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IDSA
Infectious Diseases Society of America

June 6, 2006

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

Re: Comments on Docket ID Number 2006D-0088 (Guidance for Industry: Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines)

To Whom It May Concern:

The Infectious Diseases Society of America (IDSA) appreciates the opportunity to comment on the Food and Drug Administration's (FDA) Guidance for Industry – Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines (hereinafter called "Draft Guidance"). IDSA represents 8,000 physicians and scientists devoted to patient care, education, research, and community health planning in infectious diseases. Members of the Society include experts in vaccine science, hospital epidemiology, and public health. The threat of pandemic influenza and in particular the ongoing spread of the H5N1 virus is of great concern to the Society. To address our concerns, IDSA's Board of Directors has established the Society's Pandemic Influenza Task Force (PITF) to monitor potential threats, suggest appropriate domestic and international responses, and issue specific recommendations to the Board. The PITF, which played a leading role in developing IDSA's comments below, is comprised of Drs. Kathy Neuzil (chair), Jeffrey Duchin, Kathryn Edwards, David Fedson, Kathleen Gensheimer, Frederick Hayden, Edward Janoff, Andrew Pavia, and Gregory Poland.

IDSA applauds FDA's efforts in developing the Draft Guidance. This document is a critical step forward in the nation's pandemic preparedness efforts. The rapid development, production and distribution of pandemic influenza vaccines will be essential to the ultimate goal of protecting human health during an influenza pandemic. We strongly support several aspects of the Draft Guidance that seek to streamline the licensure process for pandemic influenza vaccines, thereby accelerating the availability of vaccine for the public good.

Specifically, IDSA supports the following concepts outlined in the Draft Guidance:

- licensure of pandemic influenza vaccines may be sought either as a supplement to an existing BLA or as a new BLA using the accelerated approval regulations;
- evaluation of the immune response elicited following receipt of the vaccine may serve as a surrogate endpoint that is likely to predict clinical benefit;
- guidance on clinical data to support the accelerated approval of a pandemic vaccine may apply to several types of vaccine, including cell culture derived vaccines; and
- approval of existing vaccines for new routes of administration will be considered as a clinical supplement to a BLA.

IDSA also has several concerns about the Draft Guidance, which are addressed below.

1) IDSA strongly believes that pandemic vaccines should be evaluated differently than seasonal influenza vaccines. As such, we recommend flexibility in interpreting meaningful differences between alternative products. The emphasis in the Draft Guidance is on individual antibody titers. This emphasis must be tempered by the primacy of the need to define the most antigen sparing vaccine formulation that will be acceptably immunogenic for a population, not one that is optimally immunogenic for an individual. In this way, the greatest number of people can be protected. Protection against infection is one standard for a vaccine, however a diminution in the morbidity and mortality of disease may be sufficient for pandemic vaccines. For example, the percent of subjects achieving a protective antibody titer or a 4-fold rise in titer may be more important than the absolute GMT. Likewise, an adjuvanted vaccine with lower antigen content may be less immunogenic than an unadjuvanted vaccine with higher antigen content, but would be the better choice for protecting a population.

2) Live attenuated influenza vaccines are attractive alternatives for quickly vaccinating large populations due to the ease of preparing vaccine virus seed strains by reverse genetics, and administering the vaccine intranasally. We share FDA's concern that serological responses following administration of the live influenza vaccine are poor correlates of protection. Mucosal immunity may be a better correlate of protection. As such, it is essential that FDA participate in the development of assays to measure mucosal immunity so that more specific guidance can be provided to manufacturers of live vaccines.

3) Peptide-based vaccines should be similarly addressed in the Draft Guidance. Lack of consensus on immune correlates for these alternative vaccine candidates will delay their availability to the public.

Again, IDSA appreciates the opportunity to provide comments on this important document. We trust the FDA will strongly consider our recommendations. Should FDA representatives have questions about IDSA's comments, please contact Julie Hantman, MPH, Program Officer for Public Health and Science, at 703-299-0200.

Sincerely,

Martin J. Blaser, MD
President