Royal Society of Canada

H5N1: Evolving Situation, Evolving Research

June 19, 2023, Canadian Museum of Nature, Ottawa, Ontario

Proceedings

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List of Abbreviations

AIV	Avian influenza virus
BIPOC	Black, Indigenous, and other people of colour
CAHSN	Canadian Animal Health Surveillance Network
CFIA	Canadian Food Inspection Agency
CIHR	Canadian Institutes of Health Research
CL3	Containment level 3
CL4	Containment level 4
CPHLN	Canadian Public Health Laboratory Network
CWHC	Canadian Wildlife Health Cooperative
DAA	Direct acting antivirals
DIVA	Differentiating infected from vaccinated animals
DND	Department of National Defence
DRDC	Defence Research and Development Canada
ECCC	Environment and Climate Change Canada
FPTI	Federal/provincial/territorial/Indigenous
GWAS	Genome wide association studies
HA	Hemagglutinin
HHT	Human Health Therapeutics Research Centre
HPAI	Highly pathogenic avian influenza
NCFAD	National Centre for Foreign Animal Disease
NGO	Non-governmental organization
NML	National Microbiology Lab
NRC	National Research Council
PCR	Polymerase chain reaction
PHAC	Public Health Agency of Canada
PHL	Public Health Laboratory
PPE	Personal protective equipment
SARI	Severe acute respiratory infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Executive Summary

In June 2023, an inter-sectoral meeting was convened by the Royal Society of Canada in partnership with the Public Health Agency of Canada, the Canadian Food Inspection Agency, the National Research Council and the Canadian Institutes of Health Research at the Canadian Museum of Nature in Ottawa. This meeting was opened by Dr. Theresa Tam, Canada's Chief Public Health Officer, and closed by Dr. Mary-Jane Ireland, Chief Veterinary Officer of Canada. Over the course of the day, participants aimed to:

1. Consolidate the current state of science, knowledge, and action related to the response to highly pathogenic avian influenza A (HPAI) H5Nx virus in avian, wildlife, and domestic animal populations, and implications for prevention and preparedness for human health;
2. Discuss and identify science and research knowledge gaps and priorities for HPAI which can be addressed across disciplines and sectors;
3. Fully integrate and operationalize a One Health perspective into research planning for an emerging health threat.

An opening panel presentation addressed key questions on lessons from past spillover events from previous influenza virus pandemics and the key research challenges and gaps in science, risk reduction, and to enable the greatest connectivity across surveillance, science, policy, and practice. This was followed by group discussions to identify knowledge, capacity, and implementation gaps for research, and describe how to integrate One Health in the prevention and response to HPAI. Topic areas included:

- Diagnostics, surveillance, disease control and population health
- Assessing the risks related to H5Nx reassortants
- Pharmaceutical interventions
- Health intelligence and social sciences

A thematic analysis based on proceedings' notes was also done and in conjunction with the proceedings, the following key themes emerged:

1. <u>Research knowledge gaps</u>

Participants acknowledged that current research structures do not support, far less incentivize, multidisciplinary approaches, leading to weakened efforts to build a robust One Health framework to tackle HPAI, including effective scientific collaboration and coordination among various agencies and academics, and communication and data sharing strategies. Persistent gaps include lack of Canada's preparedness and capacity, particularly around containment level 3 (CL3) capabilities for HPAI work in Canada.

2. <u>Surveillance</u>

Participants discussed current surveillance programs and expressed the need for capacity building and tools to ensure robust surveillance. Participants provided background and context about Canada's efforts to improve avian and mammalian wildlife surveillance. Capabilities have waxed and waned as a function

of fiscal and technical (e.g. diagnostic) limitations. While surveillance programs have been considered a priority for wild birds, a formal surveillance program for wild and domestic mammals is lacking. Participants underscored the need to link resources and data sharing across disciplines and sectors to consider both domestic and wild species as well as humans.

3. Interspecies transmission

Participants were keen to understand factors operating at the human-animal interface and which promote interspecies transmission. These questions draw attention to the considerable complexity of interspecies transmission while focusing on potential intervention points in human-animal systems. Potential interventions necessitate effective communication and coordination between partners in human health, wildlife and agricultural sectors in a sustainable fashion.

4. Collaboration

Cross-disciplinary collaboration was seen as critical to integrating One Health approaches into HPAI decision making. While the importance of the federal, provincial, and territorial agencies was acknowledged, connections with rural and Indigenous communities must be sought in a more meaningful way towards prevention, preparedness and response to public health emergencies. The benefits of collaborations between intra- and extramural scientists was also underscored. These collaborations would help build the trust that is currently lacking in terms of key communication, scientific collaboration, and data sharing strategies.

5. One Health

Integrating One Health principles and research in combating HPAI challenges was a prominent theme at the workshop, and second only to research gaps. Participants observed governance, policy, and decision making, and fiscal constraints as fundamental issues hindering implementation. A key takeaway point was the need to strengthen inter-sectoral and multi-disciplinary approaches that include resources and knowledge brokering between government agencies and academics as well as a bi-directional partnerships with Indigenous communities.

6. Countermeasures

Both medical countermeasures such as antivirals and vaccines and public health measures for prevention were underscored throughout the meeting. Stockpiling and gaps in biomanufacturing of materials was discussed. Gaps in capacity around research and development for countermeasures, partially driven by limited access to CL3 facilities, and limited understanding of the underlying biology of host-virus interactions and immunity were noted.

In summary

Overall, there was consensus that a One Health approach is integral to addressing gaps in prevention, risk reduction, and science around HPAI. Robust cross-sectoral connectivity is essential for health intelligence,

policy, and research. Cohesive efforts to dismantle barriers to capacity-building, enhance inter-sectoral communication and data sharing, and build research collaborations are warranted.

Opening Panel Presentation *Current response and mitigation, globally and in Canada: Bringing emerging science forward*

This session aimed to contribute to a shared understanding of the current situation with H5Nx highly pathogenic avian influenza virus, or HPAI (nationally and globally) through short presentations by panelists addressing the following questions:

1. What lessons can we derive from past spillover events from previous influenza virus pandemics (e.g. 2009, H1N1) and epizootics from biological, epidemiological, behavioural and social perspectives?
2. What are the key research challenges and gaps in the science for the current situation, for risk reduction of H5Nx spillover into other species, and to enable the greatest connectivity across surveillance, science, policy, and practice?

Abed Harchaoui (Canadian Food Inspection Agency): Dr. Harchaoui provided an overview of the animal health situation, noting that over 7.6 million poultry (commercial operations and backyard flocks), 1,800 wild birds and 180 domestic and wild mammals have been affected in Canada (as of June 2023). At the molecular level, mammalian adaptive mutations in PB2 (part of the polymerase complex), E701D and E627K/V/A, have evolved independently and been noted in mammals and wild birds; E627K has also been documented in domestic poultry. No adaptations known to enhance transmission among mammals has been noted in the HA gene. All HPAI viruses are sequenced by the Canadian Food Inspection Agency (CFIA) and a combination of genomic and epidemiological analyses are used to generate transmission networks. Research gaps include a lack of understanding of viral determinants contributing to the expanded geographical spread compared to 2014/15, and the role(s) of selective pressures for host switches (avian to mammal; mammal to mammal; mammal to avian); the effects of innate and adaptive immunity; virus competition; mammalian host adaptive mutations in the polymerase complex; species-dependent infection phenotypes in different poultry breeds/production and wild birds; and the development of machine learning to identify markers associated with virulence and adaptation to mammals. Dr. Harachaoui also highlighted the international trade implications of this panzootic, and underscored the importance of public communications and recovery.

Peter Buck (Public Health Agency of Canada): Dr. Buck provided an overview of the human health situation as of June 2023, noting that no human cases of H5Nx HPAI have been detected in Canada, although there have been six severe cases with two deaths globally. Human cases reported to date have been linked to exposure to infected birds and their environments (e.g., recent case in Chile). The epidemiology of the virus is changing. In the past, waves have been geographically and temporally limited. However, viral activity is now pan-Canadian and ongoing. The potential for interspecies transmission,

including reverse zoonoses (e.g. pandemic H1N1 influenza viral transmission from human to swine in 2009) was underscored as a major challenge to both human and animal health, highlighting the importance, and need for, broad, early engagement across sectors. The following priorities were discussed: rapid diagnostic development and commercialization, including point-of-care testing, serodiagnostics; early characterization of emerging and novel viruses and discernment of detailed case information; and enhanced and integrated surveillance, including wastewater sequencing.

Shayan Sharif (University of Guelph): indicated that poultry vaccination initiatives are under consideration in the United States and the European Union, noting that the likelihood of control and elimination appears unlikely otherwise. Ideal vaccines are thermostable, reduce transmission, generate immune memory, and are rapidly developed, approved, and deployed through a sound global infrastructure for manufacturing and distribution. They should also be inexpensive, and ideally, effective after a single dose. Research gaps exist around vaccination strategies, including target populations, use of vaccines in outbreaks, trade issues and goals of vaccination (i.e., to reduce transmission, infection, disease, or all of these?). Partially effective and/or mismatched vaccines also pose a challenge.

Matthew Miller (McMaster University): highlighted the importance of addressing gaps around our understanding of host determinants of severe disease in people, including cohort age. Based on pre-existing data and concepts of influenza immune imprinting, individuals born between 1918 and 1952 are theoretically at lower risk since they were exposed to historical H1 viruses (more closely related to H5 viruses), whereas those born after 1968 are at higher risk of severe infection to H5 since they were exposed to H3 viruses (more closely related to H7 viruses). The importance of considering individuals at the highest risk at the human-animal interface (as we do for rabies) was underscored, and other considerations such as vaccination strategies (e.g., post-exposure, ring vaccination) and stockpiling are important. Dr. Miller noted that an H5Nx vaccination strategy is likely to differ from an annual seasonal influenza vaccine. For example, the strategy may consist of priming by targeting the HA stalk, then the development of neutralizing antibodies on boosting, and would require two (possibly different) vaccine doses. With respect to antivirals, Dr. Miller suggested that there is a limited antiviral toolkit noting that current options are limited by narrow therapeutic windows and emergence of resistance. Strong emphasis was made to address key gaps pro-actively before spillover and spread to humans occurs.

Sue Twine (National Research Council Canada): Dr. Twine noted gaps related to the availability of containment level 3 (CL3) lab capacity for viral pathogenesis and vaccine development/preclinical challenge studies as well as capacity for rapid vaccine development in Canada. They noted the importance of coordination between existing CL3 labs including on platforms, adjuvants and cell lines to develop vaccines to control spread in animal populations using a One Health approach. For clinical trials; they noted gaps in monitoring and rapid high throughput platforms for field testing. Dr Twine indicated that the National Research Council Canada (NRC) can support collaborations across Federal, Provincial/Territorial, academic and industry partners working on diagnostics, surveillance, disease control and population health, and risk assessment of H5Nx reassortants using capacity for diagnostics and therapeutics development including lab-on-a-chip technologies, development of biomarker and immunoassays and CL3 capacity for pathogen risk assessment. Specific examples of emerging

technologies included the Powerblade and ViMis for rapid, field-based diagnostics. The NRC has also established multiple cell lines and platforms for vaccine development and can produce adjuvants.

Michelle Driedger (University of Manitoba): Dr. Driedger provided an overview of the importance of clear and responsible risk communication emphasizing a need for a layered communication approach by providing increasingly more depth in the scientific details following plain language messaging to build trust and confidence. In particular, she highlighted that communication is critical across multiple situations and scenarios such as: to reduce stigmatization of imported cases; to provide guidance around domestic consumption of at risk animals; to target messaging to at risk populations, understanding those populations may change; to address the information needs of the moveable middle of vaccine-hesitant individuals by curating resources to answer different questions from credible sources; and to provide clear reasons for why initial guidance messaging may need to shift in the face of uncertainty, and to consider unintended consequences for downstream impacts particularly around the use of short-term mandates. She highlighted that there are important structural and social barriers, and systemic racism that pose considerable challenges, and the importance of understanding public health messaging will need to shift.

Several points were raised when the floor was opened:

- **Coordination**
    - Global frameworks to prevent spillover are important and Canada should engage in these
    - The importance of understanding risk and shifting to a more proactive stance was underscored
    - Strong emphasis was made around leveraging and coordinating existing capacity
    - Silos between wildlife and domestic animal efforts were noted
    - Importance of data sharing and avoiding duplication of scientific efforts. This requires coordination and collaboration
    - Overarching sentiment that we are currently short on actions around HPAI
- **Communication**
    - Messaging around vaccinating food animals will be a new challenge given vaccine hesitancy
    - Developing key messages around HPAI to communicate with the public is important to increase confidence in government
    - Enhancing basic knowledge of infectious diseases in mainstream science classes in school will enable messaging during health emergencies
    - Early engagement and co-development of programs with Indigenous communities, Elders, and services will have major impacts on receptivity. Similarly, all of society, including stakeholder groups that comprise hunters, harvesters, fishers, and country food groups should be engaged
- **Vaccines and vaccine development**
    - T and B cell responses after (universal human) influenza vaccination, developing a regulatory framework and means to test efficacy (e.g., non-inferiority trial) with seasonal vaccines is important

- Governance and decision-making around stockpiling human vaccines and antivirals merits more consideration

Breakout Discussions

The current challenges around HPAI present opportunities to apply a One Health approach in practice. This meeting intended to identify high priority knowledge gaps and potential research priorities for the most pressing questions. Breakout groups were formed under 4 key topic areas, ensuring cross-sectoral representation and reflecting diverse perspectives. Participants were asked to actively and meaningfully consider the One Health approach in their discussions, including principles of equity and enabling actions.

Participants were first tasked to detail/summarize current actors and research activities, striving for human, domestic animal, and wildlife health counterparts and researchers to interact across sectors within these groups, focusing on the most pressing issues related to the current situation. They were then asked to consider the following:

1. With a view to prevent further interspecies transmission of HPAI, what are the key gaps in our understanding of factors potentiating spillover (at molecular, viral, individual host and population scales, and from a behavioural perspective) that should be urgently addressed? What are the gaps in risk reduction research in the immediate term?
2. With a view to enhancing preparedness and response, what are the key gaps which merit immediate attention around both existing and surge capacity for research and implementation? Consider collaborative partnerships, tools, and instruments (protocols, reagents, agreements), infrastructure (biocontainment, data) and workforce.
3. How do we integrate a One Health and other holistic, systems-based approaches to prevention and response, and apply this regionally, nationally, and internationally? How do we work towards a global view of health security while managing national challenges?

Topic 1: Diagnostics, surveillance, disease control and population health

This group focused on surveillance, control, and epidemiology, including the 1) molecular detection 2) serology 3) genomics and 4) epidemiological and ecological analysis for wildlife, domestic animals and humans, how data are compiled, analyzed and to inform outbreak control and other mitigation measures.

Current key activities and capacities

Wildlife surveillance. Diagnostic capabilities exist for HPAI nucleic acid detection (polymerase chain reaction [PCR]) and serology primarily through the National Centre for Foreign Animal Disease (FCFADD-CFIA) and the Canadian Animal Health Surveillance Network (CAHSN), and to a lesser extent through academic laboratories operating either on a contractual or research basis; for example, Environment and Climate Change Canada (ECCC) contracts diagnostic labs in the CAHSN for avian influenza testing of samples collected through active disease surveillance. For wildlife surveillance, AIV surveillance partners, conducts opportunistic AIV sampling of live wild birds across Canada through existing field research

programs in accordance with Canada's Interagency Surveillance Program for Avian Influenza Viruses in Wild Birds (also known as Canada's Inter-agency Wild Bird Influenza Survey). Results from the Program are used to determine if conservation concerns exist for susceptible wildlife populations and also contribute to a One Health approach to pathogen surveillance with an aim to protect food security and human health. The Canadian Wildlife Health Cooperative (CWHC) also conducts passive surveillance on dead birds, and some surveillance through banding programs. Surveillance in mammals falls under provincial jurisdictions and occurs *ad hoc,* with some provinces having flexibility/adaptability to focus on die offs and other signals; there is no formal surveillance program for wild and domestic mammals. There are robust connections with hunters and trappers and wildlife rehabilitation facilities that could be leveraged for more active surveillance.

Surveillance in the agricultural setting. Veterinarians have been notified about the increased avian influenza risk to domestic pets/companion animals, however owners bear the costs of testing, thus this remains limited. The CFIA is responsible for the surveillance of HPAI within commercial poultry operations through a number of mechanisms. First, passive surveillance is utilized, with samples obtained when clinical signs suggestive of notifiable avian influenza are reported, followed by targeted surveillance when notifiable avian influenza is confirmed. Active surveillance activities include pre-slaughter surveillance in commercial poultry (chickens and turkeys); hatchery supply flock surveillance; and voluntary enhanced surveillance in the poultry genetic exporters sector. Census data are available for farms through provincial and regional partners, including commodity boards. Strategies for communication to industry and backyard flock owners are in place through commodity boards, dashboards, social media, and One Health communication groups. The Canadian Animal Health Surveillance System also plays an important role.

Surveillance in humans. Virus detection for seasonal influenza A and B viruses (with and without subtyping) is available for symptomatic inpatients, particularly those with severe influenza-like illness, through institutional and regional clinical and public health laboratories. Existing FluWatch (https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html) surveillance and severe acute respiratory infection (SARI) protocols can be leveraged. Poultry workers and other exposed individuals from infected premises are instructed to self-monitor and report symptoms. Currently there is no serosurveillance for H5N1 for humans in Canada. Potential sources for surveillance and control materials exist, but may be biased (e.g., Canadian Blood Services).

Diagnostic capacity. Viral whole genome sequencing is available through CFIA, but capacity is limited. Technical limitations of a commercial serology kit for avian influenza were underscored. The National Microbiology Lab (NML) supports reference diagnostic capacity and works with provincial public health laboratories (PHLs) through the Canadian Public Health Laboratory Network (CPHLN) with protocols and proficiency panels that are also available to frontline clinical microbiology laboratories. Serological testing for influenza in general for humans is restricted to research use.

Risk assessment. This is integrated between animal health groups. For example, wild bird data informs domestic animal risk assessments. From a human health perspective, integrated risk assessment activities for HPAI have been undertaken by PHAC taking a One Health approach, in collaboration with One Health

stakeholders. Joint risk assessments have been conducted by CFIA/PHAC in the past (e.g., mpox (2010), H1N1 pdm09).

Data sharing. There are some data sharing processes in place for epidemiological (Canadian Notifiable Avian Influenza Surveillance System) and genomic data (albeit limited) at the national level. Whilst a database for wild bird data exists, there are limitations. Existing databases are not well connected, having been established by different groups for different purposes; there is currently no mechanism to integrate human and animal data.

Gaps, solutions and priorities

Key knowledge gaps for preventing inter-species viral spillover:

- What drives spillover at the intersection of wild birds and farms? Do cervid and fur farms, or wild pigs represent a risk?
- A better understanding of migratory flyway dynamics as it relates to the virus (e.g. phylodynamics) would likely provide novel insights.
- What environments comprise the human-animal interface and what are the key interfaces (e.g., occupational, hunting, trapping) that warrant attention?
- More knowledge about species susceptibility and the dynamics of cryptic infections would be important to ascertain. A much better understanding of immunoepidemiology is needed across species.
- Are mammals playing an important role and is mammal-to-mammal transmission occurring? What are the barriers to, and enablers for, such events? Animal challenge experiments are an effective way to gain some understanding of virulence and transmission, but there are a limited number of CL3 laboratories approved for this work.
- Could vaccination of wildlife be used to limit interspecies transmission?
- What is the virus survivability in different environments?
- What is the appropriate use of PPE (e.g., based on infectious dose by transmission routes) for different scenarios?

Key gaps in existing and surge capacity for research and implementation

- An overarching, goal-oriented surveillance strategy with access to diagnostics for local investigation, including human surveillance, was recognized as an important gap. There is a gap in targeted surveillance at the human-animal interface at the programmatic level; the sensitivity of human case detection is limited if relying on case identification among patients with severe disease.
- Enhanced communication between human health, animal health, agricultural and environmental organizations would be important to support decision-making around post-exposure (and other high-risk individuals) human testing, including guidance and education around indications for testing of relevant species. This requires long-term, sustainable programmatic funding rather than shorter-term, piecemeal project-based support.

- For wildlife surveillance, there is a gap in surveillance for a) wild mammals and b) northern and remote regions of the country, especially for sick or dead wildlife which are less detectable on the northern landscape. Surveillance for AIV in live birds in northern regions is relatively robust.
- There is some, but not broad awareness of BSL-3 governance and current capacity; the number, and scope (*in vitro, in vivo*), regulation would be helpful to know.
- From a diagnostic development perspective, there are capacity gaps for viral genomics and serology across species at the laboratory level; there is also a paucity of inexpensive and accurate point of care diagnostics.
- A system for evaluating strategies and responses, or to exercise potential scenarios is lacking.

How do we integrate a One Health approach and work towards global health security?

- A governance structure that enables the best policy and decision-making is warranted. This includes defining the roles and responsibilities for both government and non-government decision makers.
- Mechanisms for prioritization of pathogens for investigation and pandemic preparedness would be beneficial.
- Knowledge mobilization to decision makers in government, especially related to preventive measures remains an important gap.
- There is a gap in mechanisms to support rapid, open data sharing and integration across sectors. Current research structures do not support, far less incentivize, multidisciplinary approaches, and do not currently support One Health principles.
- At the local level, there is also a diagnostic gap for wildlife sampling, which could include more community engagement and enhanced connections to human health.
- Currently, there is also limited pan-American cooperation, particularly around transboundary surveillance (e.g., migratory birds), though US, Canada and Mexico have all signed the North American Plan for Avian & Pandemic Influenza (NAPAPI) and collaborative efforts are anticipated to increase.
- There is also a deficiency in the time to complete and publish viral sequences in the public domain.
- There is an absence of a collective voice to prioritize a One Health approach and plan. Best practices in communication would be helpful.

Topic 2: Assessing the risks related to H5Nx reassortants

This group focused on current biocontainment capacity to work with HPAI and virological expertise in Canada involved in viral phenotyping and host response for risk assessment (transmission, pathogenesis, population immunity).

Current key activities and capacities

Technical capacity. There is reasonable BSL-3 capacity to work with SARS-CoV-2 in Canada, but approval to work with HPAI viruses remains a crippling challenge. The NRC has BSL-3 capacity for in vitro and small animal models, and there is some coordination between NRC, NML, Health Canada, academia, and

industry to test therapeutics. The National Centre for Foreign Animal Disease (NCFAD), part of the CFIA, has facilities to work with avian and other animal models, and shares H5Nx viruses with scientists at NML (PHAC) for experimental challenge studies; these risk assessment studies are currently ongoing. The vast majority of research and development on H5Nx viruses in Canada is being conducted by the NCFAD, who are isolating, genotyping and phenotyping Canadian reassortant viruses. The NML uses BSL-4 for animal studies which can pose limitations for pathogenicity studies. The NML is establishing capacity for serodiagnostics and has a robust reverse genetic system.

Gaps, solutions and priorities

Key knowledge gaps for preventing inter-species viral spillover

- What are the biological drivers of wild bird-domestic poultry transmission? Can poultry and other farm animal practices impact transmission? Do we know what point in the chain of transmission we would benefit most from targeting and which interventions would work best?
- What are the differences in immunity and susceptibility of different avian species? Gaps around the susceptibility of non-avian species, including pigs and other mammals (e.g., deer mice, domestic mammals) were also discussed. Understanding the difference in pathogenesis between species, immune response (e.g., shedding, recovery in wildlife), tissue tropism, co-infections in nature (including parasites and bacterial superinfections), concomitant infection and exposure to contaminants and toxins (e.g., mercury, larvicides, pesticides) is needed.
- There are substantial gaps in data from different animal challenges studies, including data on host-pathogen interactions. How are reassortant and adapted/mutated viruses impacting transmission to domestic animals and wildlife?
- Transcriptomes from infected individuals of any species may be helpful to inform risk and identify determinants for pathogenesis across species. We also need to understand the reservoir species and predictors for resistance to disease.
- Understanding the viral determinants that contribute to differences in pathogenicity in wild birds and mammals is crucial, particularly as H5Nx viruses diversify. How can viral genomic data provide functional insights, such as receptor binding affinity and change in host range, tropism, and shedding?
- From an environmental persistence perspective, there are knowledge gaps around viral thermostability and replication, and the potential effect of a range of related factors on viral tropism (respiratory versus gastrointestinal), shedding and transmission for different hosts.

Key gaps in existing and surge capacity for research and implementation

Many questions surrounded the current landscape of regulations for virological risk assessments for HPAI.

- Participants asked why H5N1 is still considered a foreign animal disease. The regulatory pathway still includes import permits and security clearance; can these processes be expedited? It would be helpful to understand the limitations on work with low pathogenicity H5 viruses as well. There is limited laboratory capacity for wild bird testing and research, encumbered by different

regulations from CFIA and PHAC for the same pathogen(s). Many BSL-3 facilities are not licensed to work with H5N1 and there are too few licensed facilities to tackle this problem domestically, despite major investments in CL3 infrastructure during the pandemic.

- There is a capacity gap for human seroimmunologic studies in people at the human-animal interface (e.g., poultry workers, animal handlers, animal rehabilitators). Access to more diagnostics (e.g., H5-specific serology) would be highly valuable. Currently, commercially available H5 serology kits do not work optimally, but are being updated.
- Immunity in wild birds and susceptibility of different birds is not well elucidated, but serological testing of wild bird samples is underway through interagency surveillance coordinated by ECCC.
- Viral genotyping, with timely public access to viral genomes detected in Canada and elsewhere, would be highly valuable. Gaps in our understanding of viral genomic epidemiology and immune escape in natural hosts merit addressing - a sampling strategy and resources for implementation are needed, along with species-specific reagents. Samples and sequences are key to facilitating research, and the need for collaboratively sharing sequences and data was noted again. The use of genome wide association studies (GWAS) for virally infected/exposed species would also be helpful.
- Modeling risk assessment predictions for spillover and large-scale epidemiological studies in birds could provide important insights.
- Research capacity also depends on available experimental models for risk assessment. *In vitro* cell lines and organoids from wildlife, along with cloned species-specific reagents and cytokines would be very helpful, in addition to *in vivo* avian models (beyond poultry). There is also a need for more containment capacity for transmission studies (e.g., ferrets). A mini-consortium could generate and share reagents, protocols and models; this may also reduce the silos between organizations.
- Enhanced surveillance in mammals, including humans, may also be warranted to enhance research capacity.
- Information sharing and people with expertise/data analysis on the ground is limited. Getting information back to the people collecting samples is important but remains a deficiency at present. There is limited awareness of data sharing agreements and data privacy guidelines between parties.
- On-premise (e.g., farm) biocontainment needs to be addressed, though it is already robust in commercial poultry operations. Should there be permits for hunting and surveillance practices that congregate wild birds?

How do we integrate a One Health approach and work towards global health security?

- An approach that aims to better understand viral ecology and virus-host-environment interactions through better environmental surveillance would enhance the incorporation of a One Health approach.
- Academic CL3 capacity (facilities and other infrastructure, highly qualified personnel, administrative processes, etc.) was substantially enhanced during COVID-19, but institutions cannot get past the regulatory hurdles to work on HPAI. A multi-species national network (for materials and data) may support these activities; the limited use of current CL3 capacity for HPAI

work also limits the degree to which Canadian scientists can support other jurisdictions and enhance global health security. The risks of inaction were underscored.

- Formal data sharing and use agreements should support those generating the data in order to maintain trust between partners.
- There is a need for strong bi-directional partnerships with Indigenous communities. Are there nature-based solutions that merit more thoughtful consideration (e.g., is habitat modification a driver ?)
- Inter-sectoral and multidisciplinary approaches that include resource and knowledge brokering between government agencies and academics to develop research collaborations was identified as an important gap.

Topic 3: Pharmaceutical interventions

This group focused on the state of play for human and animal vaccines and other countermeasures such as antivirals (human), with respect to development (virology, immunology, testing, and manufacturing).

Current key activities and capacities

Diagnostics and key reagents. Virus detection and isolation are being done in a few laboratories, but with limited communication and sharing, particularly across species and disciplines. Serology has not been performed broadly across identified risk groups.

Antivirals. Current available therapies are direct-acting antivirals (DAA) and use is associated with limitations, including a short optimal window for treatment initiation and lack of access in rural areas. Phase 3 testing of monoclonal antibodies is underway, but further work on polyclonal and combination therapies is needed. There are two main stockpiles of antivirals in Canada. For human treatment or prophylaxis, the provinces and territories hold and manage their own stockpiles, collectively known as the National Antiviral Stockpile (NAS).

Vaccines. With respect to vaccines specific for HPAI, currently, there is vaccine stockpiling in the United States, but not in Canada. Current biomanufacturing facilities include the NRC Human Health Therapeutics (HHT), and Biologics Manufacturing Centre facilities, and there is a framework for contracting and technology transfer for vaccine manufacturing. Manufacturing of candidate vaccines is often done in laboratories, but could be done within larger facilities to scale up faster. Egg-based vaccines face challenges in terms of timeliness.

From a One Health perspective, it was noted that in Asia (China, Hong Kong, Vietnam and Indonesia) there is a bivalent inactivated H5/H7 vaccine that the governments have supported for the vaccination of domestic poultry. This vaccine does not induce sterilizing immunity and therefore testing prior to exportation is in place. The Canadian Food Inspection Agency (CFIA) in Canada oversees the use of animal vaccines, including *differentiating infected from vaccinated animals* (DIVA) vaccine candidates are under development by CFIA and others.

In Canada influenza is enzootic in swine; therefore, swine are routinely vaccinated here. However, currently there is no H5N1 vaccine in use for vaccination of swine or other animals in Canada.

Gaps, solutions, priorities

Key knowledge gaps for preventing inter-species viral spillover

- There is limited understanding of antigenic crossover to determine cross protection with vaccines across species, including humans, pigs, mink/ferrets, and poultry. Understanding the antigen/antibodies and cellular immune responses, and the relative efficacy of quadrivalent, modified live, egg and mammalian cell line-produced, mRNA (or other new technologies) vaccines is critical. Sterilizing immunity to reduce viral shedding and transmission is also an important component of understanding vaccine effectiveness. The correlates of protection for H5 and other influenza vaccines under development are currently poorly defined and merit attention.
- We have limited knowledge and abilities across different vaccine platforms and host species (e.g., unaware of swine vaccines under development for H5Nx in Canada), or insights into which platforms are best suited for specific species.
- Understanding the dynamics of viral spillover would also substantially inform the development and implementation of countermeasure programs, and current surveillance efforts were felt to lack the flexibility to inform medical countermeasure development in a timely manner.
- Timely coupling of detection with functional approaches (viral phenotyping and risk assessment) is important.

Key gaps in existing and surge capacity for research and implementation

- Capacity for research and development of medical countermeasures is limited by regulatory restrictions of CL3 work, and there is limited access to the viruses isolated from surveillance activities nationally and internationally. There is an important lack of basic research to identify actionable targets for novel therapeutics
- Experimental models are lacking. Mouse models require host-adapted HPAI viruses and therefore do not translate well to humans, pigs, or other mammals; establishment of relevant pre-clinical models (e.g., ferrets) across institutions is important to ensure work can be done to ultimately enable phase 1 clinical trials for antivirals and vaccines.
- Resources and frameworks clinical trials for HPAI antivirals and vaccines are limited and remain important gaps that should be met in an equitable manner.
- Surge capacity is impeded by the paucity of domestic biomanufacturing for countermeasures for both human and animal health. Though egg and cell-based vaccine platforms and novel adjuvants exist, there are limitations around both testing and manufacturing. This includes limitations around scaling up from smaller experimental scales to large scale testing and production.
- Frameworks for universal influenza vaccine development would also be beneficial, along with best practices for initial vaccine and antiviral development, manufacturing and rollout as part of rapid response and subsequent optimization schemes. Ideally capacity would be leveraged during inter-pandemic periods for other infectious diseases of global importance (e.g., cholera).

- There are important gaps for commercialization, including a lack of technology transfer agreements across institutions, regions, and companies. The need for sustained revenue lines for manufacturers and firm commitments from purchasers was also underlined.
- Target product profiling (storage, vial access, etc.), supply chain mapping and stability testing for HPAI vaccines also suffer from lack of attention. The importance of access to vaccine components and products for Canadians from Canadian factories was further underscored.
- Coordination of vaccine implementation across jurisdictions will be important.

How do we integrate a One Health approach and work towards global health security?

- Overall, a deeper understanding of the role and implementation of countermeasures such as vaccination to prevent spillover and mitigate disease across species is needed, with prioritization of next steps depending on outcomes of interest and target populations. Feasibility and pilot studies may not translate across species, thus a comprehensive approach that examines the use of medical countermeasures in specific populations is warranted.
- Communication of "evidence quality" for decision making will be important.
- Connections with rural and Indigenous communities must be sought in a sustainable and meaningful way.
- Public health successes and opportunities for improvement can be underscored to ensure pandemic challenges are proactively addressed (e.g., polling/surveys of acceptability of non-pharmaceutical interventions).
- Prevention, preparedness and response to public health emergencies benefits greatly from collaborations between intra and extra mural scientists, connecting across sectors.
- The importance of maintaining momentum to build One Health for pandemic preparedness through continuity of discussion, funding, and training was underscored, including the embedding of One Health requirements within funding proposals. There was a call for an institute that brings this all together: "Canadian Institute of One Health for Pandemic Preparedness".

Topic 4: Health intelligence and social sciences

This group was tasked to outline current data sharing mechanisms and pathways, and the communication strategy for a) decision-makers (across regional, provincial, national, territorial and international jurisdictions), b) responders (including scientists), c) affected private sectors, d) affected communities and e) the public.

Current key activities and capacities

Governance and partnerships. Governance mechanisms in One Health and animal health at the Federal/Provincial/Territorial/Indigenous (FPTI) exist for animal health, such as tables for information sharing. From the federal animal health perspective, authorizations are in place to share data using principles that govern data consistency, privacy, management and (language) translation, across Federal/Provincial/Territorial/Indigenous (FPTI) jurisdictions. FPTI data sharing agreements exist for specific types of data; for example, information on the location of farm, size of flock, and number of

affected birds can be shared, but not ancillary data (e.g., farmer self-reported symptoms). There are important examples of data limitations that may pose significant risks, including knowledge around mink farms, making it difficult to link other key data around viral activity among domestic and wild birds.

Vertical lines of communication within agencies are well established, but horizontal information sharing between agencies and FPTI jurisdictions is inconsistent and suffers from gaps. The Public Health Network Council is supported by PHAC and is establishing an FPTI data committee for all areas of human public health. There are multiple formal and informal FPTI networks. Interdepartmental tables are needed to facilitate information exchanges. Chief Medical and Veterinary Officers have strong relations in some regions, whereas in others the connection may need to be strengthened.

Gaps, solutions, priorities

Key knowledge gaps for preventing inter-species viral spillover

- It is questionable whether One Health data systems (e.g., an open repository for Canadian H5Nx genomic sequences from all species) are adequate. Comprehensive and consistent sharing of HPAI-related data across species is an important gap; current approaches are often piecemeal and would benefit from a more open, standardized and responsive strategy. There are novel technologies and data sciences tools (e.g., artificial intelligence) that could be leveraged to anticipate and detect spillovers whilst incorporating key considerations for equity in risk assessments and models.
- There is a need to include other actors and considerations, such as the industry (producer) perspective, including the potential to link compensation with biosecurity on farms. Producers may hesitate to support testing, particularly where different species may be co-located on the same premises, in the absence of clear guidance around testing and reporting.
- Understanding the micro, meso, and macro level impacts of (human) behaviour on spillover risk and interventions may be warranted to fill an important gap in how we mitigate spillover at each of these levels. For example, which interventions are merited at the micro level before spillover occurs? There is a lack of engagement of complementary quantitative and qualitative data to understand behavioural factors at the community level that lead to spillover. Do we understand the behaviour science for spillover/spillback prevention across various contexts (e.g., local communities versus populations within and across countries)? We need to understand the best approaches for specific risks in specific contexts.
- A gap in training and protocols that adopt a One Health approach to investigation and management at the frontlines was also noted. What is the role of community (or citizen) science in addressing these issues and detecting spillover?
- People may be unaware of the risk of spillovers, particularly since the data around drivers of spillover risk remain sparse. We thus have limited knowledge of populations at risk of exposure and magnitude of impact, which will affect vulnerable populations disproportionately.
- There is a deficiency in working collaboratively with communities and two-way knowledge sharing.

- Fundamental gaps in understanding the drivers of an unprecedented number of spillovers to mammals were reiterated, including gaps in the state of evidence related to mammal to human transmission. What is the predominant mode of transmission (e.g., direct contact vs respiratory)?
- How do we understand how we support micro level responses and economic impacts (e.g., food security)?
- Do harvested species pose a food safety issue? What is the traditional and local knowledge base that communities use to make harvesting and food preparation decisions? Who are the specific knowledge holders who need to be involved in specific and tailored ways? How are animal welfare trade-offs made? How do they interact with food security trade-offs?
- What is the status of and process for testing companion animals?
- What is the role of Defence Research and Development Canada (DRDC) and the Department of National Defence (DND) and how can their resources and knowledge link into the main data sources? How do we link in security data in the event of a deliberate spillover (e.g., national security concerns)?

Key gaps in existing and surge capacity for research and implementation

- Public and stakeholder engagement is needed to build and maintain trust such that important information is shared. Data management agreements are needed with stakeholders to maintain that trust as well as privacy and confidentiality. There are COVID-19-related governance and data agreements in place - how can we build on these and progress with policies to prepare and prevent HPAI since resources are already being reallocated? The Global Health Security Initiative in New Zealand was highlighted as an example of broad data sharing using a One Health approach.
- Issues with data collection and the need to develop common definitions and platforms are warranted at national and international levels as the situation evolves to enhance unified and coordinated approaches and interoperability. How do we address barriers against data sharing across fields?
- The lack of indicators about what to measure was also mentioned.
- COVID-19 also underscored the importance of integration of social scientists in public health responses. Social sciences include diverse and strong research communities - engaged in public health but lack inter-connections with each other and with animal health and public health/medical communities. Currently social scientists remain underrepresented and have limited access to key data. Social, economic, and behavioural considerations are not often deemed upstream prevention. Appropriate behavioural, economics, and social science expertise is required to understand multiple dimensions of inequities that influence the feasibility of strategies for spillover risk reduction, and what other supports would be needed to implement them.
- Another clear lesson from COVID-19 was the importance of communicating effectively when situations bear significant uncertainty. Communicating why change (e.g., non-pharmaceutical and pharmaceutical recommendations) is needed requires context- specific social science research. It is important to build credibility and evidence-based knowledge for future situations bearing

uncertainty. Social sciences go beyond communications. What can we answer with survey data versus research data?

How do we integrate a One Health approach and work towards global health security?

- There are diverse and strong research communities across One Health sectors and the former One Health research network, but it is not well connected. There may also be opportunities to change how we fund research from an interdisciplinary approach to achieve One Health. Leadership, training, funding and inclusion underpin viable One Health programs. The gaps in what researchers know are different than policy and program knowledge gaps- means to align research capabilities and priorities were felt to be critical, along with preparedness to actively contribute to global One Health systems.
- There is a disconnect between scientific and policy communities' concept of data and information, other perspectives, and Indigenous and traditional knowledge. Bringing multiple ways of knowing together and do more to bring Indigenous knowledge, especially about animals, into decision making is of great importance.
- Although some federal and provincial tables exist for One Health for specific topics such as antimicrobial resistance, permanent FPTI One Health governance mechanisms and policy frameworks are absent. A One Health lens can also be applied to membership at network tables. FPTI and other BIPOC underserved populations co-planning tables are critical to ensure no groups are left behind; incorporating this perspective can help to address mistrust. Governments do not always have time to build consensus, at the same time, we have to deal with contradictory information, so contributors do not feel ignored. Hence, the importance of actively listening and engaging communities about what is needed (e.g., around country foods), along with the need to ensure co-development of One Health approaches with First Nations, Inuit, and Métis. There are great stories to be told of Indigenous leadership in response to COVID-19. We can also learn from northern and rural area containment programs and initiatives. A One Health investigation protocol for the front lines could be piloted. A decision-making framework that approaches the problem with a broader scope of risks and understandings is important.
- It was recognized that at the international level there are also challenges that contribute to the problem, including whether protocols from the One Health perspective is adequate to inform decisions and spur action. It is clear that, there is a need to strengthen intersectoral data sharing internationally for the prevention of pandemics; yet this is not strongly captured in the Zero Draft of the Pandemic Instrument. We can follow the Quadripartite One Health System model and establish a distributed, interoperable system, rather than a centralized system that is virtually distributed and uses a common language. We can build in a requirement to better reflect One Health as a priority instead of: "It feels like we are advocating from our respective fields." The ability to work outside of an agency mandate is important to achieve One Health. The research and knowledge we have along with gaps within One Health need to be brought together in a comprehensive actionable plan. The World Health Organization (WHO) pandemic instrument is an important opportunity to use a One Health approach, and to incorporate other international

mechanisms already in place such as the Pandemic Influenza Preparedness (PIP) Framework, to avoid duplication of efforts.

- Are data sharing issues a symptom or a cause of lack of One Health integration? Using a One Health model will lead to additional acceptance and uptake and help to gain momentum.
- It was also noted that the environment and climate change had not been discussed at this meeting, and merited attention. The complexities of One Health require tight coordination of many different groups; need to de-silo and include environmental and Indigenous and rural perspectives.
- There is a need to map knowledge and research along with gaps and prioritize actions and leaders for a comprehensive actionable plan that also mitigates the risk of duplication of work. Shared and divergent understandings need to come together within a One Health approach.
- Occupational health bears consideration, given the impact of COVID-19 on certain sectors.
- A comprehensive HPAI research agenda that is One Health focused, with deliverables and timelines is of great value. Such an agenda would need to identify knowledge gaps and quickly respond to research outputs to address them. Rather than a One Health agency, One Health should be embedded in all relevant agencies; but coordination is needed (e.g., working group, secretariat). To connect the silos a One Health research forum may be of benefit.
- How universities recognize knowledge output and the incentives for research are very different for the government; how do we break down these barriers?

Summary: the critical role of collaboration and partnerships for avian influenza science and research

During [B(1] the moderated report back sessions and plenary discussions led by rapporteurs, several overarching impressions were made in evidence. There was a strong sense of generous openness, collegiality, and willingness to collaborate among individuals. Over the course of the proceedings, participants voiced gaps in formal structural frameworks, and a paucity of systemic mechanisms for research collaboration. The point was made that this meeting served as an inception point, and that both broader and deeper discussions are warranted through ongoing dialogue. This could include but is not limited to additional contributors from individual provincial, territorial and Indigenous governments, Indigenous scholars and communities, the security and defense community, the agricultural private sector, non-governmental organizations (NGOs), inter-governmental agencies, global scholars, and international researchers.

The point that human health is interdependent with wildlife and domestic animal health was repeatedly highlighted. Also, wildlife conservation and food security through agricultural biosecurity are critical ends unto themselves, independent of human health concerns. Thus far both the response and research related to the H5Nx HPAI panzootic have depended heavily on wildlife and agricultural animal health agencies across provinces and the federal family, with involvement of extra-mural contributors through CWHC. These sectors have leveraged existing capacity to conduct substantial HPAI surveillance, virus detection,

whole genome sequencing, viral and disease phenotyping, and development of vaccine candidates. This leadership from the animal health sector has benefited the (human) public health sector, enhancing joint risk assessment efforts.

Until now, there was limited involvement of extra-mural, university-based scientists in H5Nx-related research, representing a weakness in Canadian research capacity. This could be attributed to limited engagement with intra-mural efforts, restricted access to data, and/or regulatory restrictions to work with H5Nx viruses despite ample containment level 3 (CL3) capacity across Canadian universities. Both data sharing and the ability to work with domestic H5Nx viruses in existing CL3 laboratories were repeatedly raised across discussion tables as key barriers to research. Formal and informal enablers of extra-intramural collaboration (e.g., H5Nx research forum(s) and network) would also be beneficial, further providing mechanisms through which to operationalize a One Health approach.

Thematic Qualitative Analysis

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Objective

This summary provides an initial qualitative analysis of the working documents from the June 19, 2023 Highly Pathogenic Avian Influenza (HPAI) workshop. It is intended to complement the summary report by yielding insights into and reflection on the workshop's deliberations. While this analysis isn't intended to lead to research or policy recommendations, some specific examples, concepts, and opportunities identified by workshop participants are described.

Identified Themes

7. Research knowledge gaps

Research knowledge gaps were the most frequently discussed theme during the coding of information among participants. Participants acknowledged that there is a "gap in mechanisms to support rapid, open data sharing and integration across sectors [such] that current research structures do not support, far less incentivize, multidisciplinary approaches." These obstacles create a ripple effect leading to weakened efforts to build a robust One Health framework to tackle HPAI, effective surveillance programs, collaboration/coordination among various agencies, and communication and data sharing strategies. Participants built on existing knowledges from previous pandemics (e.g. 2014/2015) in Canada and reiterated some of the gaps that continue to exist. Presently, these gaps include lack of Canada's preparedness, capacity development, and even "basic knowledge for infectious diseases in mainstream science classes in schools on health emergencies". Individual participants and breakout groups noted CL3 containment labs are few and coordination among them is weak, impacting on necessary "platforms, adjuvants and cell lines to develop vaccines to control the spread in animal population". Participants

acknowledged the abundance of CL3 capacity in terms of work on SARS-COV-2 but also stressed the need to expand capacity and provide "approval to work with HPAI viruses [which] remains a crippling challenge" in Canada.

8. Surveillance

Participants discussed current surveillance programs and expressed the need for capacity building and tools to ensure robust surveillance. On the current state of knowledge, participants provided background and context about Canada's efforts to improve wild birds' surveillance. It looked at the Interagency Wild Bird Influenza Survey established in 2005, which initially focused on "live bird surveillance and over time included dead surveillance (conducted by CWHC) [but] has waned and waxed over the years as a function of available funding". Presently, there are also technical limitations regarding commercial serology kits for testing for avian influenza. While surveillance programs have been considered a priority for wild birds, "there is no formal surveillance program for wild and domestic mammals". Participants underscored the need to link across disciplines and sectors to consider both domestic and wild species. Furthermore, agencies must work jointly together and avoid an *ad-hoc*, piecemeal approach to conducting HPAI surveillance: another manifestation of the "collaboration" theme, below.

9. Interspecies transmission

Participants were keen to understand factors operating at the human-animal interface and which promote interspecies transmission. For instance, identifying what "drives the intersection of wild birds and farms" and what "events, barriers, and enablers could drive mammal-to mammal transmissions". These questions demonstrate clear recognition of the considerable complexity of interspecies transmission while focusing on potential intervention points in human-animal systems. Interventions could take the form of surveillance activities or countermeasure programs. This strategy will be possible and effective through "access to diagnostics for local investigations including human surveillance". Further, effective "communication between human health and agricultural organizations would be important to support decision-making around post-exposure for humans". Participants concluded that "long-term, sustainable programmatic funding rather than shorter-term, piecemeal project-based support" would be necessary to reduce inter-species transmission of HPAI.

10. Collaboration

Collaboration was notably interlinked with other themes of "surveillance" and "One Health", and indeed was viewed as critical to them. Cross-disciplinary collaboration specifically was seen as critical to integrating One Health approaches into HPAI decision making. While the importance of the federal, provincial, and territorial agencies was acknowledged "connections with rural and Indigenous communities must be sought in a meaningful way... [towards] prevention, preparedness and response to public health emergencies [which] also benefits greatly from collaborations between intra- and extramural scientists, connecting across sectors". Such collaboration will help build the trust that is currently lacking in terms of key communication and key data sharing strategies. When trust is built over a sustained period between Indigenous communities and key individuals, data-sharing protocols could be

created and strengthened through data-sharing agreements. At the federal through the provincial and territorial levels, communication can be promoted through effective horizontal channels, which is presently “inconsistent and suffers from gaps”. There is a high potential to reduce the effect of agencies working in silos under such circumstances. Through such efforts decision-making processes could better incorporate “existing databases that are not well connected, having been established by different groups for different purposes, and currently [having] no mechanism in place to integrate human and animal data”.

11. One Health

Integrating One Health principles and research in combating HPAI challenges was a prominent theme at the workshop; second only to research gaps. Within the context of One Health participants observed governance, policy, and decision making, and funding (the sub-themes) as the fundamental issues hindering implementation. A key takeaway – clearly related to the previous theme of collaboration – is the need to strengthen “inter-sectoral and multi-disciplinary approaches that include resources and knowledge brokering between government agencies and academics… as well as a bi-directional partnership with Indigenous communities”. Placing such importance on One Health will ensure that momentum is built towards future preparedness against the multiple uncertainties around HPAI. Momentum could be achieved and maintained through “continuity of discussion, training, and embedding One Health requirements with funding proposals.” One breakout group proposed the “Canadian Institute of One Health for Pandemic Preparedness”, to institutionalize strategies for more tangibly advancing a holistic One Health.

APPENDICES

1. Methodology: Thematic Analysis

Thematic analysis is an established qualitative research methodology which permits identification of patterns and themes within textual data by following six steps (Byrne 2021). The initial step involves familiarization with the data: here, the jamboards and presentation notes. Second is the generation of codes, the “standalone and fundamental building blocks” of qualitative analysis (Byrne, 2021 p. 1399) which offers adequate detail for identifying the overall themes. Here, because of the small volume of text codes that were assigned manually in Microsoft Word rather than with qualitative analysis software such as NVivo. Iterative coding allowed discarding of inconsistent codes. Provisional themes were then generated by linking and aggregating codes, with sub-themes identified where relevant information would be lost through aggregation. Even though there are no restrictions on the number of themes, too many themes may lead to an incoherent analysis and too few can deprive us of exploiting the full details of the data (Byrne, 2021). Provisional themes were then refined and connected to provide a comprehensive narrative; the final step. Such narratives can be either illustrative or analytical format; respectively, description of participants’ contribution and relating results to available data or following an interrogative approach about what the participants said and contextualizing the interpretation using available literature (Terry et al., 2017). We used the illustrative format to keep the emphasis on what was

actually said at the workshop. Table 1 describes the total number of instances each code appeared in the working documents. Quotes were selected to illustrate specific attributes of themes and are presented anonymously below. All other information described from the breakout sessions is aggregated.

Table 1. Codes, sub-codes, and the total number of instances each code in the documents analyzed

Codes and sub-codes	Number of code instances (N/n)
Inter-species transmission	N=18
· Spillovers	N=6
Research knowledge gaps	N=29
Risk reduction/assessment	N=7
Pandemic Preparedness	N=4
Integrating One Health	N=24
· Governance	N=9
· Policy and decision	N=10
· Funding	N=8
Surveillance	N=11
· Serology	N=4
· Genomic sequencing	N=5
· Epidemiology	N=4
Pharmaceutical interventions	N=10
· Vaccines	N=6
· Vaccination strategies	N=9
Health intelligence	N=5
· data sharing	N=9
· communication strategies	N=10
Social science	N=2
Collaboration	N=17
· EDI/BIPOC	N=8

Annex 1: Participant List

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Tom Wong	Chief Medical Officer of Public Health	ISC

Annex 2: Background Documents from PHAC & CFIA, including research prioritizations

1. H5N1: Current State of Readiness and Collaborative Response (PDF)
2. HPAIV Interagency Prioritization Exercise Executive Summary (PDF)
3. HPAIV Prioritization Exercise Executive Summary (PDF)

Annex 3: Additional Supporting Material

1. Prevention of zoonotic spillover; https://www.who.int/publications/m/item/prevention-of-zoonotic-spillover
2. Tripartite zoonoses guide; https://www.who.int/initiatives/tripartite-zoonosis-guide
3. Quadripartite One Health Joint Plan of Action; https://apps.who.int/iris/bitstream/handle/10665/363518/9789240059139-eng.pdf?sequence=1&isAllowed=y
4. WOAH A_90SG_8_Technical Item Strategic challenges in the global control of high pathogenicity avian influenza https://www.woah.org/en/document/f_90sg_8_theme-technique/
5. Strengthening the intersectoral work for Influenza at the Human Animal Interface in the Region of the Americas: Technical Questions and Answers, https://www.paho.org/en/documents/strengthening-intersectoral-work-influenza-human-animal-interface-region-americas
6. The changing dynamics of highly pathogenic avian influenza H5N1: Next steps for management & science in North America, https://www.sciencedirect.com/science/article/pii/S0006320723001428?via%3Dihub
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