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

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September 2024

Recommendations for Local Health Departments: Influenza and Other Respiratory Virus Testing and Reporting — 2024–2025

The California Department of Public Health (CDPH) guidance for local health departments (LHDs) summarizes diagnostic testing guidelines and influenza and other respiratory virus reporting requirements for the 2024–2025 respiratory season. Influenza and RSV activity typically start increasing in the fall and peak during winter months; however, for data visualization and reporting purposes the respiratory virus surveillance season will be considered June 30, 2024–June 28, 2025 (Weeks 27–26).

HIGHLIGHTS

- Continue mandatory reporting of laboratory-confirmed influenza-associated fatal pediatric cases <18 years of age by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov).

- Continue mandatory reporting of respiratory syncytial virus (RSV)-associated fatal cases in children 0–4 years of age by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov).

- Report acute respiratory outbreaks as soon as possible by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov). Prioritize the following situations below. **Please note that acute respiratory outbreak reporting instructions in this guidance do not apply to COVID-19 outbreaks.**
    - Influenza outbreaks: occurring in institutions/congregate settings (e.g., long-term care facilities, high risk settings) 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.

* ILI is defined as fever (≥100°F or 37.8°C) plus cough and/or sore throat, in the absence of a known cause other than influenza. Persons with ILI often have fever or feverishness with cough, chills, headache, myalgia, sore throat, or runny nose. Some persons, such as older persons, children with neuromuscular disorders, and young infants may have atypical clinical presentations, including the absence of fever. In the context of a multi-pathogen outbreak that includes influenza, patients with ILI symptoms who have tested positive for another respiratory pathogen in the absence of an influenza negative test result may be considered to meet the ILI case definition; however, influenza testing is recommended in this situation because the results are helpful for infection control and clinical decision-making.

- Non-Influenza and non-COVID-19 respiratory outbreaks, including respiratory syncytial virus (RSV): occurring in institutions/congregate settings (e.g., long-term care facilities, high risk settings) with at least one case of a laboratory-confirmed respiratory pathogen, other than influenza or SARS-CoV-2, in the setting of a cluster (≥2 cases) of acute respiratory illness (ARI)[†] within a 72-hour period.

- Community settings outbreaks: assessed as having public health importance (e.g., outbreaks associated with hospitalizations or fatalities; or case(s) that have recent exposure to swine, contact with animals confirmed or suspected to have avian influenza, their environment or their raw products, or contact with a confirmed case of avian, variant, 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 of influenza. PCR testing can be used for confirmatory testing even if a 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.
  - Influenza testing by rRT-PCR should occur for all persons with ILI where recent close contacts, or exposures within 10 days of symptom onset suggest concerns for avian, variant, or novel influenza infection (e.g., variant influenza A (H3N2)v, (H1N2)v, or (H1N1)v, or avian influenza H5N1 or H7N9). For additional information see:
    - Variant Influenza Virus Infections in Humans (CDC)
    - Avian Influenza Virus Infections in Humans (CDC)
    - Avian and Novel Influenza Quicksheet (CDPH)
    - Laboratory Testing for Novel Influenza A (CDPH)
  - 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

- Confirmation and further subtyping by rRT-PCR is available at Respiratory Laboratory Network (RLN) public health laboratories (PHLs) or the CDPH Viral and Rickettsial Disease Laboratory (CDPH-VRDL).

- LHDs should work with local clinical partners (e.g., hospital clinicians and clinical laboratories) to remind them the importance of saving specimens so that further subtyping and characterization can be performed at a PHL.

DIAGNOSTIC TESTING

- Influenza rRT-PCR testing is available at CDPH-VRDL and at 24 RLN public health laboratories.

[†] ARI is defined as an illness characterized by any two of the following: fever, cough, rhinorrhea (runny nose) or nasal congestion, sore throat, or muscle aches.

- 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 onset of symptoms and no later than 5 days after onset of symptoms. For patients suspected of having avian, variant, or novel influenza, specimens may be collected no later than 10 days after symptom onset. Freeze or refrigerate specimens after collection. Ship refrigerated specimens to VRDL on cold packs. Ship frozen specimens to VRDL on dry ice. The CDPH-VRDL can receive specimens Monday through Friday.

Recommendations for RLN Laboratories

- During the 2024–2025 respiratory season, RLN laboratories are advised to continue broadened influenza surveillance testing for:
  - ILI cases, especially for hospitalized, ICU, and fatal cases
  - Outbreaks of acute respiratory illness
  - Cases where recent close contacts, or exposures within 10 days of symptom onset suggests concern for avian, variant, or novel influenza infection (e.g., variant influenza A (H3N2)v, (H1N2)v, or (H1N1)v, or avian influenza H5N1 or H7N9), as indicated above.

- To detect novel and possible reassorted viruses, it is important that PHLs NOT batch test influenza specimens and that a full rRT-PCR subtyping panel (Inf A, H3, pdm Inf A, and pdm H1) is used to determine the 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

- Batching specimens for influenza A subtyping is NOT recommended because this may delay the detection of a novel virus and is counter to the aim of having PHLs perform influenza subtyping testing.

- Specimens with rRT-PCR test results that 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**):
  - **Unsubtypable results:** with cycle threshold (Ct) value for Flu A ≤35, which might suggest a novel influenza virus inflection
  - **Inconclusive results:** for Influenza A(H1N1)pdm09 virus with Flu A Ct ≤35, which might suggest a variant influenza virus infection
  - **Co-Infections:** specimens with results suggesting the presence of more than one influenza virus (co-infections)
  - **Suspect or probable avian influenza results:** Influenza A positive specimens collected from a person meeting clinical and epidemiological criteria for avian influenza should be tested using the CDC H5 Dx Assay. Public health laboratories using the VRDL RUO reagents for the initial influenza A testing and subtyping should submit the specimen to CDPH-VRDL for testing using the CDC H5 Dx Assay or the CDC H7 Dx Assay, depending on patient history.
  - **Suspect variant (swine origin) results:** specimens with results suggestive of variant 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 VRDL General Purpose Specimen Submittal form or the VRDL Lab Web Portal, and the Influenza Reference Examination Form for instructions on submission of specimens for further characterization at CDPH-VRDL.

- For severe ILI cases or respiratory outbreak specimens that test NEGATIVE by rRT-PCR for both SARS-CoV-2 and influenza, the VRDL will accept specimens for further non-influenza respiratory virus testing. Specimens submitted to VRDL must be accompanied with a hard copy of the completed VRDL General Purpose Specimen Submittal Form (PDF) for each specimen or a form generated in the VRDL Lab Web Portal. If you have questions, please call VRDL at **510-307-8585**.

- **Influenza and SARS-CoV-2 Testing:** The CDC developed an emergency use authorization (EUA)-approved rRT-PCR multiplex assay that simultaneously detects influenza A, influenza B, and SARS-CoV-2 (Flu SC2). The CDC has proposed different scenarios in which state and PHLs may include the Flu SC2 assay in influenza diagnostic

or surveillance testing systems. The algorithm includes testing specimens: (1) with no test results for influenza or SARS-CoV-2, (2) for confirmation of rapid influenza diagnostic test (RIDT), and (3) with negative results for SARS-CoV-2 by a CLIA approved rRT-PCR assay. If a specimen tests positive for influenza A or B, influenza A subtyping or B-lineage genotyping should be completed in a timely manner regardless of the algorithm followed by the PHL.

- Each week, 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 for specimens tested during the first day of week 40 through last day of week 39. If possible, please note if test results originate from outpatient, hospitalized, ICU or fatal cases. All influenza testing done in RLN laboratories using the CDC or VRDL influenza assay or the Flu SC2 multiplex assay should be reported using the template. Specimens tested on both the Flu SC2 multiplex assay and the CDC or VRDL influenza assay should be reported only once.

- 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.**

- Submit samples to CDPH-VRDL for antiviral 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 document.

- Generally, CDPH requests the submission of at least one specimen each of laboratory-confirmed positive influenza A subtypes (i.e., H1pdm09 and H3) and one specimen each of laboratory-confirmed positive B-lineage genotypes (i.e., Victoria B-lineage and Yamagata B-lineage). In addition, please submit Yamagata B-lineage specimens as they are detected for additional characterization.
    - Submit laboratory-confirmed influenza positive specimens to CDPH-VRDL as follows:
        - At the beginning of the respiratory season: submit specimens to VRDL as they are detected in your laboratory; please do NOT batch specimens for a single shipment
        - During the peak of the respiratory season
        - At the end of the respiratory season

- Additional specimen considerations:
    - Ideally, specimens should have a CT of <30 by rRT-PCR and at least 1.0mL of clinical material.
    - Please submit two influenza B positive specimens if B-lineage data is not available.
    - During the season, the VRDL may contact PHLs requesting the submission of additional influenza positive specimens from specific jurisdictions.

- The VRDL requests SARS-CoV-2 testing status for influenza positive specimens submitted with the Influenza Reference Examination Form.

Laboratory Testing provided by CDPH-VRDL

- Testing by CDPH-VRDL will include outpatient ILI specimens submitted by sentinel providers and reference/confirmatory testing as requested by RLN and/or local PHLs. Only specimens submitted by sentinel providers will be tested for SARS-CoV-2. These specimens will be tested using the Flu SC2 multiplex assay.

- Due to the current demand for SARS-CoV-2 testing by different EUA rRT-PCR assays and the limited supply of the Flu SC2 multiplex assay, the VRDL will incorporate the latter to test specimens submitted by sentinel providers (outpatient population) and for outbreak investigations.

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

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

REPORTING OF FATAL INFLUENZA CASES

- During the 2024–2025 respiratory season, LHDs should continue mandatory reporting of influenza-associated fatal pediatric cases age <18 years.

- LHDs should report laboratory-confirmed influenza-associated fatal pediatric cases to CDPH by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov). Please upload medical records, laboratory results, and any other relevant materials to the electronic filing cabinet in CalREDIE when available. Please do NOT upload death certificates to the electronic filing cabinet in CalREDIE.
    - Please report suspect influenza-associated pediatric deaths as soon as you are notified 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.
    - Once the resolution status of an influenza-associated pediatric death is set as "confirmed" in CalREDIE, it will be included in the state weekly report and reported as confirmed to CDC.
    - If you plan to issue a press release regarding your jurisdiction's influenza-associated pediatric death(s), please ensure the case(s) has been reported to the CDPH Immunization Branch (i.e., "confirmed" in CalREDIE or paper case report form has been emailed). Please also notify the **CDPH Office of Public Affairs (media@cdph.ca.gov**) prior to the press release.
    - Influenza-associated deaths in children <18 years of age who are co-infected with RSV should be reported for both conditions.
- The CDPH Immunization Branch is collecting additional seasonal influenza vaccine information for influenza-associated fatal pediatric cases. Two supplemental forms were created for this purpose, one for pediatric cases ≥6 months, and a second birthing parent vaccine history form for pediatric cases <6 months. These forms are provider

questionnaires, administered by LHDs, that are designed to determine influenza vaccine status and/or reasons vaccine was not administered. This form is requested for fatal pediatric cases ≥6 months who were not vaccinated or with unknown vaccination status, and for cases <6 months of age if the birthing parent was not vaccinated or had an unknown vaccination status. If your jurisdiction reports a case meeting the criteria, you will receive a supplemental form request.

REPORTING OF FATAL RESPIRATORY SYNCYTIAL VIRUS CASES

- During the 2024–2025 respiratory season, LHDs should report laboratory-confirmed RSV-associated fatal cases in children 0–4 years of age.

- LHDs should report laboratory-confirmed RSV-associated fatal cases to CDPH by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov). Please upload medical records, laboratory results, and any other relevant materials to the electronic filing cabinet in CalREDIE when available. Please do NOT upload death certificates to the electronic filing cabinet in CalREDIE.
  - Once the resolution status of an RSV-associated death in a child 0–4 years of age 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 emailed). Please also notify the **CDPH Office of Public Affairs (media@cdph.ca.gov**) 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 being reported by LHDs.
  - RSV-associated deaths in children 0–4 years of age who are co-infected with influenza should be reported for both conditions.

REPORTING OF NON-TB, NON-COVID-19 RESPIRATORY OUTBREAKS

- Please note that acute respiratory outbreak reporting instructions in this guidance do not apply to COVID-19 outbreaks. COVID-19 outbreak information is available on the COVID-19 All Guidance webpage:
  - Healthcare Facilities: AFL 23-08
  - Non-Healthcare Congregate Facilities: Outbreak Definition and Reporting Guidance

- Local health jurisdictions should continue mandatory reporting of any acute respiratory outbreak, no matter when they occur, by using CalREDIE or secure email (influenzasurveillance@cdph.ca.gov). Prioritize responding to respiratory outbreaks in the following situations:

- Influenza outbreaks: occurring in institutions/congregate settings (e.g., long-term care, high risk settings) 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 respiratory season, consider influenza testing in long-term care facilities and high-risk settings 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 and testing for SARS-CoV-2 is negative. If SARS-CoV-2 and influenza are negative, submit for testing using a full respiratory viral panel. In high-risk settings, consider submitting specimens for a full respiratory viral panel as soon as a SARS-CoV-2 test is negative.
- Non-Influenza and non-COVID-19 respiratory outbreaks, including respiratory syncytial virus (RSV): occurring in institutions/congregate settings (e.g., long-term care facilities, high risk settings) with at least one case of a laboratory-confirmed respiratory pathogen, other than influenza or SARS-CoV-2, in the setting of a cluster (≥2 cases) of acute respiratory illness (ARI) within a 72-hour period.
    - Outbreaks of other respiratory viruses such as RSV in long-term care facilities and other high-risk settings may be associated with substantial morbidity and mortality. Early identification and implementation of recommended infection control precautions can reduce these impacts. Consider RSV testing in residents with respiratory illness, especially during the respiratory season. In high-risk settings, consider submitting specimens for a full respiratory viral panel as soon as a SARS-CoV-2 test is negative.
- Outbreaks in community settings that are assessed as having public health importance (e.g., outbreaks associated with hospitalizations or fatalities; or case(s) that have recent exposure to swine, contact with animals confirmed or suspected to have avian influenza, their environment or their raw products, or contact with a confirmed case of avian, variant or novel influenza).

- Laboratory confirmation for outbreak-associated cases can include any positive test performed by any clinical, commercial, or local PHL, 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 influenza antigen test results be followed up with confirmatory rRT-PCR testing.

- For outbreak cases with severe influenza, specimens should be sent for further subtyping/characterization to the local PHL or CDPH-VRDL, to enable CDPH to closely monitor influenza viruses that may be novel or resistant to antiviral medication.

ADDITIONAL QUESTIONS OR ASSISTANCE

Reporting or Surveillance Questions

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

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**