CDC STRATEGY FOR
ENHANCED SUMMER 2024 INFLUENZA SURVEILLANCE

As the multistate outbreak of avian influenza A(H5N1) in dairy cows, poultry and other animals continues and agricultural fair season approaches, conducting surveillance for seasonal influenza viruses and monitoring for novel influenza A virus infections remains critical to inform public health actions. CDC, in collaboration with STLT public health agencies, has developed a multi-faceted enhanced summer influenza surveillance strategy that will be modified as new information is learned or the situation changes warranting a revised approach.

The activities described below are aimed at identifying spread of HPAI A/H5 to and among people, beginning with those exposed to infected/potentially infected animals and extending outward to the general population .

1. Identification of human infections via symptom monitoring among workers and others with recent exposures to HPAI A/H5 infected animals on farms or other locations.
    - Partners: State and local public health; CDC and USDA support as requested
    - Activities
        i. If possible, active symptom monitoring should involve daily contact between health department staff and exposed persons using a list of names and contact information provided by the farm. This daily contact can be made through various methods based on jurisdiction resources and preferences of the persons under monitoring (i.e., text based, phone, etc.). As resources allow, ensure communication materials and methods are linguistically and culturally appropriate.
        ii. If farms do not provide the names and contact information of exposed workers to public health, the health department could (1) provide information directly to the workers or the farm owners about self-monitoring and who to contact if symptoms occur so that testing can be arranged if necessary or (2) work through an intermediary such as Department of Agriculture personnel, a facility veterinarian or a professional association to provide self-monitoring and symptom reporting information to farm workers.
2. Conduct outreach and education to people exhibiting animals (specifically swine, cattle and avian species) at or attending agricultural fairs. (A few key activities are described below but a detailed agricultural fair resource document is being developed using a one health approach and will be shared as soon as it is ready.)
    - Partners: State and local public health and departments of agriculture; CDC and USDA support as requested
    - Activities
        i. If possible, have local or state public health staff on site (or work with Department of Agriculture or fair associations who will be onsite) to provide education, assess symptoms and arrange for testing as needed
        ii. Disseminate information at the fairs regarding risks, infection prevention, symptoms to be aware of and whom to contact if symptoms develop. This can be done through the fair organizers.
        iii. Prior to the fair, provide information to individuals and groups that show animals regarding risks, infection prevention, symptoms to be aware of and whom to contact if symptoms develop.
3. Encourage ongoing influenza testing (preferably RT-PCR) of individuals with compatible illness (e.g. respiratory illness with or without a fever or conjunctivitis) throughout the summer, particularly for persons with recent history of relevant exposures (e.g., dairy cows, raw milk, wild birds, poultry, agricultural fair attendance).
    - Partners: State and local public health; CDC and USDA support as requested
    - Activities

i. Conduct outreach to health care providers to continue influenza testing throughout the summer using effective methods of communication (e.g., HANs, webinars, listservs, mailings).
ii. Consider targeted outreach to provider/clinics in areas surrounding premises with animals confirmed to have HPAI A/H5 infection (could be in person visits).

4. Enhance surveillance for novel influenza A detection among severely ill patients (i.e. hospitalized or ICU).
    - Partners: State and local public health; CDC support as requested
    - Activities:
        i. Conduct outreach to providers to request influenza testing throughout the summer for hospitalized/ICU patients presenting with compatible illness (irrespective of exposure history) and the importance of/methods for determining the influenza A subtype for all influenza A positive specimens.
        ii. Develop timely methods for identifying hospitalized patients who are influenza A positive. If possible, determine if the influenza A positive patient was in the ICU.
        iii. Arrange for subtyping of the influenza A positive specimen from all ill severely ill persons (i.e. hospitalized or ICU) either in the clinical laboratory or by shipping the specimen to the public health laboratory (PHL).
5. Enhance surveillance for novel influenza A detections in the community.
    - Partners: State and local public health; CDC support when possible and when requested
    - Activities
        i. CDC requests that jurisdictions strive to meet the 1 in 200 novel event detection goal as described in the Influenza Right Size Roadmap through increasing the number of influenza positive specimens tested in PHLs over the summer. The number of influenza positive specimens tested each week using the CDC subtyping assay to meet this goal ranges from 3 to 72, depending on the jurisdiction's population (see Influenza Right Size Roadmap Appendix A). As influenza activity declines, it may become increasingly difficult to meet this goal. However, maintaining efforts to bring in specimens for influenza testing and subtyping all influenza A positives at the PHL over the summer is important to maintain visibility of the influenza A subtypes circulating.
            1. Ask providers and clinical laboratories that submit specimens to the PHL during the fall and winter to continue doing so throughout the summer.
            2. Explore any additional providers or clinical laboratories that would be willing to submit specimens throughout the summer.
            3. CDC to provide guidance and request that commercial laboratories increase submission of influenza A and B positive specimens to state/local PHLs or national reference laboratories for additional subtyping (Appendix 1.)
            4. CDC is exploring with HRSA what role their rural health clinics might play in submitting specimens to PHLs.
        ii. PHLs should attempt to subtype all influenza A positive specimens and submit influenza specimens for additional characterization to their designation National Influenza Reference Center (NIRC).
            1. For all states, submit influenza positive specimens that meet the submission criteria outlined in Appendix 2 to the NIRC.
            2. All three NIRCs will remain operational this summer to handle the increased submission load.
        iii. Conduct whole genome sequencing of additional influenza specimens.
            1. For a state with a designated Influenza Sequencing Center (ISC), sequence influenza specimens that are not submitted to the NIRC.
            2. For states without a designated ISC, submit influenza positive specimens that meet the submission criteria outlined in Appendix 2 to the NIRC.
        iv. Unexplained clusters of respiratory illness should be investigated, including collection of specimens for testing, to determine the pathogen(s) causing illness.

6. Monitor influenza surveillance data for any unexpected patterns.
    - Partners: State and local public health, CDC
    - Activities
        i. State and local public health monitor data within their jurisdictions.
        ii. CDC analyzes the following data:
            1. Virologic data from 250 clinical laboratories (65,000 – 150,000 specimens tested weekly) and 90 PHLs (1,500 -5,000 specimens tested weekly)
            2. Outpatient respiratory illness data reported from more than 4000 outpatient providers/EDs (approximately 2.5 million patient visits weekly).
            3. Emergency department visits with influenza as a discharge diagnosis.
            4. Hospitalization data from FluSurvNet sites that are extending their traditional enrollment period (October 1 – April 30) to cover May 1– September 30.
            5. Mortality data from the National Vital Statistics Surveillance System that covers more than 99% of deaths occurring in the United States.
            6. Influenza concentrations identified in wastewater data reported by approximately 250 sites.
7. Local data anomaly detection and investigation.
    - Partners: State and local public health, CDC
    - Activities
        i. Follow-up on anomalies identified in the number of emergency department visits with influenza, influenza-like illness and conjunctivitis as a discharge diagnosis.
            1. Many state and local health departments, as well as CDC run anomaly detection algorithms to detect unexpected increases or clusters. If anomalies are identified at CDC, other influenza data sources (e.g. laboratory, hospitalization etc.) are reviewed for the area identified and results are shared with state/local public health partners.
            2. State/local public health partners review their influenza data and other relevant information (e.g. farms with A/H5 infected animals, milk producers etc.) for the area identified.
        ii. CDC will follow-up on any wastewater sites with an influenza level metric that is high (≥80 percentile) compared to values from the last season.
            1. CDC analyzes data, identifies sites reporting a high level of influenza A, reviews other data (e.g. influenza laboratory, emergency department hospitalization etc.) at CDC for the area identified and shares results with state/local public health partners.
            2. State/local public health partners review their influenza data and other relevant information (e.g. farms with A/H5 infected animals, milk producers etc.) for the area identified for the area identified.

Appendix 1: Guidance to commercial laboratories to increase submission of influenza A and B positive samples to state and local PHLs for additional subtyping (including H5)

During the week of March 25, 2024, USDA confirmed detections of influenza A(H5) highly pathogenic avian influenza (HPAI) in dairy cattle in the panhandle region of Texas. As of May 29, cows in over 65 dairy farms across 9 states have been confirmed positive for HPAI. On April 1, 2024, Texas announced that a person, who had direct exposure to cattle, had tested positive for the HPAI A(H5N1) virus. One additional person with direct exposure to cattle tested positive for A/H5 in May. In an effort to enhance surveillance of influenza infections during this outbreak, CDC in coordination with STLT public health agencies, requests that commercial laboratories prospectively increase submissions to their jurisdictional PHL during the spring and summer months when influenza transmission is normally low. This guidance has been developed to ensure the efficient transfer of clinical specimens for additional subtyping testing. Commercial laboratories are encouraged to communicate with the PHL of the patient's state of residence prior to submitting specimens to obtain the appropriate specimen submission form and any additional submission instructions. Specimens will be tested for surveillance purposes and patient specific reports may not be returned to the submitter.

CDC requests commercial laboratories continue to send the following specimens to PHLs as soon as possible for further testing and characterization.

1. Influenza A positive specimens that are subtype negative on tests designed to provide an influenza subtyping result (ex. Biofire) **and confirmed upon retest.**
2. Influenza A positive specimens that are subtype influenza A(H1) and not influenza A(H1)pdm09 on tests designed to provide an influenza subtyping result **and confirmed upon retest.**

For Awareness:

Performance characteristics for the CDC *in vitro* diagnostic reverse transcription real-time polymerase chain reaction (rRT-PCR) subtyping assays have been determined with the following human upper respiratory specimens from patients with signs and symptoms of respiratory infection and/or from viral culture:

a. nasopharyngeal swabs [NPS]
b. nasal swabs [NS]
c. throat swabs [TS]
d. nasal aspirates [NA]
e. nasal washes [NW]
f. dual nasopharyngeal/throat swabs [NPS/TS]

Performance characteristics for the CDC *in vitro* diagnostic reverse transcription real-time polymerase chain reaction (rRT-PCR) subtyping assays have been determined with the following human lower respiratory tract specimens from patients with signs and symptoms of respiratory infection:

a. bronchoalveolar lavage [BAL]
b. bronchial wash [BW]
c. tracheal aspirate [TA]
d. sputum and lung tissue

Enhanced Surveillance:

Submissions of additional influenza A and B positive specimens that have not undergone influenza subtyping testing are greatly appreciated to ensure rapid detection of any human infections of A(H5N1). While submission of as many samples as possible is preferred for the summer months ahead, CDC (in collaboration with APHL) can help to determine an appropriate and feasible number of samples each month in order to prioritize available laboratory resources. Please consider submission of samples that meet the established assay cutoff of your testing method to identify positive samples. CDC will continue to work with commercial laboratories and APHL to determine a process by which samples will be submitted to state and local public health laboratories or national reference laboratories for additional subtype testing.

Appendix 2. Summer 2024 Guidance to PHLs for Influenza Surveillance Specimen Submission

Please submit influenza positive specimens every two weeks to a national influenza reference center (NIRC) according to the new guidelines below. All three NIRCs will remain operational this summer so please submit surveillance specimens to your designated NIRC (Table 1).

Please follow instructions to complete the electronic Influenza Specimen Submission Form and provide metadata.

- Email the electronic version of the Influenza Specimen Submission Form to your designated NIRC email in Table 1.
- Print a shipping manifest from the Influenza Specimen Submission Form (preset in excel template) and include it in the shipping container.

Please send influenza virus positive specimens every two weeks to the NIRC following the same guidelines used earlier during the 2023-2024 season (described below). Please do not ship surveillance specimens directly to CDC. ISCs should sequence influenza positives not sent to the NIRC.

Specimen selection criteria for submission:

a. Original clinical specimens positive for influenza and negative for SARS-CoV-2, which have been identified during the prior two weeks. Only specimens stored in VTM, UTM or in certain specimen types, saline should be sent and not specimens stored in MTM. Saliva is not a suitable specimen for influenza virus characterization.
b. Specimens should have CT values of 28 or lower based on InfA or InfB tests using the CDC Flu SC2 Multiplex Assay or the CDC Flu rRT-PCR Dx Panel
c. Representative subtype/lineages:
    - 6 influenza A(H3N2) positive specimens
    - 4 influenza A(H1N1)pdm09 positive specimens
    - 4 influenza B/Victoria lineage positive specimens
      **All B/Yamagata lineage positive specimens should be submitted following the guidance for diagnostic specimens. It is very important to continue to conduct B genotyping to detect potential B/Yamagata lineage viruses and submit them to CDC for confirmation. However, if B genotyping can't be performed please submit only 4 influenza B positive specimens.*
d. Ideally send 0.5 mL of original clinical specimen; if 0.5 mL is not available, submit no less than 0.3 mL.

Table 1. Designated National Influenza Surveillance Reference Centers and Shipping Addresses

NIRC*	Shipping Address	Specimen Submission Laboratories All public health laboratories (state, county, or city) in the following states/territories:
California Department of Public Health, Viral and Rickettsial Disease Laboratory	CDPH/VRDL Attn: Estela Saguar/Hugo Guevara 850 Marina Bay Parkway, B262 Richmond, CA 94804 Phone: (510) 307-8497 Email: CDPHVirusIsolationProject@cdph.ca.gov	Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, New Mexico, Nevada, Oregon, Texas, US Affiliated Pacific Islands*, Utah, Washington, Wyoming *via Guam and/or Hawaii
New York State Department of Health (Wadsworth Center)	David Axelrod Institute Attn: Laboratory of Viral Diseases 120 New Scotland Ave Albany, NY 12208 Tel: (518) 474-4177 Email: fluNYS@health.ny.gov	Connecticut, Delaware, District of Columbia, Florida, Georgia, Massachusetts, Maryland, Maine, North Carolina, New Hampshire, New Jersey, New York, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, US Virgin Islands, Virginia, Vermont, West Virginia
Wisconsin State Laboratory of Hygiene	Wisconsin State Laboratory of Hygiene Attn: Communicable Disease Division (PO Box 7904) Virology Laboratory 2601 Agriculture Drive Madison, WI 53718 Phone: (800) 862-1013 Email: virus@slh.wisc.edu	Alabama, Arkansas, Iowa, Illinois, Indiana, Louisiana, Kansas, Kentucky, Michigan, Minnesota, Missouri, Mississippi, North Dakota, Nebraska, Ohio, Oklahoma, South Dakota, Tennessee, Wisconsin

Antiviral Resistance Testing Submissions

Testing for enhanced antiviral resistance surveillance will be suspended over the summer. If you have any questions regarding antiviral resistance testing, please contact Dr. Larisa Gubareva at CDC or send an email to fluantiviral@cdc.gov.

Appendix 3. Summer 2024 Guidance to PHLs for Influenza Diagnostic Specimen Submission

Please contact flusupport@cdc.gov if you have any questions regarding influenza diagnosis or referral of specimens for diagnostic rRT-PCR testing.

For Influenza Diagnostic Submissions to CDC, please contact Dr. Marie Kirby or flusupport@cdc.gov. It is very important that you rapidly contact CDC, at these addresses, if your laboratory identifies specimens that are atypical or have non-standard results. These types of results could identify a variant influenza A virus similar to those circulating in swine or other novel influenza A viruses with pandemic potential. Also, please refer specimens that are positive for influenza B virus but lineage was not able to be determined to CDC for further characterization. Specimens with non-standard test results that suggest the presence of a mixture of influenza A viruses should be submitted to CDC for confirmation. However, mixtures (i.e., co-infections) of influenza A and influenza B viruses do not need to be submitted to CDC for confirmation.

In particular, please send specimens with non-standard test results as detailed in the instructions for use of the CDC Flu SC2 Multiplex, A/ B Typing and A subtyping assays and notify CDC IMMEDIATELY **(flusupport@cdc.gov).**

Reminder: The A/H5 assay should not be performed unless the patient meets clinical and epidemiologic criteria for testing suspect specimens. PHL may run conjunctival swab specimens in the CDC H5 assay as long as they are paired with approved respiratory specimens and stored/shipped in approved media for the assay.

If presumptive positive per CDC's FDA approved instructions for use (IFU), they can be sent to CDC as a diagnostic specimen under typical diagnostic shipping protocols.

- **Any unsubtypable results from CDC H5 assay should be shipped to CDC immediately**
- **Any presumptive positive results from the CDC H5 assay should be shipped to CDC immediately**
- **Any inconclusive test results from the CDC H5 assay should be shipped to CDC immediately**

CDC is approved to run conjunctival swab specimens with this assay as a CLIA validated laboratory developed test.

To submit viruses for diagnosis please fill out one of the following forms and send along with your submission: **CDC Specimen Submission Form, CDC 50.34** (Required for CLIA reporting) or CDC Specimen Test Order and Reporting (CSTOR) | Submitting Specimens to CDC | Infectious Diseases Laboratories | CDC and indicate the following specific information**:**

- **Reason for Submission:** Diagnosis
- **If Clinical Specimen**: Indicate specimen type
- **Type/Subtype:** Inconclusive
- **Comments:**
  - Provide any relevant rRT-PCR data
  - Include patient's name and date of birth on the CDC 50.34 or CSTOR.
  - Please be sure to label the specimen with two identifiers, including patient name
  - Samples must be received frozen

Diagnostic Shipping Address:
Marie Kirby, PhD
Centers for Disease Control and Prevention
Influenza Division, H23-6
c/o STAT (unit 198)
1600 Clifton Rd, NE
Atlanta, GA 30329

Appendix 4. Summer 2024 Guidance for National Influenza Reference Centers (NIRCs)

In the influenza surveillance and specimen submission guidance sent to state PHLs (referred to as originating lab) for Summer 2024, influenza positive specimens are to be submitted to NIRCs every two weeks which meet the stated specimen selection criteria and with the following representative subtype/lineages:

6 influenza A(H3N2) positive specimens
4 influenza A(H1N1)pdm09 positive specimens
4 influenza B/Victoria lineage positive specimens

All specimens received at the NIRC will continue to undergo NGS, however not all specimens will undergo isolation. Each NIRC should randomly select specimens from each originating lab package and follow the isolation right-size number. Any specimens received from the originating lab above the isolation right-size number do not undergo isolation.

NIRC Isolation right-size number:

3 influenza A(H3N2) positive specimens
2 influenza A(H1N1)pdm09 positive specimens
2 influenza B/Victoria lineage positive specimens

Shipment to CDC should occur after the NIRC has completed the isolation workflows for selected specimens from the originating lab package/state PHL. The shipment will include all RCV tubes as well as the additional aliquots for specimens with successful isolation results bundled by the originating lab(s)/state PHL.

For example:

1) Specimens NOT chosen for isolation:
   - ISR Aliquot-NGS performed @ NIRC
   - RCV (ORIGINAL) – remaining tube sent to CDC
   - Data fields would appear as follows: Inoculation Date: null; Grow TC?: null; Passage: null; HA titer: null

2) Specimens chosen for isolation:
   - ISR Aliquot- NGS performed @ NIRC
   - RCV (ORIGINAL) – remaining tube sent to CDC
   - Successful Isolates
     - **ISA tube – NGS performed @ NIRC for all isolates**
     - REF tube – sent to CDC
     - MET tube – sent to CDC
     - RPS tube – sent to CDC
     - RHI –scintillation vial – sent to CDC
   - Data fields would appear as follows: Inoculation Date: Filled in; Grow TC?: Filled in; Passage History: Filled in if successful; HA titer: Filled in if successful.

Once received and accessioned at CDC, the date received from contract lab will be filled in signifying that NIRC workflows have been completed.