



Minutes of OFFLU Swine Influenza Virus Working Group Teleconference

December 15, 2012

Participants: Ruben Donis, Malik Peiris, Richard Webby, Marie Gramer, Sabrina Swenson, John Pasick, Sujira Parchariyanon, Taki Saito, Frank Wong, Janice Ciacci Zanella, Ian Brown, Nicola Lewis, Ariel Pereda, Hualan Chen, Amy Vincent, Kristien Van Reeth, Liz Mumford, Sara Martins, Filip Claes, Keith Hamilton, Gounalan Pavade

Agenda Items and Discussion:

Agenda 1. Discuss the recent swine-origin H3N2 reassortants in humans in North America and informally share information on any emerging subtypes or reassortants in pigs or people.

- Ruben Donis provided an update from the CDC on the recent human cases with H3N2v in the USA:
 - Between Dec 2005 and Dec 14 2011, a total 34 human cases of variant influenza viruses that are known to be circulating in pigs have been reported to CDC (13 H1N1, 19 H3N2, 2 H1N2). The median age of these cases was 10 years; 10 cases reported direct or indirect exposure to swine; in 6 cases there has been potential further human-to-human transmission. Since July of 2011, there have been 11 cases of “H3N2 variant” or “H3N2v” (triple reassortant H3N2 with M gene of the 2009 pH1N1 virus) in 5 states. All with genome sequence available and posted in public databases.
 - All H3N2v viruses have M gene from pandemic H1N1 2009 virus (H1N1pdm) and remaining genes related to previously circulating trH3N2 viruses isolated from pigs and humans
 - It is expected that there will be very little immunity to these viruses in the young population. Using a hemagglutination inhibition (HI) titer of ≥ 40 as a surrogate marker of immunity, some level of “protection” was expected in:
 - 0% of children 6-36 months of age
 - 33% of adults 18-49 years of age, this level increased to 50% for

sera collected after receiving the 2011-12 Trivalent Influenza vaccine.

- 17% of adults ≥ 65 years of age, this level increased to 40% for sera collected after receiving the 2011-12 Trivalent Influenza vaccine.
 - o All H3N2v viruses evaluated so far are resistant to the amantadine class of drugs (amantadine, rimantadine) and susceptible to the commercially available neuraminidase inhibitors oseltamivir and zanamivir.
- Richard Webby provided an update on active surveillance activities in swine in the USA. This research based project (done in collaboration with Marie Gramer) routinely collects swabs from healthy and sick animals. H1 (pandemic and classical) and H3 viruses continue to be isolated. A number of reassortant viruses have been detected, all with the M gene segment from the H1N1pdm virus. Of those H3N2 reassortant viruses sequenced, no detection of the specific H3N2v genotype have been made. A number of more contemporary isolates are being sequenced.
 - Amy Vincent updated the group on the USDA SIV surveillance that began in 2009 and recent research findings with the H3N2 reassortants in pigs. Between 2009-2011, subtypes H1N1, H1N2, and H3N2 were detected in pig populations and characterized in the USDA SIV surveillance system with approximately 2/3 of the characterized viruses being H1 and 1/3 being H3. As of mid-December 2011, there were approximately 30 H3N2 viruses detected in the USDA surveillance stream and 8 of those contained the M gene segment from the H1N1pdm virus. In addition to the H3N2-pM SIV, H1 viruses of the North American phylogenetic clusters (γ and δ) have acquired the M gene segment from H1N1pdm as well. H3N2 viruses of different genetic constellations were compared in an *in vivo* pathogenesis and transmission study in 4 week old pigs. All viruses infected and transmitted and were typical of influenza virus infection in the swine host. The H3N2 SIV with all 8 genes segments from the North American triple reassortant (TRIG) lineage was the most efficient of the 3 viruses compared, indicating that the acquisition of 2009 H1N1pdm-lineage genes may not have a selective advantage in the swine host. However, since the reassortant viruses evaluated in this study were fully successful in the challenge experiment, this suggests reassortants will likely continue to emerge in pig populations where multiple lineages of SIV co-circulate.
 - Marie Gramer reported (by email) from the University of Minnesota Veterinary diagnostic lab that 2009 H1N1pdm, gamma cluster H1N1, delta 1 cluster H1N2, delta 2 cluster H1N1, and cluster IV H3N2 viruses in the Midwestern USA with the delta cluster viruses have been found most often in the sampled pig population. About 30% (this is not a hard number) of the gamma H1, delta H1, and cluster IV H3s sequenced also possess the M gene from the H1N1pdm virus. The clinical signs described by the veterinarians submitting samples from which we obtained reassortant viruses are variable and not suggestive of increased or decreased clinical disease manifestations associated with the presence of

H1N1pdm M gene.

- Ariel Pereda reported the results of the influenza surveillance in pigs activity performed by the National Institute of Agriculture Technology (INTA), the National Animal Health Authority (SENASA) and the University of La Plata, between 2008 and 2011 in Argentina. In late 2008 a wholly human H3N2 from pigs with typical influenza symptoms was detected. Experimental reproduction of infection showed that the virus was transmitted efficiently between pigs, and that the inoculated pigs had characteristic lesions of influenza virus, suggesting that this virus is completely adapted to swine and has the potential to be maintained in the swine population. Also in 2009 the infection of pigs with the H1N1pdm virus was reported, and in 2010 and 2011 the isolation of reassortant viruses with internal genes from the H1N1pdm and the surface genes (HA and NA) from human-like H1 SIV was reported, and therefore there is some indirect evidence of circulation of human-like H1 SIVs in Argentina. In 2011 another reassortant virus was isolated with the surface genes from the wholly human H3N2 virus first isolated in 2008 and all the internal genes from the H1N1pdm virus. The clinical signs observed in all these cases correspond to typical influenza symptoms (fever, dyspnea, cough, sneezing, etc.) and absence of vaccines and the characteristics of pig production of Argentina may contribute to the emergence of these new reassortants. In summary, we have reported the first outbreak of a wholly human H3N2 subtype in Argentina and novel reassortants with the H1N1pdm.
- Kristien Van Reeth: There have been only 5 reports of variant influenza infection in humans in Europe since 2008. All infections were avian-like H1N1 SIV, 4 of the 5 patients had known exposure to swine. The most recent case was an 18-month old boy in Germany in September 2011. Information about these cases can be found in a rapid risk assessment about the H3N2v virus, which has been published on the ECDC website. There is less influenza surveillance in both pigs and people in Europe as compared to the US.
- Malik Peiris reported that swine influenza isolation rates in the abattoir surveillance in Hong Kong have increased in the last few months. Most of the viruses being isolated are various reassortants which include pandemic H1N1 genes. Of note are H3N2 viruses with pandemic H1N1 internal genes and an H3 and N2 of human seasonal influenza origin deriving from the 2004 period. Similar H3 HA and NA has been reported with the TRIG backbone in Vietnam in a publication in 2010 (our report is now online in JV). There is relatively high cross-reacting antibody in age stratified human sera to these viruses. There is also a range of H1 viruses of Eurasian avian lineage which carry various combinations of pandemic H1N1 internal genes.

Agenda 2. Review the action items and outcomes proposed from the April 2011 meeting and plans to complete before 2012 meeting.

Sub-committees were formed for driving the priority outputs at the OFFLU SIV group

meeting in April 2011.

Experts in charge of tasks 1-4 were reminded about the outputs by email before the TC. All of them plan to complete or make significant progress toward the activities before the SIV group meeting in March 2012.

1. Publication of lists of viruses and diagnostic tests by region: Marie, Kristien, Malik, Sabrina, Janice

2. Harmonization of lab protocols for influenza in pigs: Ian, Sabrina, Richard, Takehiko, Sujira, Frank

Sujira: Most of the tests follow OIE protocol. It seem that for subtype H3N2 by using chicken red blood cell gave more good result than male turkey red blood cell for HA and HI test.

3. Publication of network's statement: Ruben, Ian, Liz, John

4. Preparation of SI surveillance funding proposal: Kristien, Ruben, Filip, Richard

Some funds have been made available to RW from US NIH/NIAID to support SIV surveillance. Part of these funds will go towards supporting the OFFLU SIV technical meeting in March 2012.

5. Preparation of advocacy slide set about OFFLU SIV surveillance activity: Amy, Lina, Nicola

- A slide set was developed and circulated to group members and is available on the OFFLU website <http://www.offlu.net/fileadmin/home/en/resource-centre/pdf/SIV-Generic-slides-072011.pdf> The slides (or subset) were used in a presentation at the Emerging and Re-emerging Pig Disease conference in Barcelona, Spain (A. Vincent) and at the United States Animal Health Association, Public Health Committee meeting (S. Swenson).

6. Publish a paper on targeted surveillance: Lina, Kristien, Marie, Amy, Filip

- A proceedings drafted by Amy was circulated with an overwhelming positive response by group members to contribute regional information to turn the proceedings into a full manuscript for publication. It was proposed to combine this with the global targeted SIV surveillance mapping done by Lina.

Agenda 3. Plan the date, venue, and agenda for the 2012 meeting (it is proposed to have a 1,5-day meeting in the OIE headquarters in Paris in March 2012)

- The meeting is scheduled for March 27-28, 2012 in Paris.