A CONSULTATION TO DEVELOP A GLOBAL ANIMAL INFLUENZA RESEARCH AGENDA

Paris, 8-9 April 2014

Summary

OFFLU[1] and STAR-IDAZ[2] have partnered to develop a strategic agenda for animal influenza research. The initiative takes a global perspective and aligns the priorities of key stakeholders with interests in funding research, conducting research, and benefitting from the outputs of research.

Paris, 8-9 April 2014 - OFFLU and STAR-IDAZ convened a group of 60 key contributors to the field of influenza including animal health and public health scientists; representatives from animal production and trade (poultry, egg, and pork); the pharmaceutical sector; equine sports; policy advisers; and representatives from research funding bodies.

By way of structured group work and using feedback from a survey sent out prior to the consultation, the experts developed their vision for animal influenza research and identified areas of research which are currently of highest priority.

The group identified whether each priority was short-term applied research *(studies needed to determine effective intervention strategies with potential for immediate impact)*; longer-term applied research *(studies most likely to reduce disease burden (economic and health))*; or priority basic research *(studies which may ultimately lead to effective intervention strategies or reduced disease burden).*

In general three strong themes came out of the consultation

1) Research to identify the multifactorial determinants of health risk from influenza viruses is needed to support risk assessment, surveillance, and intervention strategies.

2) Integrated approaches to influenza research and surveillance across species (at the interface between animals and humans, and between animal species) should be taken and surveillance findings should be shared rapidly.

3) There is a need to improve technologies to develop more effective and universal influenza vaccines and diagnostics.

Research priorities may apply to a sector (poultry, pork, equine, wildlife or animal human interface), in which case this is specified, or cut across a number of these sectors. The priorities are not ranked in order of importance and categories of short-term applied, longer-term applied, and priority basic research, are considered to be of equal importance.

1 OFFLU is the joint OIE-FAO network of expertise on animal influenza

2 STAR-IDAZ is the Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses

Main outputs from the Consultation

The Consultation agreed that their vision was ***'global coordinated research to minimise animal and human health risks and maximise social, economic and environmental outcomes'***

Priority areas for research were grouped into 6 subject areas:

1. Surveillance and risk assessment

Strategic objective: To develop a better understanding of the key determinants of influenza infection and transmission dynamics to inform research, surveillance, and control

Short-term applied research priorities:

- Develop effective systems for monitoring influenza viruses in animals and in people at the animal-human interface
- Understand the viral, environmental and socioeconomic factors associated with zoonotic and interspecies transmission

Longer-term applied research priorities:

- Generate real time data on subtypes and strains of circulating influenza viruses and their prevalence, to guide disease prevention and control
- Identify the risk factors associated with international travel that increase virus shedding by vaccinated horses
- Establish complete data on influenza virus strains that are circulating globally and determine their impact on animal health and welfare in different populations of equidae including working animals in developing countries
- Obtain a complete global picture (including data about genotype and phenotype) of influenza viruses circulating in swine through improved coordination in approaches to surveillance and sharing of data
- Determine the processes involved in transmission of influenza viruses within human and swine populations, between human and swine populations (bidirectional), and the adaptation of influenza viruses to either species
- Comprehensive integration and data mining of laboratory and field data (pathogenesis, virus sequence, field metadata, production data) with coordinated analysis that will provide digested information to allow more effective risk and source attribution, surveillance, prevention and control of avian influenza
- Identify and model risk factors for influenza transmission between wild birds and poultry in different ecological settings, including the socioeconomic and human cultural aspects that contribute to or reduce such transmission

Priority basic research:

- Identify viral determinants that influence interspecies transmission, and introduce surveillance at the interfaces between species
- Analyse and describe the ecology and evolution of animal influenza viruses in all species
- Identify the determinants of key phenotypes of animal influenza viruses including the virulence and pathogenicity to different animals, receptor specificity, antigenic properties, transmissibility in different animals, host range
- Develop a predictive understanding of the link between genetic sequence data and all other available metadata (epidemiological, pathological, structural, etc.) as the basis for genetic sequence-based risk assessment

2. Diagnostic development

Strategic objective: To develop diagnostic tools that provide consistent optimal results in any setting.

Short-term applied research priorities:

- Develop an engineered cell system permissive for the replication of influenza A viruses e.g. an alternative to the currently used culture systems of embryonated chicken eggs or current cell culture systems
- Validate RT-PCR test(s) to OIE standards as fit for purpose for international movement of horses
- Optimize and validate a range of diagnostic tools and approaches to allow for improved serological and viral diversity surveillance in wild birds
- Develop sample preservation substrates which are suitable for a wide range of diagnostic sample types (faeces, tissues, blood, oral and nasal fluids, serum, environmental) and which do not rely on maintaining the cold chain
- Develop reliable diagnostic tools for rapid virus and antibody subtyping as an alternative to the current Haemagglutination Inhibition (HI) test

Priority basic research:

- Measure cross species infection with specific viruses (especially subclinical infection); increase specificity and sensitivity of assays and target correct populations

3. Prevention and control interventions (risk management)

Strategic objective: To apply targeted and effective evidence based interventions

Short-term applied research priorities:

- Validate and compare (in terms of effectiveness, cost, and social acceptability) specific interventions to decrease environmental influenza virus burden at sites where there is potential for high viral load and exposure to other species (e.g. markets, farms, mass gatherings (animal, human or both), transport)

Priority basic research:

- Improve resistance of poultry to avian influenza infection by selecting for genetic resistance or develop interventions that can block virus replication

4. Vaccine development and delivery mechanisms

Strategic objective: To improve availability, delivery and evidence based usage of efficacious cross protective vaccines to prevent infection and transmission

Short-term applied research priorities:

- Define criteria for comparing the antigenic properties of circulating influenza virus strains to those of vaccines so that well-matched and protective vaccines are available, and support internationally accepted and evidence based vaccination regimes
- Elucidate the extrinsic and intrinsic factors that impact on the immunological response to vaccination and develop strategies to minimise vaccination failure

Longer-term applied research priorities:

- Develop vaccines which induce immunological protection to a broader range of virus strains and subtypes, to reduce disease burden and risk of infection
- Develop vaccines which can elicit immunity with a single dose
- Develop vaccines for younger animals that overcome interference from maternal antibodies, and which can be applied by mass application to produce earlier onset and longer lasting immunity
- Develop vaccines that interrupt transmission of infection in addition to preventing disease and death
- Develop vaccines with protection across a broader range of virus strains and subtypes, independent of HA variability, in the face of passive or prior immunity
- Develop an immunological toolkit to measure correlates of protection (measurable signs of protection) for next generation vaccines and matching diagnostics to identify vaccinated animals or to differentiate vaccinated animals from infected animals

Priority basic research:

- Identify correlates of protection (measurable signs of protection) which result from vaccination

5. Host-pathogen interaction

Strategic objective: To improve understanding of virus-host interactions and factors that impact on the interactions such as disease pathogenesis, transmissibility, and immune responses to better inform infection control

Short-term applied research priorities:

- Identify host determinants for permissiveness, susceptibility and resistance to influenza virus infection

Longer-term applied research priorities:

- Determine the immunological mechanisms and correlates of cross-protective immune responses to influenza viruses
- Determine the pathogen, host and environmental factors in the field affecting pathogenicity, transmission, response to vaccination and viral evolution

Priority basic research:

- Determine host and viral factors associated with resistance and susceptibility to virus infection including immune and cellular responses
- Determine host, environmental and genetic factors associated with pathogenicity and clinical outcomes

6. Socioeconomics and policy

Strategic objective: To improve the effectiveness of detection, prevention and control measures through the integration of social, economic and institutional analyses of the livestock sectors affected by influenza viruses

Short-term applied research priorities:

- Identify social, economic, and institutional factors, including governance, that impede the effective implementation of influenza surveillance, prevention and control

- Develop an evidence-based system that enables the development and global implementation of One Health policies to prevent, detect, and respond to zoonotic infections

Longer-term applied research priorities:

- Understand the structure and interactions within animal sector production systems and how the dynamics of animal sectors influence infection risk
- Identify and understand how to influence social and economic behaviours along the value chain
- Understand the social and economic impact of influenza viruses in animals and their impact on humans
- Develop social and economic assessments to demonstrate the social economic profitability of the research programme proposed
- Develop social and economic assessment tools to determine the social cost-effectiveness of new technologies developed

Presentations and supplementary information are available on the OFFLU website

http://www.offlu.net/index.php?id=308

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Contributing supplementary information:

USDA Animal Influenza Virus Gap Analysis
UK Flu Research Gaps Scoping meeting
WHO Influenza Research Agenda
EU DISCONTOOLS
OFFLU Research Agenda