



## TRANSCRIPT

### Avian Influenza Symposium

**Moderator: Nina Marano**

**November 3, 2004**

**Coordinator** Hello, and welcome to today's Centers for Disease Control and Prevention Symposium on Avian Influenza conference call. All lines will be in a listen-only mode during today's presentation. We will have a question and answer session, and instructions will be given to you at that time. I would now like to turn the conference over to your host for today, Ms. Nina Marano. Ma'am, you may begin.

**Dr. Marano** Thank you. Good afternoon. Welcome to our Webcast Symposium on Avian Influenza. Prevention of avian influenza is of paramount importance to both public health and animal health sectors. Partnership between the two sectors is a critical success factor for mitigating risk and communicating prevention strategies, particularly with respect to public health impact, on farm biosecurity, worker health protection and food safety. Today, Centers for Disease Control and Prevention has arranged for four scientists to address these issues, particularly for state health department and poultry industry representatives. I would like to introduce our first speaker today. His name is Dr. Tim Uyeki. He is a medical epidemiologist and pediatrician in the Influenza Branch at CDC. He works on the epidemiology, prevention and control of influenza in the U.S. and worldwide and has extensive field experience investigating influenza outbreaks in the U.S. and internationally. He has participated in a number of emergency infectious disease investigations in other countries including Ebola, SARS and avian influenza, and has worked in Vietnam for six weeks earlier this year as a member of the World Health Organization Team investigating human infections with Avian Influenza A H5N1 virus. Please welcome Dr. Uyeki, who will discuss public health impact of avian influenza.

**Dr. Uyeki** Thanks very much, and thanks for everyone for tuning in and organizing this conference. I'd like to start with a brief outline of my talk. I'll try to start with background about influenza in humans, go over the impact of influenza, talk about Influenza A virus, talk about

pandemics that have occurred in the 20<sup>th</sup> Century; talk briefly about Avian Influenza A viruses, then talk about human infections with Avian Influenza A viruses since 1997 and talk about the recent epizootic of H5N1 in Asia and related human infections.

So in terms of background on human influenza, influenza is an acute febrile respiratory illness. It is caused by infection with influenza viruses that primarily infect the upper respiratory tract of humans. It can also infect the lower respiratory tract. The signs and symptoms of influenza in humans differ by age and underlying medical conditions. In terms of the viruses, there are two major surface glycoproteins, the Hemagglutinin and the Neuraminidase. Type A and B viruses cause substantial illness and death in humans worldwide.

In terms of the two major surface proteins, the Hemagglutinin, or what we call the HA, is the site of attachment of influenza viruses to host cells. In terms of immunity that humans acquire either through vaccine or through wild type infection, the antibody that's produced against Hemagglutinin is the major form of protection that we have. In terms of the Neuraminidase, this protein helps to release influenza virions from infected cells. Antibody against the Neuraminidase can help modify disease severity, but is not completely protective.

In terms of the worldwide impact of influenza, clearly in the northern and the southern hemisphere, in temperate regions of the world, there are seasonal influenza epidemics. So during our summer in the U.S., it is winter in the southern hemisphere, and there are seasonal epidemics of influenza in countries such as, for example, Australia, Brazil, and Argentina.

In tropical climates, such as Equatorial Africa, countries in Southeast Asia, influenza viruses circulate at a low level year round. There may be a slight increase during the rainy season when the temperature is also cooler.. Each year in the United States, there is an average of more than 200,000 influenza-related hospitalizations, and an average of more than 36,000 influenza-related deaths. The majority of these deaths and hospitals occur among elderly people as well as those with chronic underlying medical conditions. During the 20<sup>th</sup> Century, we experienced three global influenza pandemics.

Some background about Influenza A viruses. Influenza A viruses can be subtyped on the basis of the Hemagglutinin and Neuraminidase

surface glycoproteins. Examples of some currently circulating human Influenza A virus subtypes in human populations worldwide are H1N1 and H1N2, as well as H3N2 viruses. Influenza A viruses cause both seasonal epidemics as well as global pandemics, and they can infect multiple species, besides humans, clearly birds, wild birds and domestic poultry, but other mammals such as pigs, horses, dogs as well as marine mammals. We're learning more and more about the extended host species range of influenza viruses.

In terms of the natural reservoir for potential new human Influenza A virus subtypes, as I said before, there are only two Hemagglutinin subtypes circulating in humans - those are H1 viruses and H3 viruses - whereas in wild waterfowl - wild geese, wild ducks - all 15 of the known Hemagglutinin subtypes, as well as all nine of the known Neuraminidase subtypes have been identified in wild aquatic birds.

I want to talk about two concepts that apply to human infection with Influenza A viruses. One is the concept of antigenic "drift." The next one is antigenic "shift." In terms of antigenic "drift," this refers to point mutations in the Hemagglutinin gene that result in minor antigenic changes to the Hemagglutinin protein. This is a continuous process. These viruses are dynamic. They're continuing to evolve, and therefore, it's possible that immunity against one strain of virus that may be circulating one year may not be protective against a new strain of a slightly antigenically drifted variant of that virus the following year or in the future. That is the basis for the annual update that must be done for vaccine strain selection for the influenza virus vaccine. Worldwide, this is done biannually. There's a Northern Hemisphere of vaccine selection process, as well as a Southern Hemisphere vaccine strain selection process.

In the U.S., this requires approximately six to eight months to produce approximately 90 to 100 million doses that are used in the U.S. Although this year, that is reduced because of the vaccine shortage. Annual influenza vaccination in the U.S. is targeted at persons at high risk of complications from influenza. Generally, inactivated vaccine is recommended for high-risk persons and healthy persons can receive live attenuated influenza virus vaccine. The take home point is that antigenic "drift," referring to minor antigenic continuous changes to the Hemagglutinin protein is what causes seasonal epidemics of influenza.

Now, I'm going to talk about a different concept, which is antigenic "shift," which refers to a major change. It's the emergence of a novel human Influenza A virus subtype and is generally thought to occur through a process of genetic reassortment between human and animal viruses or through direct animal to human transmission. It refers to the emergence of a new Hemagglutinin subtype but can also include both a new Hemagglutinin and a new Neuraminidase.

The idea is that because human beings have not had much previous exposure to a new Hemagglutinin subtype virus, most humans would not be expected to have previous immunity. A pandemic could occur if there is efficient and sustained transmission of the novel strain from person to person. It has to be sustained transmission, not dead end.

If there is a pandemic, and we believe there will be and there clearly were three during the 20<sup>th</sup> Century, there will be widespread morbidity and mortality worldwide. Pandemics in the 20<sup>th</sup> Century caused a high proportion of deaths among young adults, in contrast to seasonal epidemics where elderly and chronically ill people are more affected. This slide is sort of a diagram of what one process that we believed happened and another is a theoretical process.

So in the above scheme where basically there was genetic reassortment between a goose virus, a quail and teal virus, and this virus was transmitted to chickens in Hong Kong, which caused widespread outbreaks, and this was an H5N1 virus. There were human infections through avian to human transmission. There was no evidence for sustained human-to-human transmission of this reassortment virus and therefore, there was no pandemic.

Theoretically, another way that a pandemic virus could arise is through co-infection of a pig. Pigs can be infected with swine Influenza A viruses, with Avian Influenza A viruses and Human Influenza A viruses. There could be some reassortment in the pig through co-infection and if there was resultant pig to human transmission and then sustained human-to-human transmission of a novel virus, that could result in a pandemic.

The estimated impact of influenza pandemics that occurred during the 20<sup>th</sup> Century, during the 1918-1919 so called Spanish Flu was the emergence of Influenza A H1N1. There were an estimated 20 to 50

million deaths worldwide and more than half a million deaths estimated in the U.S.

During the 1957-1958 emergence of the Asian Flu, H2N2, there were an estimated 70,000 U.S. deaths, and during the 1968-1969 emergence of Hong Kong Flu, H3N2, there were an estimated 34,000 deaths in the U.S. These H3N2 viruses continue to circulate worldwide.

A modeling study to estimate the potential impact in the United States of a future pandemic estimated between 89,000 and 207,000 deaths, up to 734,000 hospitalizations and many tens of millions of outpatient visits with an economic impact of roughly between \$70 million and \$160 billion. That was based upon an attack rate of the population affected of between 15% and 35%.

Now, I'll give some background about Influenza A viruses, and there are clearly people on this call that have much more expertise than I do about avian Influenza A viruses, and they can add in anything. Basically, Avian Influenza A viruses infects both the respiratory and the gastrointestinal tract of birds. So that's different than humans. In humans influenza viruses just infect the respiratory tract. Avian Influenza virus infections usually do not cause any signs of illness in wild waterfowl. Genetic reassortment definitely can occur. It can occur frequently, and then when these viruses infect domestic poultry, there can be substantial morbidity and mortality depending upon the kind of virus.

These viruses are excreted in the respiratory tract and in the gastrointestinal track. So they're present in feces. They can survive, depending on the conditions, particularly low temperatures and low humidity conditions for days up to weeks. We know that in these H5N1 outbreaks among poultry in Asia have been going on not just in cooler climates, but also during very hot and humid climates. So the viruses may have adapted to those conditions.

Avian Influenza A viruses can survive in water and they can survive on surfaces depending upon the conditions. So disinfection of an environment is definitely important in terms of public health.

Avian Influenza A viruses can be divided into low pathogenic as well as high pathogenic viruses. Low pathogenic viruses may not cause any illness in wild birds. They may be associated with mild illness in

poultry. However, they can evolve into highly pathogenic viruses, and they are associated with poultry outbreaks worldwide, including the U.S.

Highly pathogenic viruses may not cause illness in wild birds. They could, however, cause high mortality in domestic poultry. Subtypes of high path viruses that have been identified are H5 and H7, although it should be made clear that not all viruses of subtype H5 or H7 are high pathogenic viruses. There are specific molecular and pathogenicity criteria for determining what constitutes a high path virus. Briefly, I'll just mention that the H5 or H7 viruses that have been identified to be high path are those that have a multi-basic amino acid sequence at what we call the Hemagglutinin cleavage site. So that's really molecular criteria. Then there are pathogenicity criteria that I won't go into details, but basically through inoculation of poultry, there are criteria that USDA as well as OIE has in terms of what would constitute a highly pathogenic virus.

Now, I'd like to discuss human infections with highly pathogenic avian influenza viruses as well as low path viruses. Confirmed outbreaks of human infections with high path avian influenza viruses have been associated with poultry outbreaks. Probably most people are familiar with the outbreak of H5N1 among poultry in Hong Kong during 1997. The poultry infected were at live poultry markets. There were 18 human cases that were identified and six deaths during that outbreak. The primary risk factor on the basis of a case control study was visiting a live poultry market or stall within the week prior to illness onset.

Now last year, in February 2003, there were two cases of confirmed H5N1 infection in Hong Kong residents that had traveled to southern China and returned to Hong Kong. Two were confirmed; one died. I'll talk a little bit later about the ongoing epizootic of H5N1 with human cases in Vietnam and Thailand.

Last year in the Netherlands, there was a very large outbreak of highly pathogenic H7N7 among poultry. There were more than 30 million to 35 million poultry that were culled during that outbreak, and there were a number of human infections that were documented. The majority of these humans who had confirmation of H7N7 infection had mild illness, primarily conjunctivitis and they were poultry workers.

However, there were three individuals who were family members of poultry workers who did not have direct contact, suggesting some limited person-to-person spread of H7N7. They had mild symptoms. There was one fatal case in a veterinarian and who had visited and had contact with infected poultry at a commercial poultry farm. Early this year, there was an outbreak of high path H7N3 among poultry in Canada with two human H7N3 cases which I'll talk about later.

In terms of human infections with low path viruses that have been confirmed, 1998 in China, there were six cases of H9N2 virus infection that were reported in the Chinese literature with no deaths. In 1999, there were two children with confirmed H9N2 who had uncomplicated influenza-like illness and fever symptoms. They were hospitalized and completely recovered. No other cases were identified. In December 2003 in Hong Kong, there was a five-year-old boy who was also confirmed to have H9N2 virus infection. He had uncomplicated influenza illness and completely recovered. I'll talk shortly about some H7N2 virus infections in the U.S.

In North America, there have been two human infections confirmed with high path avian influenza viruses (H7N3) in the Fraser River Valley of British Columbia during March and April 2004. There were two poultry workers who were involved in culling operations who had mild illness, headache and conjunctivitis. H7N3 was isolated from them. One of these individuals was not wearing eye protection. One was wearing glasses. They were treated with the antiviral medication oseltamivir and fully recovered. These human infections occurred during a large outbreak of highly pathogenic H7N3 in chicken farms in British Columbia. The outbreaks have been controlled.

In the U.S., we've had two documented H7N2 low path virus infections of individuals. One H7N2 case was a person who was involved in culling activities during an H7N2 poultry outbreak in Virginia in 2002. He had an influenza-like illness. He was not hospitalized and fully recovered. Another individual was identified to have H7N2 virus infection in New York in 2003. We're not quite sure how he was infected. He's fully recovered from that illness and an investigation is ongoing.

I'll briefly conclude with an update about the situation of H5N1 in Asia. I think, as you know, this has been an unprecedented outbreak of high path H5N1 among poultry, involving not only commercial poultry

farms, small farms, but many backyard poultry flocks in a number of countries. There have been more than 100 million poultry that have been either culled or died. Nine countries have reported H5N1 outbreaks. In seven of those countries control of H5N1 outbreaks in poultry is unclear. Those countries include Vietnam, Thailand, Laos, Cambodia, Indonesia, Malaysia and China.

This is a map from FAO that kind of illustrates recent H5N1 outbreaks among poultry as well as the scope of outbreaks that have been reported since December 2003. The two countries in which H5N1 poultry outbreaks have been controlled are South Korea and Japan.

To summarize human cases to date, there have been 44 confirmed human H5N1 cases with 32 deaths. That includes 17 cases with 12 deaths in Thailand and 27 cases with 20 deaths in Vietnam. Overall case fatality is 73%. The majority of these cases are individuals who had direct contact with sick or dead poultry. The majority of H5N1 cases were children or young adults. The H5N1 viruses isolated from both poultry as well as from humans are resistant to the antiviral drugs amantadine and rimantadine, but they are susceptible to oseltamivir.

There's been no evidence of genetic reassortment to date. All of the genes of these H5N1 viruses isolated from humans are of avian origin. They are slightly different than the viruses isolated from people in 1997 and 2003 in Hong Kong. So the viruses have evolved. There's no current evidence for sustained human-to-human transmission of H5N1 viruses, and there is no currently available human H5N1 vaccine.

I do not believe, nor do my colleagues believe that this problem can be eradicated any time soon. It must be looked at as a longer-term problem. There are data from southern China to suggest that H5N1 viruses may circulate at an increased level during cooler months and that could occur in the upcoming several months. These viruses clearly are continuing to evolve.

There's experimental evidence that these H5N1 viruses can infect domestic cats. There is evidence that these viruses have infected tigers and leopards who have fed on H5N1 infected chickens. That comes out of Thailand as well as China. There is limited evidence, but some documentation that H5N1 viruses have infected pigs in China,



and very recently, there's experimental evidence that ducks can be infected and not have any symptoms at all and can shed H5N1 viruses for longer periods than we had previously thought.

In terms of the public health issues, for poultry workers in the U.S., both high path and low path viruses can and have been documented to spread from poultry to humans. Infection is really uncommon, but preventive measures are critical. This will be discussed in presentations following mine, but briefly, personal protective equipment is very, very important as well as decontamination of the environment. Antiviral medications for treatment of infection and prophylaxis to prevent infection definitely should be considered.

The major concern is that an individual could be co-infected with an avian virus and a human influenza A virus leading to genetic reassortment and potential transmission of a reassortant virus with pandemic potential among people.

To summarize, both low path and high path avian influenza viruses can infect and have infected people through close, unprotected direct contact with infected poultry. Human infection with high path avian influenza viruses, although it's uncommon, has resulted in mild to severe illness, including death. There's no current evidence of sustained person-to-person transmission of Avian Influenza A viruses at this time. However, these viruses are continuing to evolve and do have the potential for genetic reassortment to evolve into a virus that may be more easily transmissible among humans in a sustained fashion. It could result in a global human influenza pandemic.

Finally, the key to preventing human infections with Avian Influenza A viruses is to control poultry outbreaks of avian influenza. Thank you very much for your time.

Dr. Marano

Thank you, Dr. Uyeki. We have about five minutes for questions from the audience. So the operator will take questions, and we will answer them for the next five minutes pertaining to the presentation you just heard.

Coordinator

Thank you very much, Ma'am. We do have our first question coming from Joanna Quinn.

E. Gaunder            Actually, this is Eric Gaunder. I'm sitting in with Dr. Quinn. Has there been any evidence of subclinical infection in humans with H5N1?

Dr. Uyeki            Thanks for that excellent question. What I would say is that the surveillance that's being conducted currently in Asia, in terms of the public health surveillance, is really focused on severe illness resulting in hospitalization - so severe pneumonia - and many of those cases have died. So in fact, there has not really been surveillance for mild or subclinical infections. However, there are epidemiological investigations that are underway and ongoing to look at household contacts or different populations of individuals who have been exposed. There are really critical public health investigations that should be done. That would include sero-epidemiological studies of poultry workers, persons involved in culling activities, children, people in rural areas, etc.

But to date, the only thing I would say is that in Hong Kong in 1997, there was one study that looked at poultry workers and the seroprevalence of H5 antibody. That included more than 1,000 poultry workers, and the seroprevalence of H5 antibody was 10%. The majority of those people were never ill, or they had mild illness. We believe that mild and subclinical illness with H5N1 infection can definitely occur, but this can vary with the specific strain. The extent to which any mild or subclinical H5N1 infection has occurred in Asia related to this current H5N1 epizootic is unknown at this time.

E. Gaunder            That was a fairly prominent feature of the Netherlands epidemic as well. Was it not?

Dr. Uyeki            If you're referring to recently publicized information suggesting that there have been a lot of individuals exposed to H5N1 that were infected, these findings have not been published in any scientific journal.

If you're referring to the original description that was published in *Lancet* last year where there were 89 human H7N7 infections documented, you're right. The majority of those people who did have either RT-PCR or isolation confirmation of H7N7 infection - those people had conjunctivitis or mild influenza-like illness. So clearly, that was a high path H7N7 virus that was transmitted to humans and resulted mostly in mild illness. So you're quite correct. However, there was one H5N1-infected veterinarian who died.

- E. Gaunder            Okay. So there's like 1,000 people that are serologically positive for H7N7 in the Netherlands. At this point, it's primarily anecdotal then?
- Dr. Uyeki             This has been published on the Web site in the Netherlands or in Belgium, but it has not been published in any peer reviewed scientific journal. We know that those manuscripts have been submitted for publication, but at this time, it would premature to comment on them. One of our concerns at CDC is the methodology that was used to determine serological infection. Many of us would like to actually review what the methods were. It's unclear if they use micro-neutralization assay and confirmatory tests for the serological antibody tests.
- I think it would be premature for any of us to comment on any results that have been put out on the Web site without seeing the results in a peer reviewed scientific publication.
- Dr. Marano            Do we have any other questions?
- Coordinator           Our next question comes from David Baker.
- D. Baker               How long does this virus last in the litter and poultry houses? The second question has to do with what is the preferred disinfectant to be used and mode of application?
- Dr. Uyeki             I'm going to let some experts who are on the phone who are veterinary virologists or agriculture experts address those questions.
- Dr. Marano            Dr. Hegngi, can you please answer the question?
- Dr. Hegngi            This virus is very sensitive to heat. If you apply heat, it doesn't last that long in poultry houses. For precautionary measures, it can last just for 24 or 48 hours if the house is closed up and heated to plus 100 degrees. The virus will be out of there with the right temperature and humidity. For disinfectant, the virus, again, is also very sensitive to most of the disinfectants and detergents.
- D. Suarez             This is David Suarez. I just had one additional comment to make from what Dr. Hegngi had also said. The time that it takes for the virus to be inactivated is very much dependent on the temperature as well as

moisture. Obviously, the virus can last for many weeks at four degrees Celsius, particularly in the high protein environment that's found in the poultry litter. So it's not really possible to give a specific time when all of the virus is going to be inactivated in a particular house because it is very much time and humidity dependent as well as the substrate that it's in.

To concur with what Dr. Hegngi had said, a lot of times, in the U.S., we'll close up the house and turn the heaters on to get the temperature to a high level to inactivate the virus in just a couple of days. Again, you can go in with any of the commonly used disinfectants that will also inactivate any of those viruses, but of course, you always had to worry about the high organic loads of some of these viruses. Typically, you're going to clean the house out, get the litter out of the house first, and then disinfect the premise so that you don't have to deal with that high organic load. Did that help answer the question?

D. Baker

Yes. Thank you.

Dr. Marano

I think we have time for one more question for this session, and then at the end, we will open the floor to questions pertaining to all of the presentations. So let's take one more question and then we'll go on to the next presentation.

Coordinator

Yes, Ma'am. We have our one more question coming from David Swayne.

D. Swayne

The question is in the cases in Thailand where in hospitalization and fatalities, what were the sectors of exposure of those individuals? For example, was it primarily in the village poultry area to chicken, or village poultry to ducks, or were there cases of exposure to commercial poultry?

Dr. Uyeki

Thanks, David. The majority of human H5N1 cases in Thailand have not occurred in a commercial farm exposure setting. They're in backyard flock operations. There are few human cases in which the exposure to H5N1 viruses is believed to have been through close contact to cock fighting roosters. But the majority of the human H5N1 cases have had very direct close contact with sick or dead chickens.

In Vietnam, it's primarily the same. There are some H5N1 cases that had contact with both sick or dead chickens and ducks, but primarily, cases have occurred through contact with sick or dead chickens in rural areas.

Dr. Marano

Thank you very much. We'd like to go to the second presentation on worker health and safety. I'd like to introduce you to Lieutenant Lisa Delaney. Lisa joined the National Institute for Occupational Safety and Health Hazard Evaluation Program in 1999. She also is a Lieutenant in the United States Public Health Service Commission Corps. At the Health Hazard Evaluation Program in the Atlanta field office, Lt. Delaney is working on a four-airport transportation security administration study, evaluating employee exposures to noise, heat and diesel exhaust during checked baggage screening.

Her involvement with avian influenza began last winter when she participated in the CDC influenza and avian influenza emergency response team as a co-team lead for the infection control and occupational health group.

L. Delaney

Thank you and good afternoon. It is believed that most cases of avian influenza infection in humans have resulted from contact with infected poultry or contaminated surfaces. However, other means of transmission are also possible such as the virus becoming aerosolized and landing on exposed surfaces of the mouth, nose or eyes, or being inhaled into the lungs.

There have been several instances of human infections and outbreaks of avian influenza since 1997, and Dr. Uyeki has provided good information about those outbreaks, particularly in the Netherlands and in Canada, which occurred in the poultry workers. That's why it's so important now for us to focus in on the poultry workers and prevent the transmission from occurring during these outbreak events.

The document titled, "Interim guidance for protection of persons involved in U.S. avian influenza outbreak disease control and eradication activities," was developed last winter in response to the avian influenza outbreak. It was posted on the CDC Web site in February of 2003. It was a joint CDC USDA document that was meant to complement avian control and eradication strategies determined by the state government, industry and the USDA. This guidance was also

posted on the Occupational Safety and Health Administration, OSHA's, Web site.

The recommendations are deemed the optimal precautions to be taken during an outbreak of high pathogenic or low pathogenic strains of AI. Compared to high pathogenic strains, the health effects in humans from low pathogenic avian influenza viruses are less well established, but likely less severe.

This document contains information about basic infection control and outlines the appropriate personal protective equipment to be used during an outbreak response. Proper hand washing with soap and water, or other standard hand disinfection procedures is advised after contact with infected poultry, contact with contaminated surfaces or after glove removal. Employees should also have access to the appropriate personal protective equipment and be given instructions and training on its proper use.

This slide outlines the personal protective equipment recommendations that were provided in the guidance document during a response. Disposable gloves, such as nitrile, vinyl or heavy-duty rubber gloves should be worn. Protective clothing, preferably disposable outer garments or coveralls, plus an impermeable apron, shoe covers or rubber boots that can be disinfected should also be worn.

Workers should wear safety goggles to prevent eye exposures. If safety goggles are worn, they should be non-vented. For example, an eyecup type goggle or the minimum indirectly vented. Properly fitted indirectly vented safety goggles with a good anti-fog coating may be a good choice for poultry workers who have lower risks of exposure.

Disposable particulate respirators, such a NIOSH approved N-95, are the minimum level of respiratory protection that should be worn. However, wearing respirators that offer a higher level of protection, including full-face piece, hood, helmet or loose fitting face piece respirators also will serve to protect the eyes.

Surveillance and monitoring of workers is also recommended. Workers should watch for symptoms associated with avian influenza exposures for up to one week after the last exposure and should seek medical care if they become ill. We also emphasize the importance of practicing good respiratory and hand hygiene, such as covering your

mouth when you cough and washing your hands frequently to prevent transmission to family or medical personnel.

The CDC recommended that workers receive the current season's influenza vaccine to reduce the possibility of dual infection with avian and human influenza viruses. However, due to this year's shortage, responders are not included in the high priority list to receive the vaccination this year. Workers should also receive an influenza anti-viral drug for the duration of time exposed to infected poultry or contaminated surfaces.

In this slide, we're transitioning from the response workers to general poultry workers who may also come into close contact with infected poultry during an outbreak. Examples include poultry growers, service technicians of poultry processing companies, caretakers, lay or barn workers and chicken movers at egg production facilities.

Prior to an outbreak, poultry workers should be aware of the signs of symptoms of disease in both poultry and humans. Typical symptoms associated with human infection include fever, sore throat, muscle ache and conjunctivitis. It may also lead to pneumonia and acute respiratory distress. Workers should seek medical care if they experience any of the signs and symptoms of disease.

In the event of an outbreak, anti-viral medication and the current season's flu vaccine may also be warranted for some poultry workers. Poultry workers should consult with their healthcare provider on whether or not they should receive the anti-viral medication or the flu vaccine. Currently the CDC and OSHA only recommend that workers involved in disease control and eradication activities receive the vaccination. Again, however, due to this season's vaccine shortage, these responders are not included in the high-risk category and therefore, CDC does not recommend that poultry workers receive the flu vaccine this year.

In addition to avian influenza viruses, poultry workers are also at risk of exposures to a variety of containments including organic dust, gases such as ammonia and microorganisms. Thus, many poultry workers routinely wear personal protective equipment. There are many useful resources available to help aid in the selection of the most appropriate respiratory protection on the NIOSH Web site. The respirator section of the CDC/NIOSH histoplasmosis guidance, which can be found on the

NIOSH Web site, provides information on the advantages and disadvantages of different respirators.

Of course workers wearing respirators should be included in a complete respiratory protection program. A comprehensive program includes training, testing and identification of a program administrator, and information describing all of the elements of a complete respiratory protection program can be found on the OSHA Web site.

Eye protection is recommended in situations where workers may be at risk of acquiring infectious diseases via the ocular exposure. Eye protection serves to protect against direct contact with infectious materials and also prevent workers from touching their eyes with contraindicated fingers or other objects. There are a variety of eye protection devices that provide a range of protection to workers. Non-vented or, at a minimum, indirectly vented respirators are recommended for poultry workers.

Properly fitted indirectly vented safety goggles with a good anti-fog coating may be a good choice for the lower risk of exposure. However, such goggles are not air tight, and consequently, they will not completely prevent exposures to air borne material. Directly vented goggles and safety glasses, I believe that were described during the Canada outbreak that they were wearing just safety glasses, will provide limited protection, but are not recommended for protection against fine particles, splashes or aerosols such are required in situations when workers will exposed to infected birds.

Care should be taken to provide appropriate eyewear to workers who wear prescription lenses. These workers can wear eye protection that has the correction built into the safety lenses of the protective eyewear, has lens inserts or can be fitted over regular street wear prescription glasses. Eye protection should be fitted together with a respirator because some goggles can alter the fit of half-face piece respirators.

The CDC recently posted a document entitled, "Eye Protection for Infection Control," that provides information about the various types of eye protection and can help guide your decision in determining the most appropriate eye protection for workers. I've included the link on this slide.



Protecting clothing, which includes gloves, aprons, outer garments or coveralls and boots or boot covers should be used to prevent direct skin contact with contaminated materials and surfaces and reduce the likelihood of transferring contaminated material outside of poultry barns or worksites. Disposable protective clothing is preferred. Because protective clothing can be insulating than regular clothing, precautions should be taken also to protect workers against the effects of heat stress. Workers should also follow standard operating procedures for the proper donning and doffing of personal protective equipment to reduce self-inoculating.

As soon as workers remove their gloves, they should wash their hands thoroughly with soap and water. It is important to take measures for preventing the avian influenza virus from being spread to other areas, and to do this, disposable items of personal protective equipment should be discarded properly, and non-disposable items should be cleaned and disinfected according to the outbreak response guidelines.

NIOSH formed a joint working group with OSHA to review and expand upon the existing health and safety guidance for poultry workers potentially exposed to avian influenza viruses. The group is currently developing a guidance document that is intended to help guide poultry growers who will be making decisions on how to protect poultry workers during an avian influenza outbreak. It will present basic information about avian influenza and describe what steps should be taken to minimize exposures to the virus. Links to Internet sites will also be provided for those wanting more detailed information on avian influenza, biosecurity measures and personal protective equipment. This document is currently going through the final phases of review and clearance and will be posted on the CDC Web site.

This last slide presents information on how to access some of the resources that I mentioned during my presentation. CDC does have an avian influenza Web site that contains all of the guidance documents that we've developed, and additionally, there's information and you can contact NIOSH, the 1-800 number, or if you have questions related to worker health and safety, you can also feel free to give me a call after the Webcast.

Dr. Marano

Thank you very much. We'd like to open the lines for some questions for Lieutenant Delaney.

**CDC-NCID**

**Moderator: Nina Marano**

- Coordinator Thank you very, Ma'am. Ma'am, we do have our first question coming from Suzanne Jenkins.
- S. Jenkins This question is probably more for Tim than it is for the last speaker, but it is on worker safety. I think Tim listed the use of antivirals for workers. I would like him to elaborate on when he sees using antivirals.
- Dr. Uyeki Suzanne, thanks for that question. As Lieutenant Delaney has alluded, we've been assisting in development of some guidelines, and antivirals will be listed in there. But just to tell you my own opinion, in terms of an outbreak that occurs, whether it's a high path or low path outbreak, in terms of protection of persons who would be exposed to poultry at that farm, clearly they need full personal protective equipment. But in terms of antivirals, people who have unprotected exposure need to consider post-exposure treatment. Then those who have not exposed but who will be involved in culling operations disinfection, antiviral prophylaxis, that is pre-exposure prophylaxis needs to be considered.
- We would definitely recommend antiviral treatment for exposed persons with symptoms at all, including conjunctivitis, to be treated with oseltamivir. However, for prophylaxis, until there are data to indicate the sensitivities to amantadine or rimantadine, I think that one can make a variety of choices. Rimantadine is probably better than amantadine in terms of side effects, but rimantadine/oseltamivir could be considered. But we've been working to develop these guidelines, and those antivirals will be addressed.
- S. Jenkins Thanks very much.
- Dr. Uyeki But one of the main points I would make is that active surveillance for illness, as well as consideration of antiviral prophylaxis should be extended beyond, and I think Lisa was alluding to this, beyond the last day of exposure. So probably up to a week after the last date of exposure because infection could potentially have occurred on that last day of exposure. We don't know the true incubation period in terms of human infection with these avian viruses. So a week of prophylaxis extension and surveillance is probably indicated.
- Dr. Marano Do we have some more questions?
- Coordinator Yes, Ma'am. We do have our next question coming from Lee Myers.

- L. Myers Yes, this is Lee Myers in Georgia, the State Veterinarian. I have a couple of questions. Number one, what source of funding is available to assist the industry and first responders, which are typically at the state level initially, before assistance is available from the federal level, to comply with these guidance documents? Secondly, what are the legal liabilities in place for, or the repercussions, I guess, of not being able to comply with these because I don't know of any agriculture first responders that have been fitted for these N-95 respirators.
- L. Delaney Well, first, these are guidances that were posted on CDC and are deemed at optimal precautions. In terms of them having any regulatory impact and OSHA behind it, I don't believe that there is that kind of implication. I can't address the issue of budget, which is beyond my authority to discuss.
- L. Myers Regarding legal liability, where there any discussions regarding tort law considerations? I guess not. Okay.
- L. Delaney That's what we discussed.
- L. Myers All right. Thank you. I think these are two very serious items that all of us need to think about when placing these guidance documents out there. How are we going to have the resources to comply with these, and then what is the impact both to the industry and to those first responders? If we do not have the adequate resources and rapid training, and if we do not comply with these because we have a lack of resources, then there's going to be serious implications on disease spread even further if first responders are not able to comply with a guidance document and not able to actually respond to the incident.
- So I really think that all of us need to continue discussing this, coming up with resolutions and ways that would help us comply with these documents.
- Dr. Marano Your point is well taken, Dr. Myers. Do we have any other questions?
- Coordinator Yes, Ma'am. We do have our next question coming from David Hinsler.

D. Hinsler Hi. I thank you, the questions are for either speaker. I'll read them all at front here, and you can respond. Are there any side effects or contraindications to humans taking the latest antiviral drugs prophylactically when working in poultry-infected avian influenza premises?. Also please specify any problem with long-term use of these drugs, perhaps for up to four to 16 weeks or longer. Finally, should that same worker develop symptoms suggesting avian influenza that may be severe, are there contraindications or are there problems because they have used, perhaps, long-term prophylactic treatment? And, if they have an active case in terms of regards to treatment, and how that would work out? Thanks.

Dr. Uyeki Thanks for your question. Regarding side effects of antiviral drugs when used for chemoprophylaxis or for treatment, there are adverse events that have been associated with use of these drugs. They're different depending on what drug is used, and there's information on our Web site, the CDC Influenza Branch Web site about these drugs. Amantadine and rimantadine are associated with gastrointestinal symptoms. Amantadine has some central nervous system side effects. Oseltamivir is associated with some mild gastrointestinal side effects. In terms of these side effects developing, if they're going to develop, they tend to develop within several days of initiating treatment or prophylaxis. They tend to resolve over long-term administration.

However, clearly these are prescription drugs and depending upon the individual's underlying medical conditions, if they're taking other drugs - this clearly needs to be evaluated on a case-by-case basis. But in terms of long-term side effects, there are none that have been reported. In someone who is on one antiviral drug for prophylaxis and then has documented or suspected avian influenza virus infection, it would be very prudent to treat them with another antiviral agent. Thanks.

D. Hinsler Thank you.

Dr. Marano We have time for one more question.

Coordinator Yes, Ma'am, and that question comes from Max Coates.

M. Coates Would either of the two previous speakers care to comment or speculate on the public health or worker risk to responders in situations where you have a clinically low pathogenic presentation in

the birds with or without virus detection? Very often in responding, you need to respond prior to the time you have confirmed virus detection.

Dr. Uyeki Thanks for that question. I think that the answer is unknown, but as I discussed, clearly low path infections of humans have occurred. It probably is uncommon, but we could not speculate on the frequency or what could happen in the future. But all we can say is even when responding to a suspected but not documented outbreak, it's prudent to have full personal protection as Lieutenant Delaney has outlined.

L. Delaney Precautions should be taken whether or not it's a high path or low path strain. The goal is to protect the worker from exposures to the virus.

Dr. Marano Thank you, Lieutenant Delaney. I'd like to introduce you to our next speaker. This is Dr. Kristin Holt. She's going to speak to us today about avian influenza and food safety. Dr. Holt serves as the USDA Food Safety and Inspection Service Liaison to CDC in Atlanta, Georgia. Before reporting to this position, in August 2001, Dr. Holt served in the Food Safety and Inspection Service in the field operations program area for 18 years in Georgia.

While serving in field operations, Dr. Holt was an inspector in charge, assistant area supervisor, circuit supervisor and deputy district manager. She holds a Doctor of Veterinary Medicine degree from Louisiana State University and a Master of Public Health from Emory University. Please welcome Dr. Holt.

Dr. Holt Good afternoon. I appreciate this opportunity to speak with you about avian influenza and food safety. Interest in this topic has increased following the events in Southeast Asia in recent years.

Items on the CDC and World Health Organization Web site really capture our current thinking on this subject. From the CDC Web site, "There's no evidence that any cases of avian influenza have been acquired by eating poultry products, and from the WHO Web site, "To date, there is no epidemiological information to suggest that the disease can be transmitted through contaminated food or that product shipped from affected areas have been the source of infection in humans."

To provide a little background on the viruses we're talking about, Influenza A viruses are Type A orthomyxoviruses. They have become

endemic and cause infection and disease in humans, horses, pigs and various avian species. We have seen other species become infected in outbreaks and experimental studies. The schematic identifies Neuraminidase and Hemagglutinin glycoproteins on the surface of the virus. We've developed tests that allow for the identification of subtypes based on these surface proteins, allowing for epidemiologic study of the viruses. As was mentioned before, there are 15 Hemagglutinin subtypes and nine Neuraminidase subtypes.

The influenza ecology is quite impressive. Ducks, geese and shore birds are considered the primary or primordial reservoir with all 15 Hemagglutinin and all nine Neuraminidase subtypes found here. Wild birds typically have sub clinical infections with shedding of the virus in the feces. You already know that Influenza A viruses have a propensity to change genetically.

I've been talking generally about Influenza A viruses. So what are Avian Influenza viruses? Influenza A viruses that infect birds are referred to as "Avian Influenza Viruses." These viruses are not separate species or subspecies of the Influenza A viruses. In birds we do categorize the avian influenza viruses into two categories based on pathogenicity in birds. Bird infected with low path AI viruses tend to have subclinical infections or mild respiratory syndrome. Birds infected with these strains typically do not get systemic illness, and virus isolation is primarily limited to the respiratory tissues and intestinal tract.

We focus on the H5 and H7 subtypes of low path AI because of a concern that they might mutate to a highly pathogenic strain for birds. The high path strains tend to cause severe illness in domestic birds with systemic disease and virus replication occurring in almost all tissues. High mortality in flocks is frequently seen. The high path strains are H5 and H7 subtype, and it's important to remember that not all H5 and H7 subtypes are highly pathogenic to birds. This difference as to high path or low path is based on chicken inoculation studies looking at mortality after inoculation with the strain of interest or through specific molecular testing.

I want to emphasize that I'm speaking about pathogenicity in poultry, not humans. I'll share with you a statement from a 2003 USDA ARS review article. "The virulence of H5 and H7 viruses in chickens does

not correlate with their ability to infect and cause disease in humans.” So the picture is fairly complex and is not that straightforward.

Live birds in the U.S. There are more birds than people in the U.S., and many countries can probably say the same. Birds can be found in various settings. In the U.S., there is a large commercial poultry sector that supplies most of the poultry consumed in this country. This sector primarily consists of integrated poultry operations where poultry flocks are raised in confinement so they have little contact with wild birds.

There’s a smaller commercial sector that raises organic birds for human food and birds for backyard or hobby flocks, for hunting clubs and for live bird markets. The farming practices seen in the small sectors, such as the free-range rearing, as shown in the middle right photo: increase the exposure of poultry to wild birds, and the opportunity for exposure to avian influenza viruses. I believe Dr. Hegngi with APHIS will describe in more detail how poultry become infected. Again, the majority of our food originating from birds comes from the large commercial operation sector with a considerably smaller percentage derived from free range flocks, backyard flocks, live bird markets and birds shot by hunters. I think it’s important not to overlook birds in another sector, and that’s the entertainment sector. You see “Tweety.” With our hearing all about the large number of birds in the U.S. probably makes it obvious why we focus on avian influenza. We need to protect the nation’s poultry flocks and we need to support an environment conducive to trade. The U.S. exports billion of pounds of poultry products each year. Somewhat new to the list is the need to protect public health. This focus started with the identification of human illness and death caused by avian influenza in Southeast Asia a few years ago. At this time, we don’t see a concern for food borne infection. High path AI and low path AI with H5 and H7 subtypes in poultry are reportable disease, and early detection is our goal in the U.S.

Live birds and eggs are harvested for human food in various settings. Based on numbers of birds and poundage, most of the processing occurs in large poultry processing plants where the birds of slaughtered, and my mention of red meat slaughter plants might seem strange to some, but that is where ratites, ostriches and emus are actually processed. Eggs are, of course, harvested for table eggs and some of the shell eggs are in-shell pasteurized. Eggs also go to

breaker plants where they're processed into pasteurized egg products. These egg products go out for retail sales to consumers, and the products may also go out to other food manufacturers where they're used to make other food items like mayonnaise.

In recent years, there has been increasing focus on a growing sector where birds are processed for food, and that's being the live bird market setting. Of concern are AI strains that appear to have become endemic in the live bird market system. The AI status of birds in this sector has raise concern in the large commercial poultry sector in the U.S. For those of you not familiar with live bird markets, a consumer buys a live bird and slaughters the bird themselves. The consumer dresses the bird, meaning they remove the feathers, etc., and they take the carcass home to be cooked and consumed. The lower picture was taken at a live bird market in Minnesota where some cultures, the gathering of food, the process of just getting in and gathering it, actually sort of seems to be a social event.

As I'm talking about converting a live bird into a food item for human conception, I thought a list of what is kept for human food and what is not kept would be of value. For some in the audience, this list is stating the obvious, but I wanted to point out that diseased carcasses and parts do not go for human consumption,, and the tissues of concern related to low path AI - the head, trachea, lungs and intestines - also do not go for human consumption.

I believe there are several barriers to AI in food manufacture in the U.S. First, there is active surveillance and passive surveillance on farms and in the live bird market system. Now, I'm not saying that every bird is in a surveillance program, but the surveillance programs are continuing to grow. High path AI is dramatic with its high mortality and very obvious disease in poultry flocks. Flocks are identified and not sent to slaughter, and the flocks are destroyed. High path AI is a rare event in the U.S. with it occurring in 1983 in Pennsylvania and in Texas in 2004.

A colleague of mine recently described going into a poultry house during the 1983 high path AI outbreak in Pennsylvania - the house having 60,000 birds in it. While he was in the house for a two hour period, 5,000 birds died. But in contrast, such high mortality was not seen in the recent Texas H5N2 high path AI outbreak. You may remember that I mentioned that H5 and H7 subtypes are classified as



low path or high path in poultry based on a chick inoculation study or molecular testing.

The chicks in the Texas virus inoculation study did not die, and they also gained weight. So since the criteria is an "OR" criteria, it was reported as a high path strain based on molecular testing, but it didn't really act like a high path strain. So this was an unusual event, and some of the birds from the infected farm did reach to live bird markets. Low path AI does occur in the U.S. We primarily are focusing on the detection of the H5 and H7 subtypes. Flocks with these infections are either destroyed or they are control marketed, which means they are held until they are over their illness and then they could proceed to slaughter. There are also barriers at processing plants. In the unlikely event that birds with AI virus arrive at slaughter, there are several barriers to the virus ending up on the finished product, human food.

The birds undergo ante-mortem or before death inspection and a postmortem inspection. The picture here shows postmortem inspection by a state or federal government inspector, and a government inspects each carcass and condemns disease carcasses and parts. There's a zero tolerance for feces on the finished carcasses, and we discard respiratory tissues, the heads, trachea, lungs and the intestines. As I mentioned before, if the virus was present, it would more likely be found in these tissues.

The bird's carcasses also go through anti-microbial washes, and since these viruses are labile to environmental conditions, it seems likely that these carcass rinses may have an effect. We don't think that refrigeration or freezing have much of an effect on these viruses, and I mentioned cooking because some poultry is cooked at the manufacturing plant before it's shipped to consumers. These viruses are easily inactivated by heat treatment.

Barriers to human infection during meal preparation and consumption. The presence of live AI virus in and on food in the U.S. is an uncommon event, but in the unlikely event that the virus might be present, both the CDC and WHO Web sites make reference to the preparation of poultry meat and eggs and suggest following current guidance that exists to prevent food borne illness.

From the WHO Web site, "...good hygiene practices during handling of raw poultry meat and usual recommended cooking practices for poultry products would lower any potential risk to insignificant levels," and I'll cover these usual practices in a minute.

In a 1999 article published in the *Journal of Infectious Diseases*, findings from a case control study launched to identify risk factors among hospitalized H5N1 persons in Hong Kong in 1997 were presented. So exposure to live poultry in a market was identified as a risk factor. However, consuming poultry or poultry organs, consuming poultry in a restaurant, consuming undercooked poultry or having a household member cooking poultry products were not found to be risk factors.

Though not on the slide, I'll mention host susceptibility or the route of exposure. Again, the virulence of the H5 and H7 viruses doesn't necessarily predict the same of level of virulence in humans. Again, if a virus survives and they labile to environmental conditions, you might wonder what the saliva, what its high pH and stomach acid with its low pH might do to the viruses.

The current FIGHT BAC! campaign clearly covers what we need to do in the kitchen: Wash hands and surfaces often; separate/don't cross contaminate foods and utensils; cook to proper temperatures. One thing that's not here, because I hope this would be obvious to most is that we shouldn't handle raw poultry and then lick our fingers or rub our nose or rub our eyes.

The Thermy campaign focuses on consumers and I have a Thermy magnet on my home refrigerator and use it frequently, so if you want one give me a call. They're produced by FSIS. These recommended cooking temperatures were designed to address bacterial pathogens. Now, Avian Influenza is more sensitive to heat and normal cooking temperatures will inactivate the virus. WHO indicates an internal temperature as low as 158 degrees should be adequate and the FSIS recommended temperatures are higher than that. From the CDC Web site it is mentioned that influenza viruses, such as H5N2, H7N2, and H5N1 are destroyed by adequate heat, as are other pathogens. The CDC Web site mentions 180 degrees Fahrenheit, which corresponds to the FSIS recommended temperature for a whole bird, leg, thighs, and wings.

In conclusion, there is no evidence suggesting that humans have acquired Avian Influenza by eating poultry products. In the U.S., barriers to human infection lie in food manufacture and in proper food handling during meal preparation. There is a low incidence of AI in integrated poultry operations in the U.S. where the majority of the poultry consumed in this country comes from.

I want to acknowledge several individuals who provided assistance: David Suarez and David Swayne with ARS; Bob Brewer with FSIS; Tom Gomez with USDA APHIS; and Kevin Elfering with the Minnesota Department of Agriculture. To answer questions David Suarez is also on the line with us. Thank you.

Coordinator Thank you. We have our first question coming from Daniel Curran.

D. Curran I was involved in the Virginia 87 outbreak. I was the one diagnosed in the index case and several people were involved in the task force and the control of the disease, plus growers and a lot of individuals. That virus, even that one positive case, was serologically positive at acute and convalescent stages. So we're not really sure if that antibody existed prior to that person showed up here. So I don't think that virus was infectious at all to humans involved in this outbreak. I don't think we can make a blanket statement all H5s or all H7s or any influenza as a potential risk to humans that are in close proximity to these Avian Influenza viruses.

I wonder if we are beginning to over-estimate this risk somehow. Not all H5s and all H7s are infectious to humans. We don't know what causes infection in humans. Definitely, the H5 strain in southeast Asia has been infectious to humans. I just want to caution us going forward coming up with all of these handling precautions and things, really not knowing whether this is a high-risk situation.

Dr. Holt FSIS did not change the recommended cooking temperatures. The Thermy temperatures were current and were not changed. I think basically we know these viruses are sensitive and we want people to be careful any time they handle poultry because, of course, there are other human pathogens that potentially could be on poultry meat.

Dr Uyeki I think that the bottom line is that we really don't have a lot of information and we really need to do more scientific studies to better understand the risk of avian to human transmission with Avian

Influenza viruses in both the low path and high path situation, specifically to address asymptomatic or mild infection. It is clear that there have been very, very few documented cases of human infection with low-path viruses and not many with human infection with high-path viruses, but it definitely has been documented. Of course, we're somewhat more concerned about human infection with high-path AI viruses. I think we really don't know how large the risk is and it seems prudent, particularly to first responders in a situation of an unknown outbreak where you don't know, you don't have the virologic identification, to be very cautious in terms of trying to prevent infection as much as possible.

But I think your point is well taken and I'd be happy to talk to you about the specifics of that H7N2 human case in Virginia in 2002. At the CDC Influenza Branch our perspective is that that was an acute infection associated with exposure during that H7N2 outbreak and not from previous infections, but as I mentioned, in some studies done among poultry workers in Hong Kong in 1997, clearly, humans have been infected and had either probably asymptomatic infection or mild illness. We have unpublished data from other countries to suggest that humans have been infected with highly pathogenic Avian Influenza viruses and were not sick or maybe had unknown infection in the past. From the scientific perspective we need to better understand the risk, but it seems reasonable to be very cautious in the setting of an unknown AI outbreak.

Coordinator We do have a question coming from Robert O'Connor.

R. O'Connor I'm calling from California. I do think, specifically when we're talking about low-path Avian Influenza, of which we've had quite a few even in recent history, infections of poultry in the United State with, from my own experience in California there was an H6N2 circulating for at least three years, so you had numerous poultry that were exposed and infected and you would, at the same time, have numerous persons who were involved in the poultry industry exposed. I think before what I would call fairly drastic measures, and I agree with the person from Georgia that the cost of the measures you're recommending are almost prohibitive, especially for a low-path influenza. I think you might want to use some of the United States' low-path cases now retrospectively and examine some of the people in the poultry industry who were involved in those cases. Do I have antibodies for H6N2 Avian Influenza floating around in my blood? I mean the cases are out

there and the studies should be done now, I think, before what I would call economically prohibitive measures are placed upon the poultry industry.

Dr Uyeki I'll just comment from the public health side and allow others, if they want, to comment about these preventive measures. Of course, we would be very much interested and love to do some of the studies that you're suggesting, sero-prevalence studies. There are a lot of logistical and confounding factors to account for, but I think what you suggest is, in fact, a very good idea. We would be very interested to do these kinds of studies.

R. O'Connor I especially think you need to be very kind of sound and valid in making those types of recommendations for low-path Avian Influenza. I think that everyone needs to realize that low-path Avian Influenza is not really an exotic situation in the United States. I mean you can go back into certain states and see numerous cases of low-path Avian Influenza. I think if there was an infectious nature to most of those infections transmission to humans, I think, would have been reported. I think we'd be able to substantiate that and I think even retrospectively you might be able to substantiate that.

Coordinator Thank you.

Dr. Marano We have time for one more question.

Coordinator We have our next question coming from Hugo Mendina.

H. Mendina Actually, I have two questions. The first one is – in any of the countries that there had human Avian Influenza do they do use a human influenza vaccine on a regular basis, like we do here in the U.S.?

Dr Uyeki Thank you. The countries with human infections documented, such as The Netherlands, Hong Kong, Vietnam, Thailand, many of those do not have highly organized influenza vaccine programs for people. Some of them, like the Netherlands and Hong Kong have recommended risk groups. They do not have an organized vaccine program in Vietnam. In Thailand there's some use of influenza vaccine, but none of those countries utilize human influenza vaccine to the extent that we do in the United States.

**CDC-NCID**

**Moderator: Nina Marano**

H. Mendina I wanted to know if it would be possible to use the human yearly influenza vaccine to minimize the presence of virus, or recombination. I was wondering if that approach had been taken in the Netherlands. The second question is - if influenza vaccination is recommended for some poultry personnel, how long in advance do they need to be vaccinated to minimize the possibility of recombination?

Dr Uyeki Those are excellent questions. WHO and CDC are currently recommending for persons involved in culling operations of H5N1-infected poultry in Asia and healthcare workers caring for H5N1-infected patients to receive human influenza vaccine, and to take other preventive measures including full PPE. In terms of the antibody response following vaccination in a human, generally this takes about two weeks post vaccination, so in terms of a poultry worker or a first responder to a suspected AI outbreak at a farm, if you got vaccinated with human influenza vaccine, you would still need to be on antiviral prophylaxis for about two weeks following vaccination before you could essentially feel that you would have protective antibodies against human influenza vaccine strains. Of course, human influenza vaccine would not offer any protection against infection with an avian influenza virus.

Dr. Marano Thank you for your questions. I think we need to move on to our last talk, which will be presented today by Dr. Fidel Hegngi of the USDA. He is a Senior Staff Veterinarian with the National Animal Health Policy and Programs, Certification and Control Team within the USDA. His current work involves being involved in the National Poultry Disease Program, the National Exotic Newcastle Disease Surveillance Program, the National H5 and H7 Low-Path AI Prevention and Control Program, and the National Poultry Improvement Plan. He holds a D.V.M. from Virginia-Maryland Regional College of Veterinary Medicine and a Masters of Poultry Science from the University of Maryland. Please welcome Dr. Hegngi

Dr. Hegngi Thank you very much. Thank you for inviting me to be part of this symposium. I would like to start my talk to try to reinforce, again, go into a little bit into the background on what Dr. Delaney, Dr. Uyeki, and Dr. Holt and some of the discussions we've had already today.

Worldwide there are many strains of Avian Influenza virus that can cause varying amounts of clinical illness in poultry. Avian Influenza can infect chickens, turkeys, pheasants, quail, ducks, geese, and

guinea fowl, as well as a wide variety of other birds. Avian Influenza is classified into low-pathogenicity Avian Influenza and high-pathogenicity Avian Influenza based on the severity of the illness they cause. Most Avian Influenza virus strains are low-pathogenic and typically cause little or no clinical signs in infected birds. High-pathogenicity Avian Influenza causes severe and highly contagious illness marked by mortality approaching up to 100%.

Currently the World Organization of Animal Health, that is OIE, that classifies and regulates animal diseases considers low-pathogenicity Avian Influenza to be a low-risk disease and does not require it to be reported. That might change in the future. Today low-pathogenicity Avian Influenza poses no threat to human health.

Looking at the introduction of what I'm going to try to cover in this talk today, I will try to stress the mission of veterinary services. I will kind of define biosecurity. I will look at sources of infection; how disease spreads. I will talk about the major components of biosecurity and how you use these different components in designing a biosecurity guideline or protocol. I will look at the importance of indemnification and Avian Influenza vaccine bank on how they are used or how to get involved on the prevention and control of Avian Influenza. For the group today that is listening to this talk, I will take this opportunity also to introduce them to the United States Department of Agriculture, APHIS, low-pathogenicity Avian Influenza program and again, this will focus basically on H5 and H7.

The mission of Veterinary Services is two-fold: One, it's to prevent, control, and eliminate animal diseases. Two, monitor and promote animal health and production. These activities are vital to the health of U.S. livestock and poultry and are key to promoting trade.

We all have heard about biosecurity for quite a long time and it is a word that is used in the industry and everyone that deals with any animal production unit. Basically, biosecurity embodies all of the cumulative measures that can or should be taken to keep diseases from a farm and to prevent the transmission of diseases by humans, insects, rodents, wild birds, etc. within an infected farm to neighboring farms. Biosecurity is the first line of defense in the prevention and control of diseases like low-pathogenicity Avian Influenza. Its use has been highly successful in keeping Avian Influenza out of commercial poultry worldwide.

However, as interesting as it may be, if Avian Influenza gets introduced into commercial poultry population biosecurity again is the primary means of controlling the disease. Biosecurity, in simple terms, is informed common sense. It's for all of us working in animal commodity groups or in any animal production units to just use our common sense. As was mentioned by the Mid Atlantic Cooperative Extension (MACE), I think around 1985 during the Avian Influenza outbreak in Pennsylvania, '83/'84, they said, in simple terms, "Do not bring germs to poultry or do not bring poultry to germs."

To truly understand and develop biosecurity programs or guidelines it is necessary to first recognize the source of diseases and then take appropriate measures to reduce and, if possible, eliminate their contact with poultry. Disease transmission occurs when microbes travel from place to place by animals, trucks, other equipment, and people. Human hands, hair, clothing, shoes, as well as skin and digestive or respiratory organs of domestic animals, dogs, cats, and free-living mammals, birds, rodents, are common routes for microbe transmission. In a typical poultry house where we have improper disposal of a carcass, that again might be a source of transmission. Backyard flocks and live bird markets, as we have seen in recent incidences of low-pathogenic Avian Influenza this year, are also sources of infection.

The diagram I have on the presentation is an old pamphlet that has been distributed all over the United States and all of the poultry industry. It was produced by the USDA. It's a simple diagram that shows in a very simple way how avian influenza can be transmitted directly by sick carrier birds and indirectly by people, their possessions, vehicles, and contaminated equipment.

Looking at the next diagram that talks about the measures of spread, in infected premises feces of infected birds are the most important source of the Avian Influenza virus. Vectors are agents of disease spreads. For example, rodents, insects, wild birds can act as vectors for Avian Influenza by carrying the virus from place to place.

I will now elaborate a little bit on the major components of a biosecurity program and looking at isolation, traffic control, sanitation, cleaning and disinfection, and rodent and insect control.



Isolation is the confinement of animals within a controlled environment. The main objective here is to prevent introduction of pathogens into flocks by creating physical barriers to exclude people, vehicles, domestic animals, insects, rodents, and wildlife from flocks. A good example in providing a good, isolated environment is to provide good ventilation, good drainage, bird-proofing for the different houses you build in the facility. You have to rodent-proof the houses, and provide lockable doors and gates.

At times in the way poultry production is set, if we go back in history looking at how poultry was grown outdoors before we went to confinement growing, it is also essential that we prevent the accumulation of standing water to greater reduce the attraction of water fowl and shore birds in our poultry facilities.

Traffic control should include traffic of personnel, vehicles, equipment, and traffic patterns within the farm. The spread of Avian Influenza virus follows the movement of people and equipment. It is important for farm personnel to wear dedicated clothing, as has been mentioned before by some speakers and footwear. Visitors must be required to wear disposable coveralls, facial masks, etc.

For sanitation and cleaning and disinfection, to prevent a possible outbreak of low-pathogenicity Avian Influenza, poultry producers must use special prevention measures and precautions on their farm. These should include cleanliness of personnel, housing, equipment, and premises, disinfection of people, materials, equipment, and vehicles. It is a must to take into consideration the use of effective products, the exposure time compatibility, looking at also temperature and humidity in deciding what kind of disinfectants you're going to use. You have to monitor this regularly and have meetings with your personnel constantly to make sure that this is effective.

Usually if low-pathogenic Avian Influenza is detected on farms, farms must be totally cleaned and disinfected. It is important to remove the litter and any other organic matter before you disinfect. Organic material generally increases the resistance of Avian Influenza virus to disinfection. We know from research that low-pathogenic Avian Influenza is inactivated by heat and drying. Low-pathogenic Avian Influenza is also very sensitive to most disinfectants and detergents.

For rodent control and insect control it is important to use baits and other devices for rodent control. You have to check bait stations and rotate baits regularly. If you are using pesticides you should use them in accordance to the label.

Biosecurity operating procedures should be put in writing to educate farm personnel and force their awareness. Supervisors should try to lead by example.

In my next set of presentation I will try to introduce the listeners of this presentation to the USDA APHIS Low-Pathogenicity Avian Influenza Program. In January 2003 the United States Animal Health Association provided a proposal to the USDA that a program be developed that would prevent and control Avian Influenza in the live-bird marketing system and the commercial poultry industry. In that essence it was stressed that this program be developed to include two compartments; and again, I use the word compartments because that is very important in terms of looking at trade issues. The first compartment is commercial poultry and the second compartment would be the live-bird marketing system.

The commercial poultry segment of this program is being developed through the National Poultry Improvement Plan, NPIP. It was adopted at the Biennial Conference in San Francisco in July of this year. For those who do not know what NPIP is, NPIP is a corporate and federal state industry program that was established in 1935 for controlling certain vertically transmitted poultry diseases, such as Salmonella Pullorum or Salmonella Typhoid and now we've added Avian Influenza into this program.

I would like to emphasize that Avian Influenza has not been proven to be a vertically transmitted disease, but because of the structure of this program it was seen by APHIS and the industry and the States that it would be good for the AI program for the commercial industry to be supervised and managed through this program. This program is extremely well-known throughout the world and with most of our trading partners.

Provisions of this program are developed jointly by industry members, state and federal officials. The provisions are located on APHIS's Web site, Code of Federal Regulation 145 and 147. The oversight of the NPIP is provided by a general conference committee, which is like the

Secretary of Agriculture advisory committee on public health. This is a specific committee that is so different in most of the other animal commodity groups.

A memorandum of understanding is established between APHIS and the official state agency in each state to implement the program. There are about 48 official state agencies that take part in this program. Again, this program would be for the commercial side of the industry. An AI program for chicken and turkey breeders already was in place in 1998. Again, NPIP usually deals with the breeders. This is the first time that NPIP is going to be involved with the production side of poultry production. The program will consist of AI monitor and certification program for table-egg layers, meat-type chickens, to include: broilers, roasters, Cornish, and fryers. For people who do not know the difference, broilers usually are grown for 42 days or six weeks; roasters about nine weeks; Cornish and fryers about three weeks. There will be guidelines for state diagnostics surveillance programs and there will be guidelines for a state initial response and containment plan, which is like an emergency response plan.

Low-pathogenicity Avian Influenza would be a disease reportable to the States. The state laboratories would test for AI in all submitted cases of respiratory diseases. This is ongoing. This is just going to be an enhanced surveillance plan and that would include testing for unexplained production drops and unexplained severe mortality.

The guidelines for a state initial response and containment plan would include for states to establish standing emergency disease management committees so that they are prepared in case there is an incidence of AI in the state, they can act immediately. Like Dr. Holt mentioned, a quick response is very important in the eradication of AI. This plan should include a minimum biosecurity plan, a public awareness and education program, different procedures for initial handling and investigation of suspicious cases, strict quarantine with control and monitoring zones, and access to adequate diagnostics. It is very, very important that diagnostics are very adequate to each state.

The plan also should have ... plans for depopulation, disposal, cleaning, and disinfection, re-population, and monitoring. We can attest to the Virginia outbreak and other incidences this year to realize that when you have this problem in your state, depopulation is crucial. If you do

not have a good plan for depopulation then you're going to spread the virus around.

For the second component of the program that covers the live-bird marketing system. That program is going to be titled the Prevention and Control of H5 and H7 Low-Pathogenicity Avian Influenza Program. The contacts for the program are, Dr. Lynn Siegfried, who is here at Riverdale; myself; and Dr. Andrea Miles, who is at the eastern regional office. She is the Eastern Regional Poultry Epidemiologist. As with the commercial poultry program, the low-pathogenicity Avian Influenza program is limited to the H5 and the H7 sub-types.

We all know that once low-pathogenicity Avian Influenza H5 and H7 become highly pathogenic it will be covered under emergency diseases and this will not fall under my colleague's purview. That will fall under the emergency programs. We are under the Certification and Control Team and we deal with the certification and eradication of diseases that are domestic, that are not foreign animal diseases. When it becomes high-path that then becomes the purview of the emergency program.

Just to reinforce again, this program is limited to the live-bird marketing system and the commercial industry is covered under the NPIP Program; however, commercial birds entering into the live-bird marketing system will fall under these standards.

This diagram kind of depicts a schematic of the components of the live-bird marketing system and thanks to Dr. Zirkle, who used to be the state veterinarian from New Jersey. The components of the live-bird marketing systems are basically, you have the live-bird markets themselves, the distributors, that would include the dealers, the haulers, the auction markets, the wholesalers, and then the production units, which can be small or can be large. Each segment of the live-bird marketing system has been treated equally in this program and all of them are held in the same standards.

So where are the live-bird markets? For a survey study that was done in 1998, 72% of them are in the northeast United States retail operations that are usually in large metropolitan areas, Southeast-Miami, 22%; California, 6%; and now we're looking in other states that we haven't had data collected yet, like Texas and Illinois.

I will be going through a series of pictures for those who have not seen what a live-bird market is and what kinds of birds are really usually grown for this market. Photos are thanks to Dr. David Henzler and John Coakley.

If you look at the picture presented, you will notice that these birds are totally different from the normal birds that we go out and buy in our regular grocery stores. You can see a lot of black and red poultry. These are kind of the birds that the ethnic groups, including myself, I am originally from Cameroon. We love eating these kinds of birds and so that's why this kind of a market is extremely, extremely important for those groups. That's where they go buy their birds to eat. These usually taste differently.

A picture of a wholesaler and dealer: You could realize that this is a big business. It is said that about 20 plus million birds go into this marketing system annually. On the left side of the slide you can see some of the biosecurity measures that are already in place. That is an automatic -crate washer to make sure that those crates are washed as they deliver birds so that the trucks go back to their destination clean, without carrying infected feces.

As part of the marketing system we're looking at monitoring very seriously the auction markets, the small sales, the free markets, and swap meets. This picture depicts some of that. This part of the component of the marketing system is very crucial in our effort in looking at them to prevent the persistence of this virus in the markets.

This is what a typical live-bird market looks like. This is somewhere downtown in Boston, so they're not hidden. You could walk and see them all around the city. They look extremely powerful.

This is what the markets look like inside. You could have some of them extremely advanced. You go in, select your bird. They process it for you and you take it home.

This program, again, entitled the Control and Prevention of H5 and H7 Low-Pathogenicity Avian Influenza, has been finalized and has been published. It was published this October 2004. The program is federally based and is state assisted. The program addresses requirements for premises licensing, worker education, Avian Influenza testing, record keeping, premises sanitation and biosecurity, disease

surveillance and response when AI positives are found. Each of these requirements is covered for the live-bird marketing system for the various distributors of the marketing system and for the suppliers or producers for the live-bird marketing system. Appropriate state regulations are required for compliance with the program standards. APHIS supports the program through providing personnel resources at the federal level and personnel and laboratory resources at the state level. The latter is through cooperative agreements with the states. In addition, APHIS investigation and enforcement services is being funded to provide personnel assistance to the states in enforcing some of the Avian Influenza regulations.

Under the program all participants must be licensed and have a premises identification number and biosecurity protocol. All personnel working with the live-bird marketing system must have been trained in biosecurity principles and procedures. This effort is being presently carried on by the state. Dr. Andrea Miles has been working extensively on this.

All bird movement must be accompanied by paperwork that includes origin of birds with GPS coordinates, test certificates, dates for all sales and movement and number of birds and species. Efforts would be made to trace all positives to their origin. It is very important that we have a trace-back mechanism. I mentioned before that looking at what the USDA is doing, looking at indemnification I can tweak it to say it's a biosecurity measure. Indemnification of our systems with planning on depopulation, cleaning and disinfection would be provided at all levels of the live-bird marketing system and the commercial poultry industry. Our current regulations at 9CFR Part 53 now provides a 50% appraised value of the birds and the cost of depopulation and disposal. Future indemnification will be according to current federal regulation and allowances for the low-pathogenicity Avian Influenza program.

It was proposed at the NPIP Biennial meeting this year to increase that reimbursement to 100%. In some sense this makes sense because looking at the new OIE chapter of Avian Influenza, the low-pathogenic Avian Influenza is going to be under notifiable Avian Influenza and that will include the H5 and the H7. So if that is put in the chapter and if that is voted on in May of next year then it makes sense to treat notifiable Avian Influenza in that sense for indemnification because it is

important to indemnify so that we can response quickly and recover quickly.

In this presentation another biosecurity measure that the USDA is implementing is that, and this has been going on for years, the USDA requires imported birds: poultry, pet birds, bird exhibitions in zoos and ratites to be quarantined and tested for AI virus before entering the country. This is important in the sense that it prevents foreign strains of Avian Influenza from being introduced in the United States.

Why an AI vaccine bank? The United States Department of Agriculture Animal Health and Plant Inspection Services Center for Veterinary Biologics has awarded a five-year contract to Fort Dodge Animal Health to develop an Avian Influenza vaccine antigen bank, that will house enough antigen to produce about 40 million doses of Avian Influenza vaccine, ten million doses of vaccine for each of the following Avian Influenza sub-types: Two for the H5s and two for the H7s.

In the event of a highly pathogenic Avian Influenza outbreak the frozen antigen will be used to prepare the vaccine for possible use in poultry in order to manage the disease. The Avian Influenza vaccine bank will be a great asset in helping APHIS work to keep highly pathogenic Avian Influenza from becoming established in the United States poultry population. Under APHIS guidelines, H5 and H7 AI vaccines are allowed to be used as a tool for combating any potential outbreak of highly pathogenic Avian Influenza in the U.S., but only under APHIS supervision and control as part of an official animal disease program.

To summarize, biosecurity is a team effort and a shared responsibility. Biosecurity should be an ongoing process and must be followed at all times. Each step should be carried out judiciously to effectively reduce disease contamination. Optimal biosecurity measures need to be developed and implemented to help both disease prevention and control. The mark of a good biosecurity program is to maximize the health of the flock, minimize the risk of disease spread, and ensure the production of a clean product. Biosecurity, as I always look at it, is an investment and is not unnecessary expense.

Avian Influenza is a potentially devastating disease, which can affect a wide variety of farm and wild birds. The cost associated with Avian Influenza is enormous, both in terms of loss of international trade and

local commerce. Migrating birds are a major vector. Human intervention is a significant contributing factor. Very high biosecurity standards are essential to prevent the introduction and spread of Avian Influenza.

To conclude, like Dr. Charlie Beard said, biosecurity is compared to life insurance. If you wait until it is needed it may be too late to get it in place.

I'd like to acknowledge my colleagues listed on the next slide for their kind contribution and scientific know-how for this program and for all of the effort that the USDA is putting out there.

For more information you can contact our Web site. We do have a telephone number that you can also call if you have questions on Avian Influenza and biosecurity practices. I am now available for questions.

Dr. Marano Thank you, Dr. Hegngi. We'll take some questions for Dr. Hegngi's presentation and also for all of the previous speakers.

Coordinator Thank you very much, Ma'am. We have our first question coming from Tom Gomez.

T. Gomez Thank you. This is Tom Gomez with USDA-APHIS and actually, I'm just going back to comment on some of the past comments and discussion related to guidance for poultry workers or responders to low-path and high-path and the areas that we're dealing with as we try to develop and revise these guidelines. As we develop these guidelines, and again, for low-path we acknowledged that there are a lot of unknowns or lack of data on which we have to develop this guidance. I think, again, especially as was documented, there's very little evidence for the human infections with low-path, especially given the fact that the viral load is typically much lower for low-path versus high-path. But again, as was mentioned, given these unknowns and the lack of data we basically default with prolonged direct contact to any AI in an enclosed setting. That's our current rationale for our decisions regarding low-path.

Also, to let you know that we're not developing these recommendations or guidance in a vacuum, we are consulting with both Ag and Health in other affected countries. For example, we are



and remain in close contact with The Netherlands related to their experience and then also with Canada. It's interesting, especially for The Netherlands. Basically we've asked them the same question: Where are you going with low-path and the reasons why. At least at this point their provisional or preliminary guidance for low-path is that they would not use antivirals, but that they would recommend full personnel protective and supervision on compliance. They're also going to be putting into their protocol mandatory reporting and diagnostic evaluation of health complaints. So again, whether that's overkill we don't know, but again, I think that speaks to, what we recognize as the need to partner with, for example, industry, to do these sero-surveys to determine if, in fact, infection is occurring with low-path and if it is, what is the outcome.

We're also discussing whether we should look at low-path H7 and H5 infections and try to see if those infections and outcomes, if they occur, are any different than some of the other H types. So again, there are a lot of questions. There are a lot of issues. Dr. Lee Myers also brought up discussions, which we've been involved with for some time; one of them being funding and the second being, again, in March of this year OSHA came out with their guidance, which, as everyone is aware, when OSHA provides guidance it does carry compliance requirements. So even within the USDA we're trying to determine-how to address and implement these guidelines, especially since now they've been issued by OSHA.

There is another issue brought up by Lisa Delaney - we're in a different situation now with the lack of the influenza vaccine, so we're having to come up with guidance regarding the use of antivirals, given an outbreak of avian influenza at this point and using it prophylactically. Who is responsible for establishing the stock pile of antivirals, maintaining it, and funding it?

So just acknowledge that there are a lot of unknowns, and that guidance is going to be a living document, that it will change based on the science.

With that I'll close with my comment. Thank you.

Coordinator Thank you. We have our next question coming from Joanna Quinn.

E. Gonder

This is Eric Gonder again. I tend to kind of view the situation with the low-path isolates in a little bit of a historical context, I guess. A number of us on this call have been working with low-path for something in excess of 30 years. We have a wealth of cases and I would imagine over the years some billions of poultry affected with LPAI. If I understood you correctly, there's been like nine cases of human disease associated with it, primarily conjunctivitis, all non-fatal. With high-path we've got an unknown attack rate. In the population as a whole we have some idea that there is mortality, but we do not know the instance of sub-clinical disease in the third world.

As a risk manager I have a little difficulty trying to sell myself the idea that low path Avian Influenza represents any more of a risk to humans than either Newcastle Disease or influenza in swine. Now, if we are going to go ahead with viral prophylaxis and full PPE in the event of the presence of low-path Avian Influenza virus I would like to know how this is going to be handled in the live-bird markets where we know there is low-path H7N2, a human exposure, and a largely unprotected situation as far as the humans are concerned. Are those people and workers going to be in PPE all of the time? Are the people going through those markets going to be tracked and offered antivirals? That's the closest thing we have in this country to Hong Kong.

Dr Uyeki

Thank you very much for those comments. I think that your experience and those of your colleagues is extremely valuable. I think that we're in a situation where we're trying to do the best given the circumstances and the knowledge to date, but I think that your input and your colleagues' input, as Dr. Gomez alluded to, will be very valuable in guiding us and helping us go forward. So I can't completely respond to your questions about the live-bird markets and PPE and so forth and antivirals, but I would agree with you clearly in terms of the evidence of human infection with Avian Influenza viruses that in terms of low-path viruses there have not been many documented and in terms of illness the most severe illness has been fever and respiratory symptoms, but not pneumonia. Most of them have been much more milder infection in contrast with H5N1 and so forth. So I don't have a direct response and I don't know if Dr. Gomez or others want to respond, but we do appreciate your comments and experience of your colleagues and we'll keep in mind these are a work in progress.

E. Gonder           What would your guidance to the people running the live-bird markets be if they have an isolation of H7N2? What should they do?

Dr Uyeki            I think your point is quite valid that there have been periodic isolations of low-path viruses in these live-bird markets, as the California caller a while back alluded to outbreaks of H6 and so forth. I think that I can speak from the public health side, but I think from the agricultural side, veterinary health side, clearly it's trying to eradicate or control this problem in the markets. In terms of the people you bring up a very good question. Should these people be in full PPE? Should they be in antivirals? I think at a minimum people need to be followed pretty actively for illness, sort of perhaps on a longer-term basis. As you well know, these viruses are continuing to evolve and we don't know the situation historically, if that will hold true for the future or not. We would really benefit from some scientific studies to better understand the risk and I think that your input from your experience is suggesting that clinical illness is, in fact, pretty uncommon from unprotected close exposure to low-path viruses, but I think it would be great if we could do some more studies to document this.

So I don't have good answers other than to say we really appreciate your comments.

E. Gonder           How would you suggest we conduct these studies without getting into a negative perception of agriculture?

Dr Uyeki            Yes. The issues are very complicated. One of the other problems is that, as you know, many of the people that work in these live-bird markets are immigrants and if someone was to have evidence of antibody to various Avian Influenza viruses, unless we were looking at people who had illness and we had acute and paired, convalescent sera we wouldn't actually be able to know when and where their infections might have occurred, whether it was through exposure in live bird markets or in their countries of origin and so forth. So there are a lot of complications in terms of sorting out confounding exposures and so forth and logistic complications.

The Influenza Branch at CDC has tried to partner up to do some of these studies in the past in recent years and a number of these individuals that work in these markets actually may not be legal residents. So there are a lot of issues that make this very complicated, but I think that these kinds of studies need to be done.

Dr. Hegngi

A little bit of a historical perspective here: I just came back from the USHA meeting and fortunately, I met one of my mentors while I was in Vet school, Dr. Mallison. It was interesting that Dr. Mallison went to the agricultural library over there in Burnsville and provided me with a lot of documentation. It was really intriguing to me just with some of the discussions we're having.

In a lot of the presentations that he provided to me, looking at what is happening now and what we're concerned with and whether this live-bird market has just appeared, it's amazing that everything we're discussing today, the concerns and what, this all was carried on in 1925. These live-bird markets have been in New York, in New Jersey, in any of these metropolitan areas since 1925. I bet you one can go back and look at the history and try to look at it as it's already been mentioned that the LPI still, from all of the effort that has been provided and all of the exposures that we all who are working with the poultry industry have come in contact with, I think still is not something too significant to be implementing severe measures that are kind of not economically feasible. Just a thought.

D. Suarez

This is David Suarez. I guess I had some similar comments. One of those comments is that, obviously, I think everybody agrees that there is a lack of data to know what the real risk is for low-path Avian Influenza specifically and even with highly pathogenic Avian Influenza we're not really sure when we look at each virus that essentially you have to look at each virus differently and so it's difficult to determine what the risk is for a particular virus for human health.. So the question is - are we doing overkill? Obviously, if we have the measures that will obviously provide the most protection, but have we ever done a risk analysis to say what is the actual exposure? Are we investing too much in this one particular issue when there are many other exposures in the live-bird markets or on the farm setting that would be a much better return on value as far as protective equipment or additional things, protective measures?

The last is I'm also a little bit concerned about observational bias. I think from the studies that have been done around the world looking at serology that there does appear to be a much higher exposure of humans to Avian Influenza viruses with no agreement whether there's any clinical disease involved or not. I think the reason that we may think that high-path Avian Influenza viruses are more likely to be

involved in human infections is an observational bias because it's hard to ignore dead or dying poultry and it's easier to recognize an association of human disease when you're also having concurrent avian disease; whereas with the low-path AI situation where you're not having necessarily any poultry disease, at least severe poultry disease, you're not necessarily associating that with clinical disease in humans.

Dr Uyeki I completely agree with all of the points you just made and I think that in the process of developing these guidelines, we would certainly appreciate the input of the people on this call who have spoken and those who have not. We welcome those and I think that we need to partner and make this a team effort. So I appreciate your comments.

Dr. Marano We have time for a few more questions and then we need to wrap up.

Coordinator Thank you very much, Ma'am. We have our next question coming from Michael Cobb.

M. Cobb Yes. I was interested in FSIS and whether they're looking at changing the poultry product inspection regulations at all to remove some of the exemptions that poultry has that red meat does not, whether it's the 20,000 birds or under a year or 1,000 birds or under or this live-bird market retail exemption so that they might address some of these concerns or they might have inspection over these small operators that we don't have in red meat.

Dr. Holt I'm not aware that we're doing that. Maybe if you would look at the slide you might want to e-mail me that question because it is possible our policy people are looking at that. I'm not aware that we are. I mean basically right now we're not seeing AI as an issue related to food safety, which is our primary focus.

Coordinator Our next question comes from James Barton.

J. Hahn This is John Hahn, a veterinarian with APHIS Vet Services and I served as one of the liaison veterinarians with the task force in Canada, the USDA liaison with Canada. On the outbreak there they had some interesting problems that came up or concerns about how to deal with it. They did put their workers that were exposed on Tamiflu and they said one of the problems they were starting to have towards the end was that they had timed out on the amount of time they could take Tamiflu, which sort of relates to what I think David Hensler was saying

earlier. They told them they could only be on the Tamiflu four to five weeks and then they couldn't be on it for another year. That was starting to create personnel problems with regards to having adequate personnel to actually go out and fight the disease. Do you have any comments on that? It certainly ought to be kept in mind.

Dr Uyeki

I'm not sure I understand what the work restrictions were or the reason why they could not be on it for longer than four or five weeks and so I can't answer that question, but there certainly have been studies looking at human influenza where people have been on chemoprophylaxis with oseltamivir or Tamiflu and other antivirals for two or three months. I'm not quite sure I understand what the policy was in Canada with that H7N3 outbreak because there shouldn't be any kind of long-term side effects of oseltamivir. I don't know how to answer your question.

J. Hahn

I just know that that was their guideline that they were working under.

Dr Uyeki

I'd be very interested in learning more about that and I'd be happy if you could share that with me. I'd be interested in looking at that.

J. Hahn

I'll give you a call.

Dr. Marano

Do we have another question?

Coordinator

Yes, Ma'am, coming from Mr. Tom Gomez.

T. Gomez

Regarding the question regarding the live-bird markets, again, it comes down to, as was mentioned, trying to determine what that exposure risk is. The guidance that we developed in February of this year was developed because of the events in southeast Asia. Following our outbreak of high-path AI in Texas, we tried to define or identify at least two categories of risk for individuals. One of those categories were persons that would have prolonged direct contact with poultry. That would be essentially our first responders or the on-farm poultry workers. For the second category, which was employees in the live-bird markets, they would fall under a category that would be a more routine, occupational contact with poultry, contaminated surfaces, or equipment. These individuals would have a less intense or prolonged exposure, and therefore would not fall under the requirements or the guidance for PPE and/or antivirals, etc.

It's one of these areas where guidance was made in the absence of strong data or other information. We developed a risk categorization of exposure to try to make that separation of who needs to be protected with personal protective equipment, antivirals, etc. So again, we definitely need the studies to inform development and revisions to this guidance. Thank you.

Dr. Marano Thank you, Tom. Do we have any other questions?

Coordinator Yes, Ma'am. We do have another question coming from Richard Slemmins.

R. Slemmins Yes. This is Dick Slemmins at Ohio State. I'm sorry I got in late and you may have discussed it already, but looking for sero-prevalence of influenza specific antibodies to H5 and H7 in humans it seems like the initial survey wouldn't require the acute and convalescent sera. Is there any evidence on what the sero-prevalence is out there in people with contact with infected birds? Specifically for the United States low-path H5s and H7s viruses.

Dr Uyeki We have not done those studies in the U.S.

R. Slemmins So really you wouldn't need the convalescent sera on your initial surveillance, would you?

Dr Uyeki That's correct, but I guess the issue is that if your study was among people working at these live poultry markets or even individuals working on commercial poultry operations, if a substantial proportion of that study population were immigrants it might be difficult to know when the exposure could have occurred. Just having detectable antibody would not indicate when infection occurred and maybe the infection occurred ten years earlier. It might not necessarily be temporally related to working in a farm or in a poultry market. So it can tell you one thing, but you're right; it's a starting point.

R. Slemmins But if they're negative it doesn't make any difference.

Dr Uyeki If it's all negative that's correct; then it suggests that the risk is low. So you're right, but we actually have not been able to do those studies in the U.S. I think that we would be very much interested. They are very difficult, complicated serological assays to do. It requires microneutralization tests and then confirmatory Western Blot assays

and repeated testing. But nevertheless, I think if we could do some of these studies in the U.S. it could shed some light on this issue of the risk of low-path virus avian-to-human transmission.

Dr. Marano I think we have time for one more question and then we'll need to close the call.

Coordinator Thank you, Ma'am. Our last question comes from Lee Myers.

L. Myers Really just a comment and not so much of a question: I'd like to thank you, Dr. Marano, and your colleagues for spearheading this Webcast conference. I think it's been very enlightening. I would encourage this type of discussion to continue. I think we've raised a lot more questions, perhaps, than we have answers. As some of these documents, whether they are guidelines or programmatic policies, I would encourage us to establish a very conscious effort of including all of the multi-disciplinary subject matter experts that could have great impact and insight in developing these guidelines. So I really appreciate this Webcast and would like to encourage some type of institutionalized manner that we could continue and expand as we walk through these very difficult issues that could have tremendous impacts on our international trade, our domestic markets, animal health, public health that cross so many sectors. Again, thank you for spearheading this and please let us know a way that we can continue in more of a formalized manner.

Dr. Marano Thank you, Dr. Myers. We appreciate that feedback. We also felt that the this call raised our awareness of issues that we really need to take back to the table and work with health departments, agriculture departments and industry representatives to hammer out answers to some of these difficult questions.

With that, we have a slide up on the screen now that gives you two pieces of information: One is there will probably be a number of people who were not able to attend either today's presentation or all of today's presentation. All of these presentations can be seen starting tomorrow at this address that's posted on the slide and the transcript of our discussions will be available in about five to seven days at that same location.

If you have specific questions pertaining to each of the presentations, please e-mail them to the speakers directly. However, if you have



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comments that are more general, that don't fit in either of the specific categories, please e-mail them to me. My e-mail address is at the bottom of the slide that you got announcing this Web site - it's nmarano@cdc.gov. I will be happy to forward them on or collate the questions so that we can develop an organized strategy for responding to your questions and some of the issues that you raised. With that, I'd like to thank the audience for attending and giving up two of your precious hours to spend with us, thank our speakers, and thank those who assisted in answering questions, for being available on the call today. Thank you very much and good-bye.

Coordinator

Thank you, everyone, for joining today's conference call. Have a good afternoon. You may disconnect your lines at this time.

For more information, visit [www.cdc.gov/flu](http://www.cdc.gov/flu) or call the CDC Flu Information Line at (800) CDC-INFO (English and Spanish) or (800) 243-7889 (TTY).

November 3, 2004

Page 49 of 49