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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. FDA–2008–D–0530
Draft Guidance for Industry: Tropical Disease Priority Review Vouchers

Merck & Co. Inc. commends the Food and Drug Administration (the Agency or FDA) for its commitment to foster innovation while serving the public health needs of American citizens. We support regulatory oversight of product development that is based on sound scientific principles and good medical judgment.

In the course of development, licensure, and marketing of our drug and vaccine product candidates, Merck has acquired extensive experience that we have utilized to author these comments on the Agency's draft guidance on the priority review voucher program. Congress and the Agency's goals for the voucher program are consistent with our historical and ongoing commitment to develop novel drug and vaccine products as well as, generally, facilitate innovations to meet global health needs.

General Comments

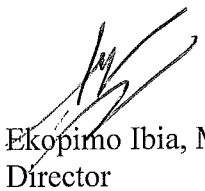
We thank the Agency for the opportunity to comment on the "Draft Guidance for Industry: Tropical Disease Priority Review Vouchers" (October 20, 2008. Docket No. FDA–2008–D–0530). We applaud the Agency's effort to provide guidance and clarity toward the implementation of the priority review vouchers for certain tropical diseases as provided for in section 1102 of the 2007 FDA Amendment Act, which added a new section 524 to the Food, Drug, and Cosmetic Act (FD&CA). We agree that such guidance is essential for effective and consistent implementation of this new incentive to develop therapies for many neglected tropical diseases with significant morbidity and mortality, especially in developing countries. We strongly recommend that FDA uses its discretion to provide sponsors some flexibility during the implementation of the provision in order to avoid any unintended consequences of minimizing the incentive inherent in the statute.

Specific Comments

In the following table (Attachment), we provide specific comments on sections of the Draft Guidance. In the left column of the table, we identify the line number, section, and subsection in the Draft Guidance; the middle column contains the original text of the Draft Guidance, the key comments and rationale to support our position; and the right column carries our suggested changes, where applicable (single strikeout for deleted text and bold/underlined type for added text). See Attachment for more details.

We appreciate the opportunity to share our comments with respect to the Draft Guidance on "Draft Guidance for Industry: Tropical Disease Priority Review Vouchers." For further information or questions, please contact me by phone 202 508 4567 or email ekopimo_ibia@merck.com.

Sincerely,



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Attachment enclosed

Attachment

Docket No. FDA–2008–D–0530; Draft Guidance for Industry: Tropical Disease Priority Review Vouchers

Line #/Section/Subsection	Original Text and Our Comment with Rationale	Proposed Change
70-72/III/B and 209-212/IV/Q10	**Text** At least 1 year in advance, the sponsor planning to use the voucher must notify FDA of intent to use the voucher and the date on which the sponsor intends to submit the application. After the voucher is issued, the sponsor redeeming the voucher must notify FDA of their intent to submit a human drug application with a priority review voucher at least 365 days prior to submission of the human drug application for which a priority review voucher will be used to obtain a priority review. **Comment and Rationale** While we acknowledge the need for sufficient notification period to enable FDA to adequately plan its review resources, we are uncertain about some aspects of the notification. By its very nature, it could be very difficult to be precise about the date of submission of an application. We believe the language of the guidance should be revised to provide the sponsor the ability to submit the application on a date later than already indicated, while keeping FDA reasonably informed. If FDA agrees with our approach, we strongly recommend revising the guidance, as it would be very difficult to determine a precise application submission date a year in advance.	At least 1 year in advance, the sponsor planning to use the voucher must notify FDA of intent to use the voucher and the **likely** date on which the sponsor intends to submit the application. **If a sponsor is unable to submit on the specified date an application for which the sponsor has notified FDA of its intent to use the priority review voucher, the sponsor should notify FDA immediately and should endeavor to keep FDA informed of the status of that application until its eventual submission. The sponsor still will be able to use the priority review voucher for the same application for which it had notified FDA of its intent to use the voucher if the application is submitted within a reasonable period of the original planned submission date.** **Alternatively, the sponsor may re-designate the human drug application for which it will use the voucher pursuant to this section with a new target date. The sponsor should notify FDA at least 365 days prior to submission of an application to which it has re-designated the use of a previously committed voucher.** After the voucher is issued, the sponsor redeeming the voucher must notify FDA of their intent to submit a human drug application with a priority review voucher at least 365 days prior to

		submission of the human drug application for which a priority review voucher will be used to obtain a priority review. **If a sponsor is unable to submit on the specified date an application for which the sponsor has notified FDA of its intent to use the priority review voucher, the sponsor should notify FDA immediately and should endeavor to keep FDA informed of the status of that application until its eventual submission. The sponsor still will be able to use the priority review voucher for the same application for which it had notified FDA of its intent to use the voucher if the application is submitted within a reasonable period of the earlier submission date.** **Alternatively, the sponsor may re-designate the human drug application for which it will use the voucher pursuant to this section with a new target date. The sponsor should notify FDA at least 365 days prior to submission of an application to which it has re-designated the use of a previously committed voucher.**
75-77/III/B and 213-215/IV/Q10	**Text** Payment of this extra fee, to which the sponsor is legally committed as a result of its intent to use the voucher, is not subject to waivers, exemptions, reductions, or refunds. In accordance with the language of the statute, FDA will consider this notification as a legally binding commitment to pay the priority review user fee for the fiscal year in which the application is submitted.	Payment of this extra fee, to which the sponsor is legally committed as a result of its intent to use the voucher, is not subject to waivers, exemptions, reductions, or refunds. In accordance with the language of the statute, FDA will consider this notification as a legally binding commitment to pay the priority review user fee for the fiscal year in which the application is submitted.

	Comment and Rationale As noted above, sponsor's date of application submission is only a best projection and not an exact date. In many, if not most, instances, sponsors cannot discern the nature of their phase III data a year prior to submission. Indeed, in a few instances, planned application submission may be canceled altogether. In the event that the sponsor is unable to submit an application as planned, it is unclear whether the sponsor can transfer internally to another application a priority review voucher for which the sponsor had earlier notified FDA of planned intention to use. We acknowledge that the statute makes notification to use a priority review voucher for an application a legally binding commitment to pay the priority review user fee. However, we also note that the statute states that FDA "may not grant a waiver, exemption, reduction, or refund of any fees due and payable under" section 524. We believe the statute leaves room for FDA discretion in applying this provision of the statute. Even if FDA would not grant waiver, exemption, reduction, or refund of any fees due and payable under section 524, we strongly recommend that the Agency allow sponsor's ability to internally re-designate the priority review voucher for which the sponsor had already committed to use.	**In the event that sponsor is unable to submit an application to which the sponsor had already committed to use the priority review voucher, the sponsor should notify FDA immediately and should endeavor to keep FDA informed of the status of the application until its eventual submission date. During this time, the sponsor may indicate if it intends to designate another human drug application for which it will use the voucher. The sponsor should notify FDA at least 365 days prior to submission of an application to which it has re-designated the use of a previously committed voucher.**
245-248/IV/Q13	**Text** We believe the intent of this section [524(a)(1)] 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.	

	Comment and Rationale We understand FDA's rationale regarding their inability to guarantee a 6-month review timeframe for an application using the priority review voucher. However, we believe the purpose of this special incentive program will be defeated if sponsors were not certain that an application using the voucher could be reviewed within 6-months, especially with at least 365 days notification and payment of additional user fees. Therefore, we urge FDA to make every effort to complete the review within 6 months.	
254-256/IV/Q14	**Text** 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. **Comment and Rationale** We note the scenario given in the draft guidance of what could render ineligible a product that was previously eligible for priority review voucher. In other words, for two developers working on a similar active ingredient (that may not be exactly the same but may have a different ester or salt form), only the first to approval likely would be awarded the priority review voucher, regardless of the stage of development of the other (which could be a few days from approval of the first). While this scenario likely is to be remote, it certainly is possible and creates a significant disincentive that could be mitigated by awarding two vouchers to similar	

	products approved at about the same time.	
303-305/IV/Q21	**Text** It is likely that a drug product meeting the requirements of section 524 will also qualify for marketing exclusivity, tax credits, fee exemptions, and orphan product grants provided under the Orphan Drug Act. **Comment and Rationale** The draft guidance provides some of the incentives to which designated orphan drug products may qualify. However, it is unclear if a waiver or reduction of the priority review user fee will apply in the rare event that the sponsor plans to use the priority review voucher for an application that is also a designated orphan drug product.	