



Meeting of Experts of OIE and FAO Reference Laboratories for Avian Influenza OIE, Paris, 5th March 2008

The first meeting of Experts from OIE and FAO Reference Laboratories for avian influenza was held at the OIE headquarters on 5 March 2008. The meeting was attended by representatives from six Reference Laboratories and other laboratories involved in diagnostics as well as representatives from FAO and WHO.

The meeting was chaired by Professor Steven Edwards, President of the OIE Biological Standards Commission and Chairman of OFFLU. In his opening address he stated that the Reference Laboratories play a critical leading role in diagnostics and animal health, it is vital that they work towards a common aim and that there is effective cooperation between the animal and human laboratory networks. He emphasised the importance of OFFLU and reminded the group that OFFLU was established in 2005 as a high level agreement between OIE and FAO to reflect their common objectives in supporting avian influenza control regimes and to assist WHO in early preparation of human influenza vaccines. OFFLU is an independent mechanism under the control of the OFFLU Steering Committee. In October 2007 there was a revision to the structure of OFFLU to create greater inclusiveness and more functionality. This was proposed by the OFFLU Steering Committee and jointly agreed by OIE and FAO.

Virus and information sharing

Dr Bernard Vallat, Director General of the OIE, welcomed the participants including WHO representation (Dr Elizabeth Mumford) and thanked them for their ongoing support of OIE. He made a strong statement concerning the obligations of Reference Laboratories and of national veterinary services to share information and material to support the global avian influenza control effort. OIE Reference Laboratories and FAO Reference Centres already accepted their mandate, of which transparency is a key element. OIE Reference Laboratories that are not transparent cannot function as part of the reference network.

It was agreed that these obligations are vital and needed to be addressed and reconfirmed in a Resolution to be proposed by the President of the Biological Standards Commission for adoption at the OIE General Session in May, 2008.

Action - OIE to prepare a Resolution on avian influenza information and material sharing for adoption at the OIE General Session in May 2008.

Action - OIE and FAO to draft a joint statement on sharing and transparency, with reference to avian influenza, based on the statement of the Director General of the OIE.

Issues concerning virus sharing have ignited international debate that now go beyond avian influenza. Mechanisms for sharing avian influenza viruses through the OFFLU network can be used as a model for other threats at the human animal interface.

In principle, OFFLU endorses the GISAID sequence database currently under development (subject to evaluation by the network scientists). Provided that it delivers as expected and meets OFFLU's needs, it will be the tool used by OFFLU scientists to deposit sequences and

data from animal viruses. In addition, Bhudipa Chodhury, the new OFFLU scientist, will make contact with the GISAID team to evaluate the possibility of using a proposed GISAID tracking system, currently under discussion.

If the GISAID sequence database is shown to meet the needs of the human health laboratory network, it will become the tool that WHO Collaborating Centres use for human influenza vaccine strain selection.

According to information provided by Ilaria Capua, the GISAID sequence database will be launched by the end of April 2008. To avoid duplication of effort, further discussion about an OFFLU database should be deferred until then.

Material Transfer Agreement (MTA)

The OFFLU MTA is available on the OFFLU website (www.offlu.net).

The OFFLU MTA is a template to facilitate sharing of material and can be amended as appropriate to reflect varying national policies.

The current template needs to be updated to reflect the following:

- Openness is part of the OFFLU agreement; shared data such as sequence data must be put into the public domain.
- It is important to store viral material in reference collections; viruses should not be destroyed.
- FAO have received several comments from their legal advisers.

Action - FAO/OIE to agree on changes that need to be made and amend the OFFLU MTA in line with the above suggestions.

Ilaria Capua spoke about the procedure at IZSVE to facilitate rapid release of data into the public domain. Following receipt of samples - containing influenza viruses or viral material - submitting laboratories are informed that if they do not lodge an objection in writing within 2 weeks, it is assumed that they agree to data and material being further shared. Submitting laboratories that lodge an objection are also asked to explain their reluctance to share information.

Standardisation and validation

The OIE Biological Standards Commission has been encouraging OIE Reference Laboratories to propose standard reagents for diagnostic tests. The process is straightforward; someone proposes a standard, the experts then exchange materials and data in order to agree whether or not it is 'fit for purpose'. This is something that the Reference Laboratories should address and is part of their mandate. There are currently no validated reagents for HPAI diagnostic tests. All participants were given a copy of the new 2nd edition of the *OIE Quality Standard and Guidelines for Veterinary Laboratories: infectious diseases*. This includes guidelines on preparing standard reagents.

Action - for the OFFLU secretariat to provide a link - on the OFFLU website - to information about the new edition of the OIE Quality Standard and Guidelines for Veterinary Laboratories: infectious diseases.

Laboratory presentations

Experts from the Reference Laboratories presented their current activities and areas of specialisation. This assisted in identifying gaps in the work and areas where effort may be duplicated. It was clear from the presentations that there was room for more coordination of

the activities of Reference Laboratories. Coordination can be improved through specific network technical activities.

Specific network technical activities

Technical activities for OFFLU, focussing on:

- 1) Previous proposals for OFFLU technical activities and
- 2) Suggestions from participating experts for further technical activities.

I. Proposed technical issues and activities

As part of the revision to OFFLU's structure, proposals have been made for OFFLU to address specific avian influenza technical issues relevant to the OFFLU objectives. Once the issues have been addressed the technical activity would cease. The choice of experts to address these issues should, where possible, result in good regional representation. The process should not duplicate existing procedures and activities within OIE, FAO or other bodies. It was agreed that where relevant, outputs from certain activities – such as the proposed diagnostic test kit and the vaccine group - should be endorsed by the OIE Biological Standards Commission. An OFFLU technical activity on molecular epidemiology should have its outputs reviewed by the OIE ad hoc group on epidemiology prior to endorsement by the OIE Scientific Commission on Animal Diseases. The proposed technical issues and activities are as follows:

I. Diagnostic kits – information about commercially available kits

Numerous commercial test kits are available in the market place. Much of the information about their performance is protected by confidentiality agreements, little is freely available.

It would be helpful to compile an inventory of commercially available kits, and, where manufacturers provided consent, list information about their performance and 'fitness for purpose'..

The 'Register of diagnostic kits certified by the OIE as validated fit for purpose(s)' provides a formal register for commercial kits.

II. Technical issues at the human animal interface

There was support to proposals for an OFFLU public health interface group. This would lead to a formalised mechanism for ongoing exchange of virological and other information – such as epidemiological information - with members representing both animal and human health networks. Unlike other proposed technical activities this would function on a permanent basis.

III. Biosafety

Guidance on minimum biosafety standards for handling avian influenza viruses is an issue that needs to be addressed for developing countries. Recommendations should be balanced to provide a model that is fit for purpose in both developing and developed countries. Representation should ensure that practical people are included in discussion.

IV. Molecular epidemiology

This activity should complement the work of the OIE funded OFFLU Bioinformatician based at VLA Weybridge and proposed FAO funded OFFLU Bioinformatician to be based in Rome.

Action – Bhudipa Choudhury to take this forward and to make contact with the GISAID sequence database representative.

V. Vaccine quality assurance

To address issues of vaccine efficacy and quality, specifically with reference to the current OFFLU project in Indonesia. To develop some text for the 'OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals' that provides guidance on matching vaccines with circulating field viruses.

Action – Peter Daniels to take forward elements of this in close collaboration with Gwenaelle Dauphin who takes FAO technical lead on the initiative in Indonesia.

2. Suggestions from participating experts for further technical activities:

I. Standardisation of reference sera for avian influenza A viruses of subtype H5

To decide on common reference antisera for H5 that are most promising (taking into account potential supply and demand). If successful this could be extended to other subtypes of avian influenza viruses. This should include developing a reference panel for ELISA antisera.

Action – Ian Brown to take this forward.

II. Reference standards for PCR.

RNA standards to be developed and validated. Initial focus on H5N1 and if successful this could be extended to other viral subtypes.

Action – Timm Harder to take this forward.

III. Proficiency testing

Investigate what Reference Laboratories are currently doing with regards to proficiency testing for avian influenza diagnostic tests and develop a set of common recommendations. This activity should include WHO (Elizabeth Mumford).

Action – Dennis Senne to take this forward

It is acknowledged that experts have demands on their time. Efforts should be made to use teleconferencing; some groups will be able to discuss the issues electronically.

All of these proposals need to be further discussed (in some cases) and formally agreed by the OFFLU Steering Committee.

Action – OFFLU Secretariat to organise a meeting of the OFFLU Steering Committee to discuss and agree the proposals and further action.

Activity at the human animal interface

There is growing interest from the public health sector towards collaborating with the animal health sector on activities at the human animal interface. The OFFLU network and public health influenza laboratory network collect information that is useful to each other; they need to develop ways of sharing this more efficiently.

The proposed OIE/WHO/FAO Conference (in principle the 6th -9th October 2008) would provide a forum for sharing such information. The conference is intended to include discussion about the virological characteristics of avian influenza that are important for zoonotic disease and pandemic potential and to look at modes of transmission and human exposure variables.

Action – OFFLU Secretariat to ensure that when the conference is confirmed that it is advertised on the OFFLU website.

Monitoring avian influenza virus variants in Indonesian poultry and defining an effective and sustainable vaccination strategy

Since 2004 Indonesia has adopted a policy of vaccination to control avian influenza. Initial unpublished research findings (David Swayne) have raised awareness to the importance of assessing efficiency and efficacy of vaccines – against circulating field strains - currently being used in Indonesia.

This USAID/AusAID funded, FAO-led project aims to assess antigenic matching of vaccines with available recent field strains and to provide recommendations on vaccine strains to be used in Indonesia. The project involves collaboration from a range of experts – including the OFFLU Scientist, based at VLA - in the OFFLU network and incorporates sequencing studies; challenge studies and antigenic cartography

It is hoped that interim results will be presented in June 2008 in Jakarta. Next steps include the development of a new vaccine strain.

Training Activities

Action – OFFLU Secretariat to make further calls for information on known training activities to populate the OFFLU training inventory.

OIE Laboratory Twinning Programme

Twinning has been adopted by the OIE as a method for improving laboratory capacity and expertise in developing and transition countries. Individual Twinning projects will create opportunities for developing and transition countries to develop laboratory diagnostic methods based on the standards of the OIE. Twinning has the objective of creating more OIE Reference Laboratories to provide support to regions where there is a need and to regions that are currently under-represented.

A Twinning project is a partnership between an OIE Reference Laboratory (or an OIE Collaborating Centre) and a Candidate Laboratory. The Reference Laboratory or Collaborating Centre provides the Candidate Laboratory with technical support, guidance and training.

As of March 10th 2008, the OIE has received proposals for 13 Twinning projects and a further 6 countries have expressed interest in applying with a view to submitting a proposal. One Twinning project is underway. The remaining proposals have either been approved 'in principle' or are in the process of being approved.

Summary

All action points were agreed and will be taken forward.

The next meeting of the heads of avian influenza Reference Laboratories will be called to coincide with a well attended conference.