December 19, 2008

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

Re: Docket Number FDA-2008-D-0530

Dear Sir or Madam:

The signatories of this letter, as members Global Health Technologies Coalition (GHTC), appreciate the opportunity to comment on the document, "Guidance for Industry: Tropical Disease Priority Review Vouchers". The GHTC is a consortium of nongovernmental organizations that support policies to accelerate research and development of global health technologies for resource-poor settings. The signatories of this letter are a partial list of GHTC's entire membership.

Without new tools to prevent, treat and diagnose the diseases of the developing world, gains achieved by the overall U.S. investment in combating these diseases could prove short-lived. Diseases change over time and can develop resistance to the drugs that are used to treat them; treatments that work today may not work tomorrow. Accurate diagnostics prevent overtreatment that can lead to drug resistance. New vaccines and microbicides will reduce the number of people needing treatment and, therefore, reduce the incidence of drug resistance.

The priority review voucher statute (Section 1102 of FDAAA) calls for the Food and Drug Administration (FDA) to award a priority review voucher to any sponsor of a newly approved drug or biologic that targets a listed neglected tropical disease. The voucher entitles the bearer to the priority review of a future new drug application. GHTC applauds the steps that FDA has taken to date in implementing the program and would like to offer the following comments on the proposed guidance (FDA-2008-D0530):

1. **Determining eligibility for priority review:** Research and development in drugs and biologics is an expensive and financially risky venture. For the program to work as an incentive to encourage new research and development, sponsors will need some degree of confidence and clarity as to whether or not their neglected tropical disease product qualifies for a priority review voucher.

   While we understand that it is unreasonable to expect FDA to provide early determination of whether a product will qualify for a voucher, one of the key variables in determining whether an application is eligible to earn a voucher is that the application must qualify for priority review. If the determination of whether an application qualifies for priority review is not made until after the application is submitted, the impact of the priority review voucher program will be limited as sponsors are unlikely to be willing to absorb the associated risk. We recommend that the appropriate review divisions work with sponsors to determine as early as possible whether or not the application will be eligible for priority review. Such predeterminations are currently made under FDA's "fast track" designations.

2. **Voucher Transferability:** Priority review vouchers are an important tool to encourage research and development in diseases that have often been neglected by industry because they are not traditionally considered profitable ventures.

   We are particularly pleased that FDA has decided that the option to use a voucher can be transferred multiple times through the use of appropriate contractual vehicles. The easier it is for entities to transfer the voucher, the greater the market value of the voucher will be, in turn creating a more powerful incentive for investing in much-needed advances in the neglected tropical disease space. We are pleased that FDA has allowed for such transfers, as unhindered transferability is the only way for priority review vouchers to achieve their full market value.

3. **Previously Approved Active Ingredients:** Section 524 of the legislation states that "The drug that is the subject of the application must contain no active ingredient (including any ester of salt of the active ingredient) that has been approved in any other application under section 505(b) (1) of the Act or section 351 of the PHS Act." Although this statement has a meaningful interpretation for exclusivity of approved drugs and well characterized therapeutic agents, we believe it may have an unintended negative impact on the development of new vaccines for global diseases.

   A number of new vaccines are improvements upon existing vaccines. A narrow interpretation of what constitutes a "previously approved ingredient" in terms of biologics could pose an unfortunate barrier to much-needed innovation; there are existing vaccines licensed almost a century ago (such as BCG for tuberculosis) which are of very limited efficacy, but which could be used to design new and much more efficacious vaccines for which there may be a significant global need.

   Most vaccines are complex biologicals, especially live or attenuated vaccines for infectious diseases, and in many cases, the "active ingredient," or in this case the antigen(s) that elicit the effective immune response, may not be known (the "correlate of immunity"). For this reason we would propose that there be more flexibility in the interpretation of "active ingredient" for complex biologics such as vaccines. In this context, there is already a precedent for using different definitions for CDER and CBER products when considering products for the FDA's 6 month priority review.

We appreciate your consideration of these comments. If you have any questions, please feel free to contact Rodrigo Daly at +1 202 350 9642.

Respectfully Submitted,

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