strengths should be combined and presented together in one Drug Product section. If the quality information is the same between all strengths, the data should only appear once.

<sup>36</sup> Flavor manufacturers can provide the composition information directly to the reviewer if the information is not available to ANDA applicants due to proprietary reasons.

<sup>37</sup> The Inactive Ingredient database is available at <http://www.fda.gov/Drugs/InformationOnDrugs/ucm080123.htm>.

<sup>38</sup> FDA recommends that applicants provide a calculation of elemental iron intake based on the maximum daily dose of the drug product.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

542 having no effect on safety or efficacy. Given that the nature of the data and information  
543 necessary to demonstrate safety and efficacy can vary by product, applicants should submit a  
544 controlled correspondence to [GenericDrugs@fda.hhs.gov](mailto:GenericDrugs@fda.hhs.gov) or consult the FDA Bioequivalence  
545 Recommendations for Specific Products Web site for current product-specific data  
546 recommendations prior to submission of the application.  
547

548 **3.2.P.2** Contains information on the pharmaceutical development of the drug product including  
549 the pharmaceutical development report and the microbial attributes — the container closure  
550 integrity testing report for sterile product, antimicrobial effectiveness testing for multi-dose  
551 sterile products, and if the sterile drug product is packaged, as single-use/dose/multi-dose and/or  
552 pharmacy bulk. If the applicant has moved toward a Quality by Design (QbD) approach,<sup>39</sup>  
553 applicants may demonstrate their methods in section 3.2.P.2. Applicants are encouraged to  
554 review FDA's information on Quality by Design for ANDAs: An Example for Modified Release  
555 Dosage Forms and An Example for Immediate-Release Dosage Forms.<sup>40</sup> For sterile products  
556 that are reconstituted (or further diluted) and stored prior to administration, the applicant should  
557 provide microbiological studies to support the worst case postconstitution or postdilution storage  
558 times, diluents, and conditions stated in the product package insert labeling. The study should be  
559 a risk assessment that shows adventitious microbial contamination does not grow (generally  
560 accepted as not more than (NMT)  $0.5\log_{10}$  growth) under the specified storage conditions.<sup>41</sup>  
561

562 **3.2.P.3** Contains information about the manufacture of the drug product including:  
563 (1) the name and full address of the facility(ies);  
564 (2) contact information for an agent at the facility (phone and fax numbers, email address);  
565 (3) function or responsibility;<sup>42</sup>  
566 (4) cGMP certification for both the applicant and the drug product manufacturer if different  
567 entities; and  
568 (5) the CFN, FEI, or DUNS numbers, if known.

569 The information provided in this section should match the information provided in Form FDA  
570 356h for the finished dosage manufacturer and all outside contract testing laboratories.  
571

572 **3.2.P.3.2** Contains the batch formula for the drug product including: (1) amounts of  
573 components including processing aids, if any, that come into contact with the drug  
574 substance or product during any stage of manufacture (quantitative comparison between  
575 the pilot scale and commercial scale in a tabular form recommended) and (2) indication  
576 and justification of any overage(s) or weight adjustment(s) used.  
577

578 **3.2.P.3.3** Contains a description of the manufacturing process and controls including:

---

<sup>39</sup> Pharmaceutical Quality by Design (QbD) is defined as systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management (Ref. 26).

<sup>40</sup> Supra note 17.

<sup>41</sup> See MAPP 5016.1 *Applying ICH Q8(R2), Q9, and Q10 Principles to CMC Review*, Supra note 33.

<sup>42</sup> Applicants are encouraged to provide the complete testing description if the facility performs testing on either the drug substance, the drug product, or both.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 579 (1) a description of the manufacturing process and facility;  
580 (2) manufacturing process flow chart showing controls;  
581 (3) master production batch record(s) for the largest intended production runs (i.e.,  
582 commercial batch records);  
583 (4) master packaging records for intended marketing container(s);  
584 (5) indication whether the drug product is a sterile product; and  
585 (6) reprocessing statement pursuant to 21 CFR 211.115 submitted by the applicant, at  
586 a minimum.

587  
588 **3.2.P.3.3.1** For sterile products, this section contains: (1) a description of the  
589 manufacturing process for the drug product, including sterilization processes and any in-  
590 process controls, and (2) the sterilization information including the sterilization and  
591 depyrogenation of packaging components and equipment.

592  
593 For products sterilized by terminal moist heat, this section will include a description of  
594 the:

- 595 (1) autoclave process and performance specifications; autoclave loading patterns;  
596 (2) methods and controls to monitor production cycles;  
597 (3) requalification of production autoclaves;  
598 (4) reprocessing; and  
599 (5) environmental monitoring, including a bulk drug solution bioburden action level  
600 prior to sterilization.

601  
602 For products sterilized by aseptic processing, this section will include a description of  
603 the:

- 604 (1) building and facilities;  
605 (2) overall manufacturing operation;  
606 (3) sterilization and depyrogenation of containers, closures, equipment, and  
607 components; and  
608 (4) environmental monitoring, including a bulk drug solution bioburden action level  
609 prior to sterilization. (Ref. 14 and MAPP 5040.1)

610  
611 **3.2.P.3.4** Contains the controls of critical steps and intermediates including: (1)  
612 acceptance criteria and test results for the exhibit batch(es); (2) comparison of controls  
613 and equipment between the pilot and commercial-batch manufacture; and (3) information  
614 about holding periods.

615  
616 **3.2.P.3.5** Contains process validation information to demonstrate that the manufacturing  
617 process produces a dosage form that meets product specifications including evaluation of  
618 data generated for the critical material attributes and critical process parameters that were  
619 found to meet the established scale-up guideline and/or acceptance criteria (Ref. 27).

620  
621 For a terminally sterilized product, this information includes: (1) validation of the  
622 production terminal sterilization process; (2) validation of depyrogenation of all product  
623 container and closures; and (3) holding periods.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

624  
625  
626  
627  
628  
629  
630  
631  
632  
633  
634  
635  
636  
637  
638  
639  
640  
641  
642  
643  
644  
645  
646  
647  
648  
649  
650  
651  
652  
653  
654  
655  
656  
657  
658  
659  
660  
661  
662  
663  
664  
665  
666  
667  
668

For an aseptically filled product, this information includes:

- (1) validation (bacterial retention studies) of sterilizing grade filters;
- (2) validation of the sterilization of sterile bulk drug or product contact equipment;
- (3) validation of sterilization and depyrogenation of product containers and closures;
- (4) validation of aseptic filling process/line/room (media fills/process simulations);
- (5) holding periods; and
- (6) actions taken after a media fill failure. (Ref. 14 and MAPP 5040.1)

**3.2.P.4** Contains information on the controls of excipients including the identity of the source of inactive ingredients and the grades (e.g., compendial or noncompendial).

**3.2.P.4.1** Contains the testing specifications including retest schedule and the excipient manufacturer's or supplier's COA.

**3.2.P.4.2** Contains the analytical procedures for the testing.

**3.2.P.4.3** Contains the validation data of the analytical procedures.

**3.2.P.4.4** Contains the justification of the specifications and includes: (1) the applicant's or drug product manufacturer's COA(s); (2) residual solvents statement(s) from manufacturer(s); and (3) bovine spongiform encephalopathy (BSE), transmissible spongiform encephalopathy (TSE), and melamine certifications, as applicable (Ref. 28).

**3.2.P.5** Contains information supporting the controls of the drug product.

**3.2.P.5.1** Contains the specifications for the drug product. These specifications include the tests, acceptance criteria, and references to methods in a tabular form. For sterile products, this section will contain the release specifications for the drug product (sterility, bacterial endotoxins, etc.). In cases where a USP monograph reports an endotoxins specification for a parenteral or intrathecal drug product, the applicant should alternatively propose a bacterial endotoxins specification based on the maximum patient dosage prescribed in the package insert labeling, not the USP monograph. The acceptance criteria for the maximum endotoxins dose to a patient are established in USP <85>.

**3.2.P.5.2** Contains the description of analytical procedures (compendial and/or in-house). For sterile products, this section will contain methods for product release tests (sterility, bacterial endotoxins (if applicable), etc.)

**3.2.P.5.3** Contains the validation of the analytical procedure including:

- (1) full validation reports for in-house methods and their equivalence to USP procedures if available for the drug product;
- (2) verification of USP <1226> procedures, when referenced;
- (3) legible spectra and chromatograms for reference standards and test samples; and

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

669 (4) the Sample Statement(s) of Availability and Identification of (a) the finished  
670 dosage form and (b) the lot numbers and strength of the drug products.<sup>43</sup>  
671

672 For sterile products, this section will contain a summary of validation procedures and  
673 results for analytical procedures (sterility, bacterial endotoxins (if applicable), etc.).  
674

675 **3.2.P.5.4** Contains the batch analysis including the executed COAs for all presentations  
676 and/or strengths of the finished dosage form.  
677

678 **3.2.P.5.5** Contains the characterization of impurities. FDA recommends controlling all  
679 potential degradation products (Ref. 16) and processing solvents if used during  
680 manufacture in the finished dosage form. FDA recommends that applicants complete the  
681 Summary Tables for the Listing and Characterization of Impurities and Justification of  
682 Limits in Drug Substance and Drug Products.<sup>44</sup>  
683

684 **3.2.P.5.6** Contains the justification of the specifications including but not limited to  
685 references to compendia (e.g., USP, JP), ICH, and/or RLD analysis. FDA recommends  
686 that applicants complete the Summary Tables for the Listing and Characterization of  
687 Impurities and Justification of Limits in Drug Products.<sup>45</sup>  
688

689 **3.2.P.6** Contains information about the reference standards or materials.  
690

691 **3.2.P.7** Contains information on the container closure system including:  
692

693 (1) a summary of the container closure system (including data for any new resin used and  
694 technical diagrams/drawings of the container closure components, a statement whether  
695 the closure for each proposed packaging configuration is child resistant or non-child  
696 resistant and a description of markings on the cap/ferrule overseals (USP General  
697 Chapters <1> Injections));

697 (2) components specification and test data;

698 (3) packaging configuration and size;

699 (4) container closure testing pursuant to USP <661> and <671> (testing should be  
700 conducted; for liquid drug products contained in plastic containers, applicants should  
701 also provide test data for leachables and/or extractables); and

702 (5) the source of supply and the supplier's address (Ref. 25).  
703

704 For controlled substances, provide a description of the tamper-evident properties of the container  
705 closure system as described in 21 CFR 1302.06. For OTC products, the applicant should  
706 confirm if the container closure system meets the requirements of 21 CFR 211.132.  
707

---

<sup>43</sup> Method validation/verification reports for all analytical methods are to be provided in section 3.2.P.5.3

<sup>44</sup> Supra note 17.

<sup>45</sup> Id.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

708 **3.2.P.8** Contains the stability data (Refs. 18 and 23).<sup>46</sup>

709

710 **3.2.P.8.1** Contains the stability and conclusions for the finished dosage form including:

- 711 (1) preapproval stability protocol;
- 712 (2) proposed expiration dating period for marketing packaging;
- 713 (3) proposed expiration dating period for bulk packaging, if applicable; and
- 714 (4) storage temperature statement.

715

716 **3.2.P.8.2** Contains the postapproval stability protocol and stability commitment. If the

717 applicant and drug product manufacturer are different entities, both will provide stability

718 commitments. For sterile products, this section contains analytical procedures and testing

719 schedule for maintenance of microbial product quality (e.g., container closure

720 integrity/sterility, bacterial endotoxins, and microbial limits) (Ref. 29).

721

722 **3.2.P.8.3** Contains stability data including:

- 723 (1) accelerated, long-term, and intermediate stability data, if applicable;
- 724 (2) batch numbers on stability records that are the same as the test batch;
- 725 (3) the date the stability studies were initiated; and
- 726 (4) the date the stability sample(s) were removed from the stability chamber for each
- 727 testing time point (Ref. 18).

728

729 For liquid or semisolid products, applicants should submit accelerated stability data

730 reflecting the worst-case storage conditions (related to orientation), at minimum. The

731 following information and data can also be included in this section:

- 732 (1) one-time special stability studies conducted to confirm quality of constituted drug
- 733 products (for example parenterals and/or powders reconstituted with diluents
- 734 and/or drug admixtures) per labeling instructions;
- 735 (2) one-time thermal cycling studies (freeze-thaw/heat-cool), as applicable; and
- 736 (3) one-time in-use stability studies for oral liquids as applicable (e.g., a solution to
- 737 be used within a certain period of opening the container per labeling instructions,
- 738 compatibility with a dropper when provided as part of the container closure
- 739 system).

740

### 741 *3. Appendices*

742

743 **3.2.A.2** Contains an appendix for Adventitious Agents Safety Evaluation for sterile products.

744 This section will contain a description of the processes used to control for potential

745 contamination with adventitious agents (e.g., TSEs, viruses). These processes may include

746 assays to detect adventitious agents, actions taken to avoid them, as well as procedures to

747 eliminate or inactivate them.

748

---

<sup>46</sup> FDA recommends three pilot-scale batches or two pilot-scale batches plus one small-scale batch with both accelerated and long-term data provided for each batch covering a period of no less than 6 months.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

### 749 4. *Regional Information*

750  
751 Section 3.2.R contains regional information for the drug substance and the drug product  
752 (§ 314.50(d)(1)(ii)(b)).

753  
754 **3.2.R.1.S** Contains the executed batch records and blank master batch records. Applicants can  
755 refer to the DMF(s) for this information. If no DMF is referenced in the application, applicants  
756 should provide the executed and blank master batch records.

757  
758 **3.2.R.2.S** Contains the comparability protocols (Ref. 30).

759  
760 **3.2.R.3.S** Contains the methods validation package. This information may also be placed in  
761 section 3.2.S.4.3.

762  
763 **3.2.R.1.P.1** Contains the executed batch records including: (1) a copy of the executed batch  
764 record(s) with equipment specified and packaging records (the packaging and labeling  
765 procedures); (2) the batch reconciliation and label reconciliation for the theoretical yield, the  
766 actual yield, and the packaged yield; and (3) the bulk package reconciliation for all bulk  
767 packaging considered a commercial container. The bulk package reconciliation is recommended  
768 if bulk packaging is used to achieve the minimum package requirement. As part of the bulk  
769 package reconciliation recommendation, the applicant should submit bulk package stability data  
770 in section 3.2.P.8.3. If bulk is to be shipped, the applicant should submit accelerated stability  
771 data at 0, 3, and 6 months; if the bulk is only warehoused for repackaging, the applicant may  
772 provide real time stability data at 0, 3, and 6 months. Provide bulk package container and  
773 closure information in section 3.2.P.7.

774  
775 **3.2.R.1.P.2** Contains information on components including and not limited to applicants'  
776 and suppliers' COAs for drug substance lots, inactive ingredients lots, and packaging  
777 components lots contained in the exhibit batches of the drug product

778  
779 **3.2.R.2.P** Contains comparability protocols, if applicable (Ref. 30).

780  
781 **3.2.R.3.P** Contains the methods validation package. This information may also be placed in  
782 section 3.2.P.5.3.

### 783 784 5. *Literature References*

785  
786 **3.3** Contains copies of any documents referred to in the application. The documents may include  
787 published articles, official meeting minutes, or other regulatory guidance or advice provided to  
788 the applicant. FDA recommends that the documents be provided in text-based PDF.

### 789 790 **D. Module 4 – Nonclinical Study Reports**

791  
792 ANDAs generally do not contain data that are required for Module 4.

793

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

### **E. Module 5 – Clinical Study Reports**

794  
795  
796 Module 5 contains all of the clinical study report data needed to support the application and  
797 demonstrate that the generic is bioequivalent to the RLD (§ 314.94(a)(7)). To facilitate the  
798 submission of complete data, FDA develops product-specific guidances,<sup>47</sup> summary data tables  
799 (as referenced in section III.B.2 of this guidance),<sup>48</sup> and multiple guidances on  
800 biopharmaceutics.<sup>49</sup> Applicants should use an eCTD Study Tagging File for each study  
801 submitted.<sup>50</sup>

#### *1. Complete Study Data*

802  
803  
804  
805 **5.2** Contains the tabular listing of the clinical studies submitted in the module.

806  
807 **5.3** Contains the clinical study reports and related information.

808  
809 **5.3.1** Contains the complete study data for the biopharmaceutic studies (Ref. 31) and the lot  
810 numbers and strength of products used in the BE study(ies); and documents the study type. The  
811 section will also contain information of in vivo and in vitro studies including, but not limited  
812 to:<sup>51</sup>

- 813  
814
- 815 • Synopsis
  - 816 • Study report
  - 817 • Protocol and amendments
  - 818 • All case report forms
  - 819 • List of independent ethics committees (IECs) or institutional review boards (IRBs) and  
consent and/or assent forms
  - 820 • IRB approval letters for protocol, amendments, and consent/assent forms
  - 821 • List and description of investigators and sites
  - 822 • Number of subjects enrolled in each site
  - 823 • Signatures of principal or coordinating investigator(s) or sponsor's responsible medical  
824 officer
  - 825 • Listing of subjects receiving test drug(s) from specified batch
  - 826 • Randomizations scheme
  - 827 • Audit certificates and reports
  - 828 • Documentation of statistical methods and interim analysis plans
  - 829 • Documentation of interlaboratory standardization methods of quality assurance  
830 procedures if used<sup>52</sup>
  - 831 • Publications based on the study<sup>53</sup>

---

<sup>47</sup> See the Bioequivalence Recommendations for Specific Products guidances on the FDA Drugs guidance Web page.

<sup>48</sup> Supra note 17.

<sup>49</sup> See the Biopharmaceutics guidances on the CDER Guidances Web page.

<sup>50</sup> See ICH M2 EWG: The eCTD Backbone File Specification for Study Tagging Files (June 2008).

<sup>51</sup> See the FDA Data Standards Resources Web Site for current FDA data standards catalog. Supra note 29.

<sup>52</sup> Supra note 17.



## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 832 • Important publications referenced in the report<sup>54</sup>
- 833 • Discontinued patients including specific reason for discontinuation<sup>55</sup>
- 834 • List of subjects included in the PP (per protocol), (M)ITT (modified/intent-to treat), and
- 835 safety populations<sup>56</sup>
- 836 • List of subjects excluded from the PP, (M)ITT, and safety populations<sup>57</sup>
- 837 • Reason for exclusion from the PP, (M)ITT, and safety populations for each subject<sup>58</sup>
- 838 • Protocol deviations including specific reason for deviation
- 839 • Demographic data
- 840 • Drug concentration data
- 841 • Treatment compliance rate data
- 842 • Individual subject's response scores/data per visit
- 843 • Adverse event listings
- 844 • Concomitant medication listings
- 845 • Listing of individual laboratory measurements by subject
- 846 • Site (identifier)
- 847 • Individual subject data listings
- 848 • In vivo and/or in vitro BE study datasets
- 849 • Summary dataset containing a separate line listing for each subject<sup>59</sup>
- 850 • Analysis dataset containing a separate line listing for each visit per subject<sup>60</sup>
- 851 • Individual Analysis datasets (e.g., adverse events, concomitant medications etc.)<sup>61</sup>
- 852 • Analysis programs
- 853 • Annotated case report form (CRF)
- 854 • Annotated ECG waveform datasets
- 855 • Image files
- 856 • Narrative safety reports for serious adverse events
- 857 • Source documents
- 858 • Clinical raw data/medical records
- 859
- 860 **5.3.1.2** Contains the comparative BA and BE study reports (e.g., fasting studies, fed studies).
- 861
- 862 **5.3.1.3** Contains in vitro-in vivo correlation study reports (e.g., comparative dissolution data).
- 863
- 864 **5.3.1.4** Contains reports of bioanalytical and analytical methods provided in individual study
- 865 reports. If a method is used in multiple studies, the method and its validation should be included
- 866 once in section 5.3.1.4 and then referenced in individual study reports.

---

<sup>53</sup> Id.

<sup>54</sup> Id.

<sup>55</sup> Id.

<sup>56</sup> Id.

<sup>57</sup> Id.

<sup>58</sup> Id.

<sup>59</sup> Id.

<sup>60</sup> Id.

<sup>61</sup> Id.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

867  
868 The data provided in all of these sections support the summary tables submitted in section 2.7.  
869 All comparative dissolution data from the in vitro-in vivo correlation study reports should be  
870 placed in section 5.3.1.3, while the dissolution summary tables should be placed in section 2.7.

871  
872 *2. Literature References*

873  
874 **5.4** Contains copies of any documents referred to in the application. The documents may include  
875 published articles, official meeting minutes, or other regulatory guidance or advice provided to  
876 the applicant. One copy of all important references cited in the QOS or individual technical  
877 reports provided in section 5.3 will also be submitted in this section (Ref. 31). FDA  
878 recommends that the documents be provided in text-based PDF.  
879

## Contains Nonbinding Recommendations

Draft — Not for Implementation

### APPENDIX A: REFERENCED GUIDANCES

880  
881  
882  
883  
884  
885  
886  
887  
888  
889  
890  
891  
892  
893  
894  
895  
896  
897  
898  
899  
900  
901  
902  
903  
904  
905  
906  
907  
908  
909  
910  
911  
912  
913  
914  
915  
916  
917  
918  
919  
920  
921  
922  
923  
924

The following documents have been referenced in this guidance document and may be relevant to applicants developing or considering development of an ANDA. This is not a comprehensive list of available information from CDER. All guidances documents listed here are available on the Drugs guidance Web page (<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>).

1. Draft Guidance for Industry *ANDA Submissions — Refuse-to-Receive Standards* (Issued by CDER, October 2013).
2. Draft Guidance for Industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (Issued jointly by CDER and CBER, January 2013 Rev. 3).
3. Guidance for Industry *Part 11, Electronic Records; Electronic Signatures — Scope and Application* (Issued by CDER, CBER, CDRH, CFSAN, CVM, ORA, August 2003).
4. Draft Guidance for Industry *Submitting Debarment Certification Statements* (Issued by CDER, CBER, and CVM, September 1998).
5. Guidance for Industry *Contents of a Complete Submission for the Evaluation of Proprietary Names* (Issued jointly by CDER and CBER, February 2010).
6. Guidance for Industry *Variations in Drug Products that May Be Included in a Single ANDA* (Issued by CDER, December 1998).
7. Draft Guidance for Industry *How to Comply with the Pediatric Research Equity Act* (Issued jointly by CDER and CBER, September 2005).
8. *Guidance for Industry Environmental Assessment of Human Drug and Biologics Applications* (Issued jointly by CDER and CBER, July 1998).
9. Draft Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (Issued by CDER, April 2013).
10. Guidance for Industry *Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications* (Issued by CDER, September 2009)
11. Guidance for Industry *ICH M4Q: The CTD — Quality* (Issued by CDER, August 2001).
12. Guidance for Industry *Submission of Summary Bioequivalence Data for ANDAs* (Issued by CDER, May 2011).

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 925 13. Guidance for Industry *Submission Documentation for Sterilization Process Validation in*  
926 *Applications for Human and Veterinary Drug Products* (Issued jointly by CDER and  
927 CVM, November 1994).  
928
- 929 14. Guidance for Industry *Sterile Drug Products Produced by Aseptic Processing — Current*  
930 *Good Manufacturing Practice* (Issued jointly by CDER and CBER, September 2004).  
931
- 932 15. Draft Guidance for Industry *Analytical Procedures and Methods Validation for Drugs*  
933 *and Biologics* (Issued jointly by CDER and CBER, February 2014).  
934
- 935 16. Guidance for Industry *ANDAs: Impurities in Drug Products* (Issued by CDER,  
936 November 2010).  
937
- 938 17. Guidance for Industry *ANDAs: Impurities in Drug Substances* (Issued by CDER, June  
939 2009).  
940
- 941 18. Guidance for Industry *Abbreviated New Drug Applications: Stability Testing of Drug*  
942 *Substances and Products* (Issued by CDER, June 2013).  
943
- 944 19. Draft Guidance for Industry *Genotoxic and Carcinogenic Impurities in Drug Substances*  
945 *and Products: Recommended Approaches* (Issued by CDER, December 2008).  
946
- 947 20. Guidance for Industry *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation*  
948 (Issued by CDER, March 2013).  
949
- 950 21. Guidance for Industry *Size of Beads in Drug Products Labeled for Sprinkle* (Issued by  
951 CDER, May 2012 Rev. 1).  
952
- 953 22. Draft Guidance for Industry *Size, Shape, and Other Physical Attributes of Generic*  
954 *Tablets and Capsules* (Issued by CDER, December 2013).  
955
- 956 23. Guidance for Industry *ANDAs: Stability Testing of Drug Substances and Products*  
957 *Questions and Answers* (Issued by CDER, May 2014).  
958
- 959 24. Guidance for Industry *Guideline for Submitting Supporting Documentation in Drug*  
960 *Applications for the Manufacture of Drug Substances* (Issued by CDER, February 1987).  
961
- 962 25. Guidance for Industry *Container Closure Systems for Packaging Human Drugs and*  
963 *Biologics* (Issued jointly by CDER and CBER, May 1999).  
964
- 965 26. Guidance for Industry *ICH Q8(R2) Pharmaceutical Development* (Issued jointly by  
966 CDER and CBER, November 2009).  
967
- 968 27. Guidance for Industry *Process Validation: General Principles and Practices* (Issued  
969 jointly by CDER, CBER and CVM, January 2011 Rev. 1).  
970

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 971 28. Guidance for Industry *Pharmaceutical Components at Risk for Melamine Contamination*  
972 (Issued jointly by CDER and CVM, August 2009).  
973
- 974 29. Guidance for Industry *Container and Closure System Integrity Testing in Lieu of Sterility*  
975 *Testing as a Component of the Stability Protocol for Sterile Products* (Issued by CBER,  
976 CDER, CDRH, and CVM, February 2008).  
977
- 978 30. Draft Guidance for Industry *Comparability Protocols -- Chemistry, Manufacturing, and*  
979 *Controls Information* (Issued by CDER, CBER and CVM, February 2003).  
980
- 981 31. Guidance for Industry *ICH M4E: The CTD — Efficacy* (Issued by CDER, August 2001).  
982

983  
984 See also:

985  
986 Draft Guidance for Industry *Providing Regulatory Submissions in Electronic Format —*  
987 *Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act*  
988 (Issued by CDER and CBER, February 2014).  
989

990 Draft Guidance for Industry *Providing Regulatory Submissions in Electronic Format —*  
991 *Standardized Study Data* (Issued by CDER and CBER, February 2014 Rev. 1).  
992

993  
994  
995  
996  
997  
998  
999  
1000  
1001  
1002  
1003  
1004  
1005  
1006  
1007  
1008  
1009  
1010  
1011  
1012  
1013

***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

1014  
1015  
1016  
1017  
1018  
1019  
1020  
1021  
1022  
1023  
1024  
1025  
1026  
1027  
1028  
1029  
1030  
1031  
1032  
1033  
1034  
1035  
1036  
1037  
1038  
1039  
1040  
1041  
1042  
1043  
1044  
1045  
1046  
1047  
1048  
1049  
1050  
1051  
1052  
1053  
1054  
1055  
1056  
1057  
1058  
1059

**APPENDIX B: COVER LETTER TEMPLATE**

*Date*

*Office of Generic Drugs (HFD-600)  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Metro Park North VII,  
7620 Standish Place  
Rockville, MD 20855*

Heading: Provide pre-assigned ANDA number, if applicable  
Indicate that the submission is an Original Application

Indicate that expedited review is being requested by providing the statement,  
“Expedited Review Request”

Reference: Provide the name of generic product name and strengths

*Dear Sir or Madam:*

Paragraph 1: Provide the name of the applicant  
Provide the name of the generic drug product and strengths  
Provide the drug product packaging description as single-use or single dose, multi  
dose and/or pharmacy bulk.

Paragraph 2: Provide the RLD NDA or ANDA number  
Provide brand and generic drug product name and strengths  
Provide the name of the RLD holder

Paragraph 3: Indicate whether the GDUFA fee has been paid and provide the amount paid  
Provide User Fee Payment ID Number  
Indicate that a copy of the Generic Drug User Fee Cover Sheet is contained in the  
application at Module 1.2

Paragraph 4: Indicate whether Controlled Correspondence were used to develop this  
application  
Provide the Controlled Correspondence numbers and indicate that copies are  
provided in Module 1.2  
Indicate whether Meeting Minutes are contained in this application  
Indicate that the Meeting Minutes are provided in Module 1.2  
Indicate whether FDA reviewed any protocols or conducted telephone  
conferences with the applicant during development of the application

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

1060 Indicate whether a Suitability Petition was approved in relation to this application  
1061 Provide the docket number and a copy of FDA’s approval letter in Module  
1062 1.12.11  
1063 Indicate whether a Citizen Petition was filed and/or granted in relation to this  
1064 application  
1065 Provide the docket number, a copy of the petition, FDA’s response (if applicable)  
1066 in Module 1.12.11  
1067

1068 Paragraph 5: Indicate that Letters of Authorization for DMFs enclosed in section 1.4.1  
1069 List all DMFs referenced in the application  
1070

Product name	DMF number	DMF holder and address	FEI/DUNS	Fee status

1071  
1072 Indicate whether any approved ANDAs are referenced  
1073 List all ANDAs referenced in the application  
1074

Product name	ANDA number	ANDA holder and address	FEI/DUNS	Fee status

1075  
1076 Paragraph 6: Indicate whether any information or data in the application should be highlighted  
1077 for a specific discipline’s review  
1078 Indicate the method of sterilization for the drug product (e.g., aseptic processing  
1079 or terminal sterilization) if applicable  
1080 Indicate whether the application contains pharm/tox data for review in Module  
1081 3.2.P.1.  
1082

1083 Paragraph 7: Identify the sites where the ANDA batches were manufactured (including FEI or  
1084 DUNS number)  
1085 Identify the sites where the marketed product will be manufactured for marketing  
1086 (including FEI or DUNS number)  
1087

1088 Paragraph 8: Indicate the proposed drug product expiration date and the basis for the request in  
1089 Module 3.2.P.8.1  
1090

1091 Paragraph 9: Provide the basis for the expedited review request (if applicable)  
1092

1093 Paragraph 10: Indicate whether the ANDA was compiled and submitted pursuant to FDA’s  
1094 guidance on electronic submissions  
1095

1096 Paragraph 11: Indicate whether a letter of Non-Repudiation Agreement for digital signatures has  
1097 been submitted to the FDA and provide the date of that submission  
1098

1099 Paragraph 12: Indicate the file structure of the labeling

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 1100  
1101 Paragraph 13: Indicate whether the RLD has a REMS  
1102 Indicate whether information on the proposed REMS has been submitted in  
1103 Module 1.16  
1104  
1105 Paragraph 14: Provide information related to the physical description of the product (tablet size,  
1106 scoring) and comparison to the RLD in Module 3.2.P.1  
1107  
1108 Provide information about the tamper-resistant properties of a controlled  
1109 substance in Module 3.2.P.7 if applicable.  
1110  
1111 Paragraph 15: Provide a summary table of subsections applicable to the ANDA  
1112  
1113 Paragraph 16: Provide the name and contact information for a technical point of contact (for  
1114 electronic submissions)  
1115  
1116 Paragraph 17: Provide the signatory's contact information  
1117  
1118 *Signature*  
1119