

Guidance for Industry User Fee Waivers, Reductions, and Refunds for Drug and Biological Products

DRAFT GUIDANCE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)
Center for Biologics Evaluation and Research (CBER)**

**March 2011
User Fees
Revision 1**

36 **Guidance for Industry**
37 **User Fee Waivers, Reductions,**
38 **and Refunds for Drug and**
39 **Biological Products**

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TABLE OF CONTENTS

76
77
78
79

80I. **INTRODUCTION..... 1**

81II. **BACKGROUND..... 1**

82III. **DEFINITIONS..... 2**

83IV. **TYPES OF WAIVERS AND REDUCTIONS..... 4**

84A. Public Health.....4

85B. Barrier to Innovation.....6

86C. Financial Considerations for Public Health and Barrier-to-Innovation
87 Waivers and Reductions.....7

88D. Small Business.....9

89V. **EXEMPTIONS AND REFUNDS..... 11**

90A. Orphan Designated Products.....11

91B. State or Federal Government Entity.....12

92C. No Substantial Work.....12

93VI. **SUBMITTING REQUESTS FOR WAIVERS, REDUCTIONS AND
94REFUNDS..... 13**

95A. Timing of Requests.....13

96B. Content and Format of Requests.....14

97C. Address for Submitting Requests.....16

98VII. **FDA RESPONSES TO REQUESTS FOR WAIVERS AND
99REDUCTIONS..... 17**

100VIII. **RECONSIDERATIONS AND APPEALS..... 17**

101A. Reconsideration Request.....17

102B. Appeal Request.....17

103IX. **DISCLOSURE OF PUBLIC INFORMATION..... 18**

104

9 *Contains Nonbinding Recommendations*

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11 *Draft – Not for Implementation*

105 **Guidance for Industry¹**
106 **User Fee Waivers, Reductions, and Refunds**
107 **for Drug and Biological Products**
108

109
110 This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current
111 thinking on this topic. It does not create or confer any rights for or on any person and does not operate to
112 bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of
113 the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA
114 staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call
115 the appropriate number listed on the title page of this guidance.
116

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118

119 **I. INTRODUCTION**

120

121 This guidance provides recommendations to applicants regarding requests for waivers, refunds,
122 and reductions of user fees assessed under sections 735 and 736 of the Federal Food, Drug, and
123 Cosmetic Act (the Act) for drugs, including biological drug products. This guidance is a revision
124 of the draft guidance entitled *Draft Interim Guidance Document for Waivers of and Reductions*
125 *in User Fees* (1993 interim guidance), issued July 16, 1993.

126

127 This revised guidance describes (1) the types of waivers, refunds, and reductions available under
128 the user fee provisions of the Act and (2) the procedures for requesting waivers, refunds, or
129 reductions, and reconsiderations and appeals of FDA decisions on such requests. The revised
130 guidance also provides clarification on related issues such as user fee exemptions for orphan
131 drugs.

132

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

138

139

140 **II. BACKGROUND**

141

142 The Prescription Drug User Fee Act of 1992 (PDUFA I) authorized FDA to assess user fees for 5
143 years in conjunction with the review of human drug applications. This authorization to assess
144 user fees was for fiscal years (FY) 1993 through FY 1997. PDUFA has been reauthorized three
145 times. The Food and Drug Administration Modernization Act of 1997 reauthorized the user fee
146 provisions for 5 years, beginning in FY 1998 (PDUFA II). The Prescription Drug User Fee

12¹ This guidance has been prepared by the Office of Regulatory Policy (ORP), Center for Drug Evaluation and
13 Research (CDER), in consultation with the Center for Biologics Evaluation and Research.

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147 Amendments of 2002 reauthorized the user fee program for another 5 years, beginning in FY
148 2003 (PDUFA III), and the Food and Drug Administration Amendments Act of 2007
149 reauthorized the user fee program for another 5 years beginning in FY 2008 (PDUFA IV). The
150 statute is up for reauthorization again in FY 2012.

151

152 The Act authorizes FDA to assess application fees for certain human drug and biological product
153 applications or supplements when those applications or supplements are submitted. In addition,
154 FDA can assess annual product fees for certain approved drug and biological products, and
155 annual establishment fees for the facilities in which those products are made in final dosage
156 form.²

157

158 Because of the way the program is structured in the Act, the total amount FDA collects in user
159 fees is independent of the number of waivers or reductions in fees that are granted. Target
160 revenues are established in accordance with a statutory formula, and the amount of each type of
161 fee (application, product, and establishment) is determined based on historical data of how many
162 applications, products, and establishments were assessed fees in the previous fiscal year.
163 Therefore, the more waivers or reductions are granted, the more fees must be increased the
164 following year for applications, products, and establishments subject to fees to meet the annual
165 statutory revenue targets.³

166

167

168 III. DEFINITIONS

169

170 For purposes of this guidance:

171

172 • The term **affiliate** means a business entity that has a relationship with a second
173 business entity if, directly or indirectly, (A) one business entity controls, or has the power
174 to control, the other business entity; or (B) a third party controls, or has the power to
175 control, both of the business entities.⁴

176

177 • The term **applicant** means the owner, holder, or sponsor of a new drug application
178 (NDA) or biologics license application (BLA).

179

180 • The term **application** includes both NDAs and BLAs.

18² Information on product, establishment, and application fees, including fee rates, PDUFA goals, and other various
19 user fee related issues can be found on FDA's PDUFA Internet site:

20 <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm>.

21³ Under the Act, FDA sets user fee target revenue each year. For example, if the FDA is to collect \$600 million in a
22 fiscal year, the \$600 million is divided by 3 and each category, applications, products, and establishments would be
23 expected to provide \$200 million. FDA divides the target revenue in each category by the number of applications,
24 products, or establishments it expects to assess fees to determine the fee for each individual application, product, or
25 establishment. The more product fees FDA waives, the higher the product fee is in the subsequent fiscal year. For
26 example, using the target revenue of \$200 million, if we assessed fees for 2500 products for fiscal year A, the fee
27 would be \$80,000 per product. If FDA waived fees for 100 products, we would expect 2400 products to be assessed
28 fees in the subsequent fiscal year, and the fee amount per product would increase (\$200 million divided by 2400 =
29 \$83,333 per product). As a result, more companies might request waivers because of higher fee assessments.

30⁴ Section 735(11) of the Act.

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181

182 • The term **drug** includes drug and biologic products.

183

184 • The term **final dosage form** means, with respect to a prescription drug product, a
185 finished dosage form which is approved for administration to a patient without substantial
186 further manufacturing.⁵ Substantial further manufacturing does not include packaging.⁶
187 FDA generally considers a product to be in final dosage form unless one or more of the
188 following operations is required but has yet to be performed: mixing, granulating,
189 milling, molding, lyophilizing, tableting, encapsulating, coating, sterilizing, and filling
190 sterile, aerosol, or gaseous drugs into dispensing containers.

191

192 • The term **human drug application** means an application for (1) approval of a new
193 drug submitted under section 505(b) of the Act or (2) licensure of a biological drug
194 product under section 351 of the Public Health Service Act (PHS Act).⁷ For purposes of
195 this guidance, the term **human drug application** does not include the following:

196

- 197 • A supplement to such an application
- 198 • An application with respect to whole blood or a blood component for transfusion
- 199 • An application with respect to a bovine blood product for topical application licensed
200 before September 1, 1992
- 201 • An application for an allergenic extract product
- 202 • An application for a device licensed under section 351 of the Public Health Service
203 Act
- 204 • An application with respect to a large volume parenteral drug product approved
205 before September 1, 1992
- 206 • An application for a licensure of a biological product for further manufacturing use
207 only
- 208 • An application submitted by a State or Federal Government entity for a drug that is
209 not distributed commercially.⁸

210

211 • The term **person** means the person subject to fees and includes any affiliates of that
212 person.⁹ The term **person** includes an individual, partnership, corporation, and
213 association.¹⁰ This document will also use the term **person** when referring to an
214 applicant.

215

216 • The term **supplement** means a request to the Secretary to approve a change in a
217 human drug application which has been approved.¹¹

218

36⁵ Section 735(4) of the Act.

37⁶ See section 735(5) of the Act.

38⁷ Section 735(1) of the Act.

39⁸ Id.

40⁹ Section 735(9) of the Act.

41¹⁰ Section 201(e) of the Act.

42¹¹ Section 735(2) of the Act.

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- 219 • The term **financial resources** means the total gross annual worldwide revenues and other
220 available financial assets of an applicant and its affiliates.

222

223 **IV. TYPES OF WAIVERS AND REDUCTIONS**

224

225 According to section 736(d) of the Act, FDA will grant a waiver of or reduction in one or more
226 user fees assessed under section 736(a) of the Act where it finds that an applicant meets the
227 eligibility criteria under one of the following provisions:

228

- 229 • A waiver or reduction is necessary to protect the public health.

230

- 231 • The assessment of the fee would present a significant barrier to innovation because of
232 limited resources available to the person or other circumstances.¹²

233

- 234 • The applicant is a small business submitting its first human drug application to the
235 Secretary for review.

236

237 The Act also provides for waiver or reduction of user fees if the fees would exceed the
238 anticipated present and future costs incurred by the Secretary in conducting the process for the
239 review of human drug applications for the person. Fees-exceed-the-costs waivers and reductions
240 are not addressed in this guidance document.¹³

241

242 **A. Public Health**

243

244 Under section 736(d)(1)(A) of the Act, an applicant may qualify for a waiver of or reduction in
245 application, product, and/or establishment fees if the waiver or reduction is necessary to protect
246 the public health. Under this provision, FDA may grant a public health waiver of or reduction in
247 user fees if the Agency finds that the following two criteria are met:

248

- 249 • The product protects the public health; and

250

- 251 • The applicant shows that a waiver or reduction is **necessary** to continue an activity that
252 protects the public health.

253

48¹² There are two additional special circumstances that may affect eligibility for waivers or reductions under the
49 barrier to innovation waiver provision. Each is addressed in a separate waiver guidance. Specifically, for
50 companies participating in the President's Emergency Plan for AIDS Relief, see the guidance document, *User Fee*
51 *Waivers for FDC and Co-Packaged HIV Drugs for PEPFAR*. For companies submitting combination products
52 under 21 Code of Federal Regulations 3.2(e), see the guidance for industry and FDA staff on *Application User Fees*
53 *for Combination Products*. We update guidances periodically. To make sure you have the most recent version of a
54 guidance, check the FDA Drugs guidance Web page at
55 <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

56¹³ There is a separate guidance document that discusses the Agency's current thinking on the fees-exceed-the-costs
57 waiver provision. For more information, see the guidance document, *Fees-Exceed-the-Costs Waivers Under the*
58 *Prescription Drug User Fee Act*, and its addendum at the guidance web page.

254 To qualify for a waiver or reduction in user fees under this provision, an applicant must meet
255 both criteria.

256

257 *1. Does the product protect the public health?*

258

259 For user fee purposes, a product that has been approved for marketing in the United States is not
260 automatically deemed to be a product that protects the public health. In evaluating whether a
261 product protects the public health, the Agency asks the following questions:

262

263 • Is the drug product a significant improvement (or does it have the potential to be a
264 significant improvement if the drug product is not yet approved) compared to other
265 marketed products, including other dosage forms or routes of administration and non-
266 drug products or therapies?

267

268 • Are there treatment alternatives? The existence of alternatives would weigh against a
269 determination that a product is necessary to protect the public health.

270

271 • Is the drug product designated as a priority drug,¹⁴ has it been granted fast track status,¹⁵
272 or has it been determined to be a new molecular entity? Affirmative answers to these
273 questions usually indicate that a product protects the public health. Other questions the
274 Agency may consider include:

275

276 • Does the drug product demonstrate an increased effectiveness in the treatment,
277 prevention, or diagnosis of disease?

278 • Does it eliminate or substantially reduce a treatment-limiting drug reaction?

279 • Does the drug product enhance patient adherence to treatment?

280 • Has the drug product shown potential evidence of safety and effectiveness for a
281 new or underserved subpopulation (e.g., treatment for a drug resistant microbe or
282 response to a homeland security concern)?

283

284 • Is the drug product intended for the treatment of a serious or life-threatening condition?

285

286 • Does the drug product address unmet medical needs or demonstrate the potential to do
287 so?

288

289 • Is the product designated as a drug for a rare disease or condition under section 526 of the
290 Act (i.e., does it have an orphan designation)?

64¹⁴ Further information regarding priority drugs can be found in the Center for Drug Evaluation and Research's
65 (CDER's) Manual of Policies and Procedures (MAPP) 6020.3R, *Review Classification Policy: Priority (P) and*
66 *Standard (S)*. MAPP 6020.3R is available on the Internet at <http://www.fda.gov>, search by MAPP number.

67¹⁵ Further information regarding fast track status can be found in CDER's guidance for industry on *Fast Track*
68 *Development Programs — Designation, Development, and Application Review*.

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292 ■ If the product is approved, is it available to the public? There is no benefit to the public
293 health if a product is not made available to the public.¹⁶

294

295 2. *Is the waiver or reduction necessary to continue an activity that protects the public*
296 *health?*

297

298 To determine whether a waiver of or reduction in user fees is necessary to continue an activity
299 that protects the public health, the Agency considers not only the benefit to the public health, but
300 also whether the waiver or reduction is necessary. The legislative history of PDUFA I states that
301 FDA may waive or reduce fees unless such a waiver or reduction is not necessary to protect the
302 public health, or it is apparent that the fee will not be a disincentive to innovation.¹⁷ It also
303 expressly notes that FDA should consider the “limited resources” of the applicant when
304 evaluating a request for a fee waiver or reduction under section 736(d).¹⁸ Therefore, the Agency
305 believes that a financial test is appropriate for the public health waiver provision. The Agency
306 considers the relationship between the annualized cost of user fees and the financial resources of
307 the applicant, including affiliates, requesting the waiver or reduction. The financial
308 considerations are discussed in section IV.C below.

309

310 **B. Barrier to Innovation**

311

312 Under section 736(d)(1)(B) of the Act, an applicant may qualify for a waiver of or reduction in
313 application, product, and/or establishment fees when the assessment of the fees would present a
314 significant barrier to innovation because of limited resources available to the applicant or other
315 circumstances. Under this provision, FDA may grant a waiver of or reduction in user fees if:

316

317 • The product or other products or technologies under development by the applicant are
318 innovative; and

319

320 • The fee(s) would be a **significant barrier** to the applicant’s ability to develop,
321 manufacture, or market innovative products or to pursue innovative technology.

322

323 To qualify for a waiver or reduction in user fees under this provision, an applicant must meet
324 both criteria.

325

326 1. *Is the product innovative or is the company pursuing other innovative drug products*
327 *or technologies?*

328

329 A product that has been approved for marketing in the United States is not automatically deemed
330 to be innovative for user fee purposes. In evaluating requests for barrier-to-innovation user fee
331 waivers or reductions, the Agency asks the following questions:

332

74¹⁶ We would consider products stockpiled for homeland security concerns as available to the public for user fee
75 waiver purposes.

76¹⁷ House Report 102-895 (1992) at 17.

77¹⁸ Id.

- 333 • Does the drug product or technology demonstrate advanced “breakthrough” research,
 334 new, progressive methods, and/or forward thinking in the treatment or diagnosis of
 335 disease, or does it have the potential to be at the forefront of new medical technology?
 336
- 337 • Does the drug product or technology introduce a unique or superior method for
 338 diagnosing, curing, mitigating, treating, or preventing a disease, or for affecting a
 339 structure or function of the body?
 340
- 341 • Is the drug product designated as a priority drug, has it been granted fast track status, or
 342 has it been determined to be a new molecular entity?
 343
- 344 • Does the applicant have an active investigational new drug application (IND) under
 345 which the applicant is evaluating a unique or superior method for diagnosing, curing,
 346 mitigating, treating, or preventing a disease, or for affecting a structure or function of the
 347 body?
 348
- 349 • Has the applicant recently received a Federal grant for innovation? Two examples of
 350 such Federal grant programs that may qualify as innovative are: (1) the National
 351 Institutes of Health’s Small Business Innovative Research Program and (2) the National
 352 Institute of Standards and Technology’s Advanced Technology Program.
 353
- 354 2. *Does the fee create a significant barrier to the applicant’s ability to develop,*
 355 *manufacture, or market innovative products or to pursue innovative technology?*
 356

357To determine whether a fee would be a significant barrier to an applicant’s ability to develop,
 358manufacture, or market innovative products or to pursue innovative technology, the Agency
 359considers the relationship between the annualized cost of user fees and the gross annual revenues
 360and financial resources of the applicant and its affiliates. The revenue considerations are
 361discussed below.

362

363C. **Financial Considerations for Public Health and Barrier-to-Innovation Waivers and** 364 **Reductions**

365

366 1. *Whose revenues are considered when evaluating a waiver or reduction request?*
 367

368When evaluating requests for waivers of or reductions in user fees under the public health or
 369barrier to innovation provisions, the Agency considers the financial resources of the applicant
 370and its affiliates, regardless of who submits a request for a waiver or reduction of user fees.

371

372Section 736(d)(2) of the Act states that, in determining whether to grant a waiver or reduction of
 373a user fee, FDA shall consider only the circumstances and financial resources of the applicant
 374and any affiliate of the applicant. Under the Act, the applicant is the **person** who is responsible
 375for payment of the fees and the **person** who must qualify for a waiver or reduction of user fees.
 376Accordingly, the statute does not allow persons other than those legally subject to user fees, such
 377as a distributor that is not an affiliate, to qualify for or receive waivers or reductions of user fees.

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379 2. *How does the agency determine whether an applicant has limited financial*
380 *resources?*

381

382The limited financial resources of an applicant and its affiliates are an important indicator of
383whether user fees are a barrier to innovation or a waiver or reduction is necessary to protect the
384public health.¹⁹ FDA will consider the total annual revenue of an applicant and its affiliates in
385determining whether the applicant has limited financial resources. Total annual revenue is an
386objective measure of the resources available to the applicant and is defined by generally accepted
387accounting principles. FDA does not intend to deduct marketing costs, including expenses in
388foreign markets that are often incurred because of an applicant’s marketing decisions, when
389calculating total annual revenue.

390

391In addition to total annual revenue of the applicant and its affiliates, FDA considers other
392available financial assets, including net proceeds, cash, and total assets. FDA may also consider
393the results of recent issuances of stock and the recently available capital raised from the sales of
394shares in the applicant company.

395

396Because even a very large applicant may have operating losses, FDA does not intend to consider
397lack of profitability as evidence of limited resources. The Agency also does not intend to
398consider product sales figures to be evidence of limited resources, because even a large and
399profitable company can have low sales figures for an individual product, but not need a waiver to
400continue an activity that is necessary to protect the public health or because the fees would
401present a significant barrier to innovation.

402

403Ordinarily, beginning with fees assessed for FY 2011, the Agency expects to determine that an
404applicant with financial resources, including the financial resources of affiliates, of less than \$20
405million has limited resources for user fee purposes.²⁰ An applicant with \$20 million or more in
406financial resources, including the financial resources of affiliates, generally will not be
407considered to have limited resources for user fee purposes.

409FDA considers the financial resources of applicants that are State or Federal government entities
410differently. The agency will consider State or Federal government entities with less than \$20
411million in total annual revenues ***from the sale of drug*** to have limited resources for user fee
412purposes. A government entity is able to devote only a small amount of money to drug
413development activities relative to the entity’s budget and the total State or Federal budget. In
414addition, government entities generally receive only a small amount of revenue, if any, from
415commercial distribution of a drug, as compared with total revenues. FDA believes that Congress
416intended to minimize the burden on State and Federal government entities by focusing attention

88¹⁹ As noted above, the legislative history states that FDA should consider the “limited resources” of an applicant
89when evaluating a request for a fee waiver or reduction under section 736(d). See House Report 102-895 (1992) at
9017. FDA therefore believes that a financial test is appropriate for both the public health and barrier-to-innovation
91waiver provisions.

92²⁰ For waivers regarding fees for fiscal years prior to 2011, the agency intends to continue to use as its general
93marker of limited resources the \$10 million benchmark cited in the 1993 interim guidance, adjusted for inflation.

417on their drug development revenues, not the overall revenues of the entity or the State or Federal
418government.²¹

419 3. *Why did FDA choose \$20 million as a marker?*

420

421When the 1993 interim guidance was issued, the Agency used \$10 million as a financial marker
422for evaluating whether a waiver or reduction was *necessary* to protect the public health and
423whether the fees were a *significant barrier* to innovation. Since 1993, the Agency has received
424several requests to adjust the \$10 million financial marker for inflation. As stated in Section II,
425the more fee waivers and reductions FDA grants, the more the fees for other applications,
426products, and establishments must be increased to ensure that FDA obtains the total annual fee
427revenues specified in the Act. However, the Agency believes that the \$10 million figure is
428outdated and should be adjusted. Based on almost 20 years of experience in implementing the
429user fee program, FDA has determined that most applicants that have annual revenues and
430financial resources of less than \$20 million are those least able to pay the fees. Therefore, the
431Agency intends to use \$20 million as its marker for evaluating whether an applicant and its
432affiliate have limited resources such that a waiver or reduction is *necessary* to protect the public
433health and/or whether the fees are a *significant barrier* to innovation.²²

434

435D. **Small Business**

436

437Under section 736(d)(1)(D) of the Act, an applicant is eligible for a waiver of the **application fee**
438if the applicant is a small business submitting its first human drug application to the Agency for
439review and does not have another product approved under a human drug application and
440introduced or delivered for introduction into interstate commerce. An applicant is eligible for a
441small business waiver when:

- 443 • The applicant employs fewer than 500 employees, including employees of affiliates;
- 444
- 445 • The applicant does not have a drug product that has been approved under a human drug
- 446 application and introduced or delivered for introduction into interstate commerce; and
- 447
- 448 • The applicant, including its affiliates, is submitting its first human drug application.

449

450To qualify for a small business waiver, an applicant must meet all of these criteria.

452To determine the size of an applicant and its affiliates, the FDA works with the Small Business
453Administration (SBA). FDA asks the SBA to determine what companies are affiliates of the
454applicant and the total number of employees for the applicant and its affiliates. After receiving a
455request from the FDA, the SBA consults with the applicant and determines the number of

99²¹ For example, the Act exempts a State or Federal government entity from application, product, and establishment
100fees for a drug product that is not distributed commercially. Sections 735(1) and (3) of the Act.

101²² If the \$10 million benchmark in the 1993 guidance, which was written to be used under PDUFA I, were adjusted
102solely for inflation since the conclusion of the PDUFA I period in 1998, it would be less than \$15 million in FY
1032011 dollars, so this adjustment to \$20 million would be expected to anticipate and eliminate the need for any
104further adjustments for inflation for at least the next 10 years.

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456employees the applicant and its affiliates have, based on SBA regulations. According to these
457regulations, SBA may contact the applicant to request the following information in the
458appropriate formats and detail:

459

460 • An application for size determination;

461

462 • A copy of the company's Articles of Incorporation and Bylaws;

463

464 • The company's last annual statement to shareholders; and

465

466 • A breakdown of the number of persons employed full time, part time, temporarily, or
467 otherwise during each of the pay periods for the 12 months preceding the company's
468 certification.

469

470Companies should not submit the information requested by the SBA to FDA, nor should they
471submit this information to SBA until contacted. If the information is not submitted to the SBA,
472the request for a small business waiver will be denied.

473

474The SBA recognizes, as does FDA, that some information provided by companies may be
475confidential. Both the SBA and FDA will treat confidential commercial or financial information
476consistent with applicable federal laws and regulations. See Section IX.

477

478Once the SBA has identified and confirmed the affiliates of the applicant and determined
479whether the applicant qualifies as a small business, FDA will evaluate whether the applicant
480meets the other criteria for the small business waiver. Specifically, FDA searches its records to
481determine whether the applicant or its affiliates have previously submitted a human drug
482application or whether the applicant has a drug product that has been approved under a human
483drug application and introduced or delivered for introduction into interstate commerce. If the
484waiver applicant meets all the criteria for a small business waiver, then FDA will notify the
485applicant that the waiver is granted.

486

487 *1. Does a small business waiver have an expiration date?*

488

489If a small business waiver is granted, the applicant should submit its human drug application
490within 1 year after the date of the SBA determination. The reason for the 1 year timeframe is
491that the circumstances supporting a small business waiver may change rapidly. For example, an
492applicant could merge with a larger company and therefore no longer be considered a small
493business. Similarly, an applicant could purchase an NDA from an unaffiliated company and,
494therefore, would have a drug product that has been approved under a human drug application and
495introduced into or delivered for introduction into interstate commerce.

496

497FDA understands that unforeseen circumstances may delay submission of an application. If an
498applicant is granted a small business waiver and is not able to submit the application within 1
499year of the SBA determination, the applicant may ask FDA to extend the expiration date.

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114

500If an extension is requested, the Agency will examine its records and will work with SBA to
501confirm that the applicant still meets the criteria for a small business waiver. If the criteria are
502no longer met, the extension request will be denied.

503

504 2. *Can a small business receive a waiver of application fees for future human drug*
505 *applications?*

506

507After an applicant or its affiliate is granted a small business waiver and submits its first human
508drug application, the applicant cannot receive another small business waiver. That means that
509the applicant or its affiliate is not eligible to receive a small business waiver for any subsequent
510human drug application or a supplement to an application.²³

511

512After an applicant or its affiliate is granted a small business waiver and submits its first human
513drug application, the applicant or affiliate is ineligible for another small business waiver even if
514the application is withdrawn or refused for filing. If an applicant does not submit the application
515for which it was granted a small business waiver, the applicant may qualify again for a small
516business waiver.

517

518 3. *Can a small business receive a waiver or reduction of product and establishment*
519 *fees?*

520

521There is no specific provision in the Act for a waiver or reduction of product and establishment
522fees for small businesses. However, small businesses may apply for a waiver or reduction of
523product and establishment fees through the public health or barrier-to-innovation waiver
524provisions. See discussions in sections IV.A, IV.B, and IV.C above.

525

526**V. EXEMPTIONS AND REFUNDS**

527

528**A. Orphan Designated Products**

529

530 1. *Application Fees*

531

532Under section 736(a)(1)(F) of the Act, a human drug application for a product that has been
533designated as a drug for a rare disease or condition (referred to as an orphan drug) under section
534526 of the Act is not subject to an application fee unless the human drug application includes an
535indication for other than a rare disease or condition. A supplement proposing to include a new
536indication for a rare disease or condition in a human drug application shall not be subject to an
537application fee if the drug has been designated under section 526 as a drug for a rare disease or
538condition with regard to the indication proposed in the supplement.

539

540If an application or supplement qualifies for an orphan exemption, the applicant does not need to
541send FDA a written request. The applicant should simply notify FDA that it is claiming the
542orphan exemption when it completes and submits the User Fee Coversheet, Form FDA 3397.²⁴

115²³ Section 736(d)(4)(B) of the Act.

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543The User Fee Coversheet should be included with the application or supplement, and a brief
544statement claiming the orphan exception should be included in the cover letter.

545

546 **2. Product and Establishment Fees**

547Under section 736(k) of the Act, a drug product designated under section 526 of the Act for a
548rare disease or condition and approved under section 505 of the Act or section 351 of the Public
549Health Service Act is exempt from the product and establishment fees if it meets the public
550health requirements contained in the Act as such requirements are applied to requests for waivers
551of product and establishment fees. In addition, the applicant must have less than \$50 million in
552gross worldwide revenue during the year preceding the request for exemption. An applicant
553seeking to avail itself of this exemption should submit a certification that its gross worldwide
554revenues including affiliates, did not exceed \$50 million for the 12 months before the request.
555See sections VI for information about how to submit a request for an exemption from product
556and establishment fees.

557

558**B. State or Federal Government Entity**

559

560An application submitted by a State or Federal government entity for a drug that is **not**
561**distributed commercially** is not considered a “human drug application” under section 735(1) of
562the Act. If the application is not considered a human drug application, then application fees are
563not assessed and product and establishment fees do not apply.

564

565For the purposes of the State and Federal exemption from user fees under the Act, **distributed**
566**commercially** means any distribution in exchange for financial reimbursement, goods, or
567services, whether or not the amount of the charge covers the full costs associated with the
568product. Any recovery by the applicant of all or part of the costs of manufacture or distribution
569of a product makes the distribution commercial.

570

571**C. No Substantial Work**

572

573Under section 736(a)(1)(G) of the Act, if an application or supplement is withdrawn after the
574application or supplement is filed, FDA may refund the fee or a portion of the fee if no
575substantial work was performed on the application or supplement after the application or
576supplement was filed.

577

121²⁴ For more information about completion and submission of the User Fee Cover Sheets, see
122<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm>.

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579 VI. SUBMITTING REQUESTS FOR WAIVERS, REDUCTIONS AND REFUNDS

580

581 A. Timing of Requests

582

583 *1. Is there a statutorily mandated deadline for requesting a waiver or reduction?*

584

585 Yes. Under section 736(i) of the Act, to qualify for a waiver of or reduction in user fees as well
586 as a refund for a fee paid, an applicant must submit to FDA a written request for a user fee
587 waiver or reduction no later than 180 calendar days after the fee is due.

588

589 For example, if an applicant receives a product and establishment fee invoice from FDA, we
590 expect the invoice to be paid by the due date. The applicant can then submit a written request for
591 a waiver, reduction or refund of the fee(s) within 180 days from the date when the invoice is due.
592 If the request is submitted within 180 days of the due date (i.e., if the request is timely), FDA
593 will evaluate the applicant's request. If FDA determines that the applicant qualifies for a waiver,
594 reduction or refund, the Agency will grant the applicant's request.

595

596 To avoid having to pay a fee, an applicant can submit a request for waiver or reduction in
597 advance of when the product and establishment fee invoice is due to be paid, or in advance of
598 submitting an application. See section VI.A.3 and 4 below.

599

600 *2. Are there consequences if user fees are not paid because an applicant has not yet*
601 *submitted a waiver or reduction request or because FDA has not yet responded to a*
602 *waiver or reduction request?*

603

604 Yes. According to section 736(e) of the Act, a human drug application or supplement submitted
605 by a person subject to fees under section 736(a) is considered incomplete and will not be
606 accepted for filing until all fees have been paid. That means that if the applicant submits an
607 application or a supplement without the application fee or is in arrears for non-payment of an
608 establishment or product fee, then the submission is incomplete and FDA will not review it.
609 However, the review status of an application or supplement submitted before the invoice due
610 date would not be affected (the review would continue and there would be no effect on the
611 review goal date).²⁵

612

613 *3. Is there a recommended time frame to submit a waiver or reduction request if an*
614 *applicant wants to avoid paying the **application** fee and then seeking a refund?*

615

616 Yes. FDA encourages applicants to submit a request for a waiver of or reduction in an
617 application fee approximately 3-4 months before submission of the application. Under normal
618 circumstances and depending on available resources, FDA will try to make its determination on
619 the waiver request before the application is submitted and the fee is due.

620

¹²⁸ See CDER's MAPP 6050.1, *Refusal to Accept Application for Filing From Applicants in Arrears*.

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133

621FDA discourages applicants from submitting application fee waiver or reduction requests more
622than 4 months before the submission of an application because the circumstances that support an
623applicant's request are subject to change, and FDA considers it unreasonable to assume that
624those circumstances will continue to exist for longer than 4 months prior to the submission of an
625application. For example, if an applicant submits an application fee waiver request on July 1 and
626plans to submit its application on March 1 of the next year, FDA considers it unreasonable to
627assume that the facts stated on July 1 will remain the same 8 months later, in the following
628March. Therefore, FDA encourages sponsors to submit their waiver or reduction requests no
629more than 4 months prior to the submission of the application.

630

631 4. *Is there a recommended time frame to submit a waiver or reduction request if the*
632 *applicant wants to avoid paying the **product and establishment fees** and then seeking*
633 *a refund?*

634

635Yes. The time frame is the same as for an advance request for an application fee waiver or
636reduction: an applicant seeking a waiver or reduction of product and establishment fees may
637submit a request for a waiver or reduction 3 to 4 months before the fee is due. Annual product
638and establishment fees are usually assessed in August and are due on October 1.²⁶ Thus, an
639applicant that wishes to obtain a waiver or reduction in advance should submit its request
640between June 1 and July 1. Under normal circumstances and depending on available resources,
641FDA will try to complete its evaluation of the request before the due date of the product and
642establishment fees.

643

644The Act does not provide for deferral of user fees, and FDA does not grant deferrals of user fees
645based on pending waiver or reduction requests. FDA therefore expects that all product and
646establishment fees will be paid without regard to a pending request for a fee waiver or reduction.
647This approach will ensure that the steady funding stream Congress intended will be achieved,
648and should deter the filing of frivolous waiver or reduction requests.

649

650Ordinarily, FDA expects to grant a reduction or waiver of a product or establishment fee only for
651the current year. If an applicant wishes to have a product or establishment fee waived or
652reduced for assessments in future years, it should make a new request for a waiver or reduction
653each year.

654

655B. Content and Format of Requests

656

657 1. *General Information for All Requests*

658

659Requests for CDER and CBER user fee waivers, reductions, and refunds will be reviewed and
660granted or denied by CDER's Associate Director for Policy.²⁷ However, reductions and refunds
661for products regulated by CBER will be reviewed and granted or denied by CBER's Center
662Director.

134²⁶ The fiscal year begins October 1 and ends September 30.

135²⁷ Waivers and reductions under the fees-exceed-the-costs waiver provision are the responsibility of FDA's Office
136of Financial Management.

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663

664FDA recommends that each waiver or reduction request be submitted in writing and that it
665contain the following information:

666

667 • Name of applicant requesting the waiver,²⁸ including company name, address, contact,
668 telephone and facsimile numbers, and e-mail address

669

670 • Identification of the specific fee(s) for which the waiver, refund, or reduction is requested

671

672 • Date on which payment was made or will be made of the fee for which a waiver or
673 reduction is requested

674

675 • Statutory provision under which a waiver or reduction is requested

676

677 • Information and analyses showing that the criteria for the waiver or reduction have been
678 met

679

680 • Rationale for why the waiver, reduction or refund request should be granted

681

682 • A list of the applicant's affiliates

683

684 • For public health and barrier to innovation waivers, a current annual financial report for
685 the applicant and the applicant's affiliates. If a current annual financial report is not
686 available, a report that includes total annual revenues, net proceeds, cash, and total assets.

687

688 *2. Additional Specific Information for Application Fee Waiver or Reduction Requests*

689

690In addition to the general information specified above, requests for waivers of or reductions in
691**application fees** should include the following :

692

693 • NDA number (including supplement number and type if there is one) or BLA number

694

695 • Trade and established names of products covered by the waiver request

696

697 • Date the application was or will be submitted

698

699 • Whether or not clinical data are required for approval

700

701 *3. Additional Specific Information Requested for Product Fee Waiver or Reduction*
702 *Requests*

703

142²⁸ If an agent is submitting a waiver request on behalf of the waiver applicant, authorization from the waiver
143applicant for the agent to act on its behalf should also be included.

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704In addition to the general information specified above, requests for waivers of or reductions in
705**product fees** should include the following:

707 • NDA or BLA number

708

709 • Trade and established names of the product

710

711 • National Drug Code (NDC) number

712

713 • Name of the application holder

714

715 • Specific strength, dosage form, and route of administration

716

717 • Invoice date and number (or copy of the invoice sheet)

718

719 *4. Additional Specific Information Requested for Establishment Fee Waiver and*
720 *Reduction Requests*

721

722In addition to the general information specified above, requests for waivers of or reductions in
723**establishment fees** should include the following :

724

725 • Name of the establishment

726

727 • Address of the manufacturing site (not a business, office, or headquarters address, but the
728 actual address of the manufacturing site)

729

730 • Establishment number as listed on the invoice

731

732 • Invoice date and number (or a copy of the invoice sheet)

734C. **Address for Submitting Requests**

735

736Original user fee waiver or reduction requests should be submitted in writing to:

737

738 Associate Director for Policy

739 Attention: User Fee Waiver Office, Michael D. Jones

740 Center for Drug Evaluation and Research

741 Food and Drug Administration

742 10903 New Hampshire Avenue

743 Bldg. 51, Room 6216

744 Silver Spring, MD 20993-0002

745

746

747**VII. FDA RESPONSES TO REQUESTS FOR WAIVERS AND REDUCTIONS**

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749FDA will review the waiver or reduction request, consulting with relevant Agency officials as
750appropriate. FDA may request additional information from the applicant during the review
751period. The Agency will respond to requests for waivers and reductions in a timely fashion
752based on available resources and collection time for additional information.

753

VIII. RECONSIDERATIONS AND APPEALS

754

A. Reconsideration Request

755

756If FDA fully or partially denies a request for a waiver or reduction of user fees, the applicant
757may request reconsideration of that decision. A request for reconsideration should be made
758within 30 days of the issuance of FDA's decision to fully or partially deny a request for a waiver,
759reduction or refund of user fees.

760

761FDA recommends that requests for reconsideration state the applicant's reasons for believing
762that the decision is in error and include any additional information, including updated financial
763information, that is relevant to the applicant's position. The Agency will issue a response upon
764reconsideration, setting forth the basis for the decision.

765

766All requests for reconsiderations should be submitted in writing to:

767

768 Associate Director for Policy
769 Attention: User Fee Waiver Office, Michael D. Jones
770 Center for Drug Evaluation and Research
771 Food and Drug Administration
772 10903 New Hampshire Avenue
773 Bldg. 51, Room 6216
774 Silver Spring, MD 20993-0002

775

B. Appeal Request

776

777If a request is denied upon reconsideration, the applicant may choose to appeal the denial. A
778request for an appeal should be made within 30 days of the issuance of FDA's decision to affirm
779its denial of a request for a waiver, or reduction of user fees. The following information should
780be included in the appeal.

781

- 782 • The original waiver request
- 783 • The denial of the original waiver request
- 784 • The reconsideration request
- 785 • The denial of the reconsideration request
- 786 • A statement of the applicant's belief that the prior conclusions were in error

787

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795The appeal request should also contain particular references to information or analyses already
796submitted to the Agency that the applicant believes is relevant to its position. No new
797information should be presented in the appeal request.

798

799All requests for appeals should be submitted in writing to:

800

801 Chief Scientist and Deputy Commissioner for Science and Public Health

802 User Fee Appeals Officer

803 Food and Drug Administration

804 c/o Matthew Warren

805 10903 New Hampshire Avenue

806 Bldg. 32, Room 4210

807 Silver Spring, MD 20993-0002Fax: 301-847-8617

808

809A copy of the request for appeal should also be submitted to the CDER Associate Director for
810Policy as noted in section VIII above. After FDA reviews the information submitted in the
811appeal request, the Deputy Commissioner will issue a written decision on the applicant's request.
812The written decision issued by the Deputy Commissioner will constitute final Agency action on
813that request.

814

815

816IX. DISCLOSURE OF PUBLIC INFORMATION

817

818FDA plans to disclose to the public information about its actions granting or denying waivers
819and reductions. This disclosure will be consistent with the laws and regulations governing the
820disclosure of confidential commercial or financial information.

821