

Alliance for Biosecurity

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February 6, 2009

The Honorable Frank M. Torti
Acting Commissioner
Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Tropical Disease Priority Review Vouchers Guidance for Industry [FDA-2008-N-0567]

Dear Acting Commissioner Torti:

On behalf of the Alliance for Biosecurity, we appreciate this opportunity to submit comments regarding the Tropical Disease Priority Review Vouchers Guidance for Industry. The Alliance is a collaboration between the Center for Biosecurity of the University of Pittsburgh Medical Center, pharmaceutical companies, and biotechnology companies working to promote the robust and sustainable research and development infrastructure necessary to prevent and treat the infectious disease threats of the 21st Century. As part of this mission, the Alliance works to advance policies and laws that support the development of medicines and vaccines for diseases that rarely impact Americans or others in the developed world and which therefore lack a viable commercial market – in spite of their public health and global security impacts. The Alliance members listed below endorse these comments.

The Alliance supports the Priority Review Voucher (PRV) program, and views it as an important tool in supporting the development of medicines and vaccines for which there is no commercial market. The PRV program is a high-value, low-cost incentive available for private firms to invest in the development of drugs for infectious diseases that disproportionately impact those living in the developing world. The Alliance is confident that the program is an important step in the right direction.

Priority Review Voucher Disease Eligibility

The PRV program's statutory authority lists 16 diseases which were included in the original authorizing legislation. There are many diseases that disproportionately impact the developing world, and for which there is consequently no serious commercial market. However, the authors of the legislation did not list dozens of diseases. Instead, they authorized the Secretary of Health and Human Services to add any infectious diseases to the program "for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations."

Bavarian-Nordic • Cangene Corporation • Center for Biosecurity of UPMC • DOR BioPharma, Inc. Dynport Vaccine Company LLC, a CSC Company • Elusys Therapeutics • Emergent BioSolutions
Hematech, Inc., a subsidiary of subsidiary of Kyowa Kirin. • Human Genome Sciences, Inc. • NanoViricides, Inc. • PharmAthene • Siga Technologies • Unither Virology

The Alliance is supportive of this authority and the flexibility it offers, and we believe that the Secretary should use it when appropriate. Furthermore, we believe that several additional infectious diseases meet the criteria for inclusion prescribed in the statute, and we contend that including these diseases in the PRV program would serve the public interest, and strengthen the PRV program overall.

Additional Eligible Diseases

As noted above, the authorizing legislation gives the Secretary the authority to add to the list of tropical diseases eligible for the PRV program:

“any other infectious disease for which there is no significant market in the developed nations and that disproportionately affects poor and marginalized populations.”

The Alliance believes that eight additional diseases unambiguously meet this requirement, and that it would advance the goals of the PRV program to include them. They are as follows:

Viral Hemorrhagic Fevers (Filoviruses – Ebola, Marburg; Arenaviruses – Junin)	Plague (<i>Yersinia pestis</i>)
Monkeypox	Melioidosis (<i>Burkholderia pseudomallei</i>)
Typhus (<i>Rickettsia prowazekii</i>)	Anthrax (<i>Bacillus anthracis</i>)
Glanders (<i>Burkholderia mallei</i>)	Tularemia (<i>Francisella tularensis</i>)

Statutory Criteria for Program Eligibility

Each of these diseases meets the three criteria laid out in the authorizing statute. They are infectious diseases, they disproportionately affect poor and marginalized populations, and they have no significant market in developed nations.

The eligibility of the eight diseases for the first of the three criteria is self evident: all eight diseases are infectious in nature.

We believe their eligibility for the second criteria is also self evident. Very few residents of the developed world (and in the case of some of these diseases, no residents of the developed world) suffer from these diseases: nearly all cases of and deaths from these diseases occur in the developing world among poor and marginalized populations. For example, over 95 percent of human cases of filovirus, Junin virus, anthrax, and plague occur in developing countries, while the incidence of these diseases in developed countries is extremely rare. The CDC

characterizes anthrax as existing in most countries in Sub-Saharan Africa and Asia, and estimates that the vast majority of deaths from anthrax occur in the developing world. Melioidosis is endemic to Southeast Asia, and the CDC reports that in some countries, it is so widespread that it is a frequent contaminant in lab-grown cultures. The WHO estimates that in 2003 – the most recent year for which it provides statistics – 98.7 percent of plague cases and 98.9 percent of deaths from plague occurred in Africa. And although the incidence of filoviruses and typhus tend to be episodic rather than consistent and ongoing, they continue to have a disproportionate impact on the developing world. Ebola and Marburg outbreaks in the Angola, Democratic Republic of Congo, Gabon, and Uganda have killed thousands in the relatively short period since the diseases were identified. Clearly, the eight diseases qualify as continuous and ongoing infectious disease burdens on the developing world.

Clearly, the impact of these infectious diseases is disproportionately weighted toward the developing world. We believe, therefore, that the qualification of these eight diseases for the first two criteria is beyond dispute.

Absence of a Significant Market in the Developed World

The Alliance also believes that each of these eight diseases meets the third criteria: that they have no significant market in the developed world. The statute does not include a definition for the term “significant market in the developed world.” However, as a matter of common usage, “market” generally refers to the commercial sector, unless otherwise specified. More importantly, defining “market” as referring to the commercial sector is consistent with the list of diseases already eligible for the PRV program. Currently, drugs for many of these diseases have a non-commercial market consisting of substantial government and not-for-profit programs, and these programs are appropriately not considered to be disqualifying “significant markets” for the purposes of the PRV program. Indeed, we are unaware of any interpretation of the PRV statute concluding that the existence of a non-commercial government or not-for-profit market for drugs and other interventions should disqualify a particular disease. Just as the existence of potential non-commercial buyers does not disqualify diseases already covered under the PRV program, it should not disqualify the eight diseases proposed for inclusion here. In addition, we would argue that even if the non-commercial programs relevant to the eight proposed diseases were considered a “market,” they are not sufficiently active in terms of actual funding outflows to reach the threshold of “significant.”

Consequently, the Alliance maintains that the eight diseases proposed for inclusion meet each of the three criteria for inclusion in the PRV program: they are infectious diseases, they disproportionately impact communities in the developing world, and they have no significant market in the developed world.

Additional Merit

Congress did not mandate that the Secretary must add every disease that meets the statutory qualification to the PRV program. Indeed, simply identifying every infectious disease that disproportionately affects poor and marginalized populations and for which there is no

significant market in the developing world would be a challenging undertaking. Instead, the Secretary was provided with the authority to designate additional diseases through a rulemaking process, so long as they meet the criteria noted above.

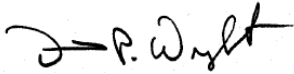
In the United States, some of the eight proposed infectious diseases are often associated with bioterrorism, given the fact that they are unlikely to occur in the developed world, but have the potential to be weaponized. But in the developing world – as discussed above, these diseases continue to be naturally occurring infectious disease threats. The fact that they have in the past been weaponized, or have the potential to be used as weapons, should not disqualify them from inclusion in the PRV program.

That said, we believe that the Secretary should not overlook the biosecurity aspect of the eight proposed diseases. The Alliance understands that security is not in the explicit mission of the PRV program, and therefore that the Secretary has the authority to disregard the corollary security benefits of adding certain diseases to the PRV program. However, we would point out that Congress did not provide any specific guidelines for the Secretary to use in determining what additional factors to consider when selecting diseases to add to the program. The Secretary has broad discretion to select the criteria with which to determine whether eligible diseases should be included. Although biosecurity is not a responsibility of the PRV program, it is an explicit responsibility of the Secretary, as well as a stated priority of the President. In fact, the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response has explicit requirements for new medicines and vaccines to counter the diseases listed above. Therefore, we believe it is appropriate for the Secretary to view favorably the relevance of a particular disease to security when considering whether to include it in the PRV program, so long as that disease meets the statutory eligibility requirements. At the very least, the fact that these diseases are considered to be among those most likely to be weaponized and used against the United States should not prejudice the Secretary against their inclusion in the PRV program.

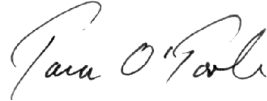
Conclusion

In conclusion, we would like to again express our support for this program and its mission. The Alliance understands and appreciates the obstacles to the development of drugs intended for diseases that rarely impact those living in the developed world, and we are deeply engaged in supporting policies and programs to overcome these obstacles. The PRV program is an excellent example of just such a program, and the Alliance will remain supportive of it whether or not it is expanded to include the eight proposed diseases. But we are convinced that including these eight diseases will strengthen the program, and further its mission of supporting the development of diseases that disproportionately impact the world's poor and marginalized.

Alliance for Biosecurity
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