In this issue of the *Journal of Infectious Diseases*, Sakabe et al report that the polymerase acidic (PA) protein component of the H5N1 influenza RNA-dependent RNA polymerase affects cytokine production in human macrophages and may be important in determining pathogenicity in mice [1]. They imply that PA may be relevant to the increased mortality mediated by hypercytokinemia in H5N1 infection in humans. The experiments demonstrating these results were conducted by generating reassortant viruses among H5N1 isolates with different cytokine induction profiles.

The reviewers and editors have considered whether the studies conducted by Sakabe et al represent examples of Dual Use Research of Concern (DURC), as discussed in the United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern [2], and if so, whether the benefits of publishing the work outweigh the risks and how best to mitigate these risks. The editors contacted the National Institutes of Health Office of Biotechnology Activities (OBA) and consulted other experts in both influenza research and biosecurity before deciding to publish the article.

Although the experiments suggest that changes in the PA protein may enhance the harmful effects of H5N1 influenza viruses, the studies do not demonstrate definitively that specific changes cause increased virulence in mice or humans. Moreover, high-level cytokine-inducing H5N1 viruses containing the PA residues identified as being important in these studies are widely found circulating in nature. In addition, this report may provide information helpful to both public health authorities and influenza research investigators (see the accompanying editorial by Donis and Cox in this issue [3]). Identifying naturally circulating viruses with high cytokine-inducing potential may help to predict outbreaks with high morbidity and mortality, and demonstrating the parts of the virus that lead to increased virulence may lead to more effective approaches to both antiviral therapy and preventive vaccines.

Decisions regarding which studies and manuscripts qualify as DURC are complex, and policies regarding how to deal with these issues continue to evolve. The *Journal of Infectious Diseases* will continue to examine each article that might have DURC issues on an individual basis. We have recently added a “check box” for reviewers to help us identify which manuscripts might fall into this category, and we will continue to monitor this evolving field.

**Note**

*Potential conflicts of interest.* Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

**References**

