Summary of the OFFLU Swine Influenza Virus (SwIAV) group technical meeting
OIE Headquarters, Paris, 27 - 28 February 2019

Participants: Amy Vincent (USDA, USA), Ariel Pereda (INTA, Argentina), Clement Meseko (NVRI, Nigeria), Frank Wong (AAHL, Australia), Gaelle Simon (ANSES, France), Janice Ciacci Zanella (EMPRAPA, Brazil), Kristien Van Reeth (Ghent University, Belgium), Marie Culhane (U Minnesota, USA), Nicola Lewis (APHA/RVC, UK), Todd Charles Davis (CDC, USA), Sabrina Swenson (NVSL, USA), Tung Nguyen (NCVD, Vietnam), Yohannes Berhane (NCFAD, Canada), Young Ki Choi (CBNU, Rep. Korea), Gounalan Pavade (OIE).

Through Skype – Huanliang Yang (HVRI, China), Richard Webby (St. Jude, USA), Taiko Saito (NIAH, Japan).

Dr Jean-Philippe Dop, the OIE Deputy Director General, Institutional Affairs and Regional activities welcomed the experts on behalf of Director General, OIE. He thanked the experts for supporting the OFFLU activities through technical advice and sharing data to capture the global swine influenza virus situation by regular meetings. He noted that surveillance for influenza in swine is important to better understand the implications of influenza viruses for humans and animals, and to minimise the impacts on health, economies and production. Finally, he wished the participants a successful and productive meeting.

The experts presented the status of Swine influenza virus (SwIAV) by region and recent updates on the research activities of SwIAV.

Australia (Frank Wong):

Systematic influenza surveillance in swine does not occur in Australia. However, snapshots of the SwIAV diversity present, have been obtained from occasional syndromic sampling associated with investigation of respiratory diseases. A recap of the known H1 and H3 subtype influenza A viruses detected in Australian swine from 2012 and 2016 was provided. Phylogenetic analysis has shown that the HA genes of H1N2 viruses in swine in Western Australian (WA) and Queensland (QLD) swine were independently derived from older H1N1 human seasonal viruses including 1977-like (in WA) and mid-1990s-like (in QLD); and that the HA genes of H3N2 swine viruses detected in WA were derived from human H3N2 viruses circulating during the 1995 influenza season. The N2-NA genes of these viruses were either from human 1968-like (WA), 2003-like (QLD) and mid-1990s-like (WA) H3N2 viruses from past human influenza pandemics or seasons. Virus sequences also showed that these SwIAV had undergone reassortment, containing mixed internal genes from the viruses in past human influenza seasons, including H3N2/1998-like, H3N2/1995-like, H1N1/1977-like and H1N1pdm2009-like. For further information on these viruses, refer to https://doi.org/10.1128/JVI.00316-18.

In December 2017, an H3N2 virus consisting of 6 virus gene segments including the HA gene derived from the 1968 pandemic virus, and NA and PA genes from other past H3N2 seasonal influenza viruses, was detected in swine sampled in the state of Victoria. In addition, a variant H3N2(v) virus with HA and NA genes derived from 1995-like H3N2 seasonal virus was detected in late 2018 for the first time in Australia, from a single case of an infected human in South Australia during routine screening of influenza positive samples sent to the WHO Collaborating Centre for Influenza Reference and Research, Melbourne. The remaining 6 internal genes were contributed by H1N1pdm2009 influenza viruses that were previously detected in swine and humans around 2009/2010. These recent H3N2 swine-origin viruses were further indication of the mix of old human influenza virus genes that may circulate in pigs over periods spanning several decades in multiple Australian states. H1N1pdm viruses have been in continuous circulation and also involved in ongoing human-swine interface interactions in Australian swine populations since 2009, contributing to the apparent SwIAV reassortment diversity in Australia. These snapshots highlight the need and importance of continued influenza virus surveillance in swine in Australia and elsewhere for informing both animal and zoonotic influenza risk assessments and pandemic preparedness.

China (Huanliang Yang):

China has about half of the world's swine population. China's pig production ranges from backyard to large-scale. Pigs were not routinely vaccinated against swine influenza. People and pigs have contacts frequently. Sporadic human infection with SwIAVs have been occasionally reported. Driven by commercial profit, long distance transportation of pigs by trucks were common before August 2018. In China the objectives of the surveillance program include to gain a better understanding of the genetic evolution of swine influenza viruses, update diagnostic assays, and vaccine seed stock products and to investigate the evolution and biologic properties (virulence, antigenicity, and transmissibility) of SwIAV.

In January - April 2018, sample collection and testing were carried out in the first stage over 3,800 nasal swab samples from 2 provinces. In November 2018 - January 2019, sample collection and testing were carried out in the second stage over 15,300 nasal and tracheal swab samples from 20 provinces. A total of 19800 nasal and tracheal swabs and more than 2000 serum samples were collected and tested.

From the first stage samples, 56 strains of SwIAVs were isolated, including 30 EA H1N1, 25 EA H1N1 and 1 H1N2. From the second stage samples, 130 strains of SwIAVs were isolated and work is still in progress. The results of HI test on 3561 serum samples showed that the antibody positive rates of 21.1 % EA H1N1, 13.2% pH1N1/2009, and 2.2%H3N2.

To summarise, multiple subtypes of influenza viruses co-circulated in pigs in China during 2017 to 2018. The EA Group2 H1N1 continues to exist in pigs and triple-reassortant EA H1N1 containing the four RNP genes (encoding PB1, PB2, PA, and NP) from 2009/H1N1 became predominant among pigs in China.

South Korea (Young Ki Choi):

The FMD outbreaks in South Korea in the past few years have significantly decreased the isolation rate of SwIAVs although the sero-prevalence rate was maintained by about 25- 30%. The decreased phenomena of SwIAV isolation rate was hypothesized to be closely associated with intense SwIAV hygiene control for FMD because overall swine viral disease cases were seemed decreased in several years.

Nevertheless, some H1N1 (n=5), H1N2 (n=1), and H3N2 (n=6) SwIAV were isolated from 2015 to 2018. Genetic and phylogenetic characterization revealed that A(H1N1)pdm09-like (1A.3.3.2 clade) influenza viruses were dominant compared with H1N2 subtypes. The swine H1N2 isolate shared its internal genes with A(H1N1)pdm09 virus-like viruses except the N2 gene which were originated from swine H3N2 viruses. HA genes of H3N2 viruses belonged to Cluster IV and they have the M gene of A(H1N1) pdm09 virus suggesting most of recent swine H3N2 were H3N2 variants viruses. Ferret infection studies demonstrated that all subtypes were well replicated in lungs and tracheal tissues with 4.8 to 5.8 log10 TCID50/g in infected ferrets. The H1N1 virus showed the higher virus titers than that of swine H3N2 viruses in nasal turbinate (5.1 Vs 3.1 log10 TCID50/g) and readily transmitted into indirect contact ferrets. However, the 2018 H3N2 isolate failed to transmit to indirect contact ferrets. To confirm the transmission ability of recent swine H3N2 virus, further studies are needed using animal models.

Japan (Taki Saito):

Active and passive surveillance for SwIAV was done in Japan in 2018. By active surveillance, 43 viruses were isolated from 914 nasal swabs belonging to 20 farms and by passive surveillance, 6 viruses were isolated. The subtypes detected include predominately A(H1N1)pdm09, H1N1-swine HA and NP, H1N2-swine HA and human NA and H3N2-human HA, human NA. SwIAV possessing either Classical H1 HA or human-like H3 HA with most of the human A(H1N1)pdm09 virus derived internal genes have cocirculated in Japanese pig populations.

Vietnam (Taki Saito):

In Vietnam, 83 SwIAV were isolated in 2018 from 1680 nasal swabs from 5 provinces belonging to 31 farms. The subtypes detected include predominantly A(H1N1)pdm09, H1N2 (two versions) and H3N2. There is continuing genetic reassortments which generate the novel combination of gene segments. Unlike human population, pre-2009 human-like H1 viruses still have circulated in Vietnamese pig population. Antigenic drifts of Vietnamese classical and pre-2009 humanlike H1 and human-like H3 SIV are evident.

Future SwIAV surveillance and research opportunities in Asia (Nguyen Tung):

The pig population of the Asia is about 60% of the world and there are five Asian countries in the top ten pork production of the world. Concerning the fact that a lot of breeding pigs are imported from Europe and the USA, Asia should be focused for conducting of surveillance and research on SwIAV. Looking at the history of influenza pandemic in human, all the SwIAV lineages established in the pig herds and almost all major swine influenza virus lineages from different continents are co-circulating in pigs in Asian countries. However, the circulation of SwIAVs in Asia is more complex than in Europe and USA. Besides, lack of information and limitation of systematic surveillance of SwIAVs in Asia results in the inadequate understanding of SwIAVs in Asia and that could be seen from SwIAVs data in Vietnam. Continuing the SwIAV surveillance and research in Asia will help to detect new viruses, keep monitoring the virus evolution, understand the impact of zoonotic infection of SwIAVs and it may also help to transfer techniques and strengthen capacity of Asian laboratory in diagnosis and surveillance of animal diseases. For the future of SwIAV surveillance and research in Asia, the region needs to maintain the current cooperation, extend the new collaborative project and especially that should be well coordinated with other plans.

Surveillance in Europe (Gaëlle Simon, Anses) :

Information on SwIAVs in Europe was collected thanks to voluntary contributions of former partners from the last European Surveillance Network for Influenza in Pigs (ESNIP) program which ended in 2013. Surveillance data obtained during the last five years (2014-2018) were kindly provided by ANSES (France), APHA (United Kingdom), DTU (Denmark), IZSLER (Italy), NVRI (Poland/Slovakia) and University of Ghent (Belgium/Netherlands). Three other governmental laboratories, which were not ESNIP3 partners, also contributed to the current overview, i.e., IZSVE (Italy), UAB (Spain) and SVA (Sweden). IDT Biologika, a German medical company that was an ESNIP3 partner, implemented diagnosis and surveillance activities in 18 European countries from 2015 to 2017 in collaboration with FLI (Germany) and was happy to share the data they accumulated too. Additionally, data from Norway and Greece were retrieved from scientific publications.

Since 2014, several labs developed molecular tools for the rapid identification of HA and NA gene lineages, based on previous knowledge provided by ESNIP3 about European SwIAVs. Also, new generation sequencing pipelines were implemented for whole genome sequencing and genotype characterizations.

Thus, the main information about SwIAV in Europe now is:

- Enzootic viruses from four genetic lineages are still co-circulating across Europe, i.e., H1avN1, H3N2, H1huN2, H1N1pdm
- H1avN1 is still by far the most important lineage
- There are significant regional variations, with novel enzootic viruses and/or disappearance of previous enzootic viruses in some countries
- A swine-divergent genogroup of H1N1pdm (versus seasonal-like H1N1pdm) has emerged
- Viral diversification continues to increase in European pigs, either by antigenic shifts (reassortments) or antigenic drifts (immune escape, host adaptation)
- There is a dramatically increasing frequency of (multi) reassortant viruses containing ≥1 gene(s) from H1N1pdm, including genotypes of public-health interest (ex: reassortant IGC with Mpdm)
- There are frequent introductions of HA or NA genes from seasonal human IAVs (H1N1pdm, H3N2)

USA Surveillance (Sabrina Swenson):

USDA surveillance program for influenza A virus in swine was presented. It included three data streams: case-compatible swine accessions submitted to the NAHLN system, swine populations epidemiologically linked to a human case of influenza A virus and swine exhibiting influenza-like illness (ILI) at events such as auctions, markets, fairs, or other swine exhibition events. The surveillance plan was drafted in 2008 and later modified in 2009 to be specific for pdmH1N1 and then broadened in 2010 to account for more subtypes. From 2012 the lab improvised the laboratory algorithm testing methods and in 2014 the Ct cut off values for virus isolation was implemented. In 2015 external review of the surveillance program was conducted and in 2016 a stakeholder meeting was held, and the algorithm changed for efficiency. The changes included matrix PCR cost no longer borne by the program, lower CT cut off values for further covered testing and selecting only one sample per herd for subtyping. In 2018 the nasal wipes were added as an approved sample type.

The NVSL holds a repository of around 7739 viruses representing around 36 states. Full genome sequencing is done on select isolates of interest at NVSL. The lab provides confirmative testing and public health investigations. In fiscal year 2017 and 2018, a total of 20250 and 28518 samples respectively were tested in the USDA system. The subtypes isolated were H1N1, H1N2, H3N1 and H3N2. 73.7% of the H3s in fiscal year 2018 were the Human-like H3s. In June -August 2018, country fair associated zoonotic transmissions were detected in country fairs of California, Indiana, Ohio and Michigan. 14 human infections were reported with detection of one H3N2v and 13 H1N2v and all linked to swine exposure at these fairs. Human viruses were genetically related to the swine viruses detected from the same fairs.

USA herd-based research (Marie Culhane):

A team of researchers at the University of Minnesota Swine Disease Eradication Center, led by Dr. Montserrat Torremorell, is dedicated to studying various vaccine combinations for IAV of swine. Influenza infection is one of the top disease problems throughout all different types of US swine farms. Vaccination is mainly taken on breeding and nursery sites. Commercial and autogenous killed vaccines are largely used in breeding female pigs and almost all pigs from nursery, finisher and wean-to-finish sites received autogenous vaccines. More than 60 percent of large breeding herds (herd size ≥ 500) in US pig farms used influenza vaccines before or at entry into the breeding herd. Both prefarrow and mass vaccination protocols reduced the odds of detecting piglets positive for influenza at weaning. Both Commercial and autogenous vaccines reduced the odds of piglets testing positive for influenza at weaning.

A pilot study was conducted to evaluate under experimental conditions, the efficacy of influenza A virus (IAV) vaccines using different prime-boost vaccination protocols in challenged pigs. The vaccine efficacy was measured by assessing serological responses pre-challenge, virus shedding, clinical signs and lung pathology post-challenge. The results showed the advantage of vaccinating pigs for IAV-S with a heterologous prime boost protocol for both killed and live attenuated influenza vaccine.

Influenza A Virus Diversity in US Swine (Marie Culhane)

The University of Minnesota (UMN) Veterinary Diagnostic Laboratory (VDL) is part of the NAHLN laboratory system that participates in the USDA SwIAV surveillance described by Dr Swenson above. In addition to receiving SwIAV samples from the USA, the UMN VDL also received samples from Mexico and Canada. In 2018, the UMN VDL sequenced 257 H1 positive virus samples. The 1A.3.3.3-gamma H1 clade was the most common H1 obtained from pigs in the US, followed by clade 1B.2.1-delta 2, 1A.3.3.2-H1N1pdm09, 1A.1.1-alpha, 1B.2.2.1-delta 1a, 1A.2-beta, 1B.2.2.2-delta 1b. For H3s,

135 H3 positive virus samples were sequenced. The 3.2010.1-human-like H3 far outnumbered the 3.1990.4-Cluster IV H3s detected. Of note, the current human seasonal H3s from 2017-2018 were detected in pigs in the USA in the 1st and 2nd quarters of 2018. A live attenuated influenza A virus (LAIV) swine influenza vaccine was introduced to the US market in November of 2017 and there have been detections of LAIV genes in the surveillance system.

There are new sampling methods for SwIAV that may be useful for swine throughout the globe. A free access publication regarding the sampling methods is published as "Comparison of individual, group and environmental sampling strategies to conduct influenza surveillance in pigs" in BMC Veterinary Research. The article is open access at the following link: https://rdcu.be/bmT4O

USA research (Amy Vincent):

The genetic diversity of H1 and H3 SwIAV HA genes reported from the USDA surveillance system between Jan 2017 and Dec 2018 was presented. Phylogenetic analyses of the HA gene showed gamma (1A.3.3.3) at 33%, H3.10.1 at 18%, Delta-2 (1B.2.1) at 11%, and Delta-1a (1B.2.2.1) at 11% as the most frequently detected HA clades in the United States during this period. However, regional differences were apparent for predominant HA/NA gene pairings. These data may influence vaccine strain selections by farm, production system, or region. Whole genome patterns were also presented, with frequent reassortment between endemic swine strains and H1N1pdm09, and these reassorted internal gene constellations found in different combinations with HA/NA pairings.

Research findings on N2 mapping by NI and recent antigenic drift in H3N2 were also presented. An update on the ongoing H3 global clade classification project was given and current status of H3 designations from different regions was shared with a request to submit new sequences to GenBank or send it to Tavis Anderson (Tavis.Anderson@ars.usda.gov) for inclusion in the nomenclature system. Vaccine platform study results with antigenically mismatched H3 viruses comparing the efficacy of HA RNA vaccine (alphavirus vectored), whole inactivated virus (adjuvanted) and live attenuated influenza virus were presented (Eugenio Abente *et al*).

Canada (Yohannes Berhane):

The 2017-18 Canadian influenza A swine surveillance was conducted in collaboration with Canadian provincial veterinary diagnostic laboratories and mainly focused on the 3 main provinces (Ontario, Quebec and Manitoba) which are responsible for almost 82% of pork production. For the current surveillance period, 182 H1N1/N2 and 112 H3N2 were analysed. The H1N1/N2 viruses detected in 2017-18 belonged to the 1A.2 (β), 1A.1 (α), H1pdm (1A.3.3.2) and δ1b (1B.2.2.2) clusters. The H3N2 viruses mainly belonged to IV and IVB clusters.

The Canadian swine H1pdm (1A.3.3.2) cluster viruses seem to be genetically diverging from the human seasonal strains, however in hemagglutination inhibition (HI) assay they still react to higher titers against reference Ca/2009 antiserum. There are two sub clusters of 1A. 2/beta viruses in Eastern Canada and they are distantly related to the USA 1A.2 viruses and they don't seem to react in HI with the reference antisera that were produced in 2013 by ARS. There are 4 subclades with in the 1A.1 (alpha) cluster. Two of these sub clusters were mainly found in Eastern Canada, the other 2 sub clusters in western Canada and in some parts of USA. We have also detected a 1B.2.2 (1b delta) cluster virus in Ontario. To our knowledge this is the first time we are detecting delta 1b viruses in Ontario since 2003-04.

The main H3 subtype viruses currently circulating in Canadian pigs belong to cluster IVB. There is a clear division between the East and West Canadian cluster IVB strains. Both East and West strains

contain multiple antigenic motifs. Within Canadian cluster IV viruses, there are 2 distinct sub clusters – 1st one in Ontario and 2nd one in Manitoba. Both cluster IV viruses are highly variable in the antigenic motif and different from the US cluster IV viruses.

Brazil update (Janice Zanella):

In Brazil since 2009 frequent outbreaks of acute respiratory disease in pigs caused by influenza A virus was reported. H1N1pdm, human seasonal origin H1N2 and H3N2 influenza viruses are the subtypes widespread in pig herds in Brazil, where they continue to evolve. Currently, influenza seroprevalence in pig herds is estimated to be 78.1%. Partial (gene segments H1s, H1pdm, H3, N1 and N2) and complete gene sequences were generated for 79 SwIAV. Out of this, 45 were H1N1pdm and multiple separate human-to-swine transmissions of H1N1pdm occurred since 2009. Other subtypes included H1N2 (18) and H1N1 (3) transmissions of H1 human seasonal viruses to pigs occurred in the early 2002 and 2006 respectively. Regarding H3N2, 13 viruses have been sequenced and studies showed the introduction of human H3N2 into pigs. All H1N2 and H3N2 viruses sequenced so far have the internal gene segments derived from H1N1pdm. These H3N2 and H1N2 SwIAV clades appear to be specific to Brazil. A recent study on 11 nurseries, with a population of 60 thousand piglets showed a prevalence of 68% positive pigs by ELISA. In all 11 nurseries, the circulation of SwIAV was identified either by detection of viral RNA by RT-qPCR in samples of nasal secretion (285/423, 67.4%) (Cut off ranging from 13.69 to 38, 87 RNA copies / uL), and also for the presence of antibodies produced against SwIAV by ELISA and HI. Among the properties, the percentage of seropositive piglets for SwIAV ranged from 27.5 to 97.5%. The HI test revealed a higher prevalence of antibodies in piglets produced against the H3N2 virus (59/283; 38.0%), followed by pH1N1 (37/283; 23.8%) and H1N2 (05/283; 23%). Of the 33 viruses sampled by nasal swabs subtyped by RT-qPCR, 18 (54.5%) were positive for the H3N2 virus (from six nurseries), nine (27.0%) were positive for pH1N1 (from two nurseries) and six (18.0%) samples from three nurseries could not be subtyped probably due to the low viral load. The data further revealed that 10.3% of the animals reacted to at least two antigens, so different viral strains of influenza are circulating in the swine population causing mixed infections and contributing to viral genetic reassortments. Antigenic cartography training, production of hyperimmune serum in piglets against Brazilian SwIAV, propagation of imported reference viruses from USDA are activities that are being carried out.

Argentina and South America (Ariel Pereda):

In Argentina research in influenza on INTA includes wild birds, equines and pigs. The swine production in Argentina, as in all Latin America differs per region of the country. Argentina has approximately 1.1 million sows, 40% of the farms are commercial and 60% are in Buenos Aires, Cordoba and Santa Fé Provinces. Little research or investigation was done on wild boars so far. Swine influenza surveillance is voluntary and on average 300 samples processed per year with detection of 40 -50 positive cases. INTA has characterized 59 viruses, and the pandemic H1N1pdm2009 was the first one that caused influenza endemic in Argentina. Today, most of the identified influenza viruses in swine have the H1N1pdm2009 internal genes. A longitudinal study was performed which included 3 farms monitored for one year. Results showed reinfection of the herds. Another study on swine from backyard farms showed no viral detection, but by serology the H1N1pdm2009 was prevalent. Antigenic characterization was done at the University of Georgia with reference antigen panel. Argentina imported a single supply of 1,500 breeding stock from Brazil but the Introduction of human viruses in the country are not related to Brazilian or Chilean sources. There are 2 commercial vaccines in Argentina, both containing non-circulating antigens in Argentina. There is autogenous vaccine in use and the sequencing and characterization is done in the lab in INTA.

Chile is the 6th pig meat exporter. There is a commercial vaccine registered in Chile (Zoetis), however it does not perform well. There is also a company producing autogenous vaccine (Newpoint) but it coincided with the outbreak of PRRS and Chile is not using it anymore. Surveillance and evolution of bird and swine influenza is funded by Mount Sinai. From December 2013 to January 2015, 39 farms (93%) were sampled in 5 sites and isolated more than 120 viruses and the characterization showed 2 large clusters. There is no delta flu in Chile and only 1 type of N2. Results showed that were 7 different introductions of pandemic N1. All internal segments are from the H1N1pdm2009. M gene is original pandemic segment. The NS showed distinct introductions. Cartography studies showed two viruses, A and B, very distinct from the pandemic and belong to old viruses. Using a panel of season human virus - H1N1 and H3N2, the serological studies compared the immune responses and analysed with the birth year of the people. The study included Chilean human sera from 1915. The results showed that in 90s there was reassortment and currently there are 4 subtypes, mainly after the introduction of the H1N1pdm2009.

Guatemala started the first study in influenza in wild birds in 2005 and in 2010 started to do serology and then virology analysis to detect influenza in pigs. From 2010 – 2011, 3 H1N1pdm2009 and then human virus distinct from the vaccine virus were detected. From 2016 – 2018, the direct sequencing of the positive sample started and now only H1N1pdm2009 detected. Ongoing work includes the sequencing of 141 flu samples. Future works associated to CDC includes the national study to establish which type of influenza virus is circulating and to study the interaction with public health. Also, the Guatemala group wants to work with Nicaragua and Honduras, consolidate a surveillance system of pig herds and convince producers that it is important.

In Colombia there are no commercial vaccines for swine influenza. There are studies on equine influenza. In swine flu there is basic serology in specific studies. The research group has Government support and organization of swine producers are studying PCV2 and influenza. Outbreak in 2007 in Antioquia characterized 3 isolates (cH1N1). Isolation of flu virus in samples from slaughterhouses with higher density of pigs in 2018 are similar in the same regions as in 2007, but the virus detected was the H1N1pdm2009. Partial sequencing demonstrated similarity to pandemic samples including Brazilian flu viruses. A study from ICA analysed and sampled 3 – 12 weeks pig nasal swabs belonging to 186 farms by RT-PCR and the results showed 30.6% positive for influenza A.

Nigeria and other African countries update (Clement Meseko):

Though Africa has a smaller number of pigs compared to America, Europe and Asia, nevertheless sizeable stocks are raised in countries like Nigeria, Ghana, Uganda and Kenya. It is also important to note that less than optimal biosecurity and weaker veterinary infrastructure in Africa make many cohorts of piggery in these countries and more likely source of pathogen emergence and circulation. Swine influenza surveillance is yet to receive deserved attention, therefore surveillance efforts by few scientists with little or no funding is limited but risk based.

Swine influenza surveillance in Nigeria for instance is focussed on slaughter slabs, live pig markets, high density pig farms and mixed farms. Yearly but seasonal surveillance in slaughter slabs revealed high prevalence of H1N1pdm 09 in pigs since it was first introduced from human during the 2009 pandemic. Both genetic materials and antibody are regularly detected. There is also evidence of interspecies transmission of avian influenza H5N1 from poultry to pigs (Nigeria and Egypt) and observation of influenza virus transmission from pigs to poultry in mixed species farms. For further information refer to https://www.nature.com/articles/s41598-018-24371-6.

It is important to note that Ghana reported fatal H1N1pdm09 among boarding school students (4 deaths and 44 hospitalised in December 2017), evidence of H1N1pdm09 has also been reported in

pigs in that country and hence the risk of future human infection from swine should be critically evaluated in Africa.

The potential for interspecies transmission and genetic reassortment of influenza in pigs (the traditional mixing vessel) require continuous surveillance and monitoring especially in Africa where co-mingling occurs.

CDC update (Todd Davis):

Influenza A(H1N2) variant virus summary (January 2018 - Feb 2019)

Human infections
13 cases of A(H1N2)v virus infection were identified in the US. Exposure to swine in an agricultural fair setting during the week preceding illness onset was reported for 11 of 13 cases. All but one case were <18 years of age. A(H1N2) infected swine were identified at each fair where cases were detected, and the viruses were determined to be closely related to the variant viruses. One case did not attend a fair and reported no swine exposure, suggesting limited person-to-person transmission. All patients fully recovered from illness. Since reporting of novel influenza A viruses became nationally notifiable in 2005, 47 human infections with A(H1)v have been reported in the US.

Genetic characterization
The A(H1N2)v viruses detected in California, Michigan and Ohio had HA gene segments from the delta 2 sublineage (clade 1B.2) of the swine H1 HA lineage. The HA and NA gene segments of these virus were closely related to 2017/2018 A(H1N2) influenza viruses circulating in the U.S. swine population and have been sporadically detected in previous A(H1N2)v zoonotic infections. All of the viruses possessed an NA gene derived from the 1998 lineage of swine influenza viruses.

Antigenic characterization
Ferret antiserum raised to the wild type strain of a WHO recommended delta 2 lineage CVV, A/Ohio/35/2017, inhibited the A(H1N2)v viruses, but with titers that were reduced 4 to 8-fold compared to the homologous virus titer. In contrast, ferret antisera raised to either the delta 2 lineage wild type A/Michigan/383/2018 or the IDCDC-RG58A CVV viruses inhibited the 2018 A(H1N2)v viruses with heterologous titers that were within 2-fold of homologous virus titers. HI reactivity of pooled, child and adult human post-vaccination sera from persons vaccinated with the 2017-2018 vaccine was below the limit of detection for all A(H1N2)v viruses tested.

Candidate vaccine viruses
https://www.who.int/influenza/vaccines/virus/candidates_reagents/variant_a_h1n1/en/

IDCDC-RG48A, A/Ohio/09/2015-like	Classical gamma lineage
CNIC-42443, A/Hunan/42443/2015	Eurasian avian-like
IDCDC-RG, A/Iowa/32/2016-like	Delta 1 lineage (pending)
NIBRG, A/Netherlands/3315/2016	Eurasian avian-like (pending)
NIBRG, A/Ohio/35/2017-like	Delta 2 lineage (pending)
IDCDC-RG, A/Ohio/24/2017-like	Alpha lineage (pending)
IDCDC-RG58A, A/Michigan/383/2018-like	Delta 2 lineage

Influenza A(H3N2) variant virus summary (January 2018 - Feb 2019)

Human infections
One A(H3N2)v virus infection was reported to the Centers for Disease Control and Prevention from Indiana. The child reported exposure to swine at an agricultural fair where swine were found to be

infected with closely related viruses. The person fully recovered from illness. Since reporting of novel influenza A viruses became nationally notifiable in 2005, 437 human infections with A(H3N2)v viruses have been reported in the USA.

A single case of a human infected with an A(H3N2)v influenza virus was detected in Australia during routine screening of influenza positive samples. The case was a child with likely exposure at a livestock exhibition. This is the first documented case of a variant influenza virus infection in Australia.

Genetic characterization
The A(H3N2)v virus from the USA, A/Indiana/27/2018, had an HA gene that was classified as the human-like or 2010.1 lineage. The virus was closely related to A(H3N2)v viruses detected in humans in several states during 2017 and viruses known to circulate in the USA swine population. Phylogenetic analyses of the HA and NA genes of the variant virus identified in Australia, A/South Australia/85/2018, showed that it grouped with A(H3N2) swine influenza viruses detected in Australia and Asia, which were likely derived from human, seasonal A(H3N2) viruses that circulated in the late 1990s. The six internal genes of A/South Australia/85/2018 were derived from A(H1N1)pdm09 viruses.

Antigenic characterization
Ferret antiserum raised to the closest wild type strain of the recommended CVV (A/Ohio/13/2017) reacted with A/Indiana/27/2018 with a heterologous titer within 2-fold of the homologous virus titer. Completion of the A/Ohio/13/2017-like CVV is pending. In HI tests performed in the presence of oseltamivir, pooled, adult post-vaccination antisera reacted with A/Indiana/27/2018 at titers that were reduced 4-fold to those against the homologous reference virus, A/Michigan/15/2014, representing the A(H3N2) component of the 2017-18 seasonal influenza vaccines. Pooled post-vaccination sera collected from young children also had reduced titers (32-fold reduced) compared to the A/Michigan/15/2014 homologous virus titer.

Candidate vaccine viruses
https://www.who.int/influenza/vaccines/virus/candidates_reagents/variant_a_h3n2/en/

NYMC X-203, A/Minnesota/11/2010	North American; cluster IV-A
NYMC X-213, A/Indiana/10/2011	North American; cluster IV-A
IDCDC-RG55C, A/Ohio/28/2016-like	2010.1 human-like
IDCDC-RG, A/Ohio/13/2017-like	2010.1 human-like (Pending)

Human population immunity against influenza viruses of swine (Kristien Van Reeth):

The 2009 pandemic H1N1 virus contained an HA that can be traced back to the human pandemic in 1918. Only people born before the 1950s still had cross-reactive antibodies against this virus, so a pandemic was possible. It is therefore important to assess the antibody titers against swine viruses in humans, to be able to anticipate on potentially pandemic swine viruses.

549 human serum samples of immunocompetent patients aged 0-97 years old were collected at Ghent University Hospital between August 2017 and January 2018. The samples contained 5-6 sera for each birth year and equal numbers of men and women. The human sera were tested for antibodies against 11 different H1 viruses. Individual sera were analysed for hemagglutination inhibition or HI antibodies and pooled serum samples per year of birth were tested for virus neutralising or VN antibodies.

Results indicated the seroprevalence for H1 swine influenza viruses is related to people's year of birth and to the origin of the swine virus. Low seroprevalences were detected for the European avian-like and for the North American human-like delta1b swine viruses. The avian-like viruses never circulated in humans before. The human-origin delta1b viruses underwent a more diverse evolution in swine as compared to other human-origin H1 swine viruses. These two virus clades thus seem to pose a potential pandemic risk for the human population.

Swine influenza risk assessment (Amy Vincent and Nicola Lewis):

An update on a swine risk assessment pipeline was provided. The project involves assessing antigenic relationships between swine and human seasonal viruses to predict potential for human risk. Hemagglutination inhibition assays (HI) and antigenic cartography allows for the quantitative analyses of antigenic relationships among strains or anti-sera. Antigenic cartography and distance data can be informative for vaccine strain selection, emerging virus analyses, monitoring of antigenic drift and pre-pandemic preparedness and risk assessment. Quantitative and harmonised virus characterisation and risk assessment generates timely and high-resolution data for both public and animal health. Currently circulating swine viruses shown to have significant antigenic distance from human vaccine strains will move along the pipeline to be tested against human sera from post-vaccination or post-exposure cohorts. Those swine strains also showing minimal cross-reactivity with human anti-sera panels can be prioritized for advanced risk assessment parameters, such as transmission studies, receptor binding, anti-viral susceptibility, etc.

Election of new co-chair:

Dr Gaelle Simon (Anses, France) was elected as the new co-chair of the Swine influenza group. Dr Taki Saito (NIAH, Japan) continues to be the Co-Chair of the group.

Setting new tasks and action points to follow up (Group discussion):

1. Surveillance in China – also invite Dr Maria Chen from Hong Kong University to present Chinese surveillance data (next meeting)
2. The SwIAV surveillance algorithm document does not need updating.
3. The OFFLU swine influenza group activities poster will be updated by Janice (Dec 2019)
4. South America regional meetings will continue to be led by Ariel and Janice.
5. The potential for African regional meetings will be explored by Clement and Yohannes to include surveillance information from Uganda, Ghana, and perhaps South Africa.
6. Regularity of OFFLU swine influenza group meetings will be approximately every 18 months. The next meeting can be tried around September 2020 subject to funding availabilities. There will be an International Pig Veterinary Society (IPVS) meeting in 2020 at Brazil. It may be a place to have an OFFLU Swine meeting and possibly an exhibitor table. Janice will follow up.
7. Possible manuscripts to be written by the group:
    a. SwIAV surveillance summaries by region: South America, Asia, Africa, Europe (March 2020).
    b. Swine-people interface with CDC – important to synthesize all information in a review: before and after, as the last review was published in 2011 (March 2020).