CDC/APHL Teleconference on Recent Influenza A(H3N2)v Human Cases – December 20, 2011

Background:

On December 20, 2011 APHL and CDC held a teleconference for state and local public health laboratories (PHLs) to discuss the impact of the recent detection of influenza A(H3N2)v human cases. The teleconference provided a review of recent influenza activity, the recommended testing algorithm for swine origin viruses, and influenza specimen submission guidance. Additionally, CDC also provided a situational update on rRT-PCR reagent availability through the Influenza Reagent Resource (IRR).

Teleconference Minutes and Important Points:

Situational Update of Current Influenza Surveillance

Dr. Daniel Jernigan provided a situational update of the current influenza surveillance. Overall influenza activity has been low, and the circulating viruses that have been tested match the vaccine strains. Resistance to antivirals has not been detected. Additionally, pediatrics mortality has not increased, and there have been few reported pediatric deaths.

Due to the low levels of circulating seasonal influenza and laboratory sample positives are currently low, CDC recommends increasing collection of (Influenza-Like-Illness) ILI samples through the means usually used in your state, and then sending these specimens to the state public health laboratory for further characterization. **Specifically, states should consider increasing collection of specimens from patients presenting with ILI in the following high priority areas**:

- ILI outbreaks, particularly pediatric influenza infections and outbreaks, as well as childcare and school settings, since these have been the settings in which some cases of the novel strain have been found.
- Unusual or severe presentations of influenza illness specifically among children.
- Medically attend ILI in children less than 18 years of age.

Since July 2011, there have been 11 cases of A(H3N2)v with the M gene from A(H1N1)pdm09 in the following states: Indiana, Pennsylvania, Maine, Iowa, and West Virginia. Of those 11 cases, 7 had direct contact with swine and 4 appear to be human to human transmission. Additionally, 1 case of classical swine H1N1 from Wisconsin and 1 case of triple reassortant swine-origin A (H1N2) from Minnesota have been confirmed. All viruses have been susceptible to antiviral medications.

> **Note:** There was an additional case identified in West Virginia as reported by CDC in an MMWR article released December 23, 2011. There is now a total of 12 cases of A(H3N2)v.

The CDC Flu rRT-PCR Dx Panel assay is able to presumptively identify these swine origin viruses. Please note that laboratory confirmation of A(H3N2)v and other swine origin viruses occurs only at the CDC Influenza Division at this time. The performance of rapid test kits (RIDTs) and other FDA-cleared influenza assays are unknown. However, some of the cases have been RIDT positive and at least one case was negative by RIDT.

CDC extends its thanks to the state health departments for their continued cooperation with identification of novel influenza cases. Prompt notification to your state epidemiologists and CDC, along with rapid referral of the specimens to CDC for confirmatory testing and detailed characterization, is essential to assure that cases are identified and investigated quickly. **This immediate referral to CDC is important in order to comply with International Health Regulations requirements.**

For additional information on public health guidance and the recent A(H3N2)v cases, please see CDC's MMWR article released December 23, 2011, "Update: Influenza A (H3N2)v Transmission and Guidelines — Five States, 2011."

Review of Influenza A(H3N2)v Testing Algorithm

Dr. Stephen Lindstrom reviewed the testing algorithm for the detection of swine origin viruses. Laboratory detection of influenza A(H3N2)v is dependent on the testing algorithm used. This virus will produce the following "inconclusive" results when the CDC real-time RT-PCR Assay is used (see package insert page 43):

- InfA/pdmInfA/H3 positive
- InfB/pdmH1/H1 negative

If a laboratory gets an inconclusive InfA/pdmInfA/H3 positive result, contact your state epidemiologist and CDC and ship the specimen to CDC immediately.

Recommended Influenza Testing Algorithm:

1. Screen specimens for InfA, InfB, and RP using the CDC Flu rRT-PCR Dx Panel Influenza A/B Typing kit.
2. Test all InfA positive specimens with the CDC Influenza A Subtyping kit using **all** primer/probe sets: H1, H3, pdmInfA and pdmH1.

Notes:

- The influenza testing 96 well plate set ups for this algorithm can be found in the CDC Flu rRT-PCR Dx Panel package insert on pages 20 and 23.
- If you have InfA/H3 positive specimens from this season that were not tested using the pdmInfA and pdmH1 primer/probe sets, CDC recommends that these specimens are retested using the Influenza A Subtyping kit as described above.

This algorithm helps to conserve reagent usage during this part of the season where prevalence of influenza is low and will identify all influenza A and B cases and seasonal H1 and H3, A(H1N1)pdm09, A(H3N2)v, and other swine-origin influenza subtypes.

Overview of Routine Surveillance Submission Guidelines

For detailed submission instructions and shipping addresses, please review the Revised Guidelines for Submitting Influenza Virus Isolates to the WHO Collaborating Center for Influenza, CDC 2011-2012 Influenza Season. **The submission instructions and shipping addresses have not changed.**

Please note that laboratories with virus isolation capacity are requested to continue maintaining this capability using appropriate biosafety practices. **Do not attempt to culture viruses that produce inconclusive results using the CDC Flu rRT-PCR Dx Panel. Specimens with inconclusive results (InfA <35) should be sent directly to the CDC for further characterization and should not be submitted to contract laboratories.**

Ancillary Reagent Availability Update

Dr. Stephen Lindstrom discussed the anticipated availability of the CDC Flu rRT-PCR Dx Panel kits for ordering from the Influenza Reagent Resource (IRR). Additional Influenza A/B Typing and A Subtyping rRT-PCR kits will be available for order on the IRR website in early January, and H5 kits will be available later in January for ordering through the IRR website. Please place orders of only 1 kit per laboratory through the IRR. Kits will not be automatically sent to laboratories.

Due to budgetary issues there will be **limits on the number of rRT-PCR kits and ancillary reagents laboratories will be able to receive this year. Laboratories will be limited to 3 typing kits, 2 subtyping kits, and 1 H5 kits.** If you think your laboratory will need additional reagents due to higher testing volumes, please contact CDC at flusupport@cdc.gov. **Influenza kits and ancillary reagents should be used wisely.**

Other Important Ordering Notes:

- Laboratories that did not receive an H5 kit will receive them first.
- The new Qiagen DSP extraction kits are available through the IRR. Please keep in mind the DSP kits have 50 reactions not 250 like the previous Qiagen Viral Mini RNA kits. Qiagen Viral Mini RNA kits for IVD use are discontinued at this time and are no longer available through the IRR; however, the kits may continue to be used until the expiration date.
- If you have a customer service issue, please contact IRR customer service at contact@influenzareagentresource.org.
- For all technical questions, please contact flusupport@cdc.gov.

Performance Evaluation Panel Update

CDC extends a thank you to all labs that have participated in the recent rRT-PCR performance evaluation panel. Data analysis is currently ongoing and reports should be sent shortly if you haven't already

received them. CDC hopes to provide a summary report to public health laboratories in the upcoming months.

Questions and Answers:

1. Will A(H3N2)v specimens be positive with the 2009 Influenza A H1N1 primers and probes as well as the seasonal Influenza A primers and probes?
    - Yes. Please refer to page 43 of the CDC Flu rRT-PCR Dx Panel package insert for more details. Page 43 also explains any non-standard results for swine origin viruses.
2. What name should we use to report 2009 Influenza A H1N1?
    - While some variations are acceptable, the WHO naming convention for this virus is Influenza A(H1N1)pdm09.
3. Is the limit of 2500 rRT-PCR reactions per state or per laboratory?
    - The ordering limitation is per laboratory.
4. Is there any guidance we can provide sentinel laboratories regarding A(H3N2)v?
    - Guidance is available in the recent CDC MMWR article released December 23, 2011, "Update: Influenza A (H3N2)v Transmission and Guidelines — Five States, 2011."
5. Do laboratories need to place an order for the subtyping kit, if they did not receive one during the first distribution wave?
    - Yes, when the kits are available, CDC requests that laboratories place an order through the IRR.
6. Should laboratories submit samples in the original 15ml VTM tubes or would CDC prefer an aliquot?
    - PHLs should submit the specimen in the original vial whenever possible in order to avoid contamination. It is also important to minimize the number of freeze-thaw cycles for original specimens.
7. How should PHLs report out suspect swine cases? Do we notify the epidemiologist?
    - Please contact and send the specimen to CDC immediately for PCR diagnostics. Results will be sent back to the submitter, with a note stating that the result is inconclusive. CDC will follow up with genetic sequence/confirmatory results to the submitter.
    - Turnaround time for results is typically 24hrs for rRT-PCR results and 48hrs for the sequence confirmation.
    - Please notify your epidemiologist of the inconclusive result. The state epidemiologist will also be contacted by CDC.
8. Will the current pyrosequencing protocols for antiviral resistance work for detecting resistance in A(H3N2)v?
    - Please do not perform antiviral resistance testing on influenza A (H3N2)v viruses. These specimens should be shipped directly to CDC.
9. On the 2011-2012 Influenza Specimen Submission Form, is there an area to indicate that the sample is for diagnostic testing?
    - Yes, please indicate on the "Reason for Submission" field on the form that the sample is being sent for "diagnosis" in order to make sure that it receives priority testing. Also, please remember to include the sender's phone and email.