Background
On September 14, 2017 APHL and CDC held a joint teleconference for state and local public health laboratories (PHLs) to provide updates for the 2017-2018 influenza season on the following topics:

- global and domestic influenza activity,
- updated national surveillance specimen submission guidance,
- diagnostic influenza specimen referral instructions.

Below are highlights from the teleconference.

Teleconference Minutes and Important Points:

Situational Update of Global and Domestic Influenza Surveillance

The WHO Vaccine Consultation Meeting is being held September 25-28, 2017 to determine the WHO recommendations for the 2018 Southern Hemisphere vaccine. CDC thanks all US public health laboratories for the data and specimens they contribute to national surveillance which aids in vaccine strain selection.

Internationally, countries in the temperate Southern Hemisphere are coming out of or still in their influenza season. South America, Australia and New Zealand had predominantly influenza A (H3N2) activity with co-circulation of influenza B. In Northern Hemisphere temperate climate countries influenza activity has remained low over the summer, with influenza B viruses predominating overall. In countries with tropical influenza seasonality, influenza activity levels and the predominant virus varied by region and country as follows:

- In the Caribbean and Central America, activity was low with both influenza A (H3N2) and influenza B viruses being reported.
- In Tropical South America, activity peaked in April and has been decreasing throughout the summer with influenza A (H3N2) predominant with some influenza B also reported.
- Eastern and Western Africa reported sporadic cases of influenza H1, H3 and B.
- In Eastern Asia there have been high levels of influenza activity reported in South China, Hong Kong and Taiwan with influenza A (H3N2) predominant.
- In Southern Asia, influenza A (H1N1)pdm09 were widespread with elevated activity reported in India, Nepal and the Maldives.
• In Southeast Asia, influenza A (H1N1)pdm09 predominated in Philippines and Myanmar. However, Vietnam reported both influenza A (H1N1)pdm09 and influenza B viruses. Singapore had co-circulation of influenza A (H1N1)pdm09, (H3N2) and B viruses.

In the US, there are typically low levels of influenza activity overall. Influenza A (H3N2) predominated overall during the 2016-17 season but influenza B viruses were reported more frequently than influenza A viruses from late March through June. In July, H3 viruses were the most frequent again, but we are still seeing sporadic H1N1pdm09 and B cases. Of the influenza B viruses, the majority are Yamagata-lineage.

CDC commended the public health laboratories (PHLs) and clinical laboratories for a strong surveillance system. Clinical laboratories reported over 1 million specimens tested which is the first time CDC has had more than 1 million reported. Furthermore, PHLs reported over 90,000 specimens tested. During summer months even though activity was low, clinical laboratories reported approximately 92,000 specimens tested and 4,000 were tested at PHLs indicating laboratories are doing a good job of continuing surveillance throughout the entire year. In recent weeks, data reported to CDC indicate a small increase in influenza activity and some sporadic outbreaks have been reported.

In regard to novel influenza A viruses, since week 20 there have been 17 H3N2v cases in the US from 3 states: ND (1), PA (1), and OH (15). There were also two H1N2v cases from OH. Prior to summer there was one additional H3N2v case in Texas. All variant virus cases seen in 2017 reported exposure to swine. Of the 19 total variant virus cases this summer, 17 out of 19 were children. Two patients were hospitalized and all fully recovered.

Internationally, China is experiencing a 5th wave of influenza A (H7N9) activity. This wave with 760 cases reported is the largest to date since the virus was first detected in 2013. This was also the most geographically widespread outbreak of (H7N9) to date.

Additional details can be referenced in the upcoming MMWR Weekly Report: Update: Influenza Activity — United States and Worldwide, May 21–September 23, 2017 which is scheduled to be published on October 6, 2017.

*Influenza Virologic Surveillance Right Size Project Update*

Given the recent large outbreak of H7N9 in China, CDC reminded everyone of the importance to remain vigilant and meet Right Size novel event detection goals. During the 2016-17 season, the US meet the 1/700 goal for novel event detection for 9 weeks and 38 states met the goal for at least 1 week. However, there are still some gaps and room for improvement. States are encouraged to focus on meeting their state goals in the upcoming season. It is important to reach novel event goals year-round. If your laboratory is unclear of your state’s specific right size goals, please contact Stephanie.chester@aphl.org or fluquestions@aphl.org to setup a call with CDC and APHL to review your goals.
Overview of Virologic Surveillance Specimen Submission Guidance

CDC provided a detailed overview of key reminders for the 2017-18 specimen submission guidance for routine surveillance:

- **Starting October 1st** submitting PHLs you are asked to send specimens directly to their assigned National Influenza Reference Center (NIRC) following the [standard submission guidance](#) for this season. The assignments have not changed from last season.

- **Please submit original clinical specimens positive for influenza virus from the previous two week period**, according to Appendix 1: 2 influenza A(H3N2) positive specimens, 2 influenza A(H1N1)pdm09 positive specimens, and 2 influenza B positive specimens.
  - If your laboratory performs influenza B lineage testing and you have recent positives from both influenza B/Victoria and B/Yamagata lineages, please submit one of each. If lineage testing isn’t done or if all your recent B viruses are from a single lineage, please still submit 2 influenza B positive specimens.
  - State PHLs are strongly encouraged to perform and report influenza B lineage genotyping using the CDC PCR assay.

- **Please remember to only ship recent viruses that were identified in the previous two weeks.** Do not batch if you don’t have enough to meet your quota, still submit what you have at that time—timeliness is very important. Specimens should have CT values less than 30 based on InfA or InfB tests using the CDC Flu rRT-PCR Dx Panel.

- **Ideally send 1.0mL of original clinical specimen; if 1.0ml is not available, submit no less than 0.6ml.** This volume is requested because the specimens get used in the following way at CDC and the NIRCs:
  - 0.6 ml for virus isolation and antigenic testing
  - 0.2 ml for genome sequencing
  - 0.2 ml is stored for repeat tests and/or isolation of vaccine virus progenitors

  If specimen volume becomes a routine issue preventing your laboratory from meeting specimen submission goals, please notify APHL or CDC as we are trying to understand the severity of this issue better.

- **Please be aware that it is a possibility for sporadic and temporary “enhanced” surveillance specimen submissions to be requested from CDC.** For example, we requested supplemental B viruses over the summer and [this is now discontinued](#).

- **There were no changes made to Influenza Specimen Submission Form for this season.** The information captured in the Influenza Specimen Submission Form is important to provide standardized and thorough data, although the CDC 50.34 specimen submission form is not mandatory. There is guidance on the CDC website that reads “If a submitter is sending in a large number of specimens, the submitter may work with a CDC lab to submit specimens using a batch form.”
  - Important Reminders:
    - Please be sure to enter a Ct value as it has important implications for whole genome sequencing surveillance testing
Use one line per specimen

Email form prior to shipment to CDC and NIRC. Electronic submission is greatly appreciated by the receiving laboratory.

In the actual package, include a paper copy of the submission form. Only print the non-pink/salmon/peach columns. The form is set to default to printing the correct columns so it should print correctly.

Please provide as much available information as possible in all columns.

Overview of Diagnostic Specimen Submission

As with previous seasons, PHLs are requested to carefully review the CDC Flu rRT-PCR Dx panel package insert for proper interpretation and referral guidance. Reminders for non-standard results can be find in the specimen submission guidance Appendix 2. If your laboratory has any non-standard results meeting this criteria, notify CDC IMMEDIATELY at flusupport@cdc.gov and send the specimen to CDC for confirmatory testing and further characterization. Furthermore, please review the specimen submission guidance Appendix 3 for diagnostic specimen referral guidance for suspect A/H5 and A/H7 (Eurasian Lineage) cases. Please contact CDC immediately and send these specimens at the highest priority. Specimens with inconclusive or non-standard results should be sent directly to the Diagnostic Development Team at CDC. These specimens should not be submitted to the National Influenza Surveillance Reference Centers. Please do not attempt to culture viruses that produce inconclusive results using the CDC Flu RT-PCR Dx panel.

For all diagnostic submissions, when you notify flusupport@cdc.gov please also provide the tracking information for the package and send the package to Attn: Stephen Lindstrom, Ph.D. to expedite receipt and testing. Please indicate the following on the Influenza Specimen Submission Form to expedite receipt and testing at CDC: Reason for Submission: Diagnosis (not surveillance); If Clinical Specimen: Indicate the specimen type; Type/Subtype: Inconclusive; Also remember to include CT values as this helps get samples into the right testing pipelines.

Due to periodic reports of inaccurate results (i.e., false positive or false negative results) from rapid influenza diagnostic tests (RIDT) and commercial molecular tests, there is concern for a potentially negative impact on public health/clinical management. The CDC Influenza Division is requesting that public health laboratories notify CDC of incidents where discrepant results are observed between a PHL confirmatory test and the commercial test in order to monitor if a particular diagnostic test is performing inaccurately. CDC has established the Commercial Influenza Diagnostic Test Discrepant Results Reporting Tool to allow voluntary reporting on the CDC FluSupport SharePoint site. The tool can be accessed by logging in to the CDC FluSupport SharePoint website under the Discrepant Dx Results tab. Please contact flusupport@cdc.gov with any questions about the new reporting tool.

CDC announced that the QIAGEN EZ1 Advanced XL and the Roche MagNA Pure 96 nucleic acid isolation systems were evaluated and qualified by the CDC Influenza Division and cleared by FDA for use with the CDC IVD Flu rRT-PCR Diagnostic Panel. These extraction platforms are cleared in addition to the previously cleared ones. Specific information for these new options are included the product update
which is available on the FluSupport SharePoint site and should be used in conjunction with the package insert for each kit. The CDC Influenza Division recommends that laboratories perform a verification when implementing a new instrument/chemistry as required under the Clinical Laboratory Improvement Amendments (CLIA). The International Reagent Resource (IRR) currently does not have reagents associated with these platforms available but does plan to make these available in the future.

For the recent Performance Evaluation Panel (PEP), there were 89 enrolled laboratories with 90% of participants correctly identifying all samples. As part of the PEP, laboratories were also asked to complete a questionnaire which indicated that 94% of participating labs are using the influenza B genotyping assay and 96% are testing for A/H5 and A/H7 viruses. Results of the PEP indicate that laboratories are adhering to the testing guidance in the package inserts. CDC is scheduling an upcoming PEP for late October or early November 2017; more information will be distributed via FluSupport and APHL Influenza News.

*Overview of Antiviral Submission Guidelines*

There are no changes for antiviral specimen submissions for surveillance or diagnostic purposes this year. Additionally the pyrosequencing protocol, reporting instructions and reporting forms have not changed. Specimens submitted to NIRCs will be tested using a phenotypic assay for neuraminidase inhibition (NI) and sequenced looking for known markers. Aggregate NI results will be sent by CDC to Laboratory Directors who are requested to forward the reports onto appropriate staff members. CDC will only send results to the Laboratory Director. As a reminder, please always prioritize submitting national influenza virologic surveillance over submitting to the pyrosequencing reference center or reporting results from in-house pyrosequencing.

Laboratories with pyrosequencing capabilities are requested to:

- Perform testing within their laboratory and report results to CDC every two weeks.
- Submit reports using the pyrosequencing reporting submission forms distributed by APHL. Email forms every two weeks to fluantiviral@cdc.gov.
  - When reporting in-house pyrosequencing results to CDC, please indicate if any of the tested viruses were submitted to national reference center or pyrosequencing center. This information is needed to avoid duplication of data.
- Note that a performance evaluation panel will be available for enrollment in the near future. Communications will be sent by APHL.

*Pyrosequencing Reporting Forms:*

- Instructions for Using the Pyrosequencing Data Reporting Form for H1N1pdm Targets
- Pyrosequencing Report Form for H1N1pdm Targets
- Instructions for Using the Pyrosequencing Data Reporting Form for H3N2 Targets
- Pyrosequencing Report Form for H3N2 Targets
Laboratories without pyrosequencing capabilities can:

- Submit up to 5 specimens every other week that are confirmed by rRT-PCR to be positive for influenza A (H1N1)pdm09 or (H3N2) using the CDC Flu rRT-PCR Dx Panel. Shipping address listed in pyrosequencing referral chart (Addendum 2; Table 1).
- Please only submit specimens with Ct values <30, and preferably 500 ul, no less than 200 ul.
- Aggregate pyrosequencing result reports will be sent to the laboratory directors. Please make sure to distribute the reports accordingly.

If your laboratory needs assistance with antiviral resistance diagnostic testing, please refer to specimen submission guidance Appendix 5 for instructions. CDC accepts requests for diagnostic antiviral testing when drug resistance is suspected by an attending physician. Influenza A and B viruses can be sent for pyrosequencing testing. Please notify CDC at fluantiviral@cdc.gov immediately and please send at least 200uL of original material.

Additional Surveillance Updates

There are no changes to FluView for the 2017-2018 season; however there is a change to FluView Interactive. CDC is going to start posting state level laboratory (clinical and PHL) data and influenza-like illness data to FluView Interactive for states that have given approval to do so. A request for approval was sent to all state influenza coordinators and they were instructed to work with health department leadership and their PHL to decide appropriate levels of data to approve for public posting on FluView Interactive. States can select if they want past seasons’ data (can select which past seasons) and/or current season data displayed. Similar to what has been presented at the national and regional level in FluView, clinical and PHL laboratory data from the previous two seasons will be displayed separately while laboratory data from the 2014-15 season and earlier will be combined. If your laboratory has not heard from your influenza coordinator about this request, we encourage you to reach out to them. As of the teleconference, CDC had responses from 40 states and plans to have the data posted in early October when the week 40 surveillance report is posted.

Starting this season, PHLs can use the reporting website to access to their aggregated reported influenza lab test and result data for their laboratory, and for all labs in their state if they are a state PHL. The site will include PHL and clinical laboratory data so you can see what data your influenza coordinator is seeing. Additionally, CDC results for antigenic characterization and genetic group will be provided on the website for labs who submit specimens to CDC for surveillance. You will only see results for your lab’s submissions – no others. Information for how to access this site will be sent out once it is live, and this should hopefully be around week 40. (It may not be this exact week, but we are aiming for as close to the start of season as possible.) This website will provide an opportunity to catch potential reporting errors or other issues so laboratories are encouraged to check it and contact CDC if anything is concerning. Additionally, it will allow you to have timely genetic group and antigenic characterization results from CDC in a downloadable format.

CDC asks that electronic reporters please monitor laboratory data feeds regularly. There are a few ways to monitor the feeds; if you need assistance with doing this, please contact Desiree Mustaquim.
As always, please let CDC know in advance if you are making any changes to yours LIMS and/or IT systems so they can help plan for the change to make sure there are no interruptions. If you are making changes to yours LIMS, it may be a good time to consider upgrading to PHLIP 2.5.1, which is aligned with the ELR standard message, adding B lineage information, or maybe mapping other respiratory pathogens. If you are not reporting influenza B lineage results and are not already working with CDC on updating your message, please contact Desiree.

**International Reagent Resource (IRR) Update**

The IRR contract is entering its 10th year in operation. CDC Flu rRT-PCR Dx Panel kits and ancillary reagents are available per usual, and there are no major changes in the ordering process that will affect laboratories this year. Laboratories should note that since June, Zika reagents are no longer available from the IRR due to lack of appropriated funds for non-influenza activities by Congressional approval. Additionally, the IRR is no longer providing plastic consumables to focus more on supporting expensive ancillary reagents that directly impact assay performance.

Please note that the IRR continues to have order limits for a single shipment. If you exceed these limits you may be denied or your order reduced; this is to minimize the financial loss if any one shipment is damaged, compromised or lost. If you need more reagents for a particular reason, please leave a note in the comments field or contact IRR customer service or CDC staff.

PCR reagents will have updates on the product page if they are approaching the expiration date. Please look at the “product description page” to help determine when to order specific products especially if you are seeking the freshest material. Later this month, the IRR will roll out a new look on its website, but nothing else is changing. Graphics will be updated and the site will be more compatible with tablets and mobile devises.

**Questions/Answers**

1. If a PHL has fatal case specimens associated with influenza, should they be sent to their designated NIRC or CDC?
   a. Unless you are trying to get a diagnostic result, these specimens can be sent to your designated NIRC. If you are trying to get a diagnostic results, please send to Xiyan Xu at CDC for pathology.

2. Our laboratory just completed a CLIA investigation and for influenza they were asking for a second level of extraction control in addition to HSC—does CDC have any advice or have other PHLs seen a similar request?
   a. If this has happened to your laboratory, please contact flusupport@cdc.gov to share more specific information on your situation. To CDC’s knowledge, as long as you are performing the assay accordingly to the package insert that has been approved by FDA (which only includes the HSC extraction control) your practices should be acceptable.
3. For Right Size novel event detection, the recommendation says that a certain number of influenza positives need to be tested at the state PHL. If hospitals are performing PCR do they still need to forward it to the PHL or can states just count those reported results?
   a. For novel event detection it is essential that the specimens be send to PHLs for testing using the CDC rRT-PCR Flu Dx assay. This is the only assay that CDC can rely on to meet novel event detection goals given its ability to detect swine variants and reliably flag inconclusive, potentially novel, specimens. In states with local laboratories performing the CDC PCR assay, that state PHL can use data reported by local labs to meet their state goal.

4. When will be the influenza pyrosequencing proficiency panel be released?
   a. CDC anticipates enrollment starting soon and the panel shipping in the beginning of October.