Pathogen Safety Data Sheets: Infectious Substances – Influenza A virus subtypes H5, H7 and H9

PATHOGEN SAFETY DATA SHEET - INFECTIOUS SUBSTANCES

SECTION I - INFECTIOUS AGENT

NAME: Influenza A virus subtypes H5, H7 and H9.

SYNONYM OR CROSS REFERENCE: *Orthomyxovirus* [1-3], influenza virus type A [1-3], *influenzavirus* A [1-3], avian influenza [1-3], and pandemic influenza [4].

CHARACTERISTICS: Influenza virus subtypes H5, H7 and H9 are members of the *Orthomyxoviridae* family of segmented, negative sense single-stranded RNA viruses. Type A influenza viruses are subdivided on the basis of the antigenic nature of their membrane-bound surface glycoproteins, haemagglutinin (HA) and neuraminidase (NA). To date, 16 HA, and 9 NA subtypes have been detected in wild birds and poultry [5-9]. Antigenic alterations occur frequently in the antigenic sites of HA and NA and are the mechanism for virus adaptation and survival. Small alterations are referred to as antigenic drift, whereas larger alterations caused by reassortment are referred to as antigenic shift. Influenza pandemics may occur as a result of antigenic shifts if the virus is able to maintain efficient human-to-human transmission [1-3].

SECTION II - HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: Avian influenza A viruses are referred to as low pathogenic avian influenza (LPAI) and highly pathogenic avian influenza (HPAI), based on the severity of illness caused in poultry. To date, only H5 and H7 subtypes have been shown to be HPAI, although not all H5 and H7 viruses are highly virulent [2, 3, 10]. Furthermore, it appears that HPAI viruses arise by mutation after LPAI viruses have been introduced to poultry [2].

Human infections from influenza A virus subtypes H5, H7 and H9 range from eye infections (conjunctivitis) to influenza-like illness (ILI) symptoms to severe respiratory illness [11-13]. Symptoms of H5N1 range from typical flu-like symptoms (e.g., fever, sore throat, cough, and muscle aches) to pneumonia, acute respiratory distress syndrome, multiple organ failure, lymphopenia, elevated liver enzyme levels and abnormal clotting profiles, diarrhoea, vomiting, abdominal pain, pleuritic pain, and bleeding from the nose and gums [11, 14, 15].

EPIDEMIOLOGY: Influenza can occur in pandemics, epidemics, localized outbreaks, and as sporadic cases. Many strains of avian influenza virus can cause varying degrees of disease in domestic poultry. Avian influenza usually does not make wild birds sick, but can cause serious illness and death in poultry [10]. HPAI is a fatal form of avian influenza that can spread rapidly in flocks, causing high mortalities. Outbreaks of HPAI have led to human infections, some of which resulted in deaths

[11]. Lack of previous exposure to the virus and high virulence of avian influenza H5N1 is a key determinant of the high fatality rate [11]. LPAI can also cause disease in humans. For example, H7N7 (1996, conjunctivitis); H9N2 (1999, ILI); H7N2 (2002, ILI); H9N2 (2003, ILI) and H7N2 (2003, ILI) [16]. Continuous existence of LPAI virus in an avian population may provide opportunities for the virus to undergo mutation and convert to a highly pathogenic strain [2].

Animal influenza A virus subtypes that have infected humans include H5N1, H7N2, H7N3, H7N7, H9N2, H10N7 and swine and avian H1 viruses.

Human cases of H5 were first reported in 1997 in Hong Kong, where avian-to-human transmission of H5N1 resulted in 18 cases of human infection and 6 deaths [15, 17]. In 2003 another outbreak in Hong Kong led to 2 cases of human infection and one death [15, 17]. In December 2003, a further outbreak of H5N1 occurred among poultry in South Korea and then later in Vietnam, Japan, Thailand, Laos, Cambodia, China, Indonesia and Malaysia [1, 18]. Since the outbreak in 2003, the World Health Organization (WHO) has reported a number of waves of avian-to-human transmission starting in Southeast Asia and spreading to areas North and West of China reaching as far as Eastern Europe and Northern Africa [19-21]. The cumulative number of human H5N1 cases reported to WHO from 2003 to May 6, 2010 is 498 cases with 294 deaths (59% mortality rate) [21].

H7 infection in humans is rare, but can occur in persons who have been in direct contact with infected birds [12, 22, 23], or in one case, seals [24]. In 2003, H7N7 was responsible for the death of a veterinarian and extensive conjunctivitis among those employed in the disposal of diseased birds in the Netherlands [12]. An outbreak of H7N3 in 2004 also led to two cases of human infection in British Columbia, Canada [23].

Since 1998, a number of human cases of H9N2 have been reported in Asia and are generally associated with mild illness [25, 26]. Transmission of H9N2 appears to be exclusively avian-to-human [26, 27].

HOST RANGE: Domestic and wild avian species. H5 and H7 are generally non-pathogenic in their natural waterfowl hosts but may become highly pathogenic once introduced into domestic poultry [3, 15]. Viral transmission of H5N1 to mammals has been reported in domestic cats, dogs, tigers and also in a stone marten (reviewed in [1, 20]).

INFECTIOUS DOSE: Unknown.

MODE OF TRANSMISSION: Influenza A infections (H5, H7, H9) in humans result predominantly from direct transmission of the virus from birds to humans. Transmission occurs primarily through contact of the mucous membranes with infectious secretions or excreta from infected wild birds or poultry. Exposure to sick poultry and the butchering of birds is associated with seropositivity for H5N1 [28, 29]. Slaughtering, de-feathering, or preparing sick poultry for cooking, playing with or handling diseased or dead poultry, handling fighting cocks or ducks that appear asymptomatic, and consuming raw or uncooked poultry or poultry products, have all been implicated as potential risk factors [14, 20]. Oral ingestion of contaminated water during swimming and direct intranasal or conjunctival inoculation during exposure to water are other potential modes of transmission, as is contamination of hands from infected fomites and subsequent self-inoculation [20, 28]. The widespread use of untreated poultry feces as fertilizer is another possible risk factor [14]. Non-sustained human-to-human spread has only been documented in a few cases [30-32]; however, the

continued circulation of virulent influenza virus H5N1 increases the potential for a new influenza virus to arise through reassortment with other circulating influenza viruses, thus increasing the threat of an influenza virus that is transmissible from person-to-person that could lead to a global influenza pandemic [1], [18], [32].

INCUBATION PERIOD: Most cases of influenza A (H5N1) occurred within two to four days after exposure [15], [18-20]. In clusters in which limited human-to-human transmission may have occurred, the incubation period appeared to be approximately 3 to 5 days, although in one cluster it was estimated to be 8 to 9 days [30], [31].

COMMUNICABILITY: Limited human-to-human transmission reported, whereby transmission probably occurred during close unprotected contact with a severely ill patient [30-32].

SECTION III - DISSEMINATION

RESERVOIR: Wild aquatic birds, predominantly ducks, geese, and shorebirds. Avian influenza viruses are generally non-pathogenic in wild birds, sometimes causing significant morbidity and mortality upon transmission to other species, including domestic birds and mammals [3], [5], [18], [20].

ZOONOSIS: Yes, from various avian species [3], [11], [12], [14], [15], [18], [20], [23], [28], [31].

VECTORS: Wild birds [3], [5], [18], [20].

SECTION IV - STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Various subtypes of H5 (H5N1), H7 (H7N3, H7N7) and H9 (N9N2) are susceptible to the neuraminidase inhibitors, oseltamivir [4], [23], [33-36], zanamivir [4], [23], [33-36], and peramivir (RWJ-270201) [34]. In the past, influenza viruses have been shown to be sensitive to M2 inhibitors, amantadine and rimantadine, although to a lesser extent than the neuraminidase inhibitors [1], [4], [35]. There is evidence of increasing resistance to M2 inhibitors by H5N1 [1], [4], [35], [36].

SUSCEPTIBILITY TO DISINFECTANTS: Susceptible to the following disinfectants: 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formalin and iodine compounds (reviewed in [37]). Also susceptible to a number of commercially available disinfectants (reviewed in [37]).

PHYSICAL INACTIVATION: Incubation at 56ºC to 60ºC for 60 min will inactivate various subtypes of H5, H7 and H9 (reviewed in [37]). Incubations in low (1 to 3) or high (10 to 14) pH solutions has also been shown to be effective at inactivating H5, H7 and H9, although the medium in which the virus is suspended may interfere with the effect of pH on virus infectivity (reviewed in [37]).

SURVIVAL OUTSIDE HOST: Influenza virus may remain infective in lake water for 4 days, in water at 22ºC, and for 30 days at 0ºC [2]. Survival in feces is likely to be influenced by the strain of the virus, type of faeces and temperature [37].

SECTION V – FIRST AID / MEDICAL

SURVEILLANCE: Identify potential exposure to H5, H7 or H9 through recent travel to or from areas with known influenza activity [1]. Monitor for symptoms of influenza. Confirm by viral culture [12, 14, 15, 18, 23], RT-PCR with strain specific primers [12, 14, 15, 18, 20, 22, 23, 31], immunostaining (Western blot, ELISA) with subtype specific antibodies [11, 15, 17, 27, 28, 30, 31], molecular sequencing [30, 31], antiviral resistance testing [30], and/or microneutralization [27, 30].

FIRST AID/TREATMENT: Antivirals must be administered early after the onset of symptoms to be effective [14, 20]. Oseltamivir is recommended for the treatment of avian influenza viruses. Oseltamivir is an oral preparation (capsule or liquid suspension), whereas zanamivir is delivered by inhalation [4, 20, 35]. Amantadine and rimantadine are also administered in countries where they are licensed if oseltamivir and zanamivir are unavailable [1, 35].

IMMUNIZATION: A vaccine for humans against the H5N1 influenza virus was approved by the Food and Drug Administration (FDA) in the United States. The immunization consists of two intramuscular injections, given approximately one month apart [38]. A vaccine for H9N2 is currently in clinical trials [1]. It is a cold-adapted, live, attenuated virus vaccine administered intranasally [1]. There are currently no human vaccines for H7 viruses, although, avian vaccines for H7 viruses are being investigated as a method to prevent outbreaks [39, 40].

PROPHYLAXIS: Chemoprophylaxis with of oseltamivir once daily for 7 days after the last known exposure is warranted for persons who have had a possible unprotected exposure H5N1 [4, 35, 38, 41]. Zanamivir (10mg twice daily) [1, 4, 35] and the M2 inhibitors, amantadine (100 mg twice daily) [1, 4, 35] and rimantadine (100 mg twice daily [1, 4, 35] are also used; however, amantadine and rimantadine are documented to be less effective as a first-line mono-therapy [1, 4, 35]. The use of human or humanized antibodies for prophylaxis and therapy are currently being investigated [32].

SECTION VI - LABORATORY HAZARDS

LABORATORY-ACQUIRED INFECTIONS: None reported.

SOURCES/SPECIMENS: Tissues, secretions and/or excretions from infected birds [1, 4, 14, 35].

PRIMARY HAZARDS: Inhalation of virus from aerosols generated when aspirating, dispensing, or mixing virus-infected samples from infected animals, especially birds [1, 4, 14, 35].

SPECIAL HAZARDS: Possible risk to people who have contact with surfaces that have been contaminated with secretions or excretions from infected birds [1, 20, 28]. Accidental inoculation is also a risk [1, 20, 28].

SECTION VII – EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 2 or 3, depending on specific virus.

CONTAINMENT REQUIREMENTS: Containment Level 2 facilities, equipment, and operational practices for work involving clinical or diagnostic specimens. Containment Level 3 facilities, equipment, and operational practices are recommended for virus isolation and laboratory manipulation of highly pathogenic H5, H7 and H9 strains of avian influenza [42]

PROTECTIVE CLOTHING: Protective solid-front gowns, gloves, shoe covers, eye protection with face seal, and N95 respiratory protection [1, 42, 43].

OTHER PRECAUTIONS: Manipulations with autopsy material or infectious material in open vessels to be carried out in a certified biological safety cabinet. Centrifugation of respiratory specimens or tissue samples to be carried out using sealed centrifuge cups or rotors,both of which are to be loaded and unloaded in a biological safety cabinet [1, 42, 43].

SECTION VIII – HANDLING AND STORAGE

SPILLS: Allow aerosols to settle, and while wearing protective clothing, gently cover the spill with paper towels and apply 1% sodium hypochlorite or other proven effective disinfectant, starting at the perimeter and working towards the centre. Allow sufficient contact time and then clean the area.

DISPOSAL: Decontaminate before disposal by steam sterilization, chemical disinfection, or incineration.

STORAGE: In sealed containers that are appropriately labelled [43].

SECTION IX - REGULATORY AND OTHER INFORMATION

UPDATED: December 2011

PREPARED BY: Pathogen Regulation Directorate, Public Health Agency of Canada.

Although the information, opinions and recommendations contained in this Pathogen Safety Data Sheet are compiled from sources believed to be reliable, we accept no responsibility for the accuracy, sufficiency, or reliability or for any loss or injury resulting from the use of the information. Newly discovered hazards are frequent and this information may not be completely up to date.

REFERENCES:

1 Thomas, J. K., & Noppenberger, J. (2007). Avian influenza: A review. *American Journal of Health-System Pharmacy, 64*(2), 149-165.

2 Alexander, D. J. (2007). An overview of the epidemiology of avian influenza. *Vaccine, 25*(30), 5637-5644. doi:10.1016/j.vaccine.2006.10.051

3 Hampson, A. W., & Mackenzie, J. S. (2006). The influenza viruses. *Medical Journal of Australia, 185*(10 SUPPL.), S39-S43.

4 Harrod, M. E., Emery, S., & Dwyer, D. E. (2006). Antivirals in the management of an influenza pandemic. *The Medical Journal of Australia, 185*(10 Suppl), S58-61.