Joint Biosafety Advisory

Influenza A(H7N9) virus

April 9, 2013

This biosafety advisory is being provided by the Public Health Agency of Canada (PHAC) and the Canadian Food Inspection Agency (CFIA) to assist clinical/ diagnostic and research laboratories in implementing proper biosafety procedures when handling samples containing influenza A(H7N9) virus which was recently identified in China. This advisory is based on currently available scientific evidence as of April 9, 2013 and is subject to review and change as new information becomes available. The Risk Group (RG) of influenza A(H7N9) virus is RG3.

1. Background

Influenza A(H7) viruses are a group of influenza viruses that normally circulate among birds. The influenza A(H7N9) virus seen in China is a reassortant virus containing genes from A(H7N9) and A(H9N2) and may be a potential pandemic agent[1,2]. It is genetically distinct from other A(H7N9) viruses previously identified in wild bird and poultry populations although clearly related to recent Eurasian lineage viruses. This virus does not appear to cause severe illness in avian populations, and represents the first H7N9 subtype to cause infection in humans. Cases of human illness resulting from influenza A(H7) viruses have been documented; however, these illnesses were generally mild and symptoms ranged from conjunctivitis to mild respiratory illness, and no human-to-human transmission was observed[3,4], moreover, these infections were associated with viruses that are highly pathogenic in poultry.

As of April 9, 2013, the influenza A(H7N9) virus recently identified in China has caused respiratory illness in 24 confirmed human cases, including 7 deaths, 14 severe cases, and 3 mild cases[5,6]. All cases to date have presented with flu-like symptoms, which progressed to respiratory illness. Although the source, reservoir, route of infection, and mode of transmission of the virus are unknown, investigations are underway to determine these factors. Human-to-human transmission has not been reported. As of April 9, 2013, no cases had been reported outside of China.

This influenza A(H7N9) virus is currently considered a Foreign Animal Disease (FAD) agent as there may be consequences if this pathogen becomes prevalent in the wild bird or poultry populations in Canada.

2. Biosafety Requirements

The following table summarizes the appropriate physical and operational containment requirements for clinical/ diagnostic and research laboratories working with influenza A(H7N9) virus. Based on the clinical presentation of severe respiratory illness and death in humans, the potential for this virus to be a pandemic agent, and that the virus is currently considered a foreign animal disease agent, this influenza A(H7N9) virus is classified as a Risk Group 3 human and animal pathogen requiring Containment Level 3 for all proliferative *in vitro* or *in vivo* activities. Non-proliferative diagnostic/clinical activities can be conducted at Containment Level 2 with additional requirements, as specified below. In the event of a non-negative human sample, it is strongly recommended that the work with the sample be stopped and the sample be transferred to the National Microbiology Laboratory (NML). In the event that a veterinary diagnostic laboratory detects a non-negative sample, the work is to be stopped and the sample be transferred to the National Centre for Foreign Animal Disease (NCFAD) as per the policy in the *Foreign Animal Disease Diagnostic Laboratory Containment Standard*[7].

The Agencies will continue to monitor this situation and will update this advisory based on new information, if appropriate. Laboratories should refer to the PHAC *Laboratory Biosafety Guidelines 3rd Edition 2004* [8] and the CFIA *Containment Standards for Veterinary Facilities* [9] for a complete listing of the biosafety requirements.

Sample Type and Activity	Minimum Containment Level Requirements		
	CL2	CL3	CL4
Non-Proliferative Clinical/Diagnostic Activities (processing specimens for packaging and distribution to laboratories, diagnostic testing activities (excluding culturing), molecular testing using non-infectious material, etc.)	●†		
Work Involving Known/likely Positive Cultures (culturing of specimens likely to contain agent, processing positive cultures for packaging and distribution to laboratories, culture of the agent, known infectious material, etc.)		●†	
***In Vivo* Work (Ag)**		●†	

† *Additional Requirements*

3. Additional Requirements

The Additional Requirements consist of the following:

Non-Proliferative Clinical/Diagnostic Activities

- All manipulations with infectious materials (e.g. nucleic acid extraction, transfers, aliquotting, etc.) must be conducted in a Biological Safety Cabinet (BSC). Additional respiratory protection (N95 mask or equivalent) is not required when working with primary specimens in a BSC.

- For activities conducted outside a primary containment device, eye and respiratory protection (N95 or equivalent) must be worn in accordance with the risk of exposure.

- A solid-front gown with tight-fitting wrists must be worn when infectious materials are directly handled and must be removed after completion of work and kept by the dedicated work area.

- Personnel must have demonstrated proficiency in microbiological practices and techniques applicable to the select pathogen.

- Leak-proof containers must be used to transport infectious material within the laboratory.

- Centrifugation of infectious materials must be carried out in closed containers placed in sealed safety cups or rotors that are unloaded in a BSC.

- Pathogen-specific disinfection and decontamination procedures must be in place.

- Infectious agents stored outside of the containment zone must be kept locked in leak-proof containers. Emergency response procedures are to take into account the existence of such infectious agents outside of the containment laboratory.

- In the event of a non-negative human sample, it is strongly recommended that all work with the sample stops and the sample be transferred to the National Microbiology Laboratory (NML).

- In the event that a veterinary diagnostic laboratory detects a non-negative sample, the work is to be stopped and the sample be transferred to the National Centre for Foreign Animal Disease (NCFAD) as per the policy in the *Foreign Animal Disease Diagnostic Laboratory Containment Standard*[7].

Work Involving Known/likely Positive Cultures and Subsequent *In Vivo* Work

- It is strongly recommended that all manipulations with human samples be conducted at the National Microbiology Laboratory (NML).
- All manipulations with positive animal samples are to be conducted at the National Centre for Foreign Animal Disease (NCFAD), as per the policy in the *Foreign Animal Disease Diagnostic Laboratory Containment Standard*[(7)].
- Respirators are to be worn as there is a risk of exposure to infectious aerosols that can be transmitted through the inhalation route.

Special Requirements for All Sample Types and Activities

- Manipulations involving growth of the influenza A(H7N9) virus are not to be performed in the same laboratory that is simultaneously culturing material that may contain human influenza virus.
- Personnel are not to come in contact with susceptible animal species for a period of 5 days after handling samples containing influenza A(H7N9), as per standard foreign animal disease protocols.

4. Transportation

Packaging, shipping and transport of specimens must comply with the requirements of the *Transportation of Dangerous Goods Regulations* [(10)], Transport Canada and the *Dangerous Goods Regulations*, International Air Transport Association.

- For air shipments, cultures (i.e. propagated virus) should be shipped as Category A, UN2814.
- For air shipments, patient/primary sample specimens should be shipped as Category B, UN3373.

For further information on how to receive training and certification in the Transportation of Dangerous Goods, please contact the Laboratory Safety Office at lsd-dsl@hc-sc.gc.ca or contact on the 24/7 emergency phone line at 613-292-6754.

5. Contact Information

Please note that this advisory is based on currently available scientific evidence and is subject to review and change as new information becomes available. Further biosafety information may be obtained from the:

- Public Health Agency of Canada on their website at: http://www.phac-aspc.gc.ca/lab-bio/index-eng.php or at (613) 957-1779, fax (613) 941-0596 and by email: biosafety_biosecurity@phac-aspc.gc.ca.
- Canadian Food Inspection Agency on their website at: http://www.inspection.gc.ca/animals/biohazard-containment-and-safety/eng/1300121579431/1315776600051 or at (613)773-6520 and by email: biocon@inspection.gc.ca.

6. References

1. Butler, D. (2013). *Novel bird flu kills two in China*. Retrieved 04/02, 2013, from http://www.nature.com/news/novel-bird-flu-kills-two-in-china-1.12728
2. European Centre for Disease Control and Prevention. (2013). *Severe respiratory disease associated with a novel influenza A virus, A(H7N9) - China*. Retrieved 04/03, 2013, from http://ecdc.europa.eu/en/publications/publications/ah7n9-china-rapid-risk-assessment.pdf
3. Belser, J. A., Bridges, C. B., Katz, J. M., & Tumpey, T. M. (2009). Past, present, and possible future human infection with influenza virus A subtype H7. *Emerging Infectious Diseases, 15(6), 859-865*. doi:10.3201/eid1506.090072; 10.3201/eid1506.090072
4. Heymann, D. L. (Ed.). (2008). *Control of Communicable Diseases Manual* (19th Edition ed.). Washington, DC: American Public Health Association.
5. ProMED. (2013). *Avian influenza, human* (26): China H7N9 case list & map
6. WHO Global Alert and Response (GAR) Human infection with influenza A(H7N9) virus in China update. Retrieved 04/09, 2013, from http://www.who.int/csr/don/2013_04_09/en/index.html
7. *Foreign Animal Disease Diagnostic Laboratory Containment Standard,* 2007, Canadian Food Inspection Agency http://www.inspection.gc.ca/english/sci/bio/anima/diag/diage.shtml
8. *Laboratory Biosafety Guidelines*, 3rd Edition, 2004, Public Health Agency of Canada http://www.phac-aspc.gc.ca/ols-bsl/lbg-ldmbl/index-eng.php
9. *Containment Standards for Veterinary Facilities,* 1st Edition, 1996, Canadian Food Inspection Agency
10. *Transportation of Dangerous Goods Regulations*, Transport Canada, http://www.tc.gc.ca/tdg/menu.htm
11. PHAC Influenza A virus subtypes H5, H7 and H9 Pathogen Safety Data Sheet (PSDS) http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/influenza-grippe-a-eng.php