



OFFLU STEERING AND EXECUTIVE COMMITTEE MEETING

6 and 7 September 2016

OIE Headquarters, Paris

Participants: Peter Daniels, Ian Brown, Billy Karesh, David Swayne, Giovanni Cattoli, Nicola Lewis, Jiming Chen, Gwenaëlle Dauphin, Lidewij Wiersma, Tianna Brand, Gounalan Pavade



Day 1:

The OIE Director General, Dr Monique Eloit provided opening comments to the Committees, thanking them for their engagement in the network especially in consideration of their busy professions. The importance of Member Countries actively contributing to the network through sharing of information, data and specimens was supported. She noted that the Committees should identify activity areas where the OIE and FAO could be supportive. This would require specific recommendations to work plans with specific objectives and budgets. This information could be further discussed at other FAO and OIE meetings such as the GF-TADs Steering Committee in early November which always has an avian influenza component or during the next Tripartite Executive

Steering Committee in January or February 2017. She concluded by noting that both organizations rely on the scientific excellence of their experts and that the OFFLU network provides a good example for other disease networks. Dr Matthew Stone, Deputy Director General, Science and Standards who has recently started at the OIE taking over from Dr Brian Evans was introduced to the Committee members.

Dr Gwenaelle Dauphin, the FAO focal point officer for OFFLU also thanked the Committee members for their valuable time in the direction and execution of various technical activities, although the OFFLU work is mostly delivered based on voluntary basis. OFFLU Committees should meet more frequently, and FAO too can give funding support. She indicated that OFFLU should focus on key technical activities that will be useful for the global scientific community rather than duplicating the work done by the parent organisations. There is new blood within the OFFLU committees and core members, in particular Nicola Lewis (Executive Committee), Jiming Chen (Executive Committee) and Lidewij Wiersma (OFFLU scientist).

Adoption of the agenda:

Dr Peter Daniels, Chair of the Steering Committee (SC) and Dr David Swayne, Chair of the Executive Committee (EC) opened the meeting and asked for agenda adoption. Dr Dauphin requested that OFFLU-WHO interactions be added and if the WHO representative Terry Besselaar could participate by teleconference at some point over the next two days. The items to be addressed under this addition included WHO's research agenda for influenza, the pandemic influenza preparedness (PIP) Framework, Tool for Influenza Pandemic Risk Assessment (TIFRA) and WHO's approach to the Nagoya Protocol requirements.

Review of all action items from the previous Steering and Executive Committee meeting:

It was agreed by all participants that the action items from the last EC/SC meeting 27-28 October 2014 be addressed according to the agenda items.

WHO Vaccine Composition Meeting – update, efforts on increasing contribution, transition to next expert and antigenic data contribution update

It was noted with that the OFFLU contributions have been coordinated by Weybridge, Padova and Geelong in turn, supported by the OFFLU scientist and OFFLU Secretariat. The significant contributions by these Reference Laboratories and FAO and OIE was acknowledged and appreciated. A letter of invitation to take over the coordinating role has been sent to Dr Mia Kim at the National Veterinary Services Laboratories, Ames, Iowa, USA. It was indicated that the new OFFLU Scientist, Dr Lidewij Wiersma, will continue to support the process. The outstanding work over many years by the previous OFFLU Scientist, Dr Filip Claes, was also acknowledged with appreciation.

The meeting recognized that OFFLU's contributions in the WHO VCM over the past two years have decreased and particularly the antigenic data from the recent avian influenza outbreaks. The Committee discussed around strategies to increase contributions of genetic and antigenic data from both nations that have experienced recent outbreaks and countries where zoonotic AI is well

established. From the last WHO VCM in February 2016, the FAO focal point compiled a list of countries that have reported outbreaks in 2015 but did not provide data, along with possible causes for lack of sharing (delays in clearance, unwillingness to share, lack of awareness) and incentives for countries to participate. A letter of acknowledgement was sent to Viet Nam after the February VCM 2016 meeting and following the selection of a poultry strain from Viet Nam as a Candidate Vaccine Virus.

It was noted that timeliness in sharing antigenic or genetic data is very important, since the purpose of the WHO VCM is to monitor recent events, for “real time” pandemic preparedness. Analyses of viruses isolated 1 to 2 years previously are not in scope. Furthermore it was noted that, in general, public health institutions in endemically infected countries were now sharing information and biological material in a proactive and transparent manner. The international engagement by animal health institutions in several countries was very minimal in comparison, and this reflects badly on the animal health sector. Effectively inducing cultural change is needed.

The meeting discussed what incentives might be useful, but this approach may have minimum impact. Even institutions receiving international research and surveillance funding are not responding with the required level of transparency. In some cases the opportunity for scientific and technical capacity building may be valued, but it is not clear whether the animal health sector may have opportunity to access funding support from nationally administered PIP Framework processes. Certainly OFFLU can continue to give high profile acknowledgement to countries that are actively participating, as it has done previously. It was noted that understanding and incentivisation has to occur at the political level as well as at the institute and Delegate levels.

The need to improve the antigenic HI testing was raised. Frank Wong has been nominated a few months ago for the coordination of the antigenic testing for the VCM. The committees discussed the need for detailed information from St. Jude on the panels of sera and antigens (reagents) to test for specific clades. There are a total of five OIE and FAO Reference Centres involved in the antigenic analysis and for the analyses to be useful these laboratories must standardize or harmonize their protocols and the reagents used. The agreed reagents must also be received in adequate time and volumes for the analyses to be completed, reported and discussed before the next VCM meeting. Some OFFLU labs have the capacities to produce ferret antisera but funding would be required for such activity; such funding should be raised from the Public Health sector.

It was noted that some OFFLU laboratories that received reagents for VCM purposes had received PIP MTAs from WHO for materials received in previous years. It was agreed to include this in the discussions with the WHO focal point during that agenda item.

Actions:

- For strategies to increase participation in sending the samples for antigenic testing, it was decided that OFFLU sends a letter to colleagues at national laboratories (the focal points at these labs need to be identified) to share the genetic data and the samples from recent isolates to the relevant Reference Centres for further analysis. The letter would explain the importance of sharing the data for the WHO VCM process. The letters would be sent out to

labs both after an immediate notification through WAHIS and also for endemic country labs reported by six monthly reports. (Chairs, Secretariat and FAO/OIE Focal Points)

- Given that all of the HPAI Reference Centres are part of the OFFLU network but some are not contributing, it was asked that OIE and FAO remind the Delegates and the designated experts of their mandate as Centres and obligations for sharing information as part of the OFFLU objectives. Specific approaches and strategies may be considered useful for countries that have patterns of being unresponsive to approaches through existing normal channels. (FAO/OIE Focal Points to progress, advise Chairs if their input is required.) .
- Another proposal to engage colleagues in countries in Southeast and East Asia is to invite them to a VCM engagement meeting. This could be done during the Avian Influenza Technical Activity (formerly the Diagnostic Technical Activity) meeting in Rome; the timing – possibly in March 2017 - will be determined through doodle managed by the OFFLU secretariat. (Leader AI TA, Chair EC, Secretariat)
- To address the issues of reception of antigenic reagents and harmonization of reagents and protocols, a teleconference will be arranged by the Secretariat by a sub-group under the VCM Human-Animal Interface activity to engage St. Jude and the five labs – Australia, UK, Italy, Germany, USA and India. Funding needs should be identified. (Leader AI TA, Secretariat)
- In addition, another teleconference will be arranged by the Secretariat amongst the OFFLU contributors to discuss the analysis, data curation and quality of report before submission to the WHO pre VCM teleconference. (Secretariat, Frank Wong)
- The OFFLU Secretariat will continue to organize letters giving high profile acknowledgement to countries that have actively participated in each VCM round. (Secretariat, Chairs)

Launch of Animal Vaccine Composition Meeting – Detailed concept note, committee members, frequency, goals, procedures, funding and ways to move forward

The Committees agreed to change the name of this Technical Activity (TA) to Influenza Virus Characterization; however, it will now be placed under the Avian Influenza TA.

There was discussion regarding whether to invite the swine influenza and equine influenza TAs to be involved. It was noted that the equine group already had an established process; therefore this group does not need the support from OFFLU but they would certainly accept to operate under OFFLU's banner. The swine influenza TA has been doing work on the methods to analyse and present antigenic data relating to influenza isolates from pigs. There is cross membership between this group and the newly recommended AI group and the scope for cross fertilization was noted.

Actions:

- A detailed concept note including terms of reference to be drafted, identifying the scope of virus diversity to be studied;, such as whether to address both H5 and H9 subtypes. (David Swayne, Ian Brown, Gwen Dauphin, Nicola Lewis)
- Projects to address scientific issues of how to measure antigenic relationships, comparing data produced using chicken or ferret sera and how to raise such antisera in a standardized manner that allowed adequate differentiation among isolates in

the chose system of analysis. (Brown and Swayne to coordinate, maybe with sub-groups and to link with the ferret antisera production)

- The Swine influenza virus TA to be consulted and the opportunities for synergies identified (Brown, Lewis)
- An influenza viral characterization meeting involving around 8 – 10 people to be planned in March/April 2017 (David Swayne, Ian Brown, Gwen Dauphin, Nicola Lewis, David Suarez, Isabella Monne)
- FAO focal point to seek funding to cover this meeting.

OFFLU Proficiency Testing (PT):

The Committees decided that the proficiency testing should be restarted amongst the 12 FAO/OIE Reference Centres only for Avian Influenza before next summer, to give confidence that the designated Reference Centres will give consistent results and have tests which will detect any avian influenza virus that may be encountered globally.

Reference Centres in turn may provide PT for national or other client labs in their regions. There should be consultation among the Reference Centres to agree the objectives of each PT round, to decide which institute will host each round, and to ensure sharing of isolates that may form the basis for the production of panels.

The system of analysis of results is to be confirmed, noting that the standard is ISO17043. (Centres that are accredited to this standard may be approached to assist in the analysis for each round.)

The proficiency testing will be conducted from within the Avian Influenza TA.

Actions:

- A letter is to be sent from OFFLU to FAO and OIE Reference Centres to inform them that the proficiency testing will recommence, noting that the proposal is for each Centre to take it in turns on a rotational basis, annually, to deliver the PT round, including panel and analysis. (Ian Brown to oversee and coordinate the process, Secretariat to assist)
- A PT round to be organized as soon as possible after the consultation among Reference Centres (Ian Brown, Secretariat)

Update of Influenza A Cleavage Site Document:

The OFFLU Scientist has been assigned to maintain an updated cleavage site document based on latest analysis and publications. Cleavage site updates, for inclusion on the OFFLU website, are important because this document is in turn is linked to the test method published in the OIE Manual.

Actions:

- Once updated and before publishing on the website the document needs to be shared with OIE and FAO Reference Centres for comments and validation. (Lidewij Wiersma)

OFFLU Wildlife TA Update (Billy Karesh):

The Wildlife TA operates by having regular TCs every 2 months, members participate according to availability.

An update was provided on draft concept notes that had been circulated that outlined the “Global Surveillance for Influenza A Viral Diversity in Wild Birds”. The Committees are in favor of the paper and encouraged the group to find a means of implementing this project. (It was noted that the proposal called for the sampling of 80,000 to 100,000 birds per year, with testing, sequencing and archiving of viruses within 6 months of collection. Hence substantial funding would be required).

There was discussion regarding what an analysis of the last 10 years data from wild bird sampling globally (numbers sampled vs strains detected) would indicate regarding the numbers that would have to be sampled to result in detections at certain defined levels and to give an indication of the complexity of the avian influenza virus population at any sampling site. This may be a matter on which the Epidemiology TA could advise. If considered a useful approach there would be required a major international collaboration to have as much data as possible from the many countries and groups conducting surveillance to be made available.

A potential project was also presented called the Global Virome Project that looks at the potential for characterization of all viruses. Conceptually the global surveillance concept note could fit into this project.

Actions:

- Follow up on the concept note on how to implement with other members of the group and possibly through the Global Virome Project. (Billy Karesh)
- Approach the Epidemiology TA regarding the options and possibilities for analysis of the 10 year history of wild bird samples. This may provide some rationale for selling the concept note to potential donors. (Billy Karesh, Gwen Dauphin)

Day 2:

Interaction with WHO (Terry Besselaar, Weigong Zhou, Sasha Kontic, Amélie Rioux, Gina Samaan)

The following points were discussed:

- WHO Research agenda (Weigong Zhou presented)

The original WHO research agenda was drafted in 2009. There are five streams to the agenda; however, stream 1 focusing on zoonotic influenza is of interest to the OFFLU network. David Swayne, Gwen Dauphin, Ian Brown, Les Sims, Richard Webby, Todd Davis, Ron Fouchier and Peter Daniels are currently participating in the working group from OFFLU Contributors to update stream 1; the update/review will be based on a published literature review. David Swayne intervened to ask whether other processes should be examined that are not in literature such as field studies. There was agreement that unpublished material and documents should be considered.

The Stream 1 technical working group will meet monthly through teleconference to finalize the agenda; there is a proposed face-to-face meeting in Geneva 6-8 December 2016 to recommend the new research agenda. In January 2017 it is expected that the research agenda will be posted on the WHO website for public comments.

PIP Framework

Sasha provided an update on the implementation of the PIP Framework, focusing on the 2016 PIP Framework Review, and the benefit sharing system under the Framework that is composed of the Partnership Contribution and the Standard Material Transfer Agreement (SMTA) 2. The PIP Framework was adopted in 2011 and is currently undergoing its first review. The eight person Review Group is tasked with (1) identifying key achievements, (2) determining whether the Framework has improved pandemic influenza preparedness and capacity to respond, and (3) identifying challenges and potential solutions. The Group has met six times, the final meeting taking place from 29 August to 2 September 2016. The final report will be transmitted to the Director-General by October 2016. The WHO Executive Board and World Health Assembly will consider it in January 2017 and May 2017, respectively.

Regarding whether there are any implications for the animal health sector the WHO advised that it could not say at this point, the report was still in preparation with a draft sent to WHO Member States just last week.

There was discussion on the SMTA 2 in relation to requests received by OFFLU labs (IZSve Padova, Italy and the South East Poultry Research Laboratory, USA) from WHO to sign the agreement because they received PIP Biological Materials (as recorded in the Influenza Virus Traceability Mechanism). In this regard, the labs wanted clarification on the “operational exemption”, which exempts an institution from having to sign an SMTA 2 its purpose for using the PIP Biological Materials to perform work on behalf of a GISRS (Global Influenza Surveillance and Response System) laboratory. Finally it was decided that the concerned labs are to send a letter to the PIP Secretariat explaining why the labs are using the PIP Biological Materials, in order to determine if the Operational Exemption applies.

Information was also provided on a study on the Nagoya Protocol currently being conducted by the WHO Secretariat. In January 2016, the WHO Executive Board requested that the WHO Secretariat analyse how the implementation of the Nagoya Protocol might affect the sharing of pathogens and the potential public health implications. The Secretariat will report back to the WHO Executive Board in this regard at the 140th session of the Board to be held in January 2017.

An update on the PIP Advisory Group (PIP AG)'s work on Genetic Sequence Data (GSD) under the PIP Framework was also provided and noted that the technical working group on data sharing submitted its report to the PIP AG in June 2016 and that the PIP AG will be providing further guidance to the WHO Director-General on this matter at its October 2016 meeting.

Actions:

- WHO focal point to forward to OFFLU the preliminary findings from the PIP review group (the draft as provided to WHO Member States last week) and the report from technical working group (Terry Besselaar, Gounalan Pavade)
- OFFLU labs receiving MTA requests from WHO should write to the PIP Secretariat explaining why each lab has received the reagents in question (and are doing this work) and to ask for the operational exemption. (Relevant OFFLU lab managers)

H5 virus evolution

Ruben Donis from CDC who was leading the group moved to BARDA and the group is not recently active.

Action:

- WHO focal point will communicate who will now lead the group and to include OFFLU in discussion on this subject. (Terry Besselaar, Gounalan Pavade)

WHO PCR Proficiency Panel

WHO indicated that this year that PCR working group meeting did not take place. The WHO PCR panels include both seasonal and zoonotic viruses, and the OFFLU committees indicated their interest in participating in these panels for zoonotic influenza. (WHO noted that the PCR Working Group, which had involved OFFLU members, had not met recently due to pressure of other matters)

Action:

- WHO focal point will consult internally to see if participation in WHO PCR Proficiency Panel is feasible and advise OFFLU Secretariat for communication to the Committees (Terry Besselaar, Gounalan Pavade)

WHO VCM update

WHO focal point informed that OFFLU contributions to the WHO VCM are practical and useful. The current agreement on the participation to VCM is valid until December 2018.

TIPRA (tool for influenza pandemic risk assessment)

Gina Samaan/WHO appreciated OFFLU experts' participation in TIPRA and requested OFFLU experts input into the H7N9 risk assessment by 9 September 2016.

OFFLU Swine Influenza Virus TA Update:

The SIV group has been able to meet face-to-face, thanks to funding support for the meeting from Centers of Excellence for Influenza Research and Surveillance (CEIRS), National Institutes of Health, USA. OFFLU thanks CEIRS for this important operational support.

The SIV group chair provided an update to the Committees about the progress of activities on contribution of sequences from global contributors. She has also noted that thanks to OFFLU there is

a lot of cross collaboration especially in peer reviewing the results. The group activities included global antigenic and genetic characterization of currently circulating swine influenza viruses (Lewis et al 2016 in eLife), standardised nomenclature for H1 viruses in pigs (Anderson et al, under review) and modelling on global swine trade for predicting viral spread globally (Nelson et al 2015 in Nature Communications).

Current activities included continued antigenic and genetic characterization of influenza viruses in pigs, with a system of analysis similar to the original “antigenic mapping” approach but refined to also be able to contribute to WHO VCM if required. Another important initiative is the development of a swine pandemic risk assessment (RA) pipeline in collaboration with CEIRS Centres including Johns Hopkins University and reaching out through the OFFLU network to other global participants. These analyses should contribute to VCM, control measures and surveillance. The RA needs the OFFLU network because it is global in nature, OFFLU can provide linkages to other countries such as China with opportunities for funding from CEIRS to include institutions and countries not currently participating in CEIRS projects.

The group also has outreach activities to stakeholders in public health and animal health such as computational workshops for analysis. She also provided an example of phylogenetic analysis and cartography that could be presented for the VCM. This model could be applicable for the avian viruses.

The FAO focal point noted that another type of platform for data sharing and analysis called Influenza Virus Monitoring (IVM) could also be used in the analysis, and noted that FLURISK is undergoing validation with 32 viral strains. There should be opportunities for cross fertilization. A document was produced by FAO, gathering information on the various risk assessment tools (including FLURISK, TIPRA, CDC IRAT and 2 other tools) and a teleconference held between the different groups to identify possible synergies and complementarities. FAO is planning to organize a meeting to validate FLURISK (Feb/March 2016). The OFFLU Applied Epi group will be requested to support this effort.

Also mentioned was the FAO surveillance project of pigs (and other livestock species) for Ebola. There will be collection of sera and swabs from pigs having nasal discharge from 15 countries of West Africa and Asia and these could be tested for Influenza A.

Actions:

- FAO to follow up with the country team in Indonesia on the OFFLU project to determine the status of IVM (Gwen Dauphin)
- FAO to follow up to see if funding could be set aside from the Ebola project specifically for the influenza A testing. (Gwen Dauphin)
- Billy Karesh to share the generic A primer standardized across 30 countries that could be used by OFFLU colleagues for the testing of these samples. (Billy Karesh)
- SIV risk assessment tool and FLURISK project to discuss about complementarity (Nicola Lewis and Gwen Dauphin to coordinate)
- The SIV antigenic analysis approach to be considered for applicability to the new AI antigenic characterization activity (Nicola Lewis, Ian Brown, David Swayne)

- Next OFFLU SIV group meeting to be organized in Rome/Paris in March 2017. CEIRS funds available for 12-13 participants. OIE and FAO to work out funding for remaining 8 participants (Gwen Dauphin, Tianna Brand, Gounalan Pavade, Nicola Lewis)

Applied Epidemiology TA:

The concept note for this TA approved by Steering and Executive Committee was further commented upon by the TA leader, seeking further clarification on the terms of reference and modus operandi. FAO indicated that it is happy to support the group.

Actions:

- The OFFLU Secretariat and Gwen to explain the OFFLU Modus Operandi through a teleconference (Gounalan Pavade, Gwen Dauphin)
- The members of the group to be reviewed again between FAO focal point and Dirk (Gwen Dauphin)

Socioeconomics TA:

A new TA on socioeconomics coming from the objectives of the OFFLU research agenda was presented by Peter Daniels. The proposed leader for this group is Jonathan Ruston. The Committees commented for a minor revision of the document and to take into consideration work done by FAO on this subject.

Actions:

- Gwen to share the work done by FAO on this subject to Peter Daniels (Gwen Dauphin, Peter Daniels)
- A revised version developed in consultation with Jonathan Rushton to be proposed by Peter Daniels so that it could be shared with the OFFLU EC and then submitted to the OFFLU SC for sign off.

Review of Other Technical Activities – how to restructure and make more operational:

The Diagnostics TA will be renamed the Avian Influenza TA, and will oversee all OFFLU activities involving laboratory work related to AI viruses. As well as initiating the new work on Avian Influenza Virus Characterization this group will oversee contributions to the WHO VCM and the associated issues of harmonization of OFFLU procedures and reagents for antigenic analysis, reinvigorate PT for designated Reference Centres and ensure that test protocols for AI are still valid and harmonized and where applicable harmonized across species more broadly. The updating of cleavage site sequences by the OFFLU scientist falls within this TA.

The Technical Activities and Projects table will be restructured in the following order:

- Active TAs
- Active activities not formally adopted as TAs
- *Ad hoc* activities as needed
- Historical (completed or discontinued) TAs, projects and other activities

Actions:

- Secretariat to implement the above decisions and circulate a revised table (Gounalan Pavade)

Restructure of OFFLU Website (tabs and contents):

The Committees discussed options for restructuring the OFFLU website with new tabs on the home page – avian influenza, swine influenza, equine influenza, and wild life technical activities, human animal interface, laboratory protocols, resources etc. There should be a hot link from the home page to laboratory protocols. There should be a section recording the scientific publications reporting work undertaken through OFFLU collaborations. Discussion about reorganization and a mock up of a revised website will be sent out to the Committees for comments.

Actions:

- OFFLU Secretariat to work with the Chair of EC in the reorganization of the OFFLU website contents (Gounalan Pavade, David Swayne)
- The OFFLU scientists (as recorded on the OFFLU Contributors list) to be emailed to advise the Secretariat of their relevant OFFLU publications (Gounalan Pavade, David Swayne)

Review of OFFLU Contributors List and Suggestions:

The Committees advised to update the list of contributors to include all the members from the various TAs as well as colleagues specifically approached by OFFLU to act as national contact points (where applicable)

OFFLU Next Meetings:

Five meetings were discussed:

- An avian influenza (AI) TA meeting involving 12 Reference Centres, St. Jude and other EC members, possibly in March 2017 in Rome. Could include up to 30 participants
- Next SC and EC meeting also in March 2017, in conjunction with the AI group meeting
- Possibility of VCM engagement meeting along with AI group meeting, although the possibility of having this in East or Southeast Asia, subject to funding, had also been discussed earlier.
- OFFLU SIV group meeting, cofunded by CEIRS and the parent organizations, in either Paris or Rome
- A possible OFFLU Technical Meeting in conjunction with the next AI Symposium in April 2018, subject to the agreement of the Symposium organizers

Actions:

- Doodle by the OFFLU Secretariat to set dates for the AI group meeting, the next combined SC/EC meeting and the SIV group meeting (Gounalan Pavade)
- Formally approach the organizers of the next AI Symposium to explore the possibility of again having an OFFLU Technical Meeting in conjunction with that event (Ian Brown, David Swayne)