Biosafety recommendations for laboratories handling human specimens suspected or confirmed to contain avian influenza A(H7N9) virus causing human disease

INTERIM RECOMMENDATIONS

Current as of 12 January 2018

Introduction

These recommendations reflect current understanding of avian influenza A(H7N9) virus causing human disease. WHO continues to monitor the situation closely for any changes that may affect the recommendations contained in this document. Should any factors change, WHO will issue a further update. The following recommendations apply to avian influenza A(H7N9) viruses causing human disease, including both highly pathogenic avian influenza (HPAI) viruses and low pathogenicity avian influenza (LPAI) viruses.

WHO recommends that laboratory work on clinical specimens taken from patients who are suspected or confirmed to be infected with avian influenza A(H7N9) virus, not involving virus propagation, be conducted according to practices and procedures described for basic laboratories – biosafety level 2 (BSL-2), as detailed in the WHO Laboratory biosafety manual, 3rd edition (1), whereas isolation or propagation of avian influenza A(H7N9) virus should be performed at higher biosafety levels (BSL-3 or above), as described below.

Final responsibility for the identification and implementation of appropriate containment measures for virus isolation or propagation in tissue culture or embryonated hens’ eggs lies with the relevant competent authorities in individual countries and institutions. However, needs vary from one country to another. Handling HPAI viruses is likely to require particular attention, with the need to fully observe specific national regulations and guidance that will supersede the general recommendations set out in this document.

Various sections of the WHO website have up-to-date information on avian influenza A(H7N9) virus (2-4). Other resources include any local and national legislation, in addition to the WHO Laboratory biosafety manual, 3rd edition (1).

Recommendations addressing essential working conditions associated with specific manipulations in laboratory settings

The recommendations provided below address essential working conditions associated with specific manipulations in laboratory settings.

a. Non-propagative laboratory procedures with clinical specimens

Diagnostic laboratory work and polymerase chain reaction (PCR) analysis should be conducted on clinical specimens from patients who are suspected or confirmed to be infected with avian influenza A(H7N9) virus causing human disease. The laboratory work and analysis should be undertaken using practices and procedures described for basic laboratory – BSL-2, as detailed in the WHO Laboratory biosafety manual, 3rd edition (1).
Examples of routine laboratory procedures that require BSL-2 include:

- diagnostic testing of serum, blood (including haematology and clinical chemistry), respiratory tract specimens or other specimens;
- treatment of clinical specimens that will inactivate any infectious virus present (lysis, fixation or other inactivating treatments); the inactivation methods should be validated, and subsequent work on purified H7N9 RNA can be performed under BSL-2 conditions; and
- routine examination of mycotic and bacterial cultures developed from respiratory tract specimens.

All manipulations of potentially infectious materials should be performed in appropriately maintained and validated biological safety cabinets (BSCs). Such procedures include those that may cause splashes, droplets or aerosols of infectious materials; for example, loading and unloading sealed centrifuge cups; grinding, blending, vigorous shaking or mixing; sonic disruption; and opening containers of infectious materials whose internal pressure may be different from the ambient pressure.

When handling and processing clinical specimens, good microbiological techniques must be used, including the following:

- no eating, drinking, smoking, applying cosmetics or handling contact lenses in any laboratory working areas;
- no mouth pipetting;
- wearing appropriate personal protective equipment (PPE), and removing that PPE before leaving the laboratory;
- performing all technical procedures in a way that minimizes the formation of aerosols and droplets;
- minimizing the use of sharps, hypodermic needles and syringes;
- always collecting contaminated sharps in puncture-proof containers fitted with covers, and treating them as infectious waste;
- using adequate biohazard containers for appropriate disposal of contaminated materials, and locating these in the immediate working area;
- decontaminating work surfaces, both after any spill of potentially infectious material and at the end of the work performed (more information on disinfection and decontamination is provided in the WHO Laboratory biosafety manual, 3rd edition (1)); and
- washing hands frequently – especially after handling infectious materials and animals, and before leaving the laboratory working areas.

An appropriate combination of PPE and physical containment devices should be used when performing procedures that cannot be conducted within a BSC. Examples of PPE are respiratory and eye protection, and examples of containment devices are centrifuge safety cups and sealed rotors.
b. Virus isolation and propagation

Virus isolation on clinical specimens from patients who are suspected or confirmed to be infected with avian influenza A(H7N9) virus should be performed only in laboratories capable of meeting the following additional biological safety containment requirements:

- practices recommended for containment laboratories – BSL-3 in the WHO Laboratory biosafety manual, 3rd edition (1) should be followed rigorously;
- a controlled ventilation system should maintain directional airflow into the laboratory room;
- in relation to exhaust air:
  - exhaust air from the laboratory room should not be recirculated to other areas within the building;
  - if exhaust air is reconditioned and recirculated within the laboratory, it should be filtered through a high efficiency particulate air (HEPA) filter;
  - when exhaust air from the laboratory is discharged to the outdoors, it should be dispersed away from occupied buildings and air intakes, and should be discharged through HEPA filters;
- laboratory workers should wear PPE appropriately, according to local risk assessment;
- a dedicated hand-wash sink should be available in the laboratory;
- all materials transported within and between laboratories should be placed in secondary containers to minimize the potential for breakage or a spill (e.g. during transfer of materials from the BSC to an incubator and vice versa), and the surfaces of containers leaving the BSC should be decontaminated;
- all cultures, stocks and potentially infectious material must be decontaminated before disposal and removal from the facility using an effective method; a method for decontamination of laboratory waste should be available within the laboratory facility (e.g. autoclave, chemical disinfection, incineration or other validated decontamination method); and
- laboratory supervisors must ensure that laboratory personnel receive appropriate and up-to-date training on all procedures and policies related to their duties, including exposure evaluation procedures.

c. Additional risks associated with virus studies

Certain experimental procedures may carry additional risks of generating virus with possible increased pathogenicity or transmissibility, or generating viruses with altered antigenicity or drug susceptibility. Specific risk assessments should be conducted, specific risk reduction measures adopted, and individual country policies and regulations should be considered before any of the following types of procedures are conducted:

- coinfection of cell cultures with different influenza viruses, or any procedures that may result in a coinfection;
- culture of viruses in the presence of antiviral drugs; and
- deliberate genetic reassortment and modification of viruses.

1 Individual countries can decide to vary these conditions, taking into account any newly acquired knowledge and effective preventive measures.
The risk assessment of such experimental studies must be considered within a social context, and individual countries may have policies and requirements that must be considered. Depending on the study design, a careful assessment should be performed in advance, to evaluate the risks of inadvertent release and potential misuse of the viruses and study outcomes. Proper control measures should be in place proportionate to any such perceived risks.

d. Work with animals infected with avian influenza A(H7N9) virus causing disease in humans

The following activities require an animal facility capable of running at BSL-3, and the associated work practices, as detailed in the WHO Laboratory biosafety manual, 3rd edition (1), should be in place:

- inoculation of animals for recovery of the agent from specimens potentially containing avian influenza A(H7N9) virus; and
- any protocol involving animal inoculation for confirmation or characterization of putative influenza A(H7N9) agents (to include the raising of A(H7N9)-specific antiserum).

e. Appropriate disinfectants

- Risk assessments should be made for the selection, preparation and use of disinfectants, including consideration of contact time.
- Disinfectants with proven activity against enveloped viruses include hypochlorite, alcohols, peroxygens, quaternary ammonium compounds and phenolic compounds (subject to the manufacturer’s recommendations).
- Those using disinfectants must be made aware of the toxic or corrosive properties of the disinfectants, and of the need to exercise caution when disinfectants are used.
- Work surfaces and equipment should be decontaminated after specimens are processed.

f. Contaminated waste

- Contaminated sharps should be collected in puncture-proof containers fitted with covers, and treated as infectious waste.
- Infectious laboratory waste should be handled, transported and disposed of according to applicable local, regional, national or international regulations. Additional information is available in the WHO Laboratory biosafety manual, 3rd edition (1) and other guidance documents available through the relevant section of the WHO website (5).

g. Occupational health

- Laboratories should develop and implement a specific medical surveillance and response plan that outlines a medical protocol for responding to exposures and potential laboratory-acquired infections.
- Any symptom or sign of infection must be reported immediately to the laboratory management team and relevant medical authorities.
- Incidents or accidents involving potential or actual exposure to avian influenza A(H7N9) virus must be reported immediately, and appropriate decontamination of any affected area or equipment must be done. Following an exposure, medical advice should be sought as soon as possible.
h. Referral of specimens to laboratories with appropriate containment measures in place

- Laboratories not able to meet recommendations a–d above should consider transferring specimens to appropriate regional, national or international reference laboratories.
- Those unable to meet recommendations b–d should consider transferring specimens to appropriate regional, national or international reference laboratories with the appropriate BSL-3 or BSL-4 facilities, to allow detailed characterization of A(H7N9) viruses.

i. Shipping requirements for avian influenza A(H7N9) virus

- Compliance with applicable national regulations for the transport of specimens within national borders is needed. In the absence of national transport regulations, applicable international modal requirements – described in the latest version of the WHO guidance on the transport of infectious substances (6) – must be followed for the transport of:
  - specimens within national borders; and
  - international shipments of avian influenza A(H7N9) virus.
- Currently, specimens suspected or confirmed to contain avian influenza A(H7N9) virus can safely be shipped as biological substance, Category B (UN 3373).
- It is recommended that laboratory isolated and propagated avian influenza A(H7N9) viruses causing human disease be shipped as Category A (UN 2814).

References