State of California—Health and Human Services Agency
California Department of Public Health

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September 2017

Recommendations for Influenza and Other Respiratory Virus Testing and Reporting — 2017–2018

The official start of the 2017–2018 influenza season is October 1, 2017. This California Department of Public Health (CDPH) guidance for local health jurisdictions (LHJs) summarizes diagnostic testing guidelines and influenza reporting requirements for the 2017–2018 influenza season (October 1, 2017–September 29, 2018).

I. HIGHLIGHTS

- Continue mandatory reporting of laboratory-confirmed influenza-associated fatal cases age 0–64 years by using CalREDIE or faxing the Severe Influenza Case History Form to **916-440-5984**.

- Continue voluntary reporting of laboratory-confirmed influenza-associated cases age 0–64 years requiring intensive care by using CalREDIE or faxing the Severe Influenza Case History Form to **916-440-5984**.

- Continue mandatory reporting of respiratory syncytial virus (RSV)-associated fatal cases age 0–4 years. Please report these cases in CalREDIE and complete the Respiratory Syncytial Virus Death Form and either fax it to **916-440-5984** or upload it to the electronic filing cabinet in CalREDIE.

- Report acute respiratory outbreaks as soon as possible by using CalREDIE or faxing the Acute Respiratory Illness Outbreak Form to **916-440-5984**, prioritizing the following situations:

    - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory-confirmed influenza in the setting of a cluster (≥2 cases) of influenza like illness (ILI) within a 72-hour period.
    - Outbreaks associated with hospitalizations or fatalities.
    - Outbreaks assessed as having public health importance (e.g., case(s) have recent exposure to swine, recent travel to an area where novel influenza is circulating, or contact with a confirmed case of swine or novel influenza).

- Laboratory testing with real-time reverse-transcription polymerase chain reaction (rRT-PCR) is the preferred testing method when there is strong clinical suspicion, even if the rapid test is negative. Rapid influenza tests may vary in terms of sensitivity and specificity when compared with rRT-PCR, with sensitivities ranging from approximately 50-70%; false positives are

common when influenza prevalence is low and false negatives can occur when influenza prevalence is high. Encourage influenza testing, by rRT-PCR, in the situations listed below:

- Hospitalized, intensive care unit (ICU) and/or fatal cases with ILI
- Acute respiratory outbreaks
- ILI in any person where history of travel, or recent close contacts or exposures within 10 days of symptom onset, suggest concern for variant or novel influenza infection (e.g., swine (H3N2v or H1N2v) influenza, avian influenza A/H7N9 or avian influenza A/H5). For additional information see:
  - Variant Influenza Virus Information (CDC)
  - Avian Influenza A (H7N9) Virus in the United States (CDC)
  - Highly Pathogenic Asian Avian Influenza A (H5N1) Virus (CDC)
  - Novel Influenza Information (CDPH)

**Influenza-like illness = fever (>100°F or 37.8°C) and cough and/or sore throat, in the absence of a known cause*

- Collect respiratory specimens for confirmation and further subtyping by rRT-PCR at a Respiratory Laboratory Network (RLN) public health laboratory or the CDPH Viral and Rickettsial Disease Laboratory (CDPH-VRDL).

- Work with community partners (e.g., hospital clinicians and clinical laboratories) to remind them of the importance of saving specimens so further subtyping and characterization can be performed at a public health laboratory.

II. DIAGNOSTIC TESTING

- Influenza rRT-PCR testing is available at CDPH-VRDL and at 27 RLN public health laboratories.

- Upper respiratory samples suitable for rRT-PCR include: nasopharyngeal (NP) swabs, nasal swabs, throat swabs, nasal aspirate, nasal washes, NP wash, and NP aspirate. For patients hospitalized with pneumonia, specimens from the lower respiratory tract should also be obtained. Lower respiratory tract samples suitable for rRT-PCR include: bronchoalveolar lavage, bronchial wash, tracheal aspirate, and lung tissue.

- Swab specimens should be collected using swabs with a synthetic tip (e.g., polyester or Dacron®) and an aluminum or plastic shaft. Swabs with cotton tips and wooden shafts are NOT recommended. Specimens collected with swabs made of calcium alginate are NOT acceptable.

- Place appropriate swab specimen in a standard container with 2–3 ml of viral transport media (VTM) or universal transport media (UTM).

- Specimens should be collected within the first 24–72 hours of symptom onset and no later than 5 days after onset of symptoms. The specimens should be kept refrigerated at 4°C and sent on cold packs if they can be received by the laboratory within 3 days of the date collected. If samples cannot be received by the laboratory within 3 days, they should be frozen at -70°C or below and shipped on dry ice. The CDPH-VRDL is able to receive specimens Monday through Friday.

Recommendations for RLN laboratories

- During the 2017–2018 influenza season, RLN laboratories are advised to continue broadened surveillance testing for all influenza viruses in persons with:
    - ILI, especially for ICU and fatal cases
    - Outbreaks of acute respiratory illness
    - Cases where history of travel, or recent close contacts or exposures within 10 days of symptom onset, suggests concern for variant or novel influenza infection (e.g., swine (H3N2v or H1N2v) influenza, avian influenza A/H7N9 or avian influenza A/H5), as indicated above.
    - CDPH and CDC recommend rRT-PCR influenza testing of all hospitalized cases with ILI, as resources permit and at the discretion of the LHJ.

- To detect novel and possible reassorted viruses, it is important that laboratories use a full rRT-PCR subtyping panel (Inf A, H3, pdm Inf A, and pdm H1) to determine subtype. Typical seasonal influenza testing results are shown below:

Influenza real-time RT-PCR results for seasonal influenza viruses

Influenza rRT-PCR Targets:	Inf A	H3	pdm Inf A	pdm H1
A/H1 2009 pdm virus*	POS	NEG	POS	POS
A/H3 seasonal virus	POS	POS	NEG	NEG

* Influenza A(H1N1)pdm09 virus

- Specimens with rRT-PCR test results that are inconclusive or meet any of the following criteria should be reported and submitted to CDPH-VRDL for further characterization as soon as possible (contact **Hugo Guevara at 510-248-9855 (cell)**):
    - Unsubtypeable results with cycle threshold (Ct) value for Flu A ≤ 35
    - Inconclusive results for Influenza A(H1N1)pdm09 virus with Flu A Ct ≤ 35
    - Specimens with results suggesting the presence of more than one influenza virus (co-infections)
    - Specimens with results suggestive of variant (swine origin) influenza:

Influenza real-time RT-PCR results suggestive of variant (swine origin) influenza virus

Influenza rRT-PCR Targets:	Inf A	H3	pdm Inf A	pdm H1
A/H1 variant virus	POS	NEG	POS	NEG
A/H3 variant virus	POS	POS	POS	NEG

- RLN laboratories should refer to the Influenza Reference Examination Form for instructions on submission of specimens for further characterization at CDPH-VRDL.

- For ILI cases that test influenza NEGATIVE, VRDL will accept specimens for further non-influenza respiratory virus testing from cases that have severe or fatal respiratory illness or are

part of an outbreak. Please use the VRDL General Purpose Specimen Submittal Form. Please be sure to complete this form online (one form per specimen) and then print out the filled-in form(s) to include with specimen(s). If you have questions, please call VRDL at **510-307-8585**.

- Each week please email influenza test results to CDPH at Influenzasurveillance@cdph.ca.gov. A template worksheet will be distributed to all RLN labs in a separate email prior to the start of the influenza season. If possible, please note if test results originate from outpatient, hospitalized, ICU or fatal cases.

- For fatal cases, refer available fresh frozen autopsy tissues to CDPH-VRDL for further testing and histopathologic analysis at CDC. On a case-by-case basis, refer to CDPH-VRDL specimens for antiviral resistance testing (e.g., a patient on treatment with persistently positive influenza PCR results). For consultation on these cases, please contact **Hugo Guevara at 510-248-9855 (cell)**.

- Submit samples to CDPH-VRDL for antiviral viral resistance (AVR) surveillance and strain-typing according to the Influenza RightSize Roadmap sample sizes for your jurisdiction. The sample sizes will be distributed to all RLN labs in a separate email.

- Generally, the CDPH requests the submission of at least one specimen each of laboratory-confirmed positive influenza A subtypes (i.e., 2009 H1 and H3) and one specimen each of laboratory-confirmed positive B-lineage samples (i.e., Victoria B-lineage and Yamagata B-lineage) as described below:

    - At the beginning of the influenza season*****
    - During the peak of the influenza season
    - At the end of the influenza season

At beginning of the season: *submit specimens to VRDL as they are detected in your laboratory: please do NOT batch specimens for a single shipment.*

NOTE 1: *Ideally specimens should have a CT of <30 by rRT-PCR and at least 1.0mL of clinical material.*

NOTE 2: *Please submit 2 influenza B positive specimens if B-lineage data is not available.*

Testing performed at CDPH-VRDL

- Testing at CDPH-VRDL will include outpatient ILI specimens submitted by sentinel providers and reference testing as requested by RLN and/or local public health laboratories.

- CDPH-VRDL and CDC will perform surveillance testing for antiviral resistance and strain-typing on the majority of specimens submitted that have been subtyped by RLN laboratories.

- Questions regarding respiratory virus testing at CDPH-VRDL can be directed to **Hugo Guevara** [*Hugo.Guevara@cdph.ca.gov* or **510-307-8565** or **510-248-9855 (cell)**].

III. REPORTING OF SEVERE INFLUENZA CASES

- During the 2017–2018 influenza season, LHJs should continue mandatory reporting of influenza-associated fatal cases aged 0–64 years.

    - Once the resolution status of an influenza-associated death is set as “confirmed” in CalREDIE, it will be included in the state weekly report, and pediatric deaths will be reported as confirmed to CDC.

- Please report **SUSPECT influenza-associated pediatric deaths** as soon as you are notified in order to help CDPH meet national reporting requirements. The CDC requires state health departments to report suspect influenza-associated pediatric deaths within two weeks of the date of death, and to close cases within two months of the date of death. We understand that there will be times when reporting deadlines cannot be met.
- If you plan to issue a press release regarding your jurisdiction's influenza-associated death(s), please ensure the case(s) has been reported to the CDPH influenza staff at the CDPH Immunization Branch (i.e., "confirmed" in CalREDIE or paper case report form has been faxed). Please also notify the State Press Office (**Office of Public Affairs, 916-440-7259**) prior to the press release.
- The resolution status should be set to "confirmed" in CalREDIE once the death meets the case definition. If fatal cases reported by your jurisdiction meeting the case definition have a "suspect" status, please confirm them as soon as your investigation permits. This will help us minimize the lag in reporting of fatal cases and allow our official counts in the state weekly report to be consistent with what is also being reported by LHJs.

- LHJs are strongly encouraged to continue voluntary reporting of laboratory-confirmed influenza-associated cases aged 0–64 years requiring intensive care.
  - Once the resolution status of an influenza-associated ICU admission is set as "confirmed" in CalREDIE, it may be included in the state weekly report.

- LHJs should report laboratory-confirmed influenza-associated fatal and ICU cases to CDPH by using CalREDIE or faxing the Severe Influenza Case History Form to **916-440-5984**. Please upload medical records, laboratory results, and any other relevant materials to the electronic filing cabinet in CalREDIE when available.

- The CDPH Immunization Branch is undertaking an effort to collect additional seasonal influenza vaccine information for pregnant/postpartum women and pediatric severe influenza cases who were not vaccinated or with unknown vaccination status. Two supplemental forms were created, one for pediatric cases ≥6 months and another for pregnant and postpartum women (also to be used for pediatric cases less than 6 months). These forms are provider questionnaires, to be completed by LHJs, and are designed to determine influenza vaccine status and/or reasons vaccine was not administered. This form is requested for all ICU and fatal pregnant/postpartum women and pediatric cases who were not vaccinated or with unknown vaccination status. If your jurisdiction reports a case meeting the aforementioned criteria, you will receive a form request.

IV. REPORTING OF FATAL RESPIRATORY SYNCYTIAL VIRUS CASES

- During the 2017–2018 influenza season, LHJs should report laboratory-confirmed RSV-associated fatal cases aged 0–4 years.

  - Once the resolution status of an RSV-associated death is set as "confirmed" in CalREDIE, it will be included in the state weekly report.
  - If you plan on issuing a press release regarding your jurisdiction's RSV-associated death(s), please ensure the case(s) has been reported to the CDPH influenza staff at the CDPH Immunization Branch (i.e., "confirmed" in CalREDIE or paper case report form has been faxed) and also notify the State Press Office (**Office of Public Affairs, 916-440-7259**) prior to the press release.
  - The resolution status should be set to "confirmed" in CalREDIE once the death meets the case definition. If fatal cases reported by your jurisdiction meeting the case

definition have a "suspect" status, please confirm them as soon as your investigation permits. This will help us minimize the lag in reporting of fatal cases and allow our official counts in the state weekly report to be consistent with what is also being reported by LHJs.

- LHJs should report laboratory-confirmed RSV-associated fatal cases to CDPH by using CalREDIE and either faxing the Respiratory Syncytial Virus Death Form to **916-440-5984** or uploading it to the electronic filing cabinet in CalREDIE. Please upload medical records, laboratory results, and any other relevant materials to the electronic filing cabinet in CalREDIE when available.

V. REPORTING OF NON-TB RESPIRATORY OUTBREAKS

- During the 2017–2018 influenza season, LHJs should continue mandatory reporting of any acute respiratory outbreaks by using CalREDIE or faxing the Acute Respiratory Illness Outbreak Form to **916-440-5984**, prioritizing the following situations:
    - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory-confirmed influenza in the setting of a cluster (≥2 cases) of ILI within a 72-hour period.
        - Even if it is not influenza season, influenza testing should occur when any resident has signs and symptoms that could be due to influenza, and especially when two or more residents develop respiratory illness within 72 hours of each other.
    - Outbreaks in institutions or congregate settings (e.g., schools, day camps) associated with hospitalizations or fatalities. If the setting is a hospice or long-term care facility, the LHJ should use its judgment as to whether the number of hospitalizations and/or fatalities is above baseline for that institution or setting.
    - Outbreaks in an institution, congregate setting or community where there has been recent exposure to swine for at least one case, or contact with a confirmed case of swine influenza (e.g., H3N2v or H1N2v).
    - Outbreaks in a community assessed by the LHJ as having public health importance.

- Laboratory confirmation can include any positive test performed by any clinical, commercial or local public health laboratory, including positive rapid antigen test, positive direct fluorescence assay, positive viral culture or positive PCR test. As rapid antigen tests may yield a relatively high proportion of false positive results when influenza prevalence is low and false negative results when influenza prevalence is high, it is recommended that rapid antigen test results be followed up with confirmatory rRT-PCR testing. For cases of severe influenza, specimens should be sent for further sub-typing/characterization to the local public health laboratory or CDPH-VRDL, to enable CDPH to closely monitor influenza viruses that may be novel or resistant to antiviral medication.

- Outbreak reports may be completed by LHJs in CalREDIE or by submitting the Acute Respiratory Illness Outbreak Form via fax to **916-440-5984**.

- Once the resolution status of an outbreak is set as "confirmed" in CalREDIE, it will be included in the state weekly report.

VI. ADDITIONAL QUESTIONS OR ASSISTANCE

Reporting or Surveillance Questions

- Contact the CDPH Immunization Branch at **510-620-3737** or the Influenza Surveillance Program by email at influenzasurveillance@cdph.ca.gov

Laboratory Testing Information or Questions

- For general specimen submission questions:
  - Contact the CDPH-VRDL at **510-307-8585**

- For specific laboratory testing inquiries:
  - Contact Hugo Guevara of the CDPH-VRDL for routine lab questions by email at *Hugo.Guevara@cdph.ca.gov* or by phone at **510-307-8565 (desk)**
  - For **urgent** situations, contact Hugo Guevara by cell phone at **510-248-9855 (cell)**