1. Case Definitions

Clinicians should consider the possibility of avian influenza A (H7N9) virus infection in persons presenting with acute febrile respiratory illness and an appropriate recent travel or exposure history. Current case definitions, last updated 7 JUN 2013, are available at: http://www.cdc.gov/flu/avianflu/h7n9-case-definitions.htm

**Confirmed Case:** A patient with novel influenza A (H7N9) virus infection that is confirmed by the Centers for Disease Control and Prevention’s (CDC) Influenza Laboratory or a CDC certified public health laboratory using methods agreed upon by CDC and the Council for State and Territorial Epidemiologists (CSTE). Confirmation of avian influenza A (H7N9) viruses may be made by public health laboratories following CDC-approved protocols for detection of avian influenza A (H7N9) virus, or by laboratories using an FDA-authorized test specific for detection of avian influenza A (H7N9) virus.

**Probable Case:** A patient with illness compatible with influenza for whom laboratory diagnostic testing is positive for influenza A, negative for H1, negative for H1pdm09, and negative for H3 by RT-PCR, and therefore subtypeable.

**Case Under Investigation:** A patient with illness compatible with influenza, meeting either of the following exposure criteria, and for whom laboratory confirmation is not known or pending, or for whom test results do not provide a sufficient level of detail to confirm novel influenza A virus infection.

- A patient who has had recent contact (within ≤ 10 days of illness onset) with a confirmed or probable case of infection with novel influenza A (H7N9) virus.

  OR

- A patient who has had recent travel (within ≤ 10 days of illness onset) to a country where human cases of novel influenza A (H7N9) virus have recently been detected or where novel influenza A (H7N9) viruses are known to be circulating in animals.

**Note:** Although laboratories performing testing on specimens collected “in-house” typically prefer nasal washes or aspirates, CDC strongly recommends that nasopharyngeal or nasal swabs be collected in addition to any other specimens collected.

2. Antiviral Treatment

While minimal data are available regarding early neuraminidase inhibitor treatment of persons infected with H7N9 virus, laboratory testing with functional assays indicates that most H7N9 viruses are susceptible to neuraminidase inhibitors (oseltamivir and zanamivir), but resistant to adamantanes (amantadine and rimantadine). Therefore, amantadine and rimantadine are not recommended for treatment of H7N9 virus infection.

- Because of the potential severity of illness associated with H7N9 virus infection, it is recommended that all confirmed cases, probable cases, and H7N9 cases under investigation receive antiviral treatment with a neuraminidase inhibitor as early as possible. Treatment should be initiated even if it is more than 48 hours after onset of illness.

- Laboratory testing and initiation of antiviral treatment should occur simultaneously; treatment should not be delayed for laboratory confirmation of influenza or H7N9 infection.

- Please see Antiviral Drugs: Dosage (ACIP) for additional guidance on the use of influenza antiviral agents. Oseltamivir is recommended for treatment of persons of any age; zanamivir is recommended for children aged 7 and older.
3. Laboratory Testing

A. Human Diagnostic Testing:
On April 22, 2013, the FDA issued an Emergency Use Authorization (EUA) for the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay (Catalog # FluEUA-01) for presumptive detection of novel influenza A (H7N9) in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (Catalog# FluIVD03) on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument. This assay provides in vitro qualitative detection and characterization of human influenza A/H7 (Eurasian Lineage) viruses on upper and lower respiratory tract clinical specimens and is to be used only for patients that present with influenza-like illness (ILI) and meet the clinical and epidemiologic criteria for testing suspect specimens (i.e. patients who meet the Case Under Investigation criteria).

Ordering site: https://www.influenzareagentresource.org/

To order a kit (only 1 kit of 1,000 reactions per lab permitted at this time) a laboratory must meet the following criteria:

- **CLIP certification** as a highly complex laboratory (http://www.tricare.mil/tma/ocmo/cclm.aspx), and
- **CDC Influenza Division Qualification** for influenza diagnostic testing.

Mr. Dan Harms (Dan.Harms@tma.osd.mil, phone: 803-781-8314/571-215-4237) is the DoD’s point-of-contact regarding DoD’s qualified laboratories with the CDC Influenza Branch.

CDCFluorder@cdc.gov will remain open to assist those labs with extenuating circumstances; however, the IRR web page is the preferred method for ordering.

Specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and submitted to your nearest military medical treatment facility laboratory for proper handling and testing. Department of Defense laboratories using the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay are:

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eisenhower Army Medical Center (EAMC)</td>
<td>USA - Fort Gordon GA</td>
</tr>
<tr>
<td>Landstuhl Regional Medical Center</td>
<td>Germany</td>
</tr>
<tr>
<td>Tripler Army Medical Center</td>
<td>USA - Honolulu HI</td>
</tr>
<tr>
<td>Brian Allgood Army Community Hospital</td>
<td>Republic of Korea</td>
</tr>
<tr>
<td>Womack Army Medical Center</td>
<td>USA - Fort Bragg NC</td>
</tr>
<tr>
<td>William Beaumont Army Medical Center (WBAMC)</td>
<td>USA - Fort Bliss TX</td>
</tr>
<tr>
<td>Brooke Army Medical Center (BAMC)</td>
<td>USA - Fort Sam Houston TX</td>
</tr>
<tr>
<td>Carl R. Darnall Medical Center (CRDAMC)</td>
<td>USA - Fort Hood TX</td>
</tr>
<tr>
<td>Madigan Army Medical Center (MAMC)</td>
<td>USA - Fort Lewis WA</td>
</tr>
<tr>
<td>US Air Force School of Aerospace Medicine (USAFSAM)</td>
<td>USA - Wright Patterson AFB OH</td>
</tr>
<tr>
<td>Naval Health Research Center (NHRC)</td>
<td>USA - San Diego CA</td>
</tr>
<tr>
<td>Naval Medical Research Unit 3 (NAMRU-3)</td>
<td>Egypt</td>
</tr>
</tbody>
</table>
Viral culture should **not** be attempted in these cases unless a **BSL 3+** facility is available to receive and culture specimens.

Please note that by using this EUA kit, there are additional requirements set forth in the EUA such as confirmation of positive result by the CDC, reporting assay performance characteristics to the CDC, and distributing CDC provided Fact Sheets with the results for Providers: [http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM349062.pdf](http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM349062.pdf) and Patients: [http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM349064.pdf](http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM349064.pdf)

Also please note that this assay, as with all assays for human diagnostics, must be verified in each laboratory per CLIA/CLIP regulations. The CDC is working with the appropriate partners to create a panel to use for this required verification of performance prior to diagnostic testing and will distribute the panel to those laboratories that have received the kits.

### B. Non-Diagnostic Testing (Surveillance/Research):

Laboratories interested in **non-clinical** testing should register with the CDC Laboratory Support for Influenza Surveillance website at [www.cdc.gov/flu/clsis](http://www.cdc.gov/flu/clsis) to procure resources for novel influenza A (H7N9) testing.

The WHO assay protocol can be found here: [http://www.who.int/influenza/gisrs_laboratory/cnic_realtime_rt_pcr_protocol_a_h7n9.pdf](http://www.who.int/influenza/gisrs_laboratory/cnic_realtime_rt_pcr_protocol_a_h7n9.pdf)

The sequences have been deposited in the EpiFlu™ Database, found on the GISAID website [http://platform.gisaid.org/epi3/frontend#457751](http://platform.gisaid.org/epi3/frontend#457751)

The below laboratories each currently have surveillance testing capability:

<table>
<thead>
<tr>
<th>Laboratory Name</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armed Forces Research Institute of Medical Sciences (AFRIMS)</td>
<td>Thailand</td>
</tr>
<tr>
<td>Naval Medical Research Unit 3 (NAMRU-3)</td>
<td>Egypt</td>
</tr>
<tr>
<td>Naval Medical Research Unit 6 (NAMRU-6)</td>
<td>Peru</td>
</tr>
<tr>
<td>Naval Medical Research Unit 2 Phnom Penh (NAMRU-2)</td>
<td>Cambodia</td>
</tr>
<tr>
<td>Naval Medical Research Unit 2 Singapore (NAMRU-2)</td>
<td>Singapore</td>
</tr>
<tr>
<td>Naval Health Research Center (NHRC)</td>
<td>USA - San Diego, CA</td>
</tr>
</tbody>
</table>

### 4. Reporting

- AFHSC recommends that possible cases of novel influenza infection be reported immediately as Reportable Medical Events (RMEs [http://afhsc.mil/reportableEvents](http://afhsc.mil/reportableEvents)) and through their local public health chain of command.
- Novel influenza strains are a Nationally Notifiable Disease (NDD) and should be reported to the CDC ([http://www.cdc.gov/nndss/default.aspx](http://www.cdc.gov/nndss/default.aspx)), your state health department, and host nation if applicable.
- Human influenza caused by a new subtype must be reported to the WHO under the International Health
Regulations.

A new Novel Influenza diagnosis screen has been added to DRSi. If you suspect an influenza A (H7N9) case, report it under this diagnosis and answer as many questions as possible.

5. Additional information

Guidance can be found at:
Armed Forces Health Surveillance Center: http://afhsc.mil
CDC: http://www.cdc.gov/flu/avianflu/h7n9-virus.htm
The NEJM article: http://www.nejm.org/doi/full/10.1056/NEJMoa1304459 (free download)

6. AFHSC POC:

For further information, contact the AFHSC’s Division of Integrated Biosurveillance (DIB) or the Division of Global Emerging Infections Surveillance & Response Systems (GEIS):

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LCDR Amy Peterson, USPHS, Veterinary Epidemiologist (DIB): 240-743-9853
CAPT Michael Cooper, Lead, Respiratory Surveillance (GEIS): 301-319-3258