

# Guidance for Industry and FDA Staff: Application User Fees for Combination Products

***DRAFT GUIDANCE—September 2004***

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner  
Office of Combination Products**

**September 2004**

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# Guidance for Industry and FDA Staff: Application User Fees for Combination Products

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner  
Office of Combination Products (OCP)  
September 2004**

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**TABLE OF CONTENTS**

<b>I.</b>	<b>PURPOSE</b> .....	<b>1</b>
<b>II.</b>	<b>BACKGROUND INFORMATION</b> .....	<b>2</b>
	<b>A. What is a combination product?</b> .....	<b>2</b>
	<b>B. How are combination products assigned for review and what type of marketing applications are required?</b> .....	<b>2</b>
	<b>C. What are user fees?</b> .....	<b>3</b>
<b>III.</b>	<b>USER FEES FOR COMBINATION PRODUCTS</b> .....	<b>4</b>
	<b>A. How are application user fees determined for combination products?</b> .....	<b>4</b>
	<b>B. What user fee waivers are available under MDUFMA?</b> .....	<b>5</b>
	<b>C. What user fee waivers are available under PDUFA?</b> .....	<b>5</b>
	<b>D. How might the PDUFA barrier to innovation waiver apply to innovative combination products for which two applications may be appropriate?</b> .....	<b>6</b>
	<b>E. What factors may be considered in determining whether a product is eligible for an “Innovative Combination Product” waiver?</b> .....	<b>7</b>
	<b>F. When would a combination product be considered innovative for the purposes of the “Innovative Combination Product” waiver?</b> .....	<b>8</b>
	<b>G. How does FDA expect to reduce application fees under the “Innovative Combination Product” waiver for innovative combination products for which two applications are required?</b> 9	
	<b>H. My product qualifies for an Innovative Combination Product waiver. How does this affect product and establishment fees payable under PDUFA?</b> .....	<b>11</b>
	<b>I. Will other waivers be available for combination products for which two applications are required?</b> .....	<b>11</b>
<b>IV.</b>	<b>PROCEDURES FOR REQUESTING WAIVERS FOR USER FEES FOR COMBINATION PRODUCTS</b> .....	<b>12</b>
	<b>A. How do I request a small business waiver under MDUFMA?</b> .....	<b>12</b>
	<b>B. How do I request a waiver for a PDUFA application, establishment, or product fee?</b> .....	<b>12</b>
	<b>C. Where can I get more information about combination products?</b> .....	<b>12</b>

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**Guidance for Industry and FDA Staff<sup>1</sup>**  
**Application User Fees for Combination Products**

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

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**I. PURPOSE**

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This document provides guidance to industry and FDA staff on marketing application user fees for combination products as defined under 21 CFR 3.2(e). The guidance document explains that combination products for which a single marketing application is submitted will be assessed the user fee associated with that particular type of marketing application. The document explains that, in the infrequent situation where FDA requires two marketing applications for a combination product, two application fees would ordinarily be assessed. The guidance also describes how the "barrier to innovation" waiver provision<sup>2</sup> under the prescription drug user fee provisions of the Federal Food, Drug, and Cosmetic Act (the Act) may be applied to innovative combination products for which FDA requires the submission of two applications. Such a waiver would provide a reduction in application user fees equivalent to the additional fee burden associated with the submission of two marketing applications.

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

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<sup>1</sup> This guidance has been prepared by the Office of Combination Products in the Office of the Commissioner in cooperation with the Center for Biologics Evaluation and Research, the Center for Drug Evaluation and Research, and the Center for Devices and Radiological Health at the Food and Drug Administration.

<sup>2</sup> Section 736(d)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379h(d)(1)).

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### 41 **II. BACKGROUND INFORMATION**

#### 42 **A. What is a combination product?**

43 A combination product is a product comprised of any combination of a drug and a device; a  
44 biological product and a device; a drug and a biological product; or a drug, device, and a  
45 biological product. Under 21 CFR 3.2 (e), a combination product is defined to include:

- 46 (1) A product comprised of two or more regulated components; i.e., drug/device,  
47 biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically,  
48 or otherwise combined or mixed and produced as a single entity;
- 49 (2) Two or more separate products packaged together in a single package or as a unit and  
50 comprised of drug and device products, device and biological products, or biological  
51 and drug products;
- 52 (3) A drug, device, or biological product packaged separately that according to its  
53 investigational plan or proposed labeling is intended for use only with an approved  
54 individually specified drug, device, or biological product where both are required to  
55 achieve the intended use, indication, or effect and where upon approval of the proposed  
56 product the labeling of the approved product would need to be changed; e.g., to reflect  
57 a change in intended use, dosage form, strength, route of administration, or significant  
58 change in dose; or
- 59 (4) Any investigational drug, device, or biological product packaged separately that  
60 according to its proposed labeling is for use only with another individually specified  
61 investigational drug, device, or biological product where both are required to achieve  
62 the intended use, indication, or effect.

63 Drug-drug, device-device, or biologic-biologic products do not meet the definition of a  
64 combination product as defined in 21 CFR 3.2 (e), and are outside the scope of this guidance.

#### 65 **B. How are combination products assigned for review and what type of marketing** 66 **applications are required?**

67 A combination product is assigned to an Agency center<sup>3</sup> that will have primary jurisdiction for  
68 its premarket review and regulation. Under section 503(g) of the Act, the assignment of a  
69 “lead center” is based upon a determination of the “primary mode of action” (PMOA) of the  
70 combination product.<sup>4</sup> For example, if the PMOA of a combination product is that of a  
71 biological product, then the combination product would be assigned to the Agency component

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<sup>3</sup> Section 503(g) of the Act defines the term “agency center” as a center or alternative organizational component of the Food and Drug Administration.

<sup>4</sup> A proposed rule defining the primary mode of action of a combination product was published in the May 7, 2004, Federal Register (69 FR 25527), and is available at <http://www.fda.gov/oc/combination/default.htm>.

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82 responsible for premarket review of that biological product. Depending upon the type of  
83 combination product, approval, clearance or licensure may be obtained through submission of  
84 a single marketing application, or through separate marketing applications for the individual  
85 constituent parts of the combination product.  
86

87 For most combination products, a single marketing application is sufficient for the product's  
88 approval, clearance or licensure. In some cases, however, a sponsor may choose to submit two  
89 marketing applications for a combination product when one application would suffice. For  
90 example, a sponsor may choose to submit two applications in order to receive some benefit that  
91 accrues only from approval under a particular type of application (e.g., new drug product  
92 exclusivity, orphan status, or proprietary data protection when two firms are involved). In  
93 other cases, FDA may determine that two marketing applications are necessary. For example,  
94 when one of the individual constituent parts of a combination product is already approved for  
95 another use, and where the labeling of the already approved product will need to be changed to  
96 reflect its new intended use in the combination product, FDA may determine that two  
97 applications are necessary if the labeling of the already approved product is subject to legal  
98 requirements different from those that will apply to the combination product. A guidance  
99 addressing the factors FDA expects to consider in determining whether a single or multiple  
100 marketing applications should be submitted for a combination product is in development and  
101 will be provided separately for public review and comment.  
102

### **C. What are user fees?**

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106 In 1992, Congress passed the Prescription Drug User Fee Act (PDUFA), P.L. 102-571. The  
107 user fee amendments were reauthorized by the Food and Drug Administration Modernization  
108 Act of 1997 and again by the Public Health Security and Bioterrorism Preparedness and  
109 Response Act of 2002. PDUFA authorized FDA to collect fees from companies that produce  
110 certain human drug and biological products. When a company requests approval of a new drug  
111 or biological product prior to marketing, it must submit an application (e.g., new drug  
112 application (NDA) or biologics license application (BLA)) along with a fee to support the  
113 review process. In addition, companies pay annual fees for each prescription drug product  
114 marketed and the establishment where the prescription drug product is manufactured. More  
115 information about PDUFA is available at <http://www.fda.gov/oc/pdufa/> and  
116 <http://www.fda.gov/cder/pdufa/default.htm> .  
117

118 The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250,  
119 amended the Act to provide for user fees for device reviews. The fees apply to certain  
120 premarket reviews of premarket approval applications (PMAs), product development protocols  
121 (PDPs), premarket reports (PMRs), biologics license applications (BLAs), certain supplements,  
122 and premarket notifications (510(k)s). More information about MDUFMA is available at  
123 <http://www.fda.gov/oc/mdufma/>.

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### 127 128 **III. USER FEES FOR COMBINATION PRODUCTS** 129

#### 130 **A. How are application user fees determined for combination products?** 131

132 As explained in the document “Assessing User Fees: PMA Supplement Definitions, Modular  
133 PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single  
134 Application, and Fees for Combination Products; Guidance for Industry and FDA” available at  
135 <http://www.fda.gov/cdrh/mdufma/guidance/1201.pdf>, a combination product with a device  
136 component (i.e., a drug-device or biologic-device product) will be subject to the fee associated  
137 with the type of application required for the product's premarket approval, clearance, or  
138 licensure. For example, a biologic-device or a drug-device combination product for which a  
139 PMA is required will be subject to the PMA fee under MDUFMA, while a biologic-device or a  
140 drug-device combination product for which a 510(k) is required will be subject to the 510(k)  
141 fee under MDUFMA.  
142

143 A biologic-device product regulated under section 351 of the PHS Act will be subject to the  
144 BLA fee under MDUFMA, if the biological component meets the definition of a device. Other  
145 biologic-device combination products (those with biologic components that do not meet the  
146 definition of a device) or drug-biologic combination products regulated under section 351 of  
147 the PHS Act, or drug-device or drug-biologic combination products regulated under section  
148 505(b) of the Act, that are human drug applications as defined in section 735 of the Act, will be  
149 subject to prescription drug user fees. Prescription drug user fees may include application and  
150 yearly product and establishment fees. More information about prescription drug user fees is  
151 available at <http://www.fda.gov/cder/pdufa/default.htm>.  
152

153 Therefore, combination products for which a single marketing application is submitted are  
154 subject to the fee associated with that type of application. Sponsors may be eligible for fee  
155 waivers or reductions (e.g., for small businesses) under PDUFA and MDUFMA. More  
156 information on available waiver options is provided below.  
157

158 In some circumstances, a sponsor may choose to submit two applications covering the various  
159 components of a combination product when one application would suffice. In such cases, two  
160 application fees would be assessed, i.e., one fee for each application. For example, a sponsor  
161 may choose to submit two applications when one would suffice in order to receive some  
162 benefit from having two applications (e.g., new drug product exclusivity, orphan status, or  
163 proprietary data protection when two firms are involved). Although sponsors may still be  
164 eligible for existing fee waivers or reductions in this circumstance, the sponsor receives benefit  
165 by submitting two applications. Review of two applications when one would suffice places  
166 extra burden on FDA review resources, and a user fee for each application would ordinarily be  
167 assessed.  
168

169 Likewise, when FDA requires two applications for a combination product, two application fees  
170 would be assessed. Sponsors may be eligible for existing waivers or reductions under PDUFA  
171 or MDUFMA. In particular, as explained below, the Agency intends to look closely at whether

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172 a PDUFA “barrier to innovation” waiver may be appropriate to reduce the additional fee  
173 burden associated with FDA’s requirement for two marketing applications.  
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176 **B. What user fee waivers are available under MDUFMA?<sup>5</sup>**  
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178 MDUFMA provides more limited user fee waiver options than those provided for under  
179 PDUFA. Other than specific situations identified in Table 1 below for which no application  
180 fee is required, standard MDUFMA fees are required for all device applications other than  
181 those from small businesses. Under MDUFMA, a small business is defined as one whose  
182 annual gross sales and revenues (for the firm and its affiliates) is ≤ \$30 million. Under  
183 MDUFMA, small businesses pay 38% of the standard PMA and BLA fee and 80% of the  
184 standard 510(k) fee. MDUFMA also provides a one-time waiver for the first premarket  
185 application from a qualified small business.  
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Category	Exemption or Waiver
Humanitarian Device Exemption (HDE)	Exempt from any fee.
BLA for a product licensed for further manufacturing use only	Exempt from any fee.
First premarket application (PMA, PDP, BLA, or premarket report) from a small business	One-time waiver of the fee that would otherwise apply.
Third-party 510(k)	Exempt from any FDA fee; however, the third-party may charge a fee for its review.
Any application for a device intended solely for pediatric use.	Exempt from any fee. If an applicant obtains an exemption under this provision, and later submits a supplement for adult use, that supplement is subject to the fee then in effect for an original premarket application.
Any application from a State or Federal Government entity.	Exempt from any fee unless the device is to be distributed commercially.

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**C. What user fee waivers are available under PDUFA?<sup>6</sup>**

PDUFA provides for a waiver of the fee for the first human drug application from a small business.<sup>7</sup> The criteria for qualifying as a small business under PDUFA are different than

<sup>5</sup> MDUFMA waivers are described in Section 738 of the Act.

<sup>6</sup> PDUFA waivers are described in Section 736(d) of the Act (21 U.S.C. 379h(d)).

<sup>7</sup> See section 736(d)(1)(D) of the Act (21 U.S.C. 379h(d)(1)(D)).



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195 those under MDUFMA.<sup>8</sup> Under PDUFA, “small business” means an entity that has fewer than  
196 500 employees for the small business and its affiliates.<sup>9</sup>

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198 PDUFA also provides for waivers or reductions of fees where:

199

- 200     ▪ such waiver or reduction is necessary to protect the public health;
- 201
- 202     ▪ the assessment of the fee would present a significant barrier to innovation because of  
203 limited resources available to such person or other circumstances; or
- 204
- 205     ▪ the fees to be paid by such person will exceed the anticipated present and future costs  
206 incurred by the Secretary in conducting the process for the review of human drug  
207 applications for such person.
- 208

209 The document “Interim Guidance Document for Waivers of and Reductions in User Fees,”  
210 available at <http://www.fda.gov/cder/pdufa/default.htm>, provides information for requesting,  
211 and the criteria for evaluating, a waiver of PDUFA application, establishment or product fees.<sup>10</sup>  
212 In addition, the document “Fees-Exceed-The-Costs Waivers Under the Prescription Drug User  
213 Fee Act,” available at <http://www.fda.gov/cder/pdufa/default.htm>, provides further explanation  
214 of the waiver option described in the third bullet above.

215

216 It should be noted that PDUFA applications (NDA or BLA) not requiring clinical data for  
217 approval are assessed half the fee that is assessed for applications that do require clinical data  
218 for approval.<sup>11</sup> Supplemental applications to NDAs or BLAs that do not require clinical data  
219 for approval are not assessed a fee.

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222 **D. How might the PDUFA barrier to innovation waiver apply to innovative combination**  
223 **products for which two applications may be appropriate?**

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225 Combination products may incorporate cutting edge, innovative technologies that  
226 hold great promise for advancing patient care. For example, by combining two  
227 different types of regulated components, treatment may be made safer or more  
228 effective than it would be using either of the components independently.

229 FDA believes that the assessment of two marketing application fees for an  
230 innovative combination product could represent a significant barrier to its  
231 development.

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<sup>8</sup> Qualifying sponsors could receive a waiver from one or both application fees for their first PDUFA and MDUFMA premarket applications. Given the different criteria for small businesses, however, some companies may qualify for one waiver but not the other.

<sup>9</sup> See section 736(d)(3) of the Act (21 U.S.C. 379h(d)(3)).

<sup>10</sup> The current mailing addresses for submitting PDUFA waiver requests can be found on the Internet at <http://www.fda.gov/cder/pdufa/addresses.htm>.

<sup>11</sup> For FY 2005, the full NDA or BLA fee is \$672,000, and the fee for an NDA or BLA that does not require clinical data for approval is \$336,000.

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232 After reviewing the various waiver options available under PDUFA and  
233 MDUFMA, FDA believes that the PDUFA barrier to innovation waiver allows the  
234 Agency to reduce the additional fee burden associated with the requirement for  
235 two marketing applications for an innovative combination product. In particular,  
236 PDUFA provides for a fee waiver or reduction when the assessment of the fee  
237 would present a significant barrier to innovation because of limited resources  
238 available to such person or other circumstances. FDA believes such “other  
239 circumstances” may exist in the infrequent case where two marketing applications  
240 are required. FDA expects to consider the factors discussed below in determining  
241 whether a particular innovative combination product is eligible for this fee  
242 reduction.

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### **E. What factors may be considered in determining whether a product is eligible for an “Innovative Combination Product” waiver?**

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To be eligible for the “Innovative Combination Product” waiver under PDUFA’s “barrier to innovation because of...other circumstances” provision, FDA expects to consider the following factors:

- 252       ▪ The combination product (as defined in 21 CFR 3.2(e)) as a whole is innovative (see  
253       Section F below for factors FDA expects to consider in determining whether a  
254       combination product is innovative).
- 256       ▪ FDA is requiring two fee-eligible<sup>12</sup> marketing applications<sup>13</sup> for the combination  
257       product.
- 259       ▪ The two components of the product are specifically intended and labeled only for use  
260       together. Applications that include independent uses of one or both components  
261       outside the combination product generally would not be eligible for this waiver.  
262       However, applications for combinations of already approved, independent products  
263       generally would be eligible if two applications are required for approval of the new  
264       combined use.
- 266       ▪ The applicant does not qualify for a PDUFA small business waiver or have limited  
267       resources. Applicants who qualify for a PDUFA small business waiver receive a full  
268       waiver of the PDUFA application fee. In addition, applicants with an innovative  
269       combination product who do not qualify for a PDUFA small business waiver, but who  
270       have limited resources, may be eligible for a standard PDUFA barrier to innovation

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<sup>12</sup> Orphan product applications, BLAs for further manufacturing use only, HDEs, pediatric device applications or other applications where a fee is not assessed would not qualify. This waiver is specifically intended to reduce the additional fee burden associated with the requirement of two fee-paying applications. In these cases, only one application would be assessed a fee.

<sup>13</sup> The two applications could be any combination of fee-eligible original or supplemental applications (e.g., two original applications, an original application and a supplemental application, or two supplemental applications).

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271 waiver, which may provide a full waiver of the PDUFA application fee because of the  
272 applicant's financial need. More information about the standard barrier to innovation  
273 waiver is available at <http://www.fda.gov/cder/pdufa/default.htm>. Applicants who  
274 believe they qualify are encouraged to explore their eligibility for the PDUFA small  
275 business or barrier to innovation waivers first.  
276

277

### **F. When would a combination product be considered innovative for the purposes of the 278 "Innovative Combination Product" waiver? 279**

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281 FDA expects to consider the following factors<sup>14</sup> in determining whether a combination product  
282 is innovative for the purposes of this waiver:  
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- 285 ■ The product addresses an unmet medical need in the treatment, diagnosis or prevention  
286 of disease, as demonstrated by one of the following:

287

- 288 • No approved alternative treatment or means of diagnosis exists; or

289

- 290 • The combination product offers significant, clinically meaningful  
291 advantages over existing approved alternative treatments. The  
292 combination product should provide for clinically important earlier or  
293 more accurate diagnosis or offer important therapeutic advantages in  
294 safety and/or effectiveness or patient compliance over existing  
295 alternatives. Such advantages may include demonstrated superiority  
296 over current treatments for effects on serious outcomes (e.g., morbidity),  
297 ability to provide clinical benefit for those patients unable to tolerate  
298 current treatments, or ability to provide clinical benefit without the  
299 serious side effects associated with current treatments.

300

- 301 ■ Factors such as whether one of the two applications includes a new molecular  
302 entity, has been designated as a priority drug or eligible for expedited device  
303 review, or has been granted fast track status, may also be considered in  
304 determining whether a product is considered innovative for the purposes of this  
305 waiver. The existence of treatment alternatives would weigh against deciding  
306 that a product is innovative.  
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<sup>14</sup> These factors are largely derived from the Agency's approach to determining the eligibility of a product for expedited or priority review, where such factors are relevant to a determination of a combination product's innovativeness.

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308 **G. How does FDA expect to reduce application fees under the “Innovative Combination**  
 309 **Product” waiver for innovative combination products for which two applications are**  
 310 **required?**  
 311

312 In evaluating how the PDUFA barrier to innovation waiver provision may apply to innovative  
 313 combination products, FDA’s goal would be to reduce the additional fee burden associated  
 314 with the requirement for two marketing applications. As noted above, waiver options under  
 315 MDUFMA are limited, and the only fee reduction under MDUFMA is for small businesses.  
 316 Therefore, for innovative combination products requiring two marketing applications, in  
 317 appropriate situations FDA would expect to reduce PDUFA application fees as follows:  
 318

- 319 ■ Products requiring a MDUFMA application and a PDUFA application. FDA would expect  
 320 to reduce the PDUFA fee by the amount of the MDUFMA fee. Thus, a sponsor would pay  
 321 the full MDUFMA fee associated with the type of MDUFMA application, and a PDUFA  
 322 fee reduced by the paid MDUFMA fee. The total amount paid would be equivalent to one  
 323 PDUFA fee.  
 324
- 325 ■ Products requiring two PDUFA applications. FDA would expect to reduce each PDUFA  
 326 fee by half. In the case where two full PDUFA fees would otherwise be required, the total  
 327 amount paid under this waiver would be equivalent to one PDUFA fee.  
 328

329 Table 2 below illustrates with a variety of scenarios how FDA would expect to reduce fees for  
 330 innovative combination products for which two marketing applications are required. The  
 331 actual fee amounts are based on the FY 2005 fee structure, and are subject to change in  
 332 subsequent fiscal years.  
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 334

<b>Table 2: Examples of Fees Under Innovative Combination Products Waiver (FY05 Fees)</b>					
Application #1	Standard Fee for Application #1	Application #2	Standard Fee for Application #2	Total Fee for both Applications (Without Waivers)	Proposed Total Fee (With Waiver)
PMA, PMA Panel-Track Supplement or MDUFMA BLA or BLA Efficacy Supplement	\$239,237	NDA/BLA	\$672,000	\$911,237	\$672,000:  \$239,237 MDUFMA, \$432,763 PDUFA
180-Day PMA Supplement	\$51,436	NDA/BLA	\$672,000	\$723,436	\$672,000:  \$51,436 MDUFMA, \$620,564 PDUFA

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<b>Table 2: Examples of Fees Under Innovative Combination Products Waiver (FY05 Fees)</b>					
Application #1	Standard Fee for Application #1	Application #2	Standard Fee for Application #2	Total Fee for both Applications (Without Waivers)	Proposed Total Fee (With Waiver)
PMA, PMA Panel-Track Supplement or MDUFMA BLA or BLA Efficacy Supplement	\$239,237	NDA/BLA Efficacy Supplement	\$336,000	\$575,237	\$336,000:  \$239,237 MDUFMA, \$96,763 PDUFA
First Small Business <sup>15</sup> PMA, PMA Panel-Track Supplement or MDUFMA BLA or BLA Efficacy Supplement	\$0	NDA/BLA	\$672,000	\$672,000	\$672,000:  \$0 MDUFMA \$672,000 PDUFA
Small Business <sup>16</sup> PMA, PMA Panel-Track Supplement or MDUFMA BLA or BLA Efficacy Supplement	\$90,910	NDA/BLA	\$672,000	\$762,910	\$672,000:  \$90,910 MDUFMA \$581,090 PDUFA
Real-Time PMA Supplement	\$17,225	NDA/BLA Efficacy Supplement	\$336,000	\$353,225	\$336,000:  \$17,225 MDUFMA, \$318,775 PDUFA
510(k)	\$3,502	NDA/BLA	\$672,000	\$675,502	\$672,000:  \$3,502 MDUFMA, \$668,498 PDUFA
510(k)	\$3,502	NDA/BLA Efficacy Supplement	\$336,000	\$339,502	\$336,000:  \$3,502 MDUFMA, \$332,498 PDUFA

<sup>15</sup> Assumes sponsor qualifies as a small business under MDUFMA but not PDUFA.

<sup>16</sup> Assumes sponsor qualifies as a small business under MDUFMA but not PDUFA.

*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

Application #1	Standard Fee for Application #1	Application #2	Standard Fee for Application #2	Total Fee for both Applications (Without Waivers)	Proposed Total Fee (With Waiver)
Original PDUFA Application (NDA)	\$672,000	Original PDUFA Application (BLA)	\$672,000	\$1,344,000	\$672,000: \$672,000 PDUFA
Original PDUFA Application (NDA)	\$672,000	PDUFA Efficacy Supplement (BLA)	\$336,000	\$1,008,000	\$672,000: \$672,000 PDUFA
PDUFA Efficacy Supplement (NDA)	\$336,000	PDUFA Efficacy Supplement (BLA)	\$336,000	\$672,000	\$336,000: \$336,000 PDUFA

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**H. My product qualifies for an Innovative Combination Product waiver. How does this affect product and establishment fees payable under PDUFA?**

The Innovative Combination Product waiver only provides for a reduction of application fees equivalent to the additional fee burden associated with the requirement for two marketing applications. This use of the PDUFA barrier to innovation waiver is not applicable to the yearly product and establishment fees. FDA intends to review requests for waivers of PDUFA product and/or establishment fees for combination products, including innovative combination products, under existing criteria established for the review of such waivers, which are applicable to both combination and non-combination products.

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**I. Will other waivers be available for combination products for which two applications are required?**

FDA has considered the various options available under PDUFA and MDUFMA, and believes the Innovative Combination Product waiver appropriately addresses the additional fee burden associated with any FDA requirement for the submission of two marketing applications for an innovative combination product. FDA will evaluate its experience in working with this guidance document, and the impact of the Innovative Combination Product waiver on the user fee program as a whole.

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*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

361 **IV. PROCEDURES FOR REQUESTING WAIVERS FOR USER FEES FOR**  
362 **COMBINATION PRODUCTS**

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**A. How do I request a small business waiver under MDUFMA?**

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367 The document “Guidance for Industry and FDA: FY 2004 MDUFMA Small Business  
368 Qualification Worksheet and Certification,” available at  
369 <http://www.fda.gov/cdrh/mdufma/guidance/1225.pdf> provides instructions for obtaining an  
370 FDA decision that a business qualifies as a small business and is eligible for reduced or waived  
371 MDUFMA application fees.

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**B. How do I request a waiver for a PDUFA application, establishment, or product fee?**

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376 The document “Interim Guidance Document for Waivers of and Reductions in User Fees,”  
377 available at <http://www.fda.gov/cder/pdufa/default.htm> provides instructions for requesting a  
378 waiver of application, establishment or product fees under PDUFA.<sup>17</sup>

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380 The same instructions should be followed for requesting the Innovative Combination Products  
381 waiver described above. The request should be clearly identified as an Innovative  
382 Combination Products Waiver Request, and be accompanied by a statement of reasons the  
383 applicant believes the Innovative Combination Products Waiver should be applied. To  
384 facilitate FDA’s consideration of the request, FDA encourages sponsors to address and  
385 substantiate each of the criteria outlined in Section III above. Current mailing addresses for  
386 submitting PDUFA waiver requests, including an Innovative Combination Products waiver, are  
387 provided at <http://www.fda.gov/cder/pdufa/addresses.htm>.

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389 Persons are encouraged to submit requests for fee waivers or reductions 90 days before the  
390 required fees are expected to be paid. In addition, under section 736(i) of the Act, to qualify  
391 for a refund of any fee collected under the user fee provisions of the Act, you must submit a  
392 written request for a refund within 180 days after such fee is due.

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**C. Where can I get more information about combination products?**

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396 The Office of Combination Products is available as a resource to sponsors and review staff  
397 throughout the development of a combination product. The Office may be reached at (301)  
398 427-1934 or by email at [combination@fda.gov](mailto:combination@fda.gov). In addition, the Office maintains an updated  
399 website with information on the regulation of combination products at  
400 <http://www.fda.gov/oc/comboination>.

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<sup>17</sup> See particularly pages 23-24 of that interim guidance document.