



THE 2013 INFLUENZA A (H7N9) VIRUS

INTRODUCTION

Microbac Laboratories, Inc. is excited to launch GLP-compliant virucidal efficacy testing services against the 2013 Influenza A (H7N9) Viruses.

The newly emerged 2013 influenza A (H7N9) virus has caused wide-spread epidemics in multiple provinces in China (World Health Organization). It was believed to be of bird origin; but it infects humans with a high mortality rate. As of 06/12/2013, there have been more than 130 reported H7N9 cases with at least 24 deaths. The number of infections and deaths are still growing to date.

There are different modes of transmission of influenza viruses among persons (Weber et al., 2008). Droplet transmission can occur during breathing, coughing, or talking (CDC, 2013; Milton et al., 2013; Lindsley et al., 2010; Stelzer-Braid et al., 2009); and contact transmission can occur via direct and indirect contact with contaminated surfaces. Many of the people infected with H7N9 are reported to have had contact with poultry. However, the sources of the virus in some cases are unknown. Currently there is no evidence of sustained human-to-human transmission of this virus. However, limited non-sustained human-to-human H7N9 virus transmission could not be excluded and remains a possibility (Li et al., 2013).

BIOLOGY AND MEDICAL TREATMENTS

The influenza A (H7N9) viruses are novel reassortants that have the “H7” surface hemagglutinin (HA) and “N9” neuraminidase (NA). They have a high mortality rate, most likely since they are so new. The H7 has not been seen in seasonal influenza nor the H9.

The virus has made the following mutations so far to adapt into humans:

- 158 Glycosylation - Binding site changes so that it binds stronger to human receptors
- E627K - Temperature changes so that it works effeciently at human body temperature rather than the higher body temperature of birds
- L226I - seen also in current H3N2, transmissibility and human binding mutations

Infectious influenza virus has been maintained on surfaces for up to two weeks (Derrick and Edward, 1941; Bean et al., 1982; Wood et al., 2010) and in water for up to seven months (Stallknecht et al., 1990). Due to the potential for transmission of influenza A(H7N9) viruses by aerosol droplets and its potential to remain viable in dry and liquid form for extended periods of time, proper safeguards should be in place to ensure protection of laboratory personnel and the environment.

Currently, there are no licensed vaccines against H7N9 virus. However several institutions are working



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diligently to develop vaccines against this virus. It has also been shown that certain anti-influenza drugs (e.g., oseltamivir and zanamivir) can be effective, especially when given early in the course of the illness.

BIOSAFETY

The virus is currently classified by the U.S. Centers for Disease Control and Prevention (CDC) as a “low pathogenic avian influenza (LPAI)” and not subject to USDA select agent requirements. However, USDA and CDC permitting requirements must be followed. Previous permits issued for general LPAI isolates are not applicable for this virus.

All in-vitro work with this virus should be conducted within BSL-3 laboratories. Due to the potential for aerosol inhalation and the pathogenicity of the virus in humans, respiratory protection is mandatory. To prevent the potential spread of this virus to birds, personnel working in the BSL-3 laboratory must avoid contact with domestic or wild birds.

EFFICACY TESTING

The rapid spread of this virus has raised a vast demand on pharmaceutical and public hygienic products that can aid in the treatment and prevention of the disease, such as vaccines, antiviral drugs, diagnostic tools, hand rubs/washes, surface cleaners and disinfectants and face masks, etc. These products along with general public health awareness and practice have been important in ensuring a successful disease prevention and control.

The efficacy and safety of these products must be adequately tested following scientifically sound and regulatory recognized methods. An important agent in these tests is the actual H7N9 influenza virus culture, which serves either as the challenge organism or the positive control. Other surrogate viruses such as the generic Influenza A isolates, although maybe similar to the 2013 H7N9 in certain ways, are different in many other aspect from the H7N9 virus.

Microbac Laboratories, Inc. has acquired the 2013 H7N9 virus and has successfully established a gfp-COMPLIANT, highly efficient cell culture based infectivity assay, available immediately to serve various testing needs for our clients. Should you require any further information, please contact us at 703-925-0100 or MBTsales@microbac.com.



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REFERENCES

<http://www.cdc.gov/flu/avianflu/h7n9/risk-assessment.htm>

Tweed SA, Skowronski DM, David ST, Larder A, Petric M, Lees W, Li Y, Katz J, Krajden M, Tellier R, Halpert C, Hirst M, Astell C, Lawrence D, Mak A. Human illness from avian influenza H7N3, British Columbia. *Emerg Infect Dis.* 2004 Dec;10(12):2196-9.

Nguyen-Van Tam, J.S., Nair P., Acheson P., Baker, A., Barker, M., Bracebridge, S., et al. Outbreak of low pathogenicity H7N3 avian influenza in UK, including associated case of human conjunctivitis. *Euro Surveill.* 2006; 11:E070531.2.

Skowronski DM, Tweed SA, Petric M, Booth T, Li Y, Tam T. Human illness and isolation of low- pathogenicity avian influenza virus of the H7N3 subtype in British Columbia, Canada. *J Infect Dis.* 2006 Mar 15;193(6):899-900.

Anonymous. Avian influenza A(H7N2) outbreak in the United Kingdom. *Euro Surveill.* 2007; 12:E060504.2

Ostrowsky, B., Huang, A., Terry, W., Anton, D., Brunagel, B., Traynor, L., Abid, S., Johnson, G., Kacica, M., Katz, J., Edwards, L., Lindstrom, S., Klimov, A., Uyeki, T. Low pathogenic avian influenza A(H7N2) virus infection in immunocompromised adult, New York, USA, 2003. *Emerg Infect Dis.* 2013; 18(7):1128-31.

Lu S, Zheng Y, Li T, Hu Y, Liu X, Xi S, et al. Clinical findings for early human cases of influenza A(H7N9) virus infection, Shanghai, China. *Emerg Infect Dis.* 2013 Jul

Weber, T.P. and Stilianakis, N.I. Inactivation of influenza A viruses in the environment and modes of transmission: a critical review. *J Infect.* 2008; 57(5): p. 361-73.

Milton, D.K., Fabian, M.P., Cowling, B.J., Grantham, M.L., McDevitt, J.J. Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks. *PLoS Pathog.* 2013; 9(3): e1003205.

Lindsley, W.G., Blachere, F.M., Thewlis, R.E., Vishnu, A., Davis, K.A., Cao, G., Palmer, J.E., Clark, K.E., Fisher, M.A., Khakoo, R. and Beezhold, D.H. Measurements of airborne influenza virus in aerosol particles from human coughs. *PLoS One.* 2010; 5(11): e15100.

Stelzer-Braid, S., Oliver, B.G., Blazey, A.J., Arent, E., Newsome, T.P., Rawlinson, W.D. and Tovey, E.R. Exhalation of respiratory viruses by breathing, coughing and talking. *J Med Virol.* 2009; 81: 1674-1679.

Derrick, G. and Edward, F.F. Resistance of influenza virus to drying and its demonstration on dust. *Lancet.* 1941; 2:664-666.



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Bean, B., Moore, B.M., Sterner, B., Peterson, L.R., Gerding, D.N. and Balfour, H.H. Jr. Survival of influenza viruses on environmental surfaces. *J Infect Dis.* 1982; 146(1): 47-51.

Wood, J.P., Choi, Y.W., Chappie, D.J., Rogers, J.V. and Kaye, J.Z. Environmental persistence of a highly pathogenic avian influenza (H5N1) virus. *Environ Sci Technol.* 2010; 44(19): 7515- 7520.

Stallknecht, D.E., Shane, M.T., Kearney, M.T., Zwank, P.J. Persistence of avian influenza viruses in water. *Avian Dis.* 1990; 34:406-411.

Cox, R.J., Madhun, A.S., Hauge, S., Sjursen, H., Major, D., Kuhne, M., Höschler, K., Saville, M., Vogel, F.R., Barclay, W., Donatelli, I., Zambon, M., Wood, J., Haaheim, L.R. A phase I clinical trial of a PER.C6 cell grown influenza H7 virus vaccine. *Vaccine.* 2009; 27:1889-1897.

Couch, R.B., Patel, S.M., Wade-Bowers, C.L., Ni o, D. A randomized clinical trial of an inactivated avian influenza A(H7N7) vaccine. *PLoS One.* 2012; 7(12): e49704.

Talaat, K.R., Karron, R.A., Callahan, K.A., Luke, C.J., DiLorenzo, S.C., Chen, G.L., Lamirande, E.W., Jin, H., Coelingh, K.L., Murphy, B.R., Kemble, G., Subbarao, K. A live attenuated H7N3 influenza virus vaccine is well tolerated and immunogenic in a Phase I trial in healthy adults. *Vaccine.* 2009; 27:3744-3753.

Suarez, D.L., Perdue, M.L., Cox, N., Rowe, T., Bender, C., Huang, J. and Swayne, D.E. Comparisons of highly virulent H5N1 influenza A viruses isolated from humans and chickens from Hong Kong. *J Virol.* 1998; 72(8): 6678-6688.