

---

# Guidance for Industry Tropical Disease Priority Review Vouchers

## *DRAFT GUIDANCE*

**This guidance document is being distributed for comment purposes only.**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be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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 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 David Roeder (CDER), 301-796-0799, or the Office of Communications, Training, and Manufacturers Assistance (CBER), 301-827-1800 or 800-835-4709.

**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)**

**October 2008  
Procedural**

---

# Guidance for Industry Tropical Disease Priority Review Vouchers

*Additional copies are available from:*

*Office of Training and Communications  
Division of Drug Information, HFD-240  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993  
Phone: 301-796-3400; Fax: 301-847-8714  
druginfo@fda.hhs.gov  
<http://www.fda.gov/cder/guidance/index.htm>*

*and/or*

*Office of Communication, Training, and Manufacturers Assistance, HFM-40  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
1401 Rockville Pike, Rockville, MD 20852-1488  
<http://www.fda.gov/cber/guidelines.htm>  
(tel) 800-835-4709 or 301-827-1800*

**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)**

**October 2008  
Procedural**

## TABLE OF CONTENTS

|             |  |          |
|-------------|--|----------|
| <b>I.</b>   | <b>INTRODUCTION.....</b>                                     | <b>1</b> |
| <b>II.</b>  | <b>BACKGROUND .....</b>                                      | <b>1</b> |
| <b>III.</b> | <b>PROVISIONS OF SECTION 524 – AN OVERVIEW .....</b>         | <b>2</b> |
| <b>IV.</b>  | <b>POLICIES AND PROCEDURES – QUESTIONS AND ANSWERS .....</b> | <b>2</b> |

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12

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

## Tropical Disease Priority Review Vouchers

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. 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.

13  
14  
15

### I. INTRODUCTION

16  
17 This guidance provides information on the implementation of section 1102 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), which adds new section 524 to the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360n). Section 524 authorizes FDA to award priority review vouchers to sponsors of certain tropical disease product applications that meet the criteria specified by the Act. A priority review voucher may be used by the sponsor who obtains it or another sponsor to obtain a priority review for a different application. A priority review voucher may be transferred from the sponsor who obtains it to another sponsor.

21  
22  
23  
24  
25 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.

26  
27  
28  
29  
30  
31  
32

### II. BACKGROUND

33  
34 Section 524 is designed to encourage development of new drug and biological products for prevention and treatment of certain tropical diseases affecting millions of people throughout the world. While diseases addressed by this legislation represent an important disease burden for humanity, there has been remarkably little progress over the past 50 years in development of drugs for these diseases. Because these diseases are found primarily in poor and developing countries, existing incentives have been insufficient to encourage development of new and innovative drug therapies. Although these tropical diseases are rare in the United States, intercontinental jet transport, immigration, tourism, and military operations are increasing the direct impact these diseases have on the health of Americans. By enacting section 524, Congress

35  
36  
37  
38  
39  
40  
41  
42

---

<sup>1</sup> This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

## *Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

43 is attempting to stimulate new drug development by offering additional incentives for obtaining  
44 FDA approval of certain tropical disease drug products. Under section 524, the sponsor of a  
45 human drug application for a qualified tropical disease may be eligible for a voucher that can be  
46 used to obtain a priority review for any subsequent human drug application under section  
47 505(b)(1) of the Act or section 351 of the Public Health Service (PHS) Act.  
48

### 49 **III. PROVISIONS OF SECTION 524 – AN OVERVIEW**

50  
51 A. What applications are eligible to receive a tropical disease priority review voucher?  
52

- 53 • The application must be for a listed tropical disease (see section IV, Question 2 of  
54 this guidance).
- 55 • The application must be submitted under section 505(b)(1) of the Act or section 351  
56 of the PHS Act.
- 57 • The drug that is the subject of the application must contain no active ingredient  
58 (including any ester or salt of the active ingredient) that has been approved in any  
59 other application under section 505(b)(1) the Act or section 351 of the PHS Act.
- 60 • The application must be submitted after the enactment of FDAAA (September 27,  
61 2007).
- 62 • The application must qualify for a priority review.  
63

64 B. What are the parameters for use of a tropical disease priority review voucher?  
65

- 66 • The voucher cannot be issued until at least 1 year after September 27, 2007, the date  
67 of FDAAA enactment.
- 68 • The application using the priority review voucher must also be a 505(b)(1) or section  
69 351 PHS Act application, and is not limited to products for tropical diseases.
- 70 • At least 1 year in advance, the sponsor planning to use the voucher must notify FDA  
71 of intent to use the voucher and the date on which the sponsor intends to submit the  
72 application.
- 73 • A sponsor using the voucher must pay an extra user fee to support the review of the  
74 application based on the average cost of a priority NDA/BLA review in the previous  
75 fiscal year. Payment of this extra fee, to which the sponsor is legally committed as a  
76 result of the notification of its intent to use the voucher, is not subject to waivers,  
77 exemptions, reductions, or refunds.
- 78 • The sponsor of a tropical disease product receiving a priority review voucher may  
79 transfer the voucher to another sponsor (see section IV, Question 8)  
80

### 81 **IV. POLICIES AND PROCEDURES – QUESTIONS AND ANSWERS**

82  
83 Since the enactment of FDAAA, the Agency has received numerous inquiries about the scope of  
84 section 524 and how various aspects of section 524 should be interpreted. The purpose of this  
85 guidance is to provide a response to these questions.  
86  
87  
88

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

### 89 **Q1. What is a tropical disease product application?**

90

91 The term *tropical disease product application* is defined in section 524(a)(4) of the Act. The  
92 term refers to an application that —

93

- 94 • is a human drug application as defined in section 735(1) of the Act<sup>2</sup>—
  - 95 ○ for prevention or treatment of a tropical disease; and
  - 96 ○ the FDA deems eligible for priority review;
- 97 • is approved after the date of the enactment of FDAAA by the FDA for use in the  
98 prevention or treatment of a tropical disease; and
- 99 • is for a human drug, no active ingredient (including any ester or salt of the active  
100 ingredient) of which has been approved in any other application under section 505(b)(1)  
101 of the Act or section 351 of the PHS Act.

102

### 103 **Q2. What tropical disease product applications may qualify for a priority review** 104 **voucher?**

105

106 Product applications for the prevention or treatment of the following tropical diseases may  
107 qualify:

108

- 109 • Tuberculosis
- 110 • Malaria
- 111 • Blinding trachoma
- 112 • Buruli Ulcer
- 113 • Cholera
- 114 • Dengue/Dengue haemorrhagic fever
- 115 • Dracunculiasis (guinea-worm disease)
- 116 • Fascioliasis
- 117 • Human African trypanosomiasis
- 118 • Leishmaniasis
- 119 • Leprosy
- 120 • Lymphatic filariasis
- 121 • Onchocerciasis
- 122 • Schistosomiasis
- 123 • Soil transmitted helminthiasis
- 124 • Yaws
- 125 • Any other infectious disease for which there is no significant market in developed nations  
126 and that disproportionately affects poor and marginalized populations, designated by  
127 regulation by the Secretary (section 524(a)(3))

128

129

---

<sup>2</sup> This definition includes drugs and most biological drugs, excluding blood components and certain other biological drug products. For details, refer to section 735(1) of the Act (21 U.S.C. 379g(1)). The definition does not cover medical devices.

## *Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

### 130 **Q3. What user fees apply to a tropical disease application?**

131  
132 User fees for human drug applications are described in sections 735 and 736 of the Act.<sup>3</sup> In  
133 general, a tropical disease application would be subject to these statutory requirements like any  
134 other application. However, we anticipate that many tropical disease applications may qualify  
135 for designation as orphan drug products. Under section 736(a)(1)(F) of the Act, if a human drug  
136 application for a prescription drug product that has been designated as a drug for a rare disease or  
137 condition under section 526 of the Act, the application is not subject to an application user fee,  
138 unless the application includes an indication for other than a rare disease or condition. In  
139 addition, section 736(k) of the Act provides for an exemption from annual product and  
140 establishment fees for certain orphan designated drugs.

### 141 142 **Q4. What is a priority review?**

143  
144 A priority review is a review conducted with a PDUFA goal date of 6 months. Normally, an  
145 application for a CDER product will qualify for a priority review if FDA determines that the  
146 product, if approved, would provide safe and effective therapy where no satisfactory alternative  
147 therapy exists or would be a significant improvement compared to marketed products, including  
148 non-drug products and/or therapies, in the treatment, diagnosis, or prevention of a disease. See  
149 CDER's Manual of Policies and Procedures (MAPP) 6020.3, "Review Classification Policy:  
150 Priority and Standard."<sup>4</sup> A CBER product will qualify for a priority review if FDA determines  
151 that the product, if approved, would be a significant improvement in the safety or effectiveness  
152 of the treatment, diagnosis, or prevention of a serious or life-threatening disease.

153  
154 FDA has committed to a goal to review and act on 90 percent of the applications that have been  
155 granted priority review status no later than 6 months after receipt, as described in the CDER  
156 MAPP and goals identified in the letters described in section 101(c) of the FDAAA.<sup>5</sup> An  
157 application that does not receive a priority designation will receive a "standard" review. Under  
158 the goals referenced in FDAAA section 101(c), FDA commits to a goal to review and act on 90  
159 percent of "standard" applications within 10 months of the date of receipt. Please note that an  
160 FDA review within a specific time frame does not mean an application will be approved within  
161 that time frame. The term "review and act on" is understood to mean the issuance of an approval  
162 or complete response letter after the review of a filed application. The action letter, if it is not an  
163 approval, will set forth in detail the specific deficiencies that need to be addressed before the  
164 application can be approved.

### 165 166 **Q5. What is a priority review voucher and when is it awarded?**

167  
168 The term *priority review voucher* is defined in section 524(a)(2) of the Act. It refers to a voucher  
169 issued by the Secretary to the sponsor of a tropical disease product application at the time of

---

<sup>3</sup> 21 U.S.C. 379g and 379h.

<sup>4</sup> Available on the Internet at <http://www.fda.gov/cder/mapp.htm>.

<sup>5</sup> See letters from the Secretary of Health and Human Services to the Chairman of the Committee on Health, Education, Labor, and Pensions of the Senate and the Chairman of the Committee on Energy and Commerce of the House of Representatives, as set forth in the Congressional Record, available on the Internet at <http://www.fda.gov/oc/pdufa4/pdufa4ltr.pdf>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

170 approval of the application that entitles the holder of such voucher to designate a single human  
171 drug application submitted under section 505(b)(1) or section 351 of the PHS Act (see section  
172 524(a)(2) of the Act) as qualifying for a priority review. Such a subsequent application would  
173 not have to meet the usual requirements for a priority review. (See Q13.)  
174

175 **Q6. Would eligibility to receive a priority review voucher be affected in any way by**  
176 **whether the sponsor intends to market or distribute the qualifying tropical disease**  
177 **product after approval?**

178 No, it does not matter if the sponsor decides not to market the product. Eligibility will be based  
179 on the criteria outlined in the statute.  
180

181 **Q7. What form will the voucher take?**  
182

183 The FDA will include information related to the priority review voucher in the approval letter for  
184 the tropical disease drug application.  
185

186 **Q8. Will these vouchers be transferable?**  
187

188 Yes, by the sponsor receiving the voucher. As the statute states (section 524(b)(2)), the tropical  
189 disease product sponsor receiving a tropical disease priority review voucher may transfer the  
190 entitlement to such voucher (including by sale) to another sponsor of a human drug application.  
191 The language of the statute allows for one transfer from the original recipient of the voucher to  
192 another sponsor of a human drug for which an application under section 505(b)(1) of the Act or  
193 section 351 of the PHS Act will be submitted after the date of the approval of the tropical disease  
194 product application. Although the statute's language imposes a limitation of one actual transfer  
195 of the voucher, FDA believes that contractual arrangements such as the use of an option or  
196 transfer of the right to designate the voucher's recipient could comply with the terms of the  
197 statute.  
198

199 **Q9. What is the procedure for voucher transfer?**  
200

201 The transfer should be documented with a letter of transfer from the tropical disease application  
202 holder granted the voucher and a letter from the new voucher owner acknowledging the transfer.  
203 These letters should be included in the application for which the sponsor wishes to redeem the  
204 priority review voucher. A voucher cannot be redeemed unless a complete record of transfer is  
205 available to the Agency.  
206

207 **Q10. When can a voucher be used?**  
208

209 After the voucher is issued, the sponsor redeeming the voucher must notify FDA of their intent  
210 to submit a human drug application with a priority review voucher at least 365 days prior to  
211 submission of the human drug application for which a priority review voucher will be used to  
212 obtain a priority review. The notification must include the date the sponsor intends to submit the  
213 application. In accordance with the language of the statute, FDA will consider this notification  
214 as a legally binding commitment to pay the priority review user fee for the fiscal year in which  
215 the application is submitted.

## *Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

216  
217  
218  
219  
220  
221  
222  
223  
224  
225  
226  
227  
228  
229  
230  
231  
232  
233  
234  
235  
236  
237  
238  
239  
240  
241  
242  
243  
244  
245  
246  
247  
248  
249  
250  
251  
252  
253  
254  
255  
256  
257  
258  
259  
260

### **Q11. What fees apply when using a priority review voucher?**

The sponsor of a human drug application that is the subject of a priority review voucher must pay FDA a priority review user fee in addition to any other fee required under the prescription drug user fee program. As the statute requires, the amount of the priority review user fee will be determined each fiscal year and based on the average cost incurred by FDA in the review of a human drug application subject to priority review in the previous fiscal year.

FDA will establish the fee amount before the beginning of each fiscal year and will publish the fee schedule in the *Federal Register*.

### **Q12. When do I pay the priority review voucher fee?**

According to the terms of the statute, the priority review user fee is due upon submission of the application for which the priority review voucher is used. The statute specifies that the application will be considered incomplete if the priority fee and all other applicable user fees are not paid in accordance with FDA payment procedures. In addition, FDA cannot collect these fees in any fiscal year until Congress has passed a law appropriating funds for these fees. Because FDA may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section of the Act and FDA may not collect priority review voucher fees prior to a relevant appropriation for that fiscal year, FDA cannot accept any application using a priority review voucher if the necessary appropriation has not become law for that fiscal year.

### **Q13. If I present a voucher to FDA for priority review, am I guaranteed a 6-month review on my new drug application?**

No. The definition of priority review in section 524(a)(1) refers to the CDER MAPP and the PDUFA goals letter.<sup>6</sup> We believe the intent of this section is that drugs for which priority review vouchers are used should be treated as if they were any other priority review drug. Therefore, these applications would be placed in the priority review group. The Agency has committed to a goal of completing 90 percent of priority reviews within 6 months.

### **Q14. Can FDA determine whether an application will be eligible to receive a voucher before an application is approved or licensed (i.e., prior to NDA/BLA submission or during review of the application)?**

No. It is important to note that a product that meets the criteria at the time of submission may not meet those same criteria at the time of the approval action and would thus not be eligible to receive a priority review voucher. This could occur if another application containing the same active ingredient is approved first. For this reason, the Agency will not make voucher determinations until the time of application approval.

### **Q15. Are combination products eligible for priority review vouchers?**

---

<sup>6</sup> The PDUFA goals can be found on the Internet at <http://www.fda.gov/oc/pdufa4/pdufa4goals.html>.

## *Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

261  
262 It depends. A combination product is eligible if the product, including all active ingredients,  
263 meets the criteria established in FDAAA. However, if the product contains any active ingredient  
264 that has been previously approved, the application is not eligible for a priority voucher (see  
265 section 524(a)(4)(C) of the Act).

266  
267 **Q16. Are products eligible that have been approved and used in other countries but have**  
268 **not previously been submitted for review by the FDA?**

269  
270 Yes, as long as they meet all the elements for a tropical disease product application described in  
271 section 524(a)(4).

272  
273 **Q17. Is a drug that is already approved for another indication eligible for a priority**  
274 **review voucher for a tropical disease application?**

275  
276 No. For an application to qualify, it must be for a human drug, no active ingredient (including  
277 any ester or salt of the active ingredient) of which has been approved in any other application  
278 under section 505(b)(1) of the Act or section 351 of the PHS Act.

279  
280 **Q18. Would a new pediatric formulation for a drug already approved for adults be**  
281 **eligible?**

282  
283 No. As noted above, an application for a product containing a previously approved drug is not  
284 eligible to receive a tropical disease priority voucher.

285  
286 **Q19. Would an application for a tropical disease product submitted to FDA prior to**  
287 **enactment of the statute but not yet approved qualify for a voucher?**

288  
289 No. The tropical disease product sponsor may not receive a tropical disease priority voucher if  
290 the application was submitted to the FDA before the date of the enactment of section 524  
291 (September 27, 2007).

292  
293 **Q20. Through what mechanism should a sponsor notify FDA that it intends to submit an**  
294 **application eligible to receive a voucher?**

295  
296 The original submission of the tropical disease application should include the sponsor's request  
297 outlining how they meet the eligibility criteria for a priority review voucher. We encourage early  
298 communication with the review division in which these issues could be discussed; however,  
299 notification before submission of the tropical disease application is not required.

300  
301 **Q21. Could a tropical disease product also qualify as an orphan drug?**

302  
303 It is likely that a drug product meeting the requirements of section 524 will also qualify for  
304 marketing exclusivity, tax credits, fee exemptions, and orphan product grants provided under the  
305 Orphan Drug Act. For information regarding these incentives, potential sponsors should contact  
306 the Office of Orphan Products Development (OOPD). These products may also qualify for new

## *Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

307 chemical entity marketing exclusivity provided under the Act. For information regarding new  
308 chemical entity marketing exclusivity, potential sponsors should contact the appropriate CDER  
309 review division.

310

311 **Q22. What are the different roles played by CDER, CBER, and the Office of Orphan**  
312 **Products Development?**

313

314 CDER and CBER

315

316 The review divisions within the Center for Drug Evaluation and Research and the Center for  
317 Biologics Evaluation and Research have the responsibility for premarket review of the tropical  
318 disease product applications and for determining whether an application meets the eligibility  
319 criteria for receiving a priority review voucher.

320

321 Office of Orphan Products Development

322

323 The Office of Orphan Products Development is located within the Office of the Commissioner  
324 and is responsible for determining whether a drug or biologic qualifies for orphan drug status.  
325 For example, to secure orphan status for the treatment of a rare disease, a sponsor demonstrates  
326 to OOPD that the disease or condition is rare in the United States (i.e., <200,000 persons in the  
327 United States are currently affected) **and** that the drug is expected to be effective (i.e., is  
328 promising) in the treatment of the disease. Orphan-drug designation must be granted prior to the  
329 submission of a marketing application. This is a separate process from the determination of  
330 whether a drug or biologic will qualify as a tropical disease drug or will ultimately be eligible for  
331 a voucher under the provisions of section 524. The latter determination will be made by CDER  
332 or CBER, as appropriate.

333

334 If the product meets the criteria of the Orphan Drug Act, OOPD will provide orphan designation  
335 that qualifies the sponsor of the product for a tax credit and the marketing incentives of the  
336 Orphan Drug Act.<sup>7</sup> Questions concerning orphan drug designations, or the benefits and  
337 requirements associated with such designations, should be directed to OODP  
338 (<http://www.fda.gov/orphan>).

339

340 **Q23. Does FDA plan to add other infectious diseases to the list? If so, when can we expect**  
341 **to see that?**

342

343 Section 524 allows FDA to designate by regulation any other infectious disease for which there  
344 is no significant market in developed nations and that disproportionately affects poor and  
345 marginalized populations. FDA intends to seek public input regarding the criteria that could be  
346 used to designate other diseases as well as specific diseases that might meet those criteria.

347

348 **Q24. What should I do if I have other questions about a tropical disease application?**

349

350 Sponsors with questions not addressed in this guidance should contact the appropriate review  
351 division within the Center for Drug Evaluation and Research (CDER) or Center for Biologics

---

<sup>7</sup> Information on the Orphan Drug Act is available at <http://www.fda.gov/orphan/progovw.htm>.

***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

352 Evaluation and Research (CBER). CDER and CBER encourage early interaction with potential  
353 sponsors so these types of questions can be discussed. Such interactions could begin as early as  
354 the pre-IND phase of drug development.  
355