DEPARTMENT OF DEFENSE (AFHSB)

Avian Influenza A (H7N9): Laboratory Testing Guidance as of 17 FEB 2016

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 history to places where H7N9 has been diagnosed in people (currently China) or an appropriate exposure history. Case definitions, last updated 26 JAN 2016, 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 meeting any of the exposure criteria below 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 not able to be subtyped.

Case Under Investigation: A patient with illness compatible with influenza, meeting any 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 suspected case of infection with avian 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 avian influenza A (H7N9) virus have recently been detected or where novel influenza A (H7N9) viruses are known to be circulating in animals,

OR

- Unprotected exposure to live avian influenza A (H7N9) virus in a laboratory.

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.

For more information: http://www.cdc.gov/flu/avianflu/h7n9-antiviral-treatment.htm

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 Polymerase Chain Reaction (RT-PCR) Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay for **presumptive detection of novel influenza A (H7N9) in conjunction** with the FDA cleared CDC Human Influenza Virus RT-PCR Diagnostic Panel on the Applied Biosystems 7500 Fast Dx RT-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).

Mr. Dan Harms (dan.e.harms.civ@mail.mil, phone: 703-681-8314/571-215-4237) is the DoD point-of-contact regarding DoD qualified laboratories with the CDC Influenza Branch.

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 RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay include:

LRMC Infectious Disease Laboratory
Landstuhl, Germany
CPT Ronald Woodbury
ronald.l.woodbury.mil@mail.mil
Civ: 49-6371-867513
DSN: (314) 590-5888

U.S. Air Force School of Aerospace Medicine (USAFSAM)
Dayton, OH (Wright-Patterson AFB)
Dr. Elizabeth Macias
Elizabeth.macias@us.af.mil
DSN: 798-3175
Civ: (937) 938-3175
Cell: (937) 581-8552

Naval Health Research Center (NHRC)
San Diego, CA
Dr. Chris Myers
Chris.myers2@med.navy.mil
Civ: (619) 553-0891

Naval Infectious Disease Diagnostic Laboratory (NIDDL)
Silver Spring, MD (NMRC at Forest Glen)
LCDR Todd Myers
Todd.e.myers.mil@mail.mil
Civ: (301) 319-3113

Tripler Army Medical Center
Honolulu, HI
LTC Jason Barnhill
Jason.c.barnhill2.mil@mail.mil
Civ: (808) 433-7923

Walter Reed National Military Medical Center (WRNMMC)
Bethesda, MD (Naval Surface Activity – Bethesda)
MAJ Robert Cybulski
Robert.cybulski@us.army.mil
Civ: (301) 295-8617

San Antonio Military Medical Center /Brooke Army Medical Center
San Antonio, TX (Ft. Sam Houston)
LTC Edward Ager
edward.p.ager.mil@mail.mil
Civ: (210) 916-1817

Brian Allgood Army Community Hospital (BAACH)
Seoul, ROK (Yongsan Garrison)
CPT Lotisha Garvin
Lotisha.e.garvin.mil@mail.mil
Civ: 011-822-7917-2041
DSN: 315-737-2041

William Beaumont Army Medical Center (WBAMC)
El Paso, TX (Ft. Bliss)
MAJ Richard Heipertz
richard.a.heipertz2.mil@mail.mil
Civ: 915-742-6471
DSN: 712-6471
Lab: 915-742-2210
DSN: 712-2210

Madigan Army Medical Center
Joint Base Lewis-McChord
Tacoma, WA
LTC James Lee
James.e.lee.mil@mail.mil
Civ: (253) 968-1925

Carl R. Darnall Army Medical Center
Fort Hood, TX
MAJ Tony Pierson
tony.pierson.mil@mail.mil
Work: 254-553-2777
Mobile: 254-768-4557
CPT Derese Getnet
derese.getnet.mil@mail.mil
Work: 254-288-8206

Womack Army Medical Center
Fort Bragg, NC
Rhonda S. Tucker
rhonda.s.tucker.civ@mail.mil
Work: (910) 907-7770

Eisenhower Army Medical Center
Fort Gordon, GA
MAJ Jim Ray Managbanag
jim.r.managbanag.mil@mail.mil
Work: (706) 787-8148

Viral culture should **not** be attempted 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

and Patients:
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 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

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

The below laboratories currently have surveillance testing capabilities:

Armed Forces Research Institute of Medical Sciences (AFRIMS)
Bangkok, Thailand
COL Louis Macareo
Louis.Macareo.mil@afrims.org
Civ: (66-2) 698-2756
Cell: +66844550343
MAJ Damon Ellison
Damon.ellison.mil@afrims.org
Civ: (66-2) 698-2756

Naval Medical Research Unit – 2
Phnom Penh, Cambodia
LCDR Jamal Dejli
Jamal.Dejli@med.navy.mil
Jamal.dejli.mil@mail.mil
jamal.dejli@namru2.org.kh

Civ: +855 (23) 884-228

Naval Medical Research Unit – 3
Cairo, Egypt
LCDR Gabriel Defang
gabriel.defang@med.navy.mil
Civ: 011-202-2348-0379

Naval Medical Research Unit – 6
Lima, Peru
Dr. Chris Mores
Christopher.mores@med.navy.mil
Civ: 511-614-4189
BB: 511-995-385373
LCDR Mark Simons
Mark.simons@med.navy.mil
Civ: (51-1) 614-4134

Naval Health Research Center
San Diego, CA
Dr. Chris Myers
Chris.myers2@med.navy.mil
Civ: (619) 553-0891

Naval Infectious Disease Diagnostic Laboratory (NIDDL)
Silver Spring, MD (NMRC at Forest Glen)
LCDR Todd Myers
Todd.e.myers.mil@mail.mil
Civ: (301) 319-3113

227th Medical Detachment (Preventive Medicine)
Camp Arifjan, Kuwait
CPT Jangwoo Lee
jangwoo.lee3.mil@mail.mil
DSN: (318) 430-7831

4. Reporting

- AFHSB recommends that possible cases of novel influenza infection be reported immediately as Reportable Medical Events (RMEs http://afhsc.mil/reportableEvents) and through their local public health chain of command. A Novel Influenza diagnosis screen has been added to DRSi. If you suspect a case of influenza A (H7N9), report it under this diagnosis and answer as many questions as possible.
- Novel influenza strains are a Nationally Notifiable Disease (NDD) and should be reported to the CDC (http://wwwn.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.

5. Additional information

Guidance can be found at:
Armed Forces Health Surveillance Branch: http://afhsc.mil

CDC: http://www.cdc.gov/flu/avianflu/h7n9-virus.htm
WHO: http://www.who.int/influenza/human_animal_interface/faq_H7N9/en/

6. AFHSB POC:

For further information, contact the AFHSB's Section of Integrated Biosurveillance (IB) or the Section of Global Emerging Infections Surveillance & Response Systems (GEIS):

Email: dha.ncr.health-surv.list.afhs-ib-alert-response@mail.mil
Phone:
Dr. Paul E. Lewis, Acting Section Chief, (IB): desk: 301-319-2235; BB: 301-412-0286
Dr. Stic Harris, Chief, Alert & Response Operations (IB): 301-319-3297; BB: 202-834-1327
CAPT Michael Cooper, Lead, Respiratory Surveillance (GEIS): 301-319-3258