# CDC/APHL Annual Seasonal Influenza Surveillance Teleconference – October 9, 2014

## Background:

On October 9, 2014 APHL and CDC held a joint teleconference for state and local public health laboratories (PHLs) to provide an overview of global influenza surveillance, a situational overview of the current influenza season, an overview of routine specimen submission for national influenza surveillance, a review of the WHO specimen submission form, and an overview of influenza specimen referral for the upcoming 2014-2015 influenza season. Below are highlights from the teleconference.

## Teleconference Minutes and Important Points:

*Enterovirus D68 (EV-D68)*

Drs. Mark Pallansch and Steve Oberste provided an update on the current CDC efforts around EV-D68 diagnostics. The current method to confirm EV-D86 is semi-nested PCR followed by sequencing; this takes number of days to complete and has led to a backlog of specimens needing testing at CDC. Four states and CDC are currently using this test method. All states others are sending specimens to CDC to differentiate EV-D68. CDC has recently developed an EV-D68 specific real-time PCR assay. The real-time PCR assay protocol will be posted on the CDC website and shared via email through APHL during the week of October 13th. APHL will host a national laboratory alert teleconference, tentatively scheduled for October 20, 2014 at 3pm ET, once laboratories have had a chance to review the protocol. Expect to see more details come from APHL next week regarding the protocol and the national teleconference. Laboratories will be responsible for validating the assay on their own.

CDC is exploring the emergency use authorization (EUA) route for distributing kits, but an emergency has not been declared at this time. There may be more information available regarding a potential EUA during the national teleconference.

*Situational Update of Global and Domestic Influenza Surveillance*

Internationally, influenza activity in the temperate Southern Hemisphere was typical. Australia and New Zealand saw predominately influenza A (H1N1)pdm09 but experienced a late increase in influenza (A(H3N2) viruses. South Africa had predominantly H3N2 activity but also reported influenza B and influenza A (H1N1)pdm09 cases. The temperate countries of South America activity are now in decline, but they saw predominantly influenza A viruses with primarily H3N2 viruses in Chile, Argentina, Uruguay and Paraguay. Countries with tropical seasonality reported low influenza activity with varying

predominant types and subtypes. From May 1 to June 27, there were 3 laboratory-confirmed cases of influenza A (H5N1) and 16 H7N9 cases.

In the US 66,006 specimens were tested for influenza between May 18 and September 20, 2014. Of those tested and reported to CDC, 4.9% (3,209 specimens) were positive for influenza. Coming out of the 2013-14 season, influenza B viruses were more commonly reported, but from mid-July through September influenza A viruses were more common. Of the influenza A viruses that were subtyped, 96% were influenza A (H3N2) and 4% were influenza A (H1N1)pdm09. Two specimens tested positive for influenza A (H3N2)v in Ohio; both had direct contact with swine.

Antigenic characterization at CDC of recently circulating viruses has shown that 100% of influenza A (H1N1)pdm09 viruses are antigenically similar to the current vaccine strain (A/California/7/2009). The influenza A (H3N2) viruses had 49% there were similar to the A/Texas/50/2012 viruses in the 2014-15 Northern Hemisphere vaccine . Of the tested influenza B viruses, 78% were B/Yamagata lineage and all were antigenically similar to the B/Massachusetts/2/2012 trivalent vaccine virus. Twenty-two (22%) percent were B/Victoria lineage and were antigenically similar to the B/Brisbane/60/2008-like quadrivalent vaccine virus. The WHO Consultation meeting was held in September 2014 to determine the WHO recommendations for the 2015 Southern Hemisphere vaccine. The recommended components for the 2015 Southern Hemisphere influenza trivalent vaccines are an A/California/7/2009 (H1N1)-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like (B/Yamagata lineage) virus. For quadrivalent vaccines, an additional component, B/Brisbane/60/2008-like (B/Victoria lineage) virus, is recommended. This represents a change in the influenza A (H3N2) and influenza B/Yamagata lineage components from the 2014 Southern Hemisphere and 2014–15 Northern Hemisphere influenza vaccine formulation.

For more information on all of the above updates, please see this MMWR article.

*Overview of Routine Surveillance Submission Guidelines*

Dr. Xiyan Xu discussed the routine surveillance submission guidelines for the 2014-2015 influenza season. 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 2014–2015 Influenza Season.

**Each laboratory should submit influenza specimens for routine surveillance as follows:**

- PHLs should submit either viral isolate **AND/OR** matching clinical specimen.
- Samples should be representative, which includes:
    - Specimens collected within 2 weeks of Shipment
    - All types/subtypes of seasonal viruses
    - Mild to severe/fatal cases

- Less than 3 viruses from a single outbreak
- Send the **first 10** early season influenza virus isolates and/or matching clinical specimens to **CDC. Immediately upon detection.**
  - Note: **Do not batch** the 10 specimens – please send specimens individually as they are identified.
- **After the first 10** specimens are sent to CDC, please send 5 most recent and representative influenza virus isolates and/or matching clinical specimens **every two weeks to your designated contract laboratory.**
- Local PHLs should work closely with state PHLs to coordinate surveillance submissions.

**PHLs should use the** 2014 Influenza Specimen Submission Form **for every influenza submission to both the CDC and contract laboratories. The submission form has been updated, please be sure to use the current submission form. For each shipment,** an electronic copy of the form and FedEx tracking information should be e-mailed to the receiving laboratory. A hard copy of the form should be enclosed in the shipment. All email addresses are listed in the Revised Guidelines for Submitting Influenza Virus Isolates to the WHO Collaborating Center for Influenza, CDC 2014–2015 Influenza Season.

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.**

*Influenza Specimen Submission Form and Instructions*

Dr. Xiyan Xu provided an overview of the2014 Influenza Specimen Submission Form. Please use this specimen submission form rather than the CDC 50.34 submission form. The only change to the form this season is the addition of influenza B-Vic and influenza B-Yam linage options. If you are using the influenza B lineage genotyping kit, please use these options as appropriate when submitting influenza B specimens.

*Specimen Shipping Guidelines*

Please see the Revised Guidelines for Submitting Influenza Virus Isolates to the WHO Collaborating Center for Influenza, CDC 2014–2015 Influenza Season for CDC and designated contract laboratory shipping addresses. One change requested this season is when submitting clinical materials to CDC or your designated contract laboratory, please transfer original clinical material to a 2ml cryovial. This will make storage and handling more efficient at the receiving laboratories.

As you start shipping influenza specimens, please remember that on Wednesday, October 1, 2014 a requirement to use a new Class 6 shipping label (for infectious substances UN 2814) and a new Class 9

shipping label (for dry ice UN 1845) took effect.

*Overview of Diagnostic Submissions*

Dr. Stephen Lindstrom discussed the diagnostic submission guidelines for the 2014-2015 influenza season. The biggest change this year is the addition of the influenza B lineage genotyping assay. For any influenza B that cannot be genotyped a Ct value of less than 35, please send to CDC for antigenic drift monitoring since it is a new assay. Ct values that are very above 35 can be reported as inconclusive; depending on the case history, you can send it to CDC for testing after contacting flusupport@cdc.gov. Adoption of the influenza B lineage genotyping kit is not required but is encouraged to help with surveillance data.

Viruses being submitted for diagnostic purposes should be sent to the same address as surveillance specimen but to the attention of Dr. Stephen Lindstrom. On the 2014 Influenza Specimen Submission Form list "diagnosis" as the reason for submission, and indicate the Ct value of the test result in the comments field. Also, submit an email to flusupport@cdc.gov so the shipment can be tracked and testing can happen as rapidly as possible.

For detailed submission instructions and guidance for inconclusive results using any of the CDC Flu rRT-PCR Dx Panel kits, please refer to the Revised Guidelines for Submitting Influenza Virus Isolates to the WHO Collaborating Center for Influenza, CDC 2014–2015 Influenza Season. Contact CDC immediately for any specimens that are suspect novel cases or inconclusive (InfA Ct <35) specimens as described on the CDC Flu rRT-PCR Dx Panel package inserts.

A change has been made to the CDC Flu rRT-PCR Dx Panel package inserts that allows primers and probes to be combined in a single tube. The package insert has been updated so it is now modular, meaning there is a separate package insert for each kit. At the beginning of each package insert there are algorithms that describe how each kit should be used in conjunction with the other kits.

CDC has been monitoring results of performance evaluation panels (PEP) in recent years. In 2012, 98% of participating laboratories scored 100% on the qualification samples. When CDC updated the procedures for H3N2v and other updates, they included those as challenge samples in the 2013 PEP. In 2013, the overall performance fell to about 85% qualification. This prompted CDC to conduct trainings; over the last year 30 labs were trained in Atlanta and additional labs were trained in Texas and California. It was determined that the decrease in qualification was not due to the performance of the assay but rather incorrect interpretation and/or transcription and specimen handling issues. These topics were addressed in the recent trainings. For the 2014 PEP, 90 labs participated and there were 9 samples in the panel. Qualifications increased to 97-98% of labs correctly identifying 100% of the PEP. This shows good performance improvement. Of the 60% of participating labs that performed the B lineage genotyping assay on the PEP samples, all correctly identified the B lineages. Remediation kits were made available. Another PEP is tentatively scheduled for November 2014; information will be distributed via APHL.

All laboratories have been invited to join the new CDC FluSupport SharePoint site which provides access to electronic package inserts, specimen submission guidance and FAQs. If you would like to enroll as qualified lab, please contact flusupport@cdc.gov.

*Overview of Antiviral Submission Guidelines*

The 2014-15 guidance for antiviral resistance testing has remained the same. Neuraminidase inhibition testing is being performed on surveillance specimens at CDC and your designated contract laboratory. Over the past year the number of specimens tested for antiviral resistance has doubled thanks to participation from PHLs. If your laboratory performs pyrosequencing for antiviral resistance, please continue to submit reports twice a week to fluantiviral@cdc.gov. CDC is still primarily concerned with receiving influenza A (H1N1)pdm09 H275Y data but is interested in any other data including H3N2 viruses. When results are submitted they are included in Fluview. Laboratories without Pyrosequencing capabilities can send 5 ADDITIONAL strongly positive 2009 H1N1 influenza clinical specimens every two weeks to the Wadsworth Center in New York. Please see the Revised Guidelines for Submitting Influenza Virus Isolates to the WHO Collaborating Center for Influenza, CDC 2014–2015 Influenza Season Appendix 2, Table 4 for additional information.

Please do not submit pyrosequencing results or specimens to CDC or Wadsworth for specimens already submitted to National Surveillance. If the results are reported there will be duplicate reporting on these isolates for antiviral surveillance. Aggregate antiviral resistance testing reports will be send to Laboratory Directors, please forward to appropriate staff.

*Public Health Laboratory Virologic Surveillance Reporting*

Thank you for reporting over the summer. Going into the season all but 3 PHLs are sending via electronic reporting. If your lab is not reporting electronically, please contact Desiree Mustaquim (dwc6@cdc.gov). The PHLIP team is currently upgrading PHLIP HL7 to match the ELR standard. More information is to come on this upgrade and labs may receive questions from your IT department. Please remember to contact CDC and your IT department if you are making any changes in your LIMS to ensure the data keeps flowing and is accurate. If you need assistance adding influenza B genotyping fields, please contact Desiree Mustaquim (dwc6@cdc.gov). Labs can also start submitting pyrosequencing data via PHLIP; contact Desiree Mustaquim (dwc6@cdc.gov) for more information.

Labs that manually report through NREVSS can also submit this data via PHLIP and once it is validated can stop manually reporting. Contact Desiree Mustaquim (dwc6@cdc.gov) or the NREVSS team for more information.

*IRR Update*

CDC Flu rRT-PCR Dx Panel kits and ancillary reagents are available per usual in the IRR. The new influenza B lineage genotyping kits are available in the IRR for ordering. Likewise, the WHO influenza kits are

available for ordering. The WHO influenza kit reagents are the same this year; you are also able to order these reagents a la carte.

Note that you can order ancillary reagents separate from CDC Flu rRT-PCR Dx Panel kits. If you already have an H5 and/or H7 kit, and it is within the expiration date, please do not order a new kit unless something has happened to that kit (e.g., freezer failure). If you do need a new kit, please explain the reason in the comments field of your IRR order. That comments field will be shared with CDC when they go to approve or deny the request. If the order is denied and you still need a kit, please respond to the denial notification as instructed in it to explain your circumstances and it will be re-reviewed.

To minimize potential financial loss (e.g., shipment loss and expiration data inventory management), there is a limit to how many reagents will be included in a single shipment. The IRR website will soon be adding a feature that allows users to see your organizations order history.

## Right Size Update

APHL and CDC are pleased to announce the release of several new and valuable Right Size resources! We will provide more information on these new resources and tools during the October 9 teleconference described above. These resources were developed based on feedback and questions from members like you — we welcome feedback on how to make these tools most valuable and ideas for future resources. All resources can be accessed from the Right Size homepage.

- Alternative Data Guidance
- Example Practices and Resources Website
- Right Size Roadmap Implementation Checklists
- Updated Right Size Sample Size Calculators

Furthermore, to help states with correctly interpreting Right Size recommendations and sampling guidance, APHL and CDC will be hosting Right Size Regional Workshops in March and April of 2014. More information will be released via APHL in the near future. States will be invited to send one laboratory and one epidemiology/influenza coordinator to their regional workshop.

Lynnette Brammer provided a few Right Size clarifications and reminders. As mentioned above, Alternative Data Guidance was recently released. States that have existing alternative data systems and states considering building a system are encouraged to review this document and learn how alternative data can assist with meeting Right Size situational awareness goals. If you have questions, please contact Stephanie.chester@aphl.org. When using the novel event detection calculator (i.e., Calculator B), it is recommended that you look at the "Flu+" tab to simplify the interpretation of the calculator output. This will tell you how many influenza positive specimens you need to test at the PHL to contribute to the national surveillance goal. You can back calculate how many ILI specimens you would need to test to get that number of positive specimens based on the time of the year/season. REMEMBER, set this calculator to "National" surveillance scale. We will go over this in more detailed at the regional workshops, but if you have questions in the meantime or are getting numbers that do not make sense or are very high,

please contact Stephanie.chester@aphl.org.

## Questions/Answers

1. Will CDC be updating the CDC Flu rRT-PCR Dx Panel package inserts for influenza A (H5) and (H7) to include the new instructions for combining primers and probes?
    a. The H5 protocol is updated in the most recent kit package insert. If you order the current inventory it does have the updated protocol, and if you have a kit that does not have the updated package insert, you can find it on the new CDC FluSupport SharePoint site.
    b. CDC will verify if the H7 package insert has been updated or not, and if not, will update it.
2. Are there any changes to the influenza antiviral resistance pyrosequencing assays?
    a. No, there are not currently any updates to these assays. CDC is anticipating updating these in the near future and once they are available the new protocols will be sent via APHL email. It will be up to each laboratory to determine if they want to update and validate the new primers.