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

Current as of 10 May 2013

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.

WHO recommends that all diagnostic laboratory work on clinical specimens taken from patients who are suspected or confirmed to be infected with avian influenza A(H7N9) virus be conducted according to practices and procedures described for basic laboratory — Biosafety Level 2 (BSL2), as detailed in the WHO *Laboratory biosafety manual*, 3rd edition.

Avian influenza A(H7N9) virus isolation procedures are recommended to be performed at higher biosafety level, as described below. Final responsibility for the identification and implementation of appropriate containment measures for virus culture, propagation and isolation studies lies with individual countries and facilities. However, needs may vary from one country to another according to the variables mentioned below and decisions should be taken in light of currently available knowledge and context.

For updated information on avian influenza A(H7N9) virus, please refer to
http://www.who.int/csr/don/en/index.html http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html
http://www.who.int/influenza/human_animal_interface/faq_H7N9/en/index.html

This document is divided into two parts:

1. Biorisk management checklist for laboratory managers and staff.

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

1. Biorisk management checklist for laboratory managers and staff

The following checklist has been developed to provide guidance for laboratories that are receiving and processing specimens from persons suspected or confirmed to be infected with avian influenza A(H7N9) virus causing human disease.

The list is not intended to be exhaustive but provides a starting point in ensuring that laboratories are prepared for the receipt of specimens and any additional workload that could arise from the heightened surveillance for infected persons and from the clinical diagnostic concerns in the WHO pandemic phases.

Other resources will include any local and national legislation, in addition to:

1. WHO *Laboratory Biosafety Manual, 3rd edition*, 2004
2. *CWA15793 Laboratory Biorisk Management, 2011*

Biorisk management checklist for laboratory managers and staff

Biorisk Management System	1. Adequate management resources (e.g. time, funds) are available 2. Staff have been advised that maintaining a safe workplace is of primary importance and procedures must be followed, and no shortcuts taken despite potentially increased workloads 3. Sufficient trained staff and other resources are available, including: • Management • Scientific staff • Specialist staff, e.g. biosafety officer (BSO) • Support staff, e.g. waste management, cleaners, maintenance, transport 4. Staff are available to cover additional working hours (e.g. evenings, weekends) 5. Reviewed and updated protocols and working practice policies are available and communicated (e.g. safe work practices, decontamination) 6. Relevant sources of information on good biosafety practices have been identified and reviewed (e.g. WHO *Laboratory Biosafety Manual*, 3rd edition)
Risk Assessment	1. Hazards associated with proposed work are identified 2. Risk is evaluated (as a function of likelihood and consequences, based on current knowledge of hazards) and appropriate mitigation measures implemented 3. Risk is regularly reviewed after implementation of control measures, to determine whether remaining risk is acceptable or additional controls need to be identified and implemented. 4. Staff with underlying medical conditions have been identified and have been informed of available options 5. Management of additional numbers of specimens, staff and other abnormal working conditions / hours have been considered 6. Infection control in the workplace (e.g. sneezing, cleaning) has been reviewed and staff have been advised
Biological Agents and Toxin Inventory and Information	1. An inventory system for proper archiving of specimens and virus isolates is in place and regularly updated 2. Sufficient storage capacity for specimens and cultures is available 3. Specimens are adequately labeled and can be identified
General Safety	1. Good housekeeping practices are in place and the laboratory is clean and tidy 2. A review of general working conditions has been conducted (e.g. electrical safety, fire safety)

Personnel and Competency	1. Training and awareness plans as well as Standard Operating Procedure (SOP) compliance programmes are in place for all staff 2. Trained and competent personnel are available, including any additional / temporary staff members required 3. Only personnel who are competent in handling respiratory virus specimens can work with potentially positive materials, including scientific and support staff
Good Microbiological Technique	4. Procedures have been reviewed for hazardous activities (e.g. generation of aerosols and droplets, use of centrifuges and biological safety cabinets (BSCs), waste management) 5. Validated, edited and updated SOPs ensuring clear, concise and consistent processes are followed
Personal Protective Equipment (PPE)	1. Adequate and appropriate personal protective equipment (PPE) has been identified, supplies (masks, respirators, lab coats, etc.) are available and staff are competent in their storage, use, cleaning and disposal
Human Factors	1. Provision has been made for adequate rest and other welfare issues (e.g. workplace stress, concern for family members) have been appropriately addressed 2. Regular team meetings and briefings are in place to ensure good communication is maintained 3. All staff (i.e. scientific and support) are informed of the risk associated with avian influenza A(H7N9) virus infection, symptoms, reporting procedures and support from the facility/organization in the event of illness
Health Care	1. Vaccination needs and provision schemes are identified, provided vaccines become available 2. A policy for availability, use, and training for the administration of antivirals is in place 3. Any symptoms to be immediately reported to laboratory management and relevant medical authorities are identified
Emergency Response and Contingency Planning	1. Stable power supply with adequate backup generators is functional, validated and available, including for essential biosafety cabinets 2. Laboratory capacity from other departments in the event of need is available and accessible 3. Fire, flooding and other risks will not be increased as a result of the changed working conditions
Accident / Incident Investigation	1. Processes exist for incident investigation and reporting
Facility Physical Requirements	1. Sufficient space for storage of specimens and other materials (e.g. waste) is available
Equipment and Maintenance	1. Access to appropriate BSCs and other essential equipment is ensured 2. Equipment is adequately maintained and validated, preferably with a stockpile of replacement parts
Decontamination, Disinfection and Sterilization	1. Procedures for adequate decontamination of all waste and other materials are identified and systematically followed 2. Adequate supplies of required disinfectants and other materials are ensured

Transport Procedures	1. Adequate supplies, including appropriate shipping containers, are available for transport 2. Procedures are in place for receipt and opening of specimens 3. Shippers are aware of required transport procedures and applicable regulations 4. Procedures are in place to ensure materials are transported safely to, within and from the laboratory
Security	1. Appropriate security measures are in place including those required to address extended working hours and abnormal conditions (e.g. additional personnel)

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

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

a. Routine laboratory procedures, including diagnostic work and PCR analysis

Diagnostic laboratory work and PCR analysis on clinical specimens from patients who are suspected or confirmed to be infected with avian influenza A(H7N9) virus causing human disease should be conducted adopting practices and procedures described for basic laboratory — Biosafety Level 2 (BSL-2), as detailed in the WHO *Laboratory biosafety manual*, 3rd edition.

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;
- Manipulations involving neutralized or inactivated (lysed, fixed, or otherwise treated) virus particles and/or incomplete, non-infectious portions of the viral genome.
- Routine examination of mycotic and bacterial cultures developed from respiratory tract specimens.

When handling and processing specimens, good microbiological techniques (GMT) should be followed:

- No eating, drinking, smoking, applying cosmetics, or handling contact lenses in any laboratory working areas.
- Wear appropriate PPE.
- Perform all technical procedures in a way that minimizes the formation of aerosols and droplets.
- Perform all manipulations of potentially infectious materials, including those that may cause splashes, droplets, or aerosols of infectious materials (e.g. loading and unloading of sealed centrifuge cups, grinding, blending, vigorous shaking or mixing, sonic disruption, opening of containers of infectious materials whose internal pressure may be different from the ambient pressure) in appropriately maintained and validated biological safety cabinets (BSCs). Consider the use of Class II BSCs to protect materials, personnel and the environment.

- Minimize the use of hypodermic needles and syringes. Always collect contaminated sharps in puncture-proof containers fitted with covers, and treat them as infectious waste.

- Never mouth pipet.

- Use adequate biohazard containers for appropriate disposal of contaminated materials and locate these in the immediate working area.

- Decontaminate work surfaces after any spill of potentially infectious material and at the end of the work being performed. More information on disinfection and sterilization is provided in the WHO *Laboratory biosafety manual, 3rd edition*.

- Wash your hands often – especially after handling infectious materials and animals, before leaving the laboratory working areas, and before eating.

- Remove PPE before leaving the laboratory.

Use an appropriate combination of PPE (including respiratory and eye protection) and physical containment devices (e.g. centrifuge safety cups or sealed rotors) when performing procedures that cannot be conducted within a BSC.

b. Virus isolation

Unless individual countries decide otherwise, taking into account any newly acquired knowledge and effective preventive measures, 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 essential containment requirements:

- Practices recommended for containment laboratories — Biosafety Level 3 in the WHO *Laboratory biosafety manual*, 3rd edition, are rigorously followed.

- A controlled ventilation system maintains directional airflow into the laboratory room.

- Exhaust air from the laboratory room is not recirculated to other areas within the building. Air should be HEPA filtered, if reconditioned and recirculated within the laboratory. When exhaust air from the laboratory is discharged to the outdoors, it must be dispersed away from occupied buildings and air intakes. This air may be discharged through HEPA filters.

- Laboratory workers should wear protective equipment, including disposable gloves, solid-front or wrap-around gowns, scrub suits, or coveralls with sleeves that fully cover the forearms, head coverings, shoe covers or dedicated shoes, eye protection (goggles or face shields), and respiratory protection (fit-tested particulate respirator, e.g. EU FFP2, US NIOSH-certified N95 or equivalent, or higher protection), because of the risk of aerosol or droplet exposure.

- 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. An example includes transfer of materials from the biological safety cabinet to an incubator and vice versa. Specimens leaving the BSC should be surface decontaminated.

c. Additional risks associated with virus isolation studies

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

- Co-infection of cell cultures with different influenza viruses, or any procedures that may result in a co-infection;
- Culture of viruses in the presence of antiviral drugs;
- Deliberate genetic modification of viruses.

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

The following activities require animal facility — Biosafety Level 3 facilities and work practices, as detailed in the WHO *Laboratory biosafety manual*, 3rd edition.

- Inoculation of animals for recovery of the agent from specimens potential containing avian influenza A(H7N9) virus
- Any protocol involving animal inoculation for confirmation and/or characterization of putative influenza A(H7N9) agents

e. Appropriate disinfectants

- Use disinfectants with proven activity against enveloped viruses including chlorine, alcohol, peroxygen, quaternary ammonium compounds and phenolic compounds, according to manufacturer's recommendations.
- Decontaminate work surfaces and equipment after specimens are processed. More information on disinfection and sterilization is provided in the WHO *Laboratory biosafety manual*, 3rd edition.

f. Contaminated waste

- Collect contaminated sharps in puncture-proof containers fitted with covers and treat them as infectious waste.
- Handle, transport and dispose of infectious laboratory waste according to applicable local, regional, national or international regulations. Consult the WHO *Laboratory biosafety manual*, 3rd edition and other relevant guidance documents available at http://www.who.int/ihr/publications/en/ for additional information.

g. Occupational health

- Immediately report any symptoms of infection to the laboratory management and relevant medical authorities.
- Immediately report incidents or accidents involving potential or actual exposure to avian influenza A(H7N9) virus and appropriately decontaminate any affected area or equipment. Following an exposure, seek medical advice as soon as possible.

h. Referral of specimens to laboratories with appropriate containment measures in place

Laboratories not able to meet the above biorisk management recommendations should consider transferring specimens to appropriate regional, national or international reference laboratories.

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

Comply with applicable national regulations for the transport of specimens within national borders. In the absence of national transport regulations or for international shipments of avian influenza A(H7N9) virus, follow applicable international modal requirements described in WHO *Guidance on regulations for the Transport of Infectious Substances 2013-2014 (Applicable as from 1 January 2013)*.

Currently, specimens suspected or confirmed of containing avian influenza A(H7N9) virus can safely be shipped as biological substance, Category B.

Cultures of avian influenza A(H7N9) virus causing human disease are recommended to be shipped as Category A.