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

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1. Access to IV Peramivir under Emergency Use Authorization

FDA has issued an emergency use authorization (EUA) for the investigational antiviral drug peramivir intravenous in certain adult and pediatric patients with confirmed or suspected 2009 H1N1 influenza infection who are admitted to a hospital. IV peramivir is authorized only for hospitalized adult and pediatric patients for whom therapy with an IV drug is clinically appropriate, based on one or more of the following:

- Adult patients:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g., enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible, or
  - the clinician judges IV therapy is appropriate due to other circumstances.
- Pediatric patients:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g., enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible.

Peramivir IV should not be used for the treatment of seasonal influenza A or B virus infections, for outpatients with acute uncomplicated 2009 H1N1 influenza infection or for pre- or post-exposure chemoprophylaxis (prevention) of influenza.

For more information, go to http://www.cdc.gov/h1n1flu/eua/peramivir.htm or to http://www.cdc.gov/h1n1flu/EUA/pdf/peramivir_qa.pdf or call 1-800-CDC-INFO (1-800-232-4636).

2. 2009 H1N1 influenza infection among pregnant women

On October 19, 2009, CDC established a support line (404-368-2133) for healthcare providers that will be staffed 24 hours/7 days a week to provide clarification on CDC guidance for pregnant women via telephone consultation with a board-certified OB/GYN. Healthcare providers can call the support line directly to obtain information. CDC also has guidance available on its website regarding the care and treatment of pregnant women including the following links: http://www.cdc.gov/h1n1flu/clinician_pregnant.htm and http://www.cdc.gov/h1n1flu/recommendations.htm

Please share this information with healthcare providers in your jurisdiction. Note: women <2 weeks postpartum should now be considered high risk for influenza complications and prioritized for antiviral treatment.

To better understand severe influenza in pregnant and postpartum women, CDC has also established a voluntary reporting system to improve the timeliness, completeness, accuracy, and level of detail in nationwide reporting of deaths and ICU admissions for influenza in pregnant women and in women with symptom onset up to 6 weeks postpartum.
CDPH is requesting that local health jurisdictions report severely ill pregnant and postpartum cases to CDPH via current mechanisms using the CDPH Severe Influenza Case Report Form - Hospitalized/Fatal Cases. CDPH will complete the CDC case report form and report those cases to CDC. Please send available medical records on such patients to facilitate this process. Local health jurisdictions may also choose to complete the CDC case report form themselves (see attached – Influenza-Report of Severe Illness (ICU Admissions) or Death in Pregnant and Post Partum Women Form) and send it to CDPH in addition to the CDPH Severe Influenza Case Report Form-Hospitalized/Fatal Cases.

CDC will inform California healthcare providers who utilize the hotline to report cases of 2009 H1N1 influenza in pregnant women to their local health jurisdiction; however, for any cases reported directly to the CDC via the hotline, CDC will forward the information to CDPH within 24 hours of the report. CDPH will then forward that report on to the appropriate local health jurisdiction as soon as possible. Questions about reporting of cases among pregnant women can be directed via email to: swineflureport@cdph.ca.gov .

The second attachment is a template for an email to providers in your jurisdiction about the hotline and about the reporting system for pregnant women.

3. Reporting of adverse events temporally associated with influenza vaccine
CDPH, Los Angeles County, and the California Emerging Infections Program are conducting surveillance for Guillain Barre Syndrome (GBS) as part of surveillance for adverse events temporally associated with receipt of 2009 H1N1 or seasonal influenza vaccine. This surveillance includes weekly hospital ICD-9 discharge code queries for GBS, reports from neurologists and other providers, and a testing program to look for infectious triggers of GBS.

Other serious adverse events may also be associated temporally with receipt of influenza vaccine and require investigation. A serious event is defined as one in which one of the following outcomes is reported: death, life threatening illness, hospitalization ≥24 hours, prolongation of a hospitalization, permanent disability, congenital anomalies, or other medically important conditions.

Events of particular interest include:

Neurologic events occurring within 30 days of vaccine receipt:
Bell's Palsy
Demyelinating diseases of the nervous system (including optic neuritis)
Encephalitis/myelitis
Seizures
Cerebrovascular accident
Other serious neurologic event

Pregnancy-related events within 7 days of vaccine receipt:
Stillbirth
Spontaneous abortion
Pre-eclampsia and eclampsia

Other events within 7 days of vaccine receipt:
Myocarditis or pericarditis
Anaphylaxis

In all counties except Los Angeles County, please contact Carol Glaser at: carol.glaser@cdph.ca.gov or 510-952-6038 or Kathy Harriman at kathleen.harriman@cdph.ca.gov or 651-699-2970 to notify them of any of these potential adverse events, particularly if the patient is hospitalized or has died.

In Los Angeles County, please notify the Adverse Events Consultation line at: 1-866-756-1513.

4. Testing of severely ill or fatal cases of suspect 2009 H1N1 influenza
CDPH is aware of severely ill and fatal cases of 2009 H1N1 influenza who were PCR- negative for influenza when upper respiratory tract specimens (i.e., NP swabs) were tested, but positive when lower respiratory tract or autopsy specimens were tested.

Therefore, CDPH would like to emphasize the following specimen collection guidelines, which are posted on the VRDL website at:
http://www.cdph.ca.gov/programs/vrdl/Pages/DiagnosticTestingforSwineInfluenzaA(H1).aspx

Minimum Specimen Requirements

Respiratory Specimens

- At a minimum, collect a nasopharyngeal swab (nasopharyngeal wash or nasopharyngeal aspirate are also acceptable). Oropharyngeal (throat) swabs are acceptable, but may not have as high a yield. If oropharyngeal specimens are collected, they should be accompanied by a specimen from the nasopharynx. Place the swabs in a standard container with 2-3 ml of viral transport media (VTM).
- If the patient is hospitalized with pneumonia, specimens from the lower respiratory tract (e.g., tracheal aspirate, bronchoalveolar lavage) should also be obtained.
- Use dacron-tipped swabs only. Cotton or calcium alginate swabs are not acceptable for PCR testing.

For fatal cases, local health jurisdictions should work with their pathologists, medical examiners and coroners to collect both fresh-frozen and fixed tissue at time of autopsy.
With influenza, viral antigens and nucleic acids may be focal and sparsely distributed in patients. Extensive sampling of both the upper and lower airway ensures the best chance of detecting the virus by immunohistochemical stains, PCR tests and culture.

Tissue specimens

The preferred specimens are fresh frozen and wet fixed tissue specimens representing extensive samples from the following pulmonary sites in addition to specimens from other organs showing pathology:

1. Central (hilar) lung with segmental bronchi, right and left primary bronchi, trachea (proximal and distal).
2. Representative pulmonary parenchyma from right and left lung.
3. For patients with suspected myocarditis, encephalitis, rhabdomyolysis or gastrointestinal symptoms, specimens should include myocardium (right and left ventricle), CNS (cerebral cortex, basal ganglia, pons, medulla, and cerebellum), skeletal muscle and gastrointestinal tract, respectively.
4. Specimens should be included from any other organ showing significant gross or microscopic pathology.

Specimen submission

1. Wet tissue: Multiple 1 x 2 cm pieces of tissue from sites listed above in 10% neutral buffered formalin.
2. Fresh-frozen tissue: (sent **separately** on dry ice) Single piece of tissue as listed above.
3. Paraffin-embedded tissue blocks: Blocks can be submitted in addition to wet and fresh-frozen and are the preferred type of specimen to submit in cases where tissues have been in formalin for a significant time. Prolonged fixation (>2 weeks) may interfere with some immunohistochemical and molecular diagnostic assays.

CDPH requests that all specimens on fatal cases be sent to VRDL using the VRDL specimen submittal form available at:
http://www.cdph.ca.gov/programs/vrdl/Documents/SwineInfluenzaSurveillanceSpecimenSubmittalForm520.pdf

Please call 510-307-8585 before sending specimens so that testing can be expedited.

5. Referral of specimens to VRDL for influenza testing

For the 2009-10 influenza season, VRDL requests that all public health laboratories in the Respiratory Laboratory Network submit:

- RNA extract or original specimens on all fatal cases of 2009 H1N1 or seasonal influenza
- RNA extract or original specimen on all pediatric cases hospitalized in an ICU with 2009 H1N1 or seasonal influenza (severe pediatric influenza surveillance)
- Five RNA extracts per week on influenza positive specimens with CT<30 for surveillance for antiviral resistance

RLN laboratories are also requested to continue reporting influenza PCR results each week to VRDL. Our new format requests that reports of laboratory data be broken down into categories as follows:

Number	2009 H1N1	Seasonal A/H3	Seasonal A/H1	Seasonal B
Outpatient				
Hospitalized				
ICU				
Fatal				
Outbreak				

Since public health laboratories are handling the primary load for testing of hospitalized cases, this information is a very important part of our surveillance and is critical to understanding the level of activity and circulating types and subtypes, as well as informing antiviral treatment guidance for clinicians.

VRDL will continue to serve as the state reference laboratory, providing assistance with testing of sentinel provider specimens, further characterization of specimens from fatal cases, surveillance for antiviral resistance, and support for jurisdictions that do not have a public health laboratory or need additional assistance with outbreaks etc.

Thank you for your ongoing commitment to the 2009 H1N1 response.