SUMMARY
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INFLUENZA VACCINE SHORTAGE

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***Please note:** Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases; therefore updates may be forthcoming elsewhere on this website, through publications such as CDC's Morbidity and Mortality Weekly Report or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations*

OVERVIEW:

Because of an urgent vaccine supply situation, CDC, in coordination with its Advisory Committee for Immunization Practices (ACIP), has issued interim recommendations for influenza vaccination during the 2004–05 season. These interim recommendations were formally recommended by ACIP on October 5, 2004, and take precedence over earlier recommendations. The following conference call followed.

This October COCA call will be focused on influenza and this week's vaccine statement. It is just by chance that the news of our lowered vaccine supply was announced two days ago, thus we are honored to have two physicians, both CDC medical experts, to speak to us today:

> Dr. Strikas has worked on adult immunization issues, particularly influenza and pneumococcal vaccines, and pandemic influenza preparedness in response planning. In addition, he was also a physician trainer, and directed smallpox preparedness and response activities, all with the National Immunization Program, known here as NIP at the Centers for Disease Control and Prevention. As of May 2004, Dr. Strikas is the Associate Director for Adult Immunization in the Immunization Services Division at NIP.
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> Dr. Tim Uyeki is the medical epidemiologist and pediatrician in the Influenza Branch. He works on epidemiology prevention and control of influenza in the United States and worldwide, and he has extensive field experience investigating influenza outbreaks in the United States and internationally. In fact, Dr. Uyeki has participated

in a number of emergency infectious disease investigations in other countries, including Ebola, SARS, and avian influenza. Dr. Uyeki will begin.

PART I: Dr. Timothy Uyeki:

CURRENT INFLUENZA ACTIVITY

- Currently, there has not been very much influenza activity in the U.S.
- Summer is typically a low season (in the U.S.), but we do occasionally hear of sporadic influenza outbreaks. During our summer, it is winter in the Southern Hemisphere
- In the Southern Hemisphere, much of the influenza activity has been due to influenza A H3N2 viruses
- There has been very sporadic activity of influenza A H1N1, or influenza type B viruses. We have not heard about any unusual human influenza viruses that have been circulating lately
- We cannot predict how severe this influenza season is likely to be, nor can we predict when it will peak
- We will have an influenza season, and the typical influenza season peaks sometime between November and April in the U.S.

ENHANCED URGENT SURVEILLANCE

- Last season CDC initiated Enhanced Urgent Surveillance for pediatric influenza-associated deaths on a national basis
- We asked state health departments to report to CDC any deaths in a child who is a U.S. resident, age less than 18 years old, with laboratory evidence of influenza virus infection. This could be through any one of a number of different tests for influenza virus infection, including rapid diagnostic tests, immunofluorenscence, and viral culture
- Some autopsy specimens on previously unexplained deaths were sent to CDC and tested by special means that our pathologists can do to identify influenza virus infection.

This is preliminary data, and this data is subject to change as we are trying to conduct our final analysis this summer and fall. For the 2003-2004 influenza season:

- 153 pediatric influenza-associated deaths were reported by 40 states to CDC. The median age was three years
- Sixty were age less than two years, and 96 were age less than five years, approximately 60 percent.
- Very few of these children had been vaccinated with influenza vaccine last season. We do not know how this data compares with any other season because we have never conducted any kind of surveillance or pediatric influenza-associated death

In addition, most children and most adults who acquire influenza virus infection are never tested, and so there is no national data about how many laboratory-confirmed cases of influenza there are each season. And we do not know anything about how many laboratory confirmed influenza- associated deaths there are each season, so this was really the first season that we had done such surveillance. A previous modeling study estimated an average of 92 deaths attributable to influenza occurred each year among children less than five years. However, that just was a modeling study.

Starting with the 2004-2005 season this fall, pediatric influenza-associated deaths are now a nationally notifiable condition reportable to CDC. Again, these would be any U.S. citizen less than 18 years old who dies with evidence by laboratory testing of influenza virus infection.

ANTIVIRALS

There are prescription antiviral medications that can be used for treatment of influenza. It is important to realize that these must be prescribed by a physician, and for ideal benefit, they should be started within the first 48 hours of illness onset. If an adult or a child has been sick for five, six, seven days with influenza illness, antiviral medications have very limited benefit, if any.

There are four approved antiviral drugs for treatment of influenza:

- **amantadine**
- **rimantadine**
- **oseltamivir**
- **zanamivir**

They all differ by:

- Approved age groups
- Different trade names
- Cost
- Route of administration
- Side effects that have been reported with them.

Antiviral medications available to treat influenza.

- They are for treatment of uncomplicated influenza
- For further details see the 2004 Advisory Committee on Immunization Practices. Recommendations for the prevention and control of influenza were published by CDC and ACIP in May of this year and are available on the Web.

Rapid diagnostic tests are also available for the diagnosis of influenza, as well as other tests that are available in the hospital laboratory setting.

- The gold standard for diagnosis of influenza virus infection is viral culture:
    - obtaining respiratory specimens
    - generally a nasal pharyngeal aspirate
    - nasal pharyngeal swab, or a nasal swab, that is sent to a laboratory and placed in tissue cell culture to try to grow influenza viruses

- There are other methods that can detect influenza virus infection in a shorter time, because viral culture takes two to seven to ten days to get a result.
    - These are called are rapid diagnostic tests.
    - There are ten different tests available. Nine of those tests are what I would call rapid antigen tests. These can yield results in 10 to 30 minutes, and that can be useful for management of patients and also for public health purposes to detect influenza outbreaks in institutions, such as nursing homes.

There are limitations to rapid diagnostic tests:

- The sensitivity of these tests is not as good and may produce false negative results
- Immunofluorenscence, also called direct florescent antibody staining, or indirect florescent antibody staining, can also be used generally in a hospital laboratory setting to diagnose influenza virus infection. These methods take approximately three to four hours.

AVIAN INFLENZA – CURRENT UPDATE

There has been a widespread, unprecedented outbreak of avian influenza virus type A, subtype H5N1 in Asia. There have been nine Asian countries that have reported outbreaks among poultry. Seven of these countries have reported outbreaks in 2004 that, at least to our assessment, it's unclear how well controlled those are:

- China
- Laos
- Vietnam
- Cambodia
- Thailand,
- Malaysia
- Indonesia

- In December of 2003 and January of 2004, South Korea and Japan reported outbreaks of H5N1 among poultry. Our assessment is that those outbreaks were limited and have been controlled. However, the outbreaks among poultry in China, Laos, Vietnam, Cambodia, Thailand, Malaysia, and Indonesia were widespread involving domestic poultry—that is chickens and ducks—in small farms and large farms and backyard farms. They are widespread through most of these countries.

- From the human public health side there have been millions of people exposed to sick or dead poultry in these countries. Since December 2003, a total of 43 confirmed human cases of avian influenza A H5N1 have been reported from two countries: Vietnam and Thailand. Of those 43 cases that have been confirmed, 31 have died, for a case fatality proportion of 72 percent. In Vietnam there have been 27 cases with 20 deaths. In Thailand, there have been 16 cases with 11 deaths.

- Further human H5N1 cases may occur in these countries because highly pathogenic H5N1 viruses are widespread among poultry in these countries, and people are in contact with them. CDC and the World Health Organization (WHO) have published recommendations about protection of people involved in the culling of poultry—that is killing of poultry, slaughter of poultry—during these outbreaks. And also about guidance for state health departments for assessing travelers who have returned from these countries who might have had poultry exposure and might have severe respiratory illness.

- At this time there is no evidence of efficient and sustained human-to-human transmission of H5N1 viruses. Recently, you may have heard, in Thailand there has been reported probable cluster of human-to-human transmission of H5N1. However, this was viewed as a dead-end transmission; that is transmission is likely to have occurred from a child who died who had poultry contact, but was not confirmed to have H5N1 yet, and she was cared for in the hospital by her mother. The mother had no contact with poultry. The mother had a confirmed case of H5N1 and died.

- The aunt, who also cared for the girl, might have had poultry contact, she is also a confirmed case. The son of the aunt got sick, but testing is underway. Both the aunt and the son of the aunt have recovered, but the original index case, who was an unconfirmed but suspected case, died and her mother died. We are extremely concerned about a potential H5N1 pandemic. However, at this time, the viruses have not acquired the capacity to efficiently transmit from person to person, and have sustained transmission. Therefore, at this time, there is no evidence for sustained human-to-human transmission.

- There is no human H5N1 vaccine available. There is work being done to try to develop a vaccine. Contracts to produce experimental vaccine for clinical trials have been awarded, but at this time, there is no H5N1 vaccine that is available.

- There are antiviral drugs that are available for treatment of influenza, as well as chemoprophylaxis for prevention of influenza. Those same drugs, amantadine, rimantadine, are available, but the viruses in Asia, isolated from humans with confirmed H5N1, have been shown to be resistant to amantadine and rimantadine. Therefore, CDC has recommended the use of oseltamivir for patients with avian influenza virus infection, or who might have exposure to avian influenza virus infection.

Q&As WITH DR. UYEKI:

Q: Do you have any data either in vitro or in vivo on the efficacy of oseltamivir against the H5N1 strains?
A: *What I would say is that in clinical use, there are absolutely no controlled trials. Oseltamivir has been used both in Thailand and in Vietnam, but the majority of cases that have presented have not come in within 48 hours of illness onset. Some patients have presented at day two, day six, day seven, and therefore, they are still receiving treatment, but the benefit is unknown.*

In terms of sequencing of these viruses, these viruses have been shown to have the characteristic mutations consistent with amantadine and rimantadine resistance. But when they've been looked at in terms of neuraminidase inhibitor resistance, they've been shown to be susceptible to neuraminidase inhibitors. Therefore, that is the basis of our recommendation to use oseltamivir. I can't provide you with much more than that. Obviously, we would like to have better data. But, consistently, the virus is isolated from poultry in both Thailand and Vietnam and humans have been resistant to amantadine, rimantadine, but sensitive to oseltamivir. The viruses from other countries in Asia are slightly different. That's the best I can answer your question.

Q: Actually, I have two questions; 1] Do you think this limited human to human transmission is enough to suggest that if we see patients with possible avian flu in this country, we need to keep them on airborne pre cautions, or would droplet precautions be sufficient? 2] Will the tests, and the rapid diagnostic tests that we have here, detect the H5N1?
A: *The second question first:* ***Rapid diagnostic tests for detection of influenza****. There are ten available right now in the U.S. Six of these detect and distinguish between influenza A and B; the others do not. What those tests do, they are antigen tests and they detect viral nucleoprotein, so all that they can do in terms of influenza A viruses is detect the type. They cannot determine subtype. If you are testing a patient—and we certainly hope this doesn't happen, but it sure could occur in the future—where there are human influenza A viruses, H1N1 or H3N2 viruses circulating in the community, and avian influenza H5N1 is imported, the use of a rapid diagnostic test cannot distinguish between Influenza A H5N1 or H3N2 or H1N1. And actually, this is a situation that we have, fortunately, not experienced in this country. But in Thailand and Vietnam, clearly, there have been H3N2 viruses circulating during this calendar year, at the same time that H5N1 viruses were infecting humans.*

There are obvious limitations to rapid diagnostic tests for detection of human influenza A viruses, but they are further confounded if H5N1 viruses are circulating. The positive predictive value to detect H5N1 is really going to drop, depending upon the prevalence of H3N2 or H1N1 viruses. They can be used to detect influenza A virus infection period, and they have been shown to detect this virus, both use in the field and in the laboratory setting, but they can't determine what it is.

One of the limitations that we have or we are concerned about with these tests is that viral shedding of H5N1 is a little bit unclear. In some patients, it may be, in fact, less than in a typical human patient infected with human influenza A viruses and therefore the sensitivity of these tests to detect H5N1 may be actually even lower than for detecting of human viruses. And already, we have some sub-optimal sensitivities to detect human viruses.

***A:** you're the first question: **Airborne precautions**. At this time, there is really no evidence of much human-to-human transmission. If we go back and look at all of the H5N1 investigations that have been done, and the outbreaks starting back in Hong Kong in 1997, in one epidemiological study in Hong Kong, there were two healthcare workers who were exposed to H5N1 patients, and two healthcare workers seroconverted out of hundreds that were actually tested, and there were no further transmissions after that.*

If we look at family clusters in Vietnam and Thailand over the past year, as well as in 2003, a family in Hong Kong had traveled to southern China and there were two family members with confirmed H5N1. We have circumstantial evidence, and we have suspicion of person-to-person transmission, but we have no conclusive evidence. However, the situation in this family cluster in Thailand is a little more convincing. Although, in the index case, that case has not been confirmed to have H5N1 yet, due to a limitation of clinical specimens.

At this time, I think the current recommendations for H5N1 are similar to the SARS infection control guidelines. Although we believe that most of transmission of avian H5N1 viruses is similar to transmission of human influenza viruses, in which large droplet transmission is really the modality of transmission, we are recommending the same as the SARS guidelines; droplet, contact, and airborne precautions. However, this could potentially—obviously in a pandemic—overwhelm a hospital's ability to deal with airborne precautions.

There is really no evidence other than this family cluster, and all we can say is, it's a probable case of person-to-person transmission. There is no other evidence at this time. But as you know, these viruses are continuing to evolve and the situation for genetic re-assortment with human influenza A viruses is a theoretical risk and could occur, and that would be a devastating consequence, potentially for public health.

<u>PART II</u> Dr. Raymond Strikas

CURRENT VACCINE SUPPLY
(Information from abstract of interim influenza vaccine recommendations for 2004-2005)

- On October 5th, CDC was notified by the Chiron Corporation that none of its influenza vaccine Fluvirin™ would be available for distribution in the U.S. for this influenza season, 2004-2005

- The company indicated that the Medicines and Healthcare Products Regulatory Agency, commonly abbreviated MHRA, in the United Kingdom, where Chiron's vaccine is produced, has suspended the company's license to manufacture the Fluvirin vaccine in its Liverpool factory for three months, thereby preventing any release of this vaccine for this influenza season.

- This action reduces by approximately one-half the expected supply of the trivalent inactivated vaccine, or the flu shot, available in the United States for this year. Chiron had expected or promised, many say, to deliver 46 million to 48 million doses of vaccine after they announced what they thought was a delay in their production, down from an original 50 million dose estimate, and now there will be no vaccine as best we can tell.

- The remaining supply of the vaccine available in the U.S. is expected to be, as of yesterday, about 55.4 million doses. That's a little more than is written in the recommendations, though not significantly different.

- Aventis announced yesterday they could produce an additional million doses. The timing of that is a little uncertain. And the MedImmune Inc. hopes to produce an additional million doses, as much as that on top of the 1.1 million doses that they had originally projected. That means, say if we are using 55 million as the estimated vaccine available today, last year 83 million doses were estimated to have been distributed. Most of that was expected, and we believe was used.

- As best we can estimate, only about 15 million of that 83 million might have been used in non-high risk people; that is in populations not included in the high risk groups listed below

- That leaves 68 million people who got vaccinated who were in the highest groups or priority groups listed below, and 55 million doses of vaccine. Thus, there is an instant shortfall even at these rough calculations, and that leads us to the serious problem we have.

PRIORITY GROUPS

- In consultation with the Advisory Committee of Immunization Practices (ACIP), realizing the shortfall, CDC and ACIP issued interim vaccine recommendations for this year on October 5th and these take precedence over the earlier recommendations issued in the spring.

- A number of priority groups who are listed for influenza vaccination, and in summary, all of the people identified earlier as at high risk of complications of influenza, are still a priority group. The groups that have been excluded are largely the contacts of those people with two exceptions.

- Within the priority groups at high risk of influenza complications who should still receive influenza vaccine are:

    - all children age six months to 23 months
    - adults age 65 years and older
    - persons age two to 64 years with underlying chronic medical conditions
    - all women who will be pregnant during the influenza season
    - residents of nursing homes and long-term care facilities
    - children age six months to 18 years on chronic aspirin therapy

- The priority groups, non-high risk who were still included as important contacts of high risk people, are the healthcare workers involved in direct patient care. And we have had questions about, what's direct patient care? We are working on a better definition, because all it says is direct patient care.

- The working definition that we have used informally is hands-on care. The receptionist in the office or in the medical ward of the hospital wouldn't fit that definition. People who go touch patients would, and therefore, phlebotomists right now are in the definition. So you can use those examples, however, you need to say to people if they press you on this, "These are working definitions and CDC hopes to issue firmer direct language as soon as possible."

- The last group of contacts is out of home caregivers and household contacts of infants less than six months of age. This is the only group of non-healthcare work contacts selected for vaccination for two reasons: Those infants are extraordinarily high risk of hospitalization, regardless of their health status related to influenza infection, and those infants cannot receive vaccine themselves, it's not licensed for them and they cannot receive antiviral drugs. So they have no means of protection except to protect those people around them, and therefore, they were singled out to have there household contacts and out-of-home caregivers vaccinated. We encourage folks in these priority groups to search for vaccine locally if the healthcare provider doesn't have it available.

- The intranasal vaccine, FluMist, should be encouraged for healthy persons five to 49 years of age, who aren't high risk, aren't pregnant. And that means the household contacts I mentioned, and healthcare workers can all receive FluMist with the exception of healthcare workers who are taking care of seriously immunocompromised people in a protective environment. A classic example here is a bone marrow transplant patient in what used to be called reverse isolation.

- We recommend that children less than nine years who are high risk should receive at least one dose of vaccine. You shouldn't hoard vaccine for their second dose, because many of them need two doses, and one should vaccinate those kids with the vaccine available. One dose will offer more protection than zero doses, though not, perhaps, as much as two doses.

If people are not included in these priority groups, we should inform them about the urgent situation we have and ask them to forgo vaccination for right now. If more vaccine becomes available later, perhaps, we can loosen these recommendations, but that is where we are. CDC is working aggressively with Aventis Pasteur and MedImmune, the companies that still have vaccine for sale and distribution, to see what is feasible about reallocation of their vaccine that hasn't yet been distributed from non-high risk, non-priority groups to priority groups and there are conversations ongoing. We hope to have a plan very quickly.

Q&AS WITH DR. STRIKAS:

Q: Has any Chiron vaccine been distributed in the United States?
A: *As far as we know is, no. Some of Chiron's vaccine is in the U.S. It's embargoed. It is not to be distributed until we get clarification from the FDA. And frankly our estimate at this point, is that it is unlikely to be distributed or used; though the FDA is still concluding its conversations and investigations in the U.K., and those won't be completed until the weekend.*

Q: Are we going to import vaccine from other countries?
A: I don't know. This is something we're looking into. I personally think it is unlikely to be able to do it in a timely way, but we are looking into it.

Q: Can one use a half-dose?
A: *Some of you may have heard that there have been studies done as recently as several years ago, of using a half-dose of the current vaccine. The data from the study published in 2002 in Vaccines by NIH, FDA and CDC, suggested that a half-dose in healthy adults through 49 years of age, does work about as well as a full dose does, that is seven and a half micrograms of hemagglutinin versus 15. We have no data, though, with the current vaccine in the priority groups we're talking about, with the exception of the healthy healthcare workers, which is a small number of people in these priority groups. Getting a half-dose licensed for use this year merits some further conversation, but I think that is unlikely, and the most FDA might do is to say that those healthcare*

workers less than 50 years of age who are otherwise healthy could receive a half dose, which would be a help, but we don't know yet.

Q: What are you recommending for laboratory workers who are processing the specimens for viral logic diagnosis of influenza? Should they receive the vaccine?
A: They're not included in the risk groups. I can't quantify the risk to them of acquiring influenza. You may know the data better that I do. The response is: They're not listed in the priority group unless they meet one of the other standards.

Q: I should have mentioned, we had a recommendation for people of 50 or 64 years, regardless of health status to be received vaccine. However, if those people are healthy, under 65 years of age, they are not in a priority group either. [Dr. Uyeki] Do you have any comment on the risk for those people of acquiring influenza?

A: I really cannot comment on the risk. What I would say is the people who actually obtaining the respiratory specimens, whether it is a physician, a nurse, a nurses assistant, or whoever, those people are obviously hands-on, very close contact with a symptomatic patient, and are clearly at risk of transmission. But a laboratory worker handling clinical specimens; we have not heard about such a risk. And so far it remains theoretical, at least anticipating a potential question about someone handling specimens potentially infected with H5N1. To my knowledge, there has never been any documented transmission to laboratory workers of H5N1.

If you have such a case, or a suspicious case, as someone who is critically ill, a returned traveler, or an immigrant with poultry exposure, those specimens really should be processed under Biosafety Laboratory Level 3; BSL 3 level conditions, but I just simply can't comment about any increased risk for someone handling specimens in a laboratory. I would clearly want them to take precautions (gloves and so forth), but I can't comment on the risk.

Q #1: Yes, I have a couple of questions, but they are going to be quick—regarding the live attenuated [vaccine] and the healthcare workers. Are we being given basically, a little more wiggle room this year to think about ways, programmatically, that we could bring that into certain areas within the hospital?

Q #2: Fifty some-odd million doses is a lot of doses to get pulled from the market, and I'm wondering if you can give us any sense of whether it would be possible to re-evaluate whether the same concern that had the vaccine pulled in the first place is really equally distributed across all 50 million doses; or whether there might be a consideration that at least some portion of this is salvageable? "Is the Chiron vaccine salvageable?" I realize you probably can't say instantaneously today, yes. But whether the concerns about why the action was taken in the first place, might, in fact, not taking a more detailed look at the situation, really apply to all 50 million doses. Or is this just so black and white that there really is no likelihood that any portion of the Chiron allotment is salvageable?

A: Yes, I don't know the details to the second question, where all that I am told is that it's unlikely to be salvageable because the regulatory authorities felt that the factory was just not producing vaccine in a sanitary way, whatever that means. Serratia bacteria have been implicated as contaminates; I've seen it in the press. And the secretary of Health and Human Services, Mr. Thompson, acknowledged yesterday that he's got the team out there looking into it. I guess we feel we've done everything possible to look at the issue and understand it.

Because this is a big problem this year, but we definitely want to get these folks back on line for next year and making vaccine. This year is an immediate problem and it's very important, but the long-term is even more important. And if there are things that need to be fixed that are problematic, we need to do everything possible to

get this company back on line. There are two issues here; the immediate and the later. All that I can say is what the secretary said: "It is unlikely that any of that vaccine will be available." They are holding out hope to say not ever, never, but unlikely and that's all I know. We may know more come [soon], but I'm told that the final visits, inspections, and conversations will be completed through the weekend. Regarding healthcare workers, what I said about healthcare workers is exactly the language, published in more detail in the ACIP recommendations from . . . [May 28, 2004]

The recommendations for which healthcare workers can be vaccinated with live vaccine are the same as in the May 28th. That has not changed. Therefore, if the healthcare worker fits the license criteria for FluMist, we encourage healthcare workers to receive that. And the ACIP recommendations, again the only exclusion in terms of what work the healthcare worker does is taking care of severely immunocompromised people in a protective environment or again, reverse isolation, assuming the healthcare worker is otherwise without high risk medical problems and is not pregnant. Those recommendations are detailed in the earlier statement and we've reiterated that, although I agree, very briefly, in the interim recommendations. [See page 17]

Q: We have had discussion with the company that makes FluMist and it's our understanding that they are not releasing any FluMist for distribution to healthcare organizations until, I guess, after some directions from the CDC. Can you comment on that, please?
A: Not directly. First of all, they were waiting for some final clearance and it was felt to be routine, not a problem from the FDA to release their vaccine and that should be happening very quickly. We are in conversations with them because it has been reported in the press, and we heard yesterday: 1] They may make some more vaccine. 2] The military may buy a lot of their vaccine several 100,000 doses. There should be hundreds of thousands of doses available, which is not a heck of a lot across this country and they propose to make some more. But I think they were waiting to have some direction about what the military wants to do in particular. CDC is part of that conversation, but somewhat indirectly. We have a contract with them for public health entities to buy vaccine. But they can do so independent of direction from us, and we've encouraged the public health [departments] to buy vaccine, but folks simply aren't used to that product and on the public health side, they haven't bought any as yet that I know of. That is about the best that I can answer that question.

Q: It is my understanding that 30 million doses have already been shipped from Aventis Pasteur. Is there going to be a reallocation of vaccine that has already been shipped, or is someone going to be in charge of that reallocation or will it happen?
A: Discussions are underway with Aventis, as well as MedImmune on how best to use the existing vaccine. Right now, it seems unlikely that vaccine that has already been shipped; that is purchased and shipped to end users is going to be taken over by the government or any such thing. At a minimum, all of those customers who've already received vaccine, have it in their possession from Aventis and MedImmune—if that's happened, then I'm not aware of it—are going to be reminded of who the priority groups are for this year, urged to target vaccine to those groups and not to others, and if they end up with extra vaccine, to work with colleagues and public health to reallocate it. But at this time, I don't think this is going to chang. But stay tuned, as there is no plan to take possession of or pull back vaccine that has already been shipped from Aventis or MedImmune to the government or back to the companies for redistribution.

What we're talking about is the small amount of vaccine, which has not yet been shipped, or firmly allocated to customers and see what one can do with that, where one can learn if these folks who have ordered it have targets in the priority groups, and if they don't, ask them to reduce their order; that sort of thing. It's a process working through the vaccine company at the present time, and that's where we are. You can quote me as to what's going on today, and I don't have any inkling that that will change, but I can only tell you what is going on today.

Q: In the indication of which healthcare workers should <u>not</u> get the intranasal vaccine, [the information] said something about severely suppressed oncology patients. In the notice that came out on Tuesday, it made it sound as if it was a little bit broader than what was in the ACIP records, and I don't know if that was intentional.
A: That is not the intent. Clearly the intent is to echo the ACIP recommendations. Obviously, we tried to make this thing brief so people could digest it quickly, but I'll emphasize in my understanding from listening to the discussion it was meant to clearly be consistent with the earlier recommendations, and if the abbreviated language seems to migrate from that, then go back to the original recommendation.

Thank you. A reminder that there is a multitude of information available on the Web at www.cdc.gov/flu. Questions can be answered by e-mailing: coca@cdc.gov and clinician phone calls are quickly handled by our 24/7 Clinician Information Line: 877.554.4625.

Post Script on H5N1 from Dr. Uyeki:
Please make a note that the majority of the confirmed human H5N1, again 43 cases, 31 deaths, in Vietnam and Thailand, have been among children and young adults who have had ***direct contact*** with sick or dead poultry. CDC has been notified of a number of returning travelers coming from different Asian countries since earlier this year with respiratory illnesses. All of these cases that I have been involved with have been among adults. And some of them have had uncomplicated symptoms, just high fever, respiratory symptoms, some have had severe pneumonia. The majority of these cases have had human influenza virus infection. The take- home message is that we are always going to have travelers, returned Americans or people from other countries coming back, probably with respiratory illnesses. Influenza, particularly human influenza, should be very high in the index of suspicion, the differential diagnosis for such travelers.

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