

## Experts Differ on HHS Select-Agent Proposal for H5N1

Robert Roos, CIDRAP, 26 December 2012; [www.cidrap.umn.edu](http://www.cidrap.umn.edu)

Some professional groups and scientists think it's a good idea to classify highly pathogenic avian (HPAI) H5N1 influenza viruses as "select agents" requiring special research precautions, while others say the step is unnecessary and would impede research, according to comments they have filed with the US Department of Health and Human Services (HHS).

For example, the Infectious Diseases Society of America (IDSA), a physician organization, says H5N1 viruses should be in the select agent category, whereas the American Society for Microbiology (ASM) argues against the idea, noting that circulating H5N1 viruses have poor transmissibility in humans.

Several vaccine manufacturers recommend that the attenuated H5N1 strains used to make vaccines should not be included in any select agent designation, because that could slow vaccine development if an H5N1 strain gained greater human transmissibility.

Aside from the select agent question, the IDSA and some scientists suggest that H5N1 vaccination should be required for lab workers who handle H5N1 strains that can spread among mammals.

In mid-October HHS asked the public to comment on whether H5N1 should be designated an HHS special agent, which means that labs handling it would have to register with the agency and meet special requirements for physical security and personnel screening and training.

The department also asked for comments on whether special safety and containment measures are needed for research involving H5N1 strains with increased transmissibility in mammals. The request followed the publication earlier this year of two controversial studies describing genetically modified H5 strains that were capable of aerosol transmission in ferrets.

Officials originally had set a Dec 17 deadline for commenting, but last week they extended the deadline to Jan 31, 2013.

Because of the threat they pose to poultry, HPAI H5N1 viruses are already listed as select agents in the US Department of Agriculture's (USDA's) Select Agent Program. But the viruses are not on HHS's select agent list.

HHS's request for comments followed a determination by a federal interagency committee that H5N1 viruses may pose a severe threat to human health and safety. The finding came from the Centers for Disease Control and Prevention's (CDC's) Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC), which includes members from various HHS and USDA agencies and the departments of Homeland Security and Defense.

The committee considered the findings concerning the transmissibility of genetically modified H5N1 viruses among ferrets, along with the virus's virulence and the low level of immunity in the population.

The comments submitted have been posted on an HHS Web site.

#### IDSA favors designation

In comments dated Dec 14, the IDSA said circulating H5N1 strains don't pose a severe threat to public health because they don't readily spread among humans, but H5N1 strains with increased mammalian transmissibility do pose such a threat, making select agent designation appropriate.

"It is crucial that extensive biosafety and biosecurity measures be taken to prevent accidental release or an act of bioterrorism," IDSA President David A. Relman, MD, wrote in the comments. Noting that the USDA already regulates H5N1 as a select agent, he said an HHS designation would ensure that the impact on human health is considered.

Relman also recommended that HHS consider "more extensive" biosafety and biosecurity requirements for work with H5N1 strains that have been lab-modified to increase their pathogenicity or transmissibility. Research on such strains is currently done in enhanced biosafety level 3 (BSL-3) conditions, according to previous reports.

In particular, Relman suggested that researchers who work with H5N1 strains that have increased transmissibility should receive an H5N1 vaccine when available.

#### Opposing views

In contrast to the IDSA, the ASM voiced opposition to regulating H5N1 as an HHS select agent. "Due to the extremely limited number of human illnesses seen despite widespread circulation of the virus and very poor transmissibility, it is hard to argue that currently circulating viruses represent a severe threat to public health and safety," the group wrote.

Because H5N1 is on the USDA's select agent list, "HPAI H5N1 already falls under the safety, security, and handling provisions of the select agent rule," the ASM said. "Adding HPAI H5n1 viruses to the HHS select agent list will not add any additional protections or oversight."

The group also said it "strongly disagrees" with the idea of making HPAI H5N1 a "Tier 1" select agent—a new HHS category that requires additional physical and personnel security precautions beyond those required for other select agents.

"Such a designation would inhibit important research activities related to these viruses," the ASM said.

An official with the Center for Biosecurity at the University of Pittsburgh Medical Center agreed that a Tier 1 designation could hinder important H5N1 research, especially work involving international collaboration. But Gigi Gronvall, PhD, a senior associate at the center, said it is a "logical step" to list HPAI H5N1 as an HHS select agent, since it's already on the USDA select agent list.

But Robert Webster, PhD, an eminent virologist and avian flu researcher at St. Jude Children's Research Hospital in Memphis, wrote that putting H5N1 on the HHS select agent list "will further impede field surveillance in endemic regions of the world where the potential risks exist and prevent introduction of early containment." He added that a Tier 1 designation for circulating H5N1 viruses would make matters even worse.

On the other hand, Webster allowed that it might make sense to use the Tier 1 classification on lab-modified H5N1 strains that can spread between mammals via respiratory droplets.

In addition, he strongly supported the idea of giving an H5N1 vaccine to lab workers who handle H5N1 vaccines with increased transmissibility, saying it should be "absolutely mandatory." He also called for increased respiratory protection.

A vaccine maker's view

A Sanofi Pasteur official urged that lab-attenuated H5N1 strains used to make vaccines should be exempt from any HHS select agent designation. He did not comment on whether HPAI H5N1 strains should be treated as select agents.

"We believe that LPAI [low-pathogenicity] strains should be exempt from CDC select agent status for reasons similar to those that are already used to exempt them from USDA select agent status," said Philip H. Hosbach, the company vice president for immunization policy.

If attenuated strains were classified as select agents, the additional regulatory burdens would delay vaccine development if a pandemic H5N1 strain emerged, Hosbach wrote.

Similar views were expressed by two other vaccine makers, MedImmune and Novartis Vaccines and Diagnostics.