Novel Influenza A H1NI Investigation Update and Guidance for Clinicians

Timothy Uyeki, MD, MPH, MPP and Anthony Fiore, MD

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Coordinator: Welcome and thank you for standing by. At this time all participants are in a listen-only mode. To ask a question during the question and answer session, please press star 1 on your touchtone phone. Today's conference is being recorded. If you have any objections, you may disconnect at this time.

I will now turn the meeting over to Mr. Justin Williams. Sir, you may begin.

Justin Williams: Good afternoon and welcome to today's COCA Conference Call on the Novel Influenza A H1NI Investigation Update and Guidance for Clinicians. We are very excited to have Dr. Anthony Fiore and Dr. Tim Uyeki present on this call.

Dr. Fiore is a Medical Officer and Dr. Uyeki is a Medical Epidemiologist in the Influenza Division here at the Centers for Disease Control and Prevention in Atlanta, Georgia.

We will not be using a Power Point Presentation and there will be no continuing education credit contact hours available for this call.

I will now turn the call over Dr. Fiore and Dr. Uyeki.

Tim Uyeki: Good afternoon. What we're going to do is a give a very brief overview of the situation, briefly review some of our guidance particularly on antiviral treatment and chemoprophylaxis and then open it up for questions. And so I will just start with giving a little bit of an overview on the national picture.

So what we have been - what states are doing now is reporting probable and confirmed cases to CDC and we are posting these Monday, Wednesday, Friday. And so what I'm going to go over are data, at least the latest data that's been posted on our website, and these are being updated Monday, Wednesday, Friday, again.

So our latest data shows 6,764 confirmed cases from 47 states plus the District of Columbia. And I'm sure tomorrow those numbers will go up a lot more.

Now, prior to a few weeks ago, CDC had been confirming all cases of Novel Swine-Origin Influenza A H1N1 virus infection. However, now that almost all state health departments have this capacity, as well as some other laboratories, most of the confirmation for this new virus infection is being done at the state level.

CDC continues to confirm some cases, as well, that are in clinical specimen submitted by state health departments.

Now, in terms of hospitalizations, we have had hospitalizations that have increased in the last several weeks and overall this will vary by state. So far roughly the median age is about 18 years and about 50% of the hospitalized cases have occurred among children.

In terms of the median time from illness onset to hospital admission, it's about four days - about four to five days and the median length of stay is also about four days.

In terms of ICU admissions, we are seeing some severe cases hospitalized primary with pneumonia including respiratory failure progressing to the acute distress - respiratory distress syndrome. We have had deaths that have occurred. Most of these deaths have had underlying medical conditions.

In terms of the hospitalized cases, many of these cases have had underlying conditions that are similar to risk factors for severe complications of seasonal influenza, although we are not seeing many elderly patients that have been hospitalized.

So the kinds of symptoms that are being reported are feverishness or the sign of fever, cough, shortness of breath, weakness or fatigue, rhinorrhea, myalgia, chills, headache, vomiting, sore throat. There have been some patients that have experienced diarrhea. Some of these patients have also had wheezing on admission.

In terms of some of the underlying conditions, by far and away, the - if we group them together, underlying conditions that stand out are asthma or COPD. We have had about 20% of the hospitalized cases having diabetes, primarily non-insulin dependent diabetes.

Some patients, about 14% of patients, have had chronic cardiovascular disease. We have had pregnant women cases that have been hospitalized. We have had some patients with underlying neuromuscular disorders.

To a smaller extent, some of the patients that have been hospitalized have had obesity and in particular a substantial obesity, almost morbid obesity and so forth.

So far at least what we have posted on the website we have had ten deaths with confirmed - laboratory confirmed Novel H1N1 virus infection, although that number will go up and we expect unfortunately death to occur.

In terms of the overall epidemiology of the country, we're seeing some regional outbreaks. There are some cities, metropolitan cities that have experienced pretty significant increases in Influenza like illness over the past couple of weeks. That is not true for the whole country.

Again, there are local jurisdictions that are experiencing rather widespread outbreaks. One could argue that there's community-wide transmission occurring in some areas. In other areas there's virtually no activity.

Let's see. I think I'll just stop there other than to say that our preliminary data on some of these hospitalized patients suggests that of the pneumonia patients, most of them appear to have findings that are consistent with viral pneumonia.

We have really seen very, very little evidence of secondary bacterial infection, although there have been a few cases that may have had nosocomial bacterial infection.

The caveat is that most of these - virtually all of these patients are being administered antibiotics upon hospital admission. Not all patients have been administered antivirals right away at admission, but that is increasing and Dr. Fiore will talk about some of our antiviral treatment recommendations.

So I think what I'll do is I'll just stop there and turn it over to Dr. Fiore who will go over some of our more pertinent recommendations for clinicians.

Anthony Fiore: Thanks Dr. Uyeki.

We have had for some time now guidance on use of antiviral recommendations for patients who have infections with Novel Influenza A H1N1 virus. And these recommendations have not changed at this point.

They focus on two groups of people. One is persons that are hospitalized, regardless of whatever underlying risk factors they might have versus that are hospitalized and are suspected or confirmed as having this particular virus infection are recommended to get antibiotic - sorry, antivirals as soon as possible.

And the antivirals of choice in this instance are Oseltamivir or Zanamivir because these viruses are consistently resistant to Amantadine and Rimantadine.

You might recall over the course of this past Influenza season there was the combination therapy recommended because of Oseltamivir resistance and some of the seasonal Influenza viruses. We're not seeing that resistance in the Novel Influenza A H1N1 viruses. So that's the one group of persons to focus on for giving antivirals; hospitalized persons.

The other group are people who have risk factors for more severe infection regardless of whether or not they need to be hospitalized. If they come into an office setting or into a hospital setting ill with what's suspected to be this Novel H1N1 virus infection, they should receive antivirals.

And the sorts of people who have increased risk for Influenza complications include persons - children that is younger than the age of five years old, older children and adults who have chronic medical conditions, chronic pulmonary, cardiac, hepatic, neurologic conditions, things like that and also adults over the age of 65.

So those are people to focus on for giving antivirals to.

What we found with looking at the hospitalization data that we have so far is that many people are actually not getting antivirals. Only about 50% of a recent case series that came from California and was published last week in the MMWR only about 50% of those patients had gotten antiviral treatment and only 5 out of that 30 in that case series had received antivirals within 48 hours of onset.

Now, of course, you can't get antivirals within 48 hours of onset when the timeframe for best benefit is thought to be - if a patient doesn't come in within 48 hours of their illness onset. However, we do recommend antivirals be started as soon as possible after the patient presents, even if it's more than 48 hours after onset.

We don't have data yet on antiviral effectiveness for this particular strain of influenza, but based upon our experience with seasonal influenza, there is some data to indicate that even starting treatment more than 48 hours after illness onset provides some benefit for hospitalized patients.

So it's important to get those antivirals in as quickly as possible and to think about influenza, in particular this Novel Influenza A H1N1 virus, when you see a patient with respiratory symptoms and fever or pneumonia.

Influenza pneumonia, seasonal Influenza pneumonia is well known as a very serious complication of Influenza and that is showing itself to be true also with the limited data we have so far from hospitalized patients with this Novel Influenza virus.

There are also new guidance up on the website from our Division of Healthcare Quality Commission here at CDC having to do with use of facemasks in a variety of different settings.

That guidance on use facemasks in respirators have been sort of scattered amongst the various guidance documents up to now and now they've been condensed into a single guidance document that became available over the weekend and I encourage you to look at that.

There are not actually many changes in that document compared to some of the earlier documents that you've seen, in particular for persons who are providing healthcare. Respirators continue to be recommended for persons caring for patients with known, probable or suspected Novel H1N1 or Influenza like illness.

And that persons - healthcare workers, that is, who are at increased risk of severe illness and those are like the group that I just listed to you a minute ago, those increased risks should definitely use a respirator and also potentially consider temporary reassignment if they're coming into contact with many patients who might have Influenza virus infection.

One more thing that Dr. Uyeki is reminding me and that is going back to the antiviral recommendations, it's important to avoid in children use of any aspirin or aspirin containing products.

And that's something to tell patients but also to avoid using yourself because of the risk for Reye Syndrome, and that's not something we've talked about much in recent years, but it's something of concern to us now. We haven't seen cases of that yet, but there's a well-known association between the use of aspirin and subsequent development of Reye Syndrome in children.

So those aspirin containing products, many of which are available over the counter and patients might not suspect have aspirin in them, people should definitely avoid those products.

And with that, I think we can open it up for questions here.

Coordinator: Thank you. At this time we will begin the question and answer session.

To ask a question, please press star 1 on your touchtone phone. Please unmute the phone and record your first and last name slowly and clearly. To withdraw the question, please press star 2.

Once again, please press star 1 to ask a question. One moment please.

You may ask your question.

Question: Yes, thank you very much for the presentation.

I had a question regarding the use of Tamiflu and the recommendations regarding the non-Novel Influenza virus and the fact that Tamiflu can be resistant to it. How can a provider distinguish - determine whether or not to use Tamiflu knowing that there still is circulating non-Novel Influenza virus circulating?

Anthony Fiore: That's an excellent question and there are communities, as you pointed out, that continue to see some seasonal Influenza viruses circulating.

When you're providing apparent treatment for patients and you can't tell the difference, you're going to have to go with the recommendations that came out last December before this Novel flu showed up and use either Zanamivir or Oseltamivir, combination of Oseltamivir plus one of the adamantane drugs that is Amantadine or Rimantadine.

You can seek confirmation on whether or not this is Novel flu fairy quickly now with the state health department having the capacity to do this testing, so it's - for hospitalized patients. It's possible you might be able to narrow the therapy down at some point into their illness.

But empiric treatments, you're right; you are stuck with having to use either the combination or Zanamivir alone.

Question cont'd: Thank you.

Coordinator: Our next question. You may ask your question.

Question: I had a question regarding the vaccinations status of some of the severe hospitalized cases. I know they've reported that there's been a good number that have been vaccinated, but has anyone distinguished whether they were all vaccinated with the trivalent in activated injectable vaccine or if there were any that were vaccinated with live, attenuated nasal vaccine?

Anthony Fiore: We don't have that information yet.

As you said, we have a relatively small number of patients to look at to see whether there's any effect of seasonal vaccine.

Certainly the immunologic data is not promising for either one of these two vaccines in the sense that the people who have been vaccinated with either the live, attenuated or the trivalent vaccine, don't show rises in antibody pre and post vaccinations to the Novel Influenza A virus.

So from that perspective it's not immunologically speaking, it would not seem probable that you would get much protection.

Question cont'd: I was wondering if the live vaccine has, you know, more of a cell-mediated component to its immunity that wouldn't be measured with standard, you know, HAI assays?

Anthony Fiore: I think that's a good question.

We don't have those data available to us yet. And we'll be looking at that as the virus continues to circulate. But so far relatively few people have been vaccinated who we have - who have been hospitalized and it's not really clear whether the vaccine is providing any effect by either one of the two vaccines.

And as you know, the live, attenuated vaccine certainly a lot less of that ends up being used especially in adults and so we really have very few people to look at to assess your question.

Coordinator: Your next question. You may ask your question.

Question: Yes, is the commercial testing considered sufficiently reliable for surveillance and for therapeutic decision-making?

Tim Uyeki: Could you just clarify what you mean by commercial testing?

Question cont'd: There are now commercial laboratories offering the Swine flu testing in addition to state laboratories.

Tim Uyeki: Right. So our understanding is that some of the large commercial laboratory services are actually using the CDC primer (unintelligible) that's specific so it's real-time RT-PCR, same as what the states are using and the same as what CDC is using. They're using the CDC developed assay.

And so that's our understanding and so we would expect that those results should be the same as, you know, other laboratory - state health department laboratories or CDC. That's our understanding.

In terms of the turnaround time, we can't comment on the turnaround time.

Question cont'd: Thank you.

Coordinator: The next question. You may ask your question.

Question: Hello?

Tim Uyeki: Hi Michelle.

Question cont'd: Hi. Thank you.

A question and I apologize if I missed something you said earlier, in terms of treating with antivirals.

Are you seeing different responses in different age groups and also is there any information on the impact of antivirals and continued of shedding of virus.

Tim Uyeki: So that's a great question.

I don't think we really have any data to talk about clinical antiviral treatment effectiveness at this time for this new virus. Certainly, you know, there are data for seasonal Influenza virus infection, but for this particular new virus, we don't have such data available. I mean, we're very interested in it.

In terms of impact upon viral shedding, similarly we don't have such data available. We are trying to - there are some studies to try to collect such data. It's an important question, but as you probably know with seasonal Influenza virus infection, there are studies that have shown somewhat different results.

So, some studies of antiviral treatment, when administered early, show reduction in clinical signs and symptoms but in fact no reduction in viral shedding, whereas other studies have shown reduction in symptoms, as well as, a reduction in viral shedding.

So again, that's for seasonal influenza. For this virus, you know, we're also very interested in this but don't have those data available.

Question cont'd: Thank you.

Coordinator: The next question. Your line is open. Please check the mute switch on your phone.

Your line is open. Go ahead with your question. Go ahead with your question. Your line is open. I'll clear the line.

This is line, sorry, go ahead. Your line is open. Go ahead with your question ma'am.

Question: Yes.

Coordinator: Go ahead with your question.

Question cont'd: Can you hear me?

Tim Uyeki: Yes.

Question cont'd: Okay, my question is about chemoprophylaxis for healthcare workers. Are there any changes to the guidelines?

Anthony Fiore: No, not since the guidelines that were put out about ten days ago - no, more like two weeks ago at this point. No, there are not changes.

Chemoprophylaxis in general is for - meant for healthcare workers who have had an unprotected exposure to somebody who is suspected of having H1N1 infection - suspected, confirmed or probable H1N1 infection.

Coordinator: Your next question.

Question: Yes, thank you.

Two questions, one, do persons treated with antivirals still develop antibodies or not? And second, what's the status of a Novel H1N1 Influenza vaccine?

Anthony Fiore: Persons who are treated with antivirals often do develop antibodies, so yeah, but what's not known is whether those antibodies differ in some functional way from antibodies that occur with natural infection. But yeah, people who get antivirals do get the antibodies.

As far as the vaccine goes, we're going through the process that we normally do with seasonal vaccine with making it. The first steps are to develop (unintelligible) that are good candidates for scaling up production of a vaccine and that's the stage that we're at right now.

The timeframe for doing this is somewhat set and there's not much you can do to contract that timeframe. It probably would be in best case scenario not until later probably in the fall before a vaccine would be - would have any sort of widespread availability just because of the various constraints with growing it up and checking immunogenicity and safety and figuring out ways to really scale up production to make a vaccine for hundreds of millions of doses.

So we're proceeding down the path to that and it's going about like it usually goes every year for seasonal flu vaccine, but it does take time.

Question cont'd: Thank you.

Anthony Fiore: Four to five months at the very least.

Question cont'd: Thank you, because if we see a lot of this in the southern hemisphere, as well know, than the chances of a pandemic increase, don't they?

Anthony Fiore: Well certainly if we saw widespread dissemination in the southern hemisphere during their Influenza season which is just getting started now, we would have

every reason to think that this will be back in the fall, and that's the planning assumption right now.

Question cont'd: Thank you sir.

Coordinator: The next question. Your line is open.

Question: Yes, any recommendation for continuous daily prophylaxis for healthcare workers in a pandemic situation as opposed to post-exposure prophylaxis? Are they the same in efficacy? What do you recommend?

Anthony Fiore: At this point there's pretty limited circumstances when we'd recommend pre-exposure prophylaxis, given a couple of constraints. One is concerns that we have enough antivirals; another is that while pre-exposure prophylaxis is quite effective, we don't have much data on using it beyond six weeks or so.

And given how long this virus is expected to circulate, a person would have to be on pre-exposure prophylaxis for quite some time.

There may be some limited circumstances of persons, healthcare workers with high risk conditions - conditions that put them at higher risk for Influenza complications where pre-exposure prophylaxis might be appropriate. I think this is sort of a case-by-case basis and would apply to a really small minority of healthcare workers.

The reliance right now for protection of healthcare workers is largely based upon use of personal protective equipment and post-exposure prophylaxis when it's appropriate.

Question cont'd: Thank you.

Coordinator: Once again, to ask a question, please press star 1 on your touchtone phone. One moment, please. One moment please while a question has just populated.

The next question. Your line is open.

Question: Yeah, thank you.

My question has to do with the utilization of N95 for the healthcare worker. In this first wave, you all posted some guidance on the Wednesday morning that actually lightened the rules for the community in utilizing N95s in healthcare workers and then by the afternoon that was mitigated.

My concern and I do appreciate the OSHA standards for the utilizations of N95 for those in isolation or having symptoms because of the spread of the virus, but my concern is availability of N95s. We contacted our suppliers and opportunity to obtain those was very limited.

And so, I just wondered if there had been any consideration as far as the ability to obtain those N95s given the shortened supply during the pandemic. And what type of guidance if those supplies are exhausted will be given to the healthcare workforce to utilize then instead of N95 that will keep us in compliance with our regulations as I work in long-term care.

Anthony Fiore: These are tough questions.

I know that at the macro level that the Division of Healthcare Quality Promotion here reached out to manufacturers of N95 masks and found that supplies were quite adequate.

But again, that's at the, you know, macro level and not necessarily something that might be reflected in - at a local level where your usual supplier might have shortfalls in the distribution system and might have difficulties getting N95 masks.

You're right that this has been one of the most difficult issues we've dealt with since the whole thing has started because there are a very wide range of opinions about whether the recommendation for use of N95 should be relaxed for healthcare workers and go back to the sorts of precautions that one uses for seasonal influenza, versus concerns, especially from the occupational health world and from some groups of healthcare workers themselves that they were, you know, putting themselves at risk in a situation where there's no vaccine, where there's very little ability to tell when somebody really has H1N1 infection and might not be opportunities to take timely post-exposure prophylaxis and knowing that our main reliance on avoiding infection is use of personal protective equipment.

And again, we also don't have all the information we might like to have yet about how this virus is transmitted. It looks a lot like seasonal influenza. The initial epidemiologic investigations, but whether there might be some potential for transmission in ways that a N95 would better prevent is still - I think still an open question.

And so with all that, I think you'll see this guidance for use of respirators in healthcare settings, you're going to - this isn't the final word on it, I suspect. I think you're going to see this continue to be tailored according to what evidence is available.

But right now the folks making these guidances have felt that we don't yet have compelling evidence that an N95 is not necessary, that N95 masks are

available for - are available adequate for the U.S., notwithstanding that there might be shortages in some local levels.

So if you do run into that kind of problem, that's definitely something you would want to let your local or state health department know and potentially even in CDC because these are the kinds of things that play into our decision-making about how practical our decisions are. Our recommendation is also important in addition to the evidence and the science base.

Question cont'd: Yeah, I appreciate that.

We work in 24 states and so we were certainly watching in our centers that were in the southern part of the United States and our major supplier was not able to obtain what they needed in a timely manner, so we're having to look at or relook at this situation.

Tim Uyeki: The only thing I would add is that let's say in the fall/winter, if there would be a tremendous demand and there really were substantial shortages of N95 respirators, CDC and the Strategic National Stockpile does have N95 respirators, and, you know, this would be a state request.

So there is the potential - I don't think right now as Dr. Fiore said, we're not aware that there are widespread shortages of N95 respirators and clearly there are issues about, you know, the appropriate fit tested model and size and so forth, but what I'm raising is the potential that in a high demand situation where there is a shortage, national shortage, that there is the potential for state health departments to have - for CDC to deploy N95 respirators out to a state health department.

Question cont'd: Okay, thank you.

Coordinator: Once again, if you would like to ask a question, you may press star 1. One moment please.

I currently have no questions.

Justin Williams: All right, well, with that Dr. Uyeki and Dr. Fiore, thanks again for providing our listeners with this information and I'd also like to thank our participants for joining us in this call today.

If you have any additional questions, please send an email to coca@cdc.gov. That's C-O-C-A @ cdc.gov. A recording of this call and the transcript will be posted on the COCA website emergency.cdc.gov/coca as soon as we get this.

Please remember to check the CDC Novel Influenza A H1N1 site regularly for any updated information or guidance at http://www.cdc.gov/h1n1flu, and thanks again for participating and I hope you all have a wonderful day.

Coordinator: Sir, another question did populate. Would you like to take it?

Tim Uyeki: Sure.

Justin Williams: Sure.

Coordinator: Your line is open.

Question: Thank you.

Just a short one, test methodologies existing for the H1N1 Swine proved not to be effective as the result it seems the bulk of the identification had to come

from CDC with PCR testing and supposedly that technology was shipped out to the state lab.

I think out of 120 specimens, I'm familiar with being shipped to the local health department, 61 results are not yet received.

How do you see in the future testing for new virus be done at the local levels?

Tim Uyeki: That's a great question and it does illustrate some of the challenges.

So clearly, you know this was a Novel virus and what was helpful was that CDC had already developed sort of a real time PCR - RT-PCR assay that was aimed at detecting highly pathogenic H5N1 virus, if it were to be introduced into the U.S., which it has not.

But having at least some primer probe set for real time RT-PCR that then could be adapted using targeting specific probes and primers for this new virus allowed sort of a rapid development of a very highly specific assay which was used first at CDC but then clearly there's an issue of producing all the reagents and so forth to get that out to state health departments.

And this has really been done quite rapidly and so that specific real time PCR assay to detect this virus was sent out to states and virtually - I don't know the latest numbers, but almost all the states, at least as of last week, had the capacity to detect the specific virus and did not have to send specimens to CDC.

But you bring up an issue that in a very high demand situation what would actually be needed, I think at CDC our perspective is this: Clearly not every patient who is ill needs to be tested. In fact, people that - who are not very ill,

don’t need to actually present for medical care and don’t need treatment. That’s sort of a national recommendation.

However, those people who have - who are ill and have certain underlying conditions that put them at higher risks for severe complications of both seasonal Influenza and what would appear to be for risk factors for this new virus infection for severe complications, those people should probably be evaluated early on in their illness.

And one could consider sort of an empiric antiviral treatment for those individuals.

Now whether or not everyone needs to be tested is an issue and for most clinicians, what you have available are rapid Influenza diagnostic tests. For a hospital based clinician, you may have immunofluorescence. Very few hospitals will have the ability to do this kind of specific PCR.

And so you do highlight an issue. There are challenges with using or at least with interpreting the results of rapid Influenza diagnostic tests, which can produce false negatives, may miss infections, in addition, a small extent there could be some false positives.

And the other problem is if there are seasonal Influenza A viruses circulating, a rapid test will not distinguish between this new virus infection and seasonal viruses. And so they won’t be very helpful to target therapy against this specific virus infection.

But, you know, for seasonal Influenza during peak activity in a community, clearly most people with Influenza do not seek medical care. Those that do, very few of them actually get tested for seasonal influenza.

But our national recommendations are certainly any hospitalized patient that's suspected or, you know, is a probable case should have specimens collected at admission specifically to test for this virus infection.

In terms of the outpatient setting for people who are not hospitalized, one could prioritize testing of patients with certain underlying conditions including pregnant women and including young children.

But even if one were to prioritize among young children, certainly there are a lot of kids that have febrile Influenza like illness due to other etiology.

So you raise a very important question that I don't think anyone has the answer to, but at the time - at this time there are no rapid diagnostic tests that are specifically going to detect this virus infection only.

And there are efforts underway to produce those - to develop those kinds of tests, but they're not available yet.

So other than say you raise a very good point and there are sort of priorities should be placed upon testing hospitalized patients and then those with underlying conditions in the outpatient setting, you know, clearly not every patient needs to be tested. I think it's an issue for treatment decisions, really.

Question cont'd: I think that there was too much reliance that the existing kits at the local level would turn positive with H1N1 strain and we found it not to be the case. We had a clear cut negative on a rapid that was confirmed by CDC as a positive for SW, so...

Tim Uyeki: Yeah, the use of rapid test clearly is going to miss cases. You will - you know, the sensitivity for seasonal Influenza virus infection is sub-optimal and we don't have data available.

We have some anecdotal data available for this new virus infection, but we would expect rapid diagnostic test, point of care test that can yield a result in 10 to 15 minutes to detect some but not all infections with this new virus.

And so exactly what you're saying does occur that people can test negative on a rapid test, but they are still infected. And so, you know, we've posted guidance about how to interpret rapid Influenza diagnostic test on the CDC web pages.

And I think even in the absence - even when we do have some good data about the performance of these rapid tests to detect this new virus infection, it's likely that what we have for interpretation is not going to change.

That one really has to understand what a negative result might be and what a positive result might be. And either a negative or a positive does not necessarily indicate the absence or the presence of this virus.

And so it's a difficult message to get out for clinicians, but people have to be aware of the limitations of these tests.

Question cont'd: And the only other comment I have, too, is that the manufactures of the rapid kits were telling me that they hadn't received any of the actual virus specimen from CDC until at least three to four weeks into this outbreak.

Tim Uyeki: So I guess - I can't comment about that, but, you know, the point is that laboratories, not necessarily the manufacturers, but clinical laboratories need to produce the data.

In other words, in the real world of what's happening, you know, real clinical practice, we'd like to know how these tests perform against a gold standard of, you know, real time RT-PCR for this specific virus infection.

So not sure how to respond to the issue about the companies not having the virus, but what we would like to know, and I think it's important for clinicians is how do these tests perform in real clinical practice for patients who may or may not have this virus infection.

Question cont'd: Yeah, data collection site on just this last four week period comparison of the rapid to the CDC result or PCR testing would be real interesting.

Tim Uyeki: Right, and as - you know, there are a number of factors that need to go into it and I think these would include not just whether it's positive or negative, but what was the time from illness onset to specimen collection, what is the age of patient and so forth.

I think, you know, experience from seasonal Influenza suggest that young children and likely to have higher viral concentrations in their upper respiratory track than adults and older children and elderly and also young children may shed virus for longer periods of time.

With this new virus, of course, we are assuming it's going to behave similar to seasonal Influenza virus infection, but in fact we need data. So, there are a number of caveats beyond just is it positive or negative sort of overall results that would be useful.

I think the other point that Dr. Fiore made was that in parts of the country there are communities that are still experiencing seasonal Influenza A and B virus activity and this does definitely pose additional challenges to interpreting the results of these rapid tests.

Question cont'd: And that's true. We did turn a seasonal virus type A which put all parties that received that result into shock and panics of all different types because there was obviously a lot of hysteria about the time that we turned the regular seasonal.

Coordinator: I do have another question. Your line is open, sir.

Question: Thank you. I had two questions. I think they'll be fairly straight-forward if you're willing to take them, and I apologize if it's redundant base on the information you gave before I tapped in, but I wanted to get a sense as to how secure or how set you all believe that a two-dose regimen will be the planning assumption for when the Swine flu vaccine is available.

And would that potentially be effected or altered if in fact the timing is such that it comes out after the availability and distribution of the regular seasonal flu vaccine?

And my second question has to do with the pediatric population. If the Swine flu comes back and it's a good bit more of a virulent actor than it has been so far, could you all anticipate a EUA type approach to lower the age threshold for in the infant population?

Anthony Fiore: Okay, with regard to the first question about requirement for two doses, that is the working assumption based on the fact that people don't appear to have

underlying antibodies with the exception of some segment of the population over the age of 50 or so.

There are some people who have some underlying antibodies - pre-existing antibodies, rather, which we don't whether or not those antibodies are in any way protective or whether bumping those antibodies with a single dose indicates protection.

I think the answer to your question is going to have to wait for the immunogenicity studies for the candidate vaccine. It's likely that the Swine flu vaccine or a Novel H1N1 vaccine, that is, would be given as a monovalent vaccine, so a vaccine that just contains that one antigen that TIV and LAIV which are for the most part already produced at this point would be a separate vaccination and a separate program, even.

So you might end up seeing sequential vaccination of people who get their seasonal flu vaccine early in the vaccination season and this would be a great season to get those patients in and vaccinated early rather than waiting until October or November and then follow that up with a monovalent vaccine. And whether that's one or two does really is going to depend on immunogenicity study.

The EUA, I think you might be referring to a EUA for use of the vaccine in children younger than the age of 1 - sorry, than the age of six months where it's currently licensed.

There is some data for the seasonal vaccine that children younger than six months do get some response and sure, if we were - certainly any sorts of options like EUA for that lower age group would be explored, just as they

were explored, and in fact, EUA does not exist for use of antivirals in children less than one.

The FDA has been quite proactive and quick to be able to invoke the use of the EAU when it's appropriate. And so, yeah, you might see something like that.

Question cont'd: Thank you.

Coordinator: And currently no questions.

Justin Williams: All right. Again, thank you to Dr. Uyeki and Dr. Fiore for taking the time to speak with us today and thank you for the participants for dialing in. And please look forward to the next COCA call on this or another topic. Thanks again.

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