

June 6, 2006

Dockets Management Branch (HFA-305)

Food and Drug Administration

5630 Fishers Lane

Room 1061

Rockville, MD 20852

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**Re: Draft Guidance for Industry on Clinical Data Needed to Support the
Licensure of Pandemic Vaccines**

Docket ID: [2006D-0088](#)

Dear Dr. Chandler and Dr. Geber:

This letter constitutes Medimmune's written response to the draft guidance entitled, 'Clinical Data Needed to Support the Licensure of Pandemic Vaccines.'

The location of the text that is being discussed is in bold and precedes the corresponding comment.

III.B. Paragraph 1

This section states that "*because of the theoretical concern for reassortment between a live attenuated pandemic influenza vaccine strain with other circulating influenza strains, it is anticipated that a licensed live attenuated influenza vaccine would be labeled for use only after the onset of a pandemic influenza outbreak.*"

It is not clear from the guidance document what regulatory or governmental body would declare the onset of a pandemic and how would the declaration be done. A timely and well-defined starting point of the pandemic is necessary to initiate an effective distribution and administration of stockpiled vaccines.

Guidance on the labeling language would allow and facilitate vaccine distribution prior to a pandemic while ensuring that health care professionals do not use vaccine until a pre-specified time.

Recommendations

- MedImmune recommends that the FDA provide additional information to clarify the timing, the scope, and the definition of the "onset of a pandemic."
- MedImmune recommends that the FDA provide guidance on labeling.

III.B. 1. Immunogenicity and III. B. 2 Safety

These sections discuss the clinical studies *performed in advance of a pandemic influenza outbreak that are* required to support the appropriate dose and regimen of a live attenuated pandemic influenza vaccine. The FDA states that *subjects should be isolated during the study period to minimize the potential for transmission of the influenza vaccine viral strain.* Furthermore, the FDA does not specify what age groups the immunogenicity and safety should be conducted in; however, the FDA indicates that “*Local and systemic reactogenicity events and symptoms of influenza illness should be well defined in all age groups for whom approval of the vaccine is sought.*” MedImmune would like to point out the impracticality and the ethical considerations of conducting the requested studies in pediatric populations in isolation, and the impracticality of conducting studies in adult populations of more than approximately 30 subjects if isolation is required.

Recommendations

- The FDA should provide more details on the study population and isolation requirements, taking into consideration the real world circumstances associated with the studies (e.g., the number and age of subjects that can be studied in an isolation facility).
- MedImmune recommends that initial safety and immunogenicity studies of a pandemic vaccine include assessment of duration and magnitude of vaccine virus shedding and, based on those data, that CBER decide whether future studies of that vaccine may be done without isolation of subjects. This will allow expanded (i.e., larger number of subjects) safety and immunogenicity studies to be performed.
- Alternatively, if isolation is required for all safety and immunogenicity studies of pandemic vaccines, MedImmune recommends that these studies should evaluate only subjects who are 18 years of age or older as are performed for new seasonal vaccine strains and that the label indication for pandemic vaccines would include the entire age recommendation (including the pediatric age range), following the annual process for release of the seasonal vaccine.
- MedImmune seeks a comparable requirement and statement associated with the Trivalent Inactivated Influenza Vaccine (**III.A 1st Paragraph**): *Once a pandemic influenza vaccine against a new influenza subtype has been licensed, further clinical data with a variant of that subtype would likely not be needed for licensure.*

III.C. 5th Paragraph; III.D.1; and III.B.1: Immunological Surrogates of Efficacy

In sections **III.C. 5th paragraph** and **III.D.1**, the FDA acknowledges that there are no identified immune surrogates associated with live attenuated influenza vaccines; however, in section **III.B.1**, the FDA recommends the following endpoints for the live attenuated vaccine: *1) the percent of subjects achieving an HI antibody titer > 1:40, and 2) rates of seroconversion, defined as a four-fold rise in HI antibody titer post-vaccination.*

Recommendations

- MedImmune suggests not specifying immunogenicity endpoints for live attenuated influenza vaccines. Medimmune recommends not restricting the

immunological endpoints to the HI antibody titers and including the following statement that “other assays and endpoints may be more relevant.”

- In the absence of validated immunological correlates for efficacy, MedImmune suggests the inclusion of other assays that would evaluate immune responses associated with vaccine take.

Some proposed assays include IgG or IFN γ (or other cytokines) Enzyme-Linked Immunospot (ELISPOT) assays; microneutralization assays; effector B cell responses; and neuraminidase assays. The characterization of the immune response (vaccine take) may also incorporate assays determining cytokine responses and localized immune responses.

MedImmune thanks the FDA for the opportunity to comment on the draft guidance. If FDA would like further information or to discuss the contents of this letter, please feel free to contact me at (301) 398-4627 or via email at kavanaugh@medimmune.com.

Sincerely,

Nancy Kavanaugh, PhD.
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MedImmune Vaccines