



July 3, 2008

RADM W. Craig Vanderwagen, MD  
Assistant Secretary for Preparedness and Response  
U.S. Department of Health and Human Services  
VIA EMAIL: [Panflucomments2@hhs.gov](mailto:Panflucomments2@hhs.gov)

RE: Proposed Guidance on Antiviral Drug Use during an Influenza Pandemic

Dear Dr. Vanderwagen:

The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) support the continued need for strong federal leadership as the nation builds the capacity necessary to respond to an influenza pandemic. We are pleased to comment on the federal government's June 2008 revision of its two draft antiviral guidance documents, the "Proposed Guidance on Antiviral Drug Use during an Influenza Pandemic" ("the Use Guidance"), and the "Proposed Considerations for Antiviral Drug Stockpiling by Employers in Preparation for an Influenza Pandemic" ("the Employer Guidance").

These comments largely build upon IDSA's December 14, 2007 letter (enclosed) regarding the prior October 2007 iterations of the guidance documents. IDSA and SHEA support efforts to develop strategies for antiviral treatment and prophylaxis of the United States population. IDSA, now joined by SHEA, continues to urge greater federal funding for antiviral purchase particularly in light of the new recommendation for workplace prophylaxis.

## **EMPLOYER GUIDANCE and USE GUIDANCE**

### Federal Support for Antiviral Prophylaxis

IDSA and SHEA recognize the importance of assuring prophylaxis in certain workplace settings including healthcare facilities and the critical infrastructure sector. We agree that antivirals should be provided in order to ensure worker perception of safety and thereby preserve high levels of workplace attendance during a pandemic. We note that the Employer Guidance newly recommends that employers that provide frontline healthcare and emergency services purchase and provide antivirals for employees at high and very high risk of exposure. The guidance also recommends that critical infrastructure employers "strongly consider" providing antivirals to critical workers and it suggests

other employers may consider antiviral prophylaxis in an effort to maintain business continuity.

After assessing these recommendations, several concerns expressed in IDSA's December letter persist. An ample national stockpile will allow a more flexible, equitable and appropriate use of antivirals during a pandemic than will employer purchase. Many businesses and healthcare facilities cannot afford such purchases. Further, many businesses outside the healthcare sector lack not only the medical infrastructure for appropriate prescription and dispensing of antivirals but also the capacity to handle the many legal, logistical and other implications noted by the Employer Guidance.

Therefore, we strongly recommend that federal authorities expand the antiviral Strategic National Stockpile to allow adequate supplies for prophylaxis of the indicated groups.

Federal purchase is the most rational approach and one which will ensure equity across workplaces. Federal authorities also should clarify the definition of 'critical worker' to help ensure adequate protection and equitable access to prophylaxis within workplaces. Federal oversight also may be needed to coordinate and ensure access across federal and private sources. Finally, in its pandemic planning the business community should include considerations for working with state and local authorities in order to accomplish the goal of providing antiviral prophylaxis from the national stockpile to appropriate workers.

## **USE GUIDANCE**

### Withholding of Recommendation on Post-Exposure Prophylaxis (PEP)

We endorse the decision to withhold a general recommendation for post-exposure prophylaxis (PEP) for household contacts. We agree there is a need to assess feasibility, purchase and stockpiling considerations before such a recommendation is made.

### Periodic Reassessment of the Guidance

IDSA and SHEA applaud the Use Guidance's language, new to this version, of the need for "periodic reassessment of national antiviral drug guidance...based on scientific and technological advances." IDSA's December 2007 letter had recommended this type of review and furthermore urged that work be done to identify an appropriate independent panel or existing advisory committees to undertake such review. A workgroup of the National Biodefense Science Board (NBSB) is discussing this issue as well, with an emphasis on identifying a mechanism for timely scientific and independent review of evolving data. We urge HHS to quickly implement the NBSB's recommendations.

### Guidance Assumptions

IDSA and SHEA are concerned about several critical assumptions in the Use Guidance. The document assumes that the pandemic will be severe, that the supply of effective antiviral agents will be extensive and continuous, and that in the absence of antiviral PEP, community mitigation measures will reduce the pandemic attack rate by one-half. On the

latter point, we caution that a substantially lower assumption of 20-25% may be more reasonable. We recommend that HHS provide the basis for its assumptions.

Further, we recommend that HHS address, in this or future guidance documents, the following considerations and their respective impact on the Guidance:

- A moderate pandemic scenario (as was addressed in the vaccine use guidance)
- The possibility of a higher mortality rate among young adults (as in the 1918 pandemic)
- Varying degrees of antiviral drug availability
- Vaccine availability
- Varying dosages or durations of antiviral treatment
- The potential for antiviral resistance and the need for stockpile diversification
- Data from studies to determine pediatric dosing

We appreciate the invitation to comment on these proposed federal antiviral strategy guidance documents for pandemic influenza. Should you have any questions, please feel free to contact Julie Hantman, MPH, IDSA's Senior Program Officer for Public Health, at [jhantman@idsociety.org](mailto:jhantman@idsociety.org) or (703) 299-0015; or Nancy Olins, SHEA's Policy and Strategic Initiatives Manager, at [nolins@shea-online.org](mailto:nolins@shea-online.org) or (703) 684-0761.

Sincerely,



Anne Gershon, MD, FIDSA  
IDSA President-Elect



Patrick J. Brennan, MD  
SHEA President

Attached: IDSA Letter to Dr. Benjamin Schwartz, Department of Health and Human Services, December 14, 2007



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December 14, 2007

Benjamin Schwartz, MD  
Senior Science Advisor  
National Vaccine Program Office  
U.S. Department of Health and Human Services

Dear Dr. Schwartz:

The Infectious Diseases Society of America (IDSAs) supports the continued need for strong federal leadership as the nation builds the capacity necessary to respond to a severe influenza pandemic. We are pleased to comment on the federal government's draft antiviral guidance documents, which include the "Overview of Proposed Federal Guidance on Antiviral Drug Strategies and Stockpiling," the "Proposed Guidance on Antiviral Drug Use Strategies during an Influenza Pandemic," and the "Proposed Considerations for Antiviral Drug Stockpiling by Employers in Preparation for an Influenza Pandemic."

IDSAs applauds the intense federal interest and commitment in determining appropriate strategies for antiviral treatment and prophylaxis of the United States population in the event of a pandemic. However, the time frame provided for public comment has made it difficult for us to undertake a thorough examination of the implications of the guidances. We believe these complicated issues require careful discussion before priorities can be established. Nonetheless, we offer the following comments on the draft antiviral guidance documents and on their implementation.

## THE ANTIVIRAL STRATEGY GUIDANCE DOCUMENTS

### Guidance Assumptions

IDSAs recognizes that the strategies outlined in the federal antiviral guidance must remain dynamic, allowing room for change as new information becomes available. Guidance must be evidence-based and reflect ethical principles and the latest science.

Planning frameworks must be based on a range of reasonable assumptions. The antiviral guidance is based on the assumptions that community mitigation measures, absent antiviral post-exposure prophylaxis, will reduce the attack rate in a pandemic by one-half; the pandemic will be severe; that the supply of antiviral agents will be extensive; and treatment and prophylaxis recommendations will not change in a way that would make fewer courses of antiviral drug available.

IDSAs is concerned about the uncertainties underlying each of these assumptions. Most notably, the guidance reflects a new critical assumption that community

mitigation strategies will reduce the attack rate in a pandemic by one-half, reducing the illness attack rate to 15 percent of the population with commensurate reductions in pandemic mortality. The basis for this core assumption should be clarified and clearly referenced in the antiviral guidance. The implications of this assumption on the estimate on antiviral drug strategy should be discussed.

In addition, the antiviral guidance document assumes a severe pandemic and an abundant supply of antivirals. It does not address strategies in the event of development of viral resistance to stockpiled drugs, the implications of higher or lower pandemic attack and case-fatality rates, or the potential, as suggested by some investigators, that the dose and/or duration of therapy might need to be higher than currently assumed.

Therefore, we recommend that consideration be given to the following:

- Develop antiviral drug guidelines for a moderate pandemic scenario (analogous to the pandemic vaccine use guidance) and account for varying degrees of antiviral drug availability;
- Assess the possible dramatic impact on strategy should the dose or duration of antiviral drugs be greater than currently assumed;
- Anticipate how much antiviral drug will be stockpiled for pandemic use and indicate how the growing size of the stockpile will affect priorities;
- Incorporate results of additional studies determining pediatric dosing and strategy for children; and
- Discuss the impact of vaccine availability on antiviral drug use guidance.

Similar to the pandemic vaccine guidance, federal antiviral guidance should be based on estimates across a range of assumptions. IDSA recommends adding an appendix to the guidance, outlining a set of assumptions that provides the foundation for the antiviral guidance.

#### Additional Surveillance and Data Review Mechanism

To maintain credibility, trust and responsiveness, a transparent mechanism should be in place to allow for prompt review of scientific data on the efficacy and effectiveness of antiviral treatment, antiviral resistance data, adverse effects, and optimal dosing and prophylactic use. This would allow timely modifications to the recommendations. IDSA suggests an independent panel, comprised of government and non-governmental experts, to function in this capacity.

#### The Use of Antiviral Prophylaxis

Given the current level of knowledge, IDSA recommends that the national guidance assure a sufficient supply of antivirals for the extended prophylaxis of health care workers and essential emergency personnel for the duration of a pandemic. We recognize that it will be important to have a consistent and uniform approach for prophylaxis of health care workers nationwide. Therefore, we recommend developing detailed federal guidance on the prophylactic use of antivirals for the health care sector and essential emergency personnel. The document should

discuss risks and potential benefits — antiviral safety, how they should be administered, and how their use should be monitored for efficacy and safety. It should include a prioritization scheme for when drug supplies are limited. We think that it is highly unlikely that there will

be adequate supplies to achieve all of the goals of prophylaxis. The document should provide a much more explicit rationale and strategy for prioritization.

If the decision is made to use post-exposure prophylaxis in conjunction with the voluntary quarantine of cases, the evidence supporting its use for household contacts should be examined more closely. In addition, practical aspects of beginning post-exposure prophylaxis of household contacts within 24 hours of exposure to the index case must be addressed, including accurate diagnosis of the index case, identifying who should determine the need for prophylaxis and ensuring prompt drug delivery when the health care system may be overwhelmed.

### **IMPLEMENTING THE ANTIVIRAL STRATEGIES GUIDANCE**

In the original planning document, HHS envisaged an antiviral stockpile large enough to treat 25 percent of the U.S. population. However, procurement has been slow; the federal portion is 72 percent complete, whereas state purchases are only 36 percent complete. Funding to complete both stockpiles, particularly the state portion, is uncertain. States vary in their willingness to purchase their antiviral allotments, and many states do not have sufficient resources. There appears to be little enthusiasm among state public health officials and legislatures to purchase additional supplies of antivirals beyond current targets.

#### Shared Responsibility

IDSA agrees in principle with the concept of shared responsibility among federal, state, local, and private parties, but in practice this approach to an antiviral strategy is not realistic and will lead to fragmented, unequal, and ultimately unsuccessful implementation. We strongly recommend that the federal government ensure equity of the antiviral supply throughout the United States so that all individuals have equal access to antiviral drugs regardless of the state or locality in which they live.

Inequalities in access to antiviral stockpiles exist, and will be greatly exacerbated during expansion, unless specific attention is paid to equity. We cannot build an equitable strategy for antiviral treatment and prophylaxis on a foundation that is already unequal. Therefore, IDSA suggests that the federal government first focus on creating consistency among state antiviral stockpiles for treatment and secondly, focus on establishing stockpiles intended for the prophylaxis of the health care sector and essential emergency personnel.

The states and municipalities have the enormous responsibility to distribute and track antiviral drugs. However, they have varying ability to purchase additional stockpiles. We feel that the responsibility of the Federal Government is to assure that all Americans will have equal access to antivirals based on the priority schemes. It is not acceptable that one's access depends on the state in which one lives or the institution for whom one works.

#### Health Care Institution Stockpiles

As stated earlier, IDSA strongly supports extended antiviral prophylaxis for health care workers for the duration of a pandemic. Because of logistical issues and concerns about eminent domain, many health care institutions have already chosen not to stockpile antiviral agents

out of fear of incurring expenses without clear benefit. In addition, many institutions that wish to purchase antivirals do not have the funds to do so.

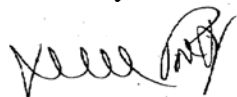
The federal government should provide resources to either purchase or subsidize antiviral agents for health care institutions. IDSA suggests that the federal government work with the appropriate health care system stakeholders to define optimal stockpiling strategies and mechanisms, including where and how the antivirals will be stored, shelf life extension, how storage will be paid for, and how the antivirals will be delivered when they are needed.

#### Operations Research

Although the commissioning of the Institute of Medicine report clearly recognizes the importance of pre-positioning, distribution, and dispensing, there is a real need for additional research in these areas that will contribute to a detailed plan for implementing the antiviral recommendations, including specifics on the logistics of storage, distribution, administration, monitoring effectiveness, and ongoing evaluation of all aspects of antiviral use during a pandemic.

Again, we appreciate the invitation to comment on the federal antiviral strategies guidance for pandemic influenza. Should you have any questions, please feel free to contact Beth Rada, MS, IDSA's program officer for science and research at [brada@idsociety.org](mailto:brada@idsociety.org) or (703) 299-1216.

Sincerely,



Donald Poretz, MD  
IDSA President

cc: Carter Mecher, MD, Director for Medical Preparedness Policy, White House Homeland Security Council  
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