Managing Avian Flu:
A Science Roadmap and Action Plan
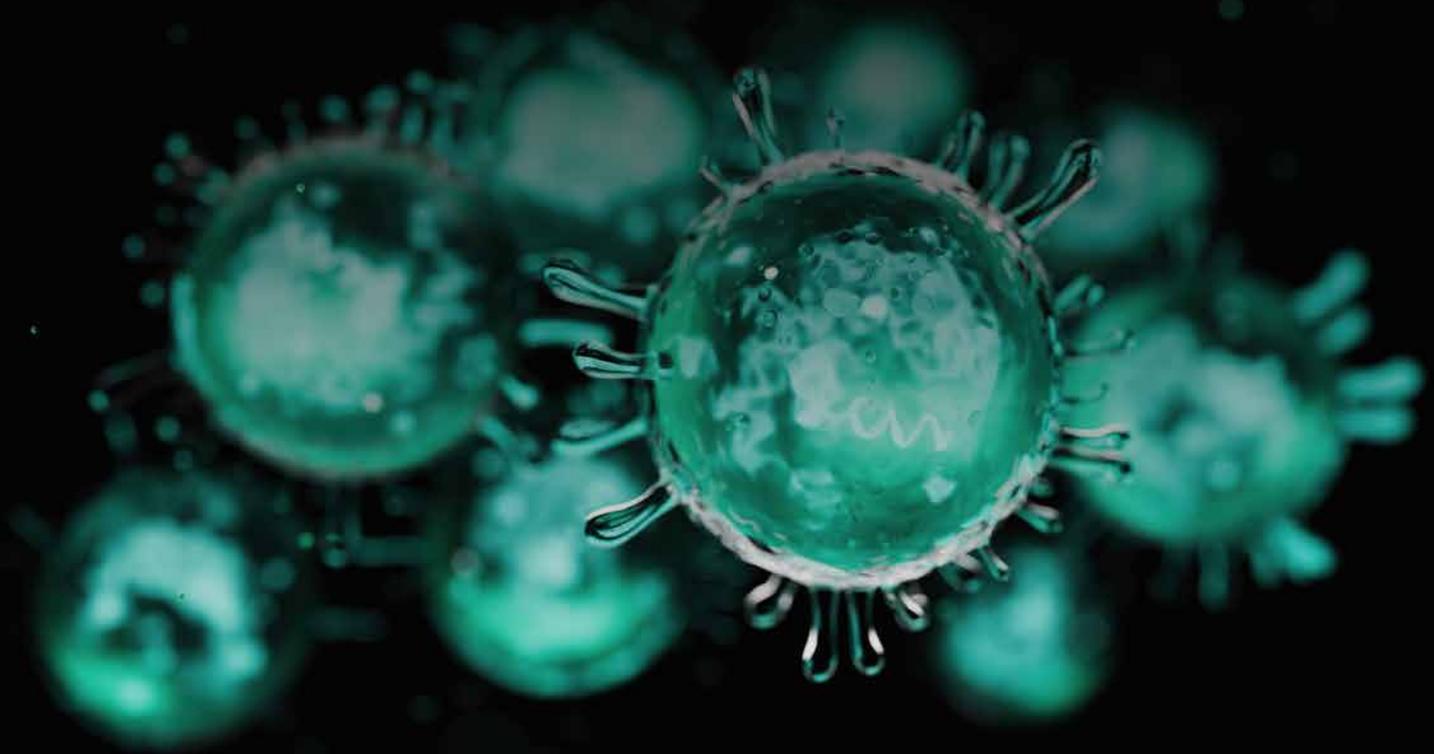
A Report from the Chief Science Advisor of Canada

February 2025

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MANAGING AVIAN FLU: A SCIENCE ROADMAP AND ACTION PLAN

EXECUTIVE SUMMARY

Context

Large-scale outbreaks of highly pathogenic avian influenza are currently spreading across several countries, affecting many animal species beyond birds. The disease, commonly known as avian or bird flu, is caused by the H5N1 virus, which has spread widely among wild birds around the globe since 2020-21, resulting in unprecedented mortality in wild birds and domestic poultry. The current virus strain, clade 2.3.4.4b, differs from the one circulating prior to 2020. It is increasingly spreading beyond wild birds to a wide variety of land and marine mammals, including more recently to dairy cattle in the US. In addition to its devastating effect on the welfare of birds and other animals, there are increasing socioeconomic concerns stemming from the impact of H5N1 on the agrifood sector with consequences on food security and pricing. The detection of the H5N1 virus in hundreds of bird species and over 200 mammals highlights its threat to biodiversity and species at risk.

The new H5N1 virus clade has also demonstrated the ability to spread to humans through contact with infected animals, making it an occupational hazard for farm workers, veterinarians and those handling wild species. The disease presentation in humans includes mild to severe respiratory symptoms and pink eye. So far, there is no evidence of human to human transmission, but the current circulating H5N1 strain has the potential to evolve or reassort (including with other influenza viruses) which could result in a virus capable of widespread infection and severe illness in people with little forewarning.

What is Needed

All influenza viruses that affect people and other mammals were initially derived from avian influenza viruses, necessitating a One Health approach with integrated, unifying actions to balance and optimize the health of people, animals and the environment. Among other, scientific data is urgently needed about where and how the H5N1 virus is spreading (transmission) and on animal and environmental reservoirs of the virus. Basic knowledge of virus biology is essential, including how the virus evolves and how it interacts with different hosts to cause infections that range from mild to fatal, depending on the species (pathogenicity). Host characteristics influencing susceptibility to infection and immunity to the virus need to be clarified and target organs must be identified. Methods should be elaborated for effective environmental monitoring and detection in many species and contexts (monitoring and diagnostics) as well as preventative infection control approaches. Last, but not least, effective vaccines and treatments that can be deployed at-scale must be developed to prevent and control outbreaks in animals and humans.

Science Roadmap and Action Plan

It is with this in mind that an integrated science roadmap and action plan (the Roadmap) is being proposed. Key principles underpin the Roadmap recommendations and deliverables. They include evidence informed decisions, open and secure science, equity and trust, harm reduction and respectful community engagement.

Given the progression of H5N1 within and across species, it is suggested that priority efforts focus on advancing H5N1 fundamental knowledge, data and medical countermeasures. Similar approaches can be ultimately extended to other avian flu viruses, such as highly pathogenic H7.

SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

CROSS-CUTTING OBJECTIVES

- Rapid avian flu virus detection for timely response and risk assessment
- Continued protection of agrifood, wildlife and eco-systems
- Prevention, treatment and management of avian flu infection and illness in animals and people

Pathway Goals	Recommended Priority Scientific Actions
Pathway #1 **Monitor Avian Flu Virus Spread and Understand the Virus and its Threats**	1. Data and situational awareness 2. Risk assessment 3. Pathogenicity and virus biology 4. Modes of transmission
Pathway #2 **Mitigate Avian Flu Impact on the Environment, Animals and Humans**	5. Strengthen virus detection and monitoring 6. Limit animal spread 7. Reduce spillover and infection in people
Pathway #3 **Enhance Avian Flu Pandemic Prevention, Readiness and Response**	8. Deploy effective medical countermeasures for people and animals 9. Adopt prevention and preparedness strategies 10. Protect vulnerable populations and promote occupational health and safety 11. Minimize impact on society
Pathway #4 **Strengthen Supportive Platforms and Systems**	12. Effective monitoring systems, laboratory and testing capacity 13. Integrated one health partnerships, networks and governance models leveraging current capabilities 14. Open and secure science and data platforms

Conclusion

The ongoing spread of H5N1 to a large number of wild, farmed and companion animals must be urgently addressed and requires focused and coordinated research, data collection and tools development. H5N1 is considered to be among the most pathogenic of the avian flu viruses with associated high mortality rates in birds and mammals, including humans. Even though the risk of illness from H5N1 infection for the general population is currently characterized as low with little to no evidence of transmission between people, the increased spread provides a potential for the virus to evolve or reassort into one that is far more efficient at infecting people and causing a new pandemic. It is therefore essential to monitor and limit virus spread and to prepare effective medical countermeasures to prevent and manage disease in animals and humans alike.

The *Science Roadmap and Action Plan for Avian Flu Management serves as a guide for collaborative avian flu* scientific action to optimize the interconnected health and well-being of humans, animals and the environment. It addresses the four essential elements that underpin effective emergency preparedness and response, namely data; fundamental knowledge of virus-host interactions; medical countermeasures tools and products; and, methods and platforms, including effective communication. Advancing the proposed priorities will require collaboration, coordination and data sharing among many federal government departments, as well as with sub-national governments and academic and industry partners. Addressing the evidence gaps and developing effective medical countermeasures is instrumental to enhancing our prevention efforts and our state of readiness to protect economic security and well being.

SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

I. CURRENT SITUATION AND CONTEXT

There is currently a large scale, global, *panzootic* (affecting many different animals) outbreak of highly pathogenic avian influenza caused by the H5N1 virus, commonly known as avian or bird flu[1]. Panzootic H5N1 has spread widely among wild birds around the globe since 2020-21 with unprecedented numbers of deaths in wild birds and domestic poultry. Panzootic H5N1 virus clade 2.3.4.4b is different from previous circulating avian flu prior to 2020. It is increasingly spreading beyond wild birds to a wide variety of land and marine mammals[1], including more recently to dairy cattle in the U.S.[2]. In addition to the devastating impact of avian flu on the welfare of birds and other animals, there are serious concerns regarding potential repercussions on the agrifood sector and food pricing as well as negative environmental effects, including on biodiversity and species at risk.

Currently, the risk of H5N1 infection for the general population is characterized as low with little to no evidence of transmission between people[3]. Direct exposure to H5N1 infected animals, as well as contaminated environments, pose the greatest risk for human H5N1 infection. Precautions to minimize or avoid exposure and spread are recommended.

Avian influenza is not new[4,5]. Prior to the relatively recent emergence of H5N1, large scale poultry outbreaks of virulent H7 subtype avian flu, known early on as "fowl plague", were documented from the turn of the 19th century,[4,5]. H7 continues to circulate. In 2024, Australia experienced multiple avian influenza poultry outbreaks, specifically involving H7N3, H7N9, and H7N8 subtypes[6]. H7 has also been associated with human infections, for example, resulting in over 600 deaths between 2013 to 2017 in the People's Republic of China; cases stopped after a poultry vaccination program was introduced[4]. There is the potential for the current circulating H5N1 strain of avian flu to evolve or reassort (including with H7 or another influenza virus) into a virus capable of widespread infection and severe illness in people, with little forewarning.

II. WHY A FEDERAL SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU?

Avian flu outbreak surveillance, preparedness and response requires coordination and harmonization across a large number of Canadian federal departments and agencies. Key organizations include the Canadian Food Inspection Agency with the lead role in responding to animal influenza outbreaks. Partners include Environment and Climate Change Canada who is responsible for conservation and protection of migratory birds, Parks Canada responds to detections in wildlife in national parks, Fisheries and Oceans helps with sample collection and testing of wild marine mammals, and Agriculture and Agrifood Canada provides support to industry for the impacts of outbreak response.

The Public Health Agency of Canada is responsible for addressing human pandemic influenza preparedness and response, while Health Canada ensures regulatory preparedness and plays a role in assessing food safety. Indigenous Services Canada supports preparedness and response efforts in First Nations on reserve and for Inuit. Public Safety operates the Government Operations Centre for emergency events of national significance. Innovation, Science and Economic Development Canada (ISED) supports innovation through science and technology, notably through *Canada's Biomanufacturing and Life Sciences Strategy*[7]. Lastly, Health Emergency Readiness Canada is a recently created special operating agency within ISED, supported by Health Canada and the Public Health Agency of Canada. It is focused on ensuring that Canada can respond to health emergencies by supporting the development and production of medical countermeasures (MCMs), including vaccines, therapeutics, and diagnostic tools. Annex 1 provides an overview of federal organizations implicated in avian flu outbreaks, adapted from the *North American Plan For Animal and Pandemic Influenza*.

A key lesson from the recent COVID-19 pandemic is the importance of science prioritization, science advice coordination and a whole-of-government approach to ensure availability of evidence for decision making and emergency management. Given the unusual scale and impact of avian flu in birds and an increasing concern about the rising number of species affected globally, in May 2024, the Chief Science Advisor (CSA) convened Canadian federal organizations involved in emergency preparedness and management activities related to the current animal outbreak of avian flu. The meeting was arranged in consultation with the Canadian Food Inspection Agency and the Public Health Agency of Canada to focus on science needs and knowledge gaps for mitigating the spread and impact of avian flu. All participants agreed on the need for a coordinated scientific research approach to avian flu in Canada to fill knowledge gaps and support science-informed policies and public communication.

The *Science Roadmap and Action Plan for Avian Flu Management* will support evidence-informed, concerted action for early detection and containment of avian flu in Canada. This proposed approach supports the objective of Canada's Federal Policy for Emergency Management to "*promote an integrated and resilient whole-of-government approach to emergency management planning, which includes better prevention/mitigation of, preparedness for, response to, and recovery from emergencies*". The scientific updates and deliberations from the May 2024 meeting noted above, recent scientific literature up to December 2024, and expert input inform this report. The roadmap relates to flu of avian origin, including highly pathogenic avian flu viruses (H5 and H7), as well as other emergent strains. Given the present state of H5N1 spread, priority action should be on H5N1.

III. WHAT WE KNOW ABOUT THE CURRENT H5N1 OUTBREAK

During 2020, H5N1 clade 2.3.4.4b viruses evolved in Asia and Europe. In late 2021, these viruses crossed to Canada and the United States, spreading through migratory wild birds, and subsequently spread to South America in October 2022[8]. The saliva, nasal secretions, feathers litter, and feces of infected birds, as well as contaminated surfaces and water, are sources of infection for other birds and animals who can, in turn, spread it further[9,10]. Human influenza viruses are predominately transmitted through the respiratory route, whereas avian influenza viruses are spread between birds primarily through direct contact[11,12]. Influenza is a well-studied virus which has developed devastating strains causing global pandemics in the past, such as the 1918-20 avian influenza virus H1N1 also known as the Spanish Flu, which killed more than 50 million people worldwide, including nearly 50,000 Canadians[13].

Avian Flu Affects Many Wild and Domestic Birds and Mammals

The United Nations recently reported that avian flu has led to the death of over 300 million birds worldwide affecting 108 countries and five continents. Avian flu is a significant threat to biodiversity[14], for wild bird populations (decimating colonies of endangered species, reaching critical areas) and mammals with mass mortality events[15].

Since 2022, mass die-offs have occurred in a broad range of infected wild bird species as well as poultry on farms which undergo strict protocols to stamp out all infection to keep the food supply as safe as possible. The USDA APHIS has reported H5N1 virus in more than 200 mammals, including domestic cats, dogs, wild and farmed foxes, farmed mink and alpacas, as well as marine animals, such as seals[16]. While some ducks and other birds act as reservoirs of infection, the H5N1 virus is lethal in many birds and scavenging mammals that have ingested contaminated carcasses. The current outbreak of avian flu has resulted in the deaths of over 11 million birds in Canada alone, either from infection or through culling to stop the spread[17]. Cats have also had a high death rate (50%) after consuming raw milk from H5N1 infected dairy cows in the US[18].

In October 2024, an H5N1 virus infection was confirmed in a pig in a backyard farm in the US for the first time[19]. Pigs are a particular concern as they are susceptible to influenza viruses spread from other pigs, humans and birds. Reassortment or avian flu viral gene swapping in pigs likely led to the 2009 influenza A (H1N1) pandemic. By the end of 2024, H5N1 was detected in poultry in almost all US states and in dairy cattle across more than 14 states. To date, there have been no dairy cattle or swine cases of H5N1 reported in Canada. With the fall bird migration, in November 2024, there were rising active avian flu infected premises of bird flocks in Canada, the majority in British Columbia, and western Canada[17].

Food Safety

Research studies show that pasteurization inactivates H5N1 virus[20]. All retail milk sampling and testing for avian flu in Canada to-date have been negative[21]. Raw milk is never safe to consume given the risk of many foodborne illnesses and it is against the law to buy and sell raw milk in Canada[22]. A recent US Department of Agriculture study showed that avian flu virus is inactivated using recommended cooking procedures (above 63C) in ground beef[23]. Evidence also demonstrates that standard pasteurization methods inactivate influenza viruses in milk[24]. There is no evidence to suggest that the consumption of pasteurized milk or fully cooked poultry, beef, game meat, organs or eggs can transmit influenza virus to humans.

Human Cases are Slowly Rising

Globally, from 2003 to September 2024, 904 cases of human infection with H5N1 virus were reported from 24 countries. Of these 904 cases, 464 were fatal (case fatality rate of 51%)[25] which could be an overestimate given mild or asymptomatic cases often go unreported.

There were about 65 sporadic human avian flu cases reported in the US during the 2024 outbreak[26] and 76 cases worldwide, mostly farm workers[14]. Note that before 2024, only one human H5N1 case had been reported in the US[27]. At the time this report was written, almost all of the US human cases reported originated from close contact with infected poultry or cattle[26]. There was one case of life-threatening H5N1 illness in Louisiana related to exposure from backyard birds (a D1.1 genotype also detected in wild birds and poultry in the United States)[28]. The majority of the recent US cases had clinically mild illness, most with conjunctivitis and a third with respiratory illness; early detection and antiviral treatment may have played a role[27]. Two confirmed H5N1 cases had no identified route of exposure in 2024. One was an adult Missouri resident with a history of severe underlying clinical illness[29] and the second was a young child from California with a confirmed H5N1 clade 2.3.4.4b infection consistent with genotype B3.13 viruses detected in the US in humans, dairy cattle and poultry[30]. A recent analysis of exposed dairy farm workers in two US states reported that 7% had serologic evidence of infection with H5N1[31] indicating it is likely people have been infected without being aware. While human avian flu cases are slowing rising, there is no evidence to-date of sustained human-to-human transmission[3].

Canada had its first human case of avian influenza in mid-November 2024 reported in British Columbia (BC), with a severe clinical presentation. The 13-year-old girl who was previously healthy with a history of mild asthma and an elevated body mass index was hospitalized in critical condition with acute respiratory distress[32]. The source of exposure remains unknown despite extensive investigation[33]. The viral genome sequence uploaded to GISAID[34] confirmed H5N1 clade 2.3.4.4.b D1.1 which is related to the same strain circulating in wild birds and poultry in BC[35]. Two rare mutations[32] were identified that could signify a concerning shift to a potential preference for a2,6 sialic acid receptors found in mammals, versus the a2,3 sialic acid receptors predominantly in birds[36]. In this case, as in the other human cases, there was no evidence of human-to-human transmission after extensive testing of possible contacts[32].

The World Health Organization considers avian flu H5Nx viruses of the Orthomyxoviridae family, including H5N1, to be priority pathogens capable of causing a pandemic. Avian flu viruses are classified as either high (H5 and H7) or low pathogenicity (LPAI) to poultry and are important to monitor. H5N1 could rapidly mutate and evolve to a strain that is more easily spread between people. Seasonal human influenza viruses (e.g. H1, H2 and H3) that circulate every year could mix or reassort with H5N1 and lead to a serious form of human flu; with little prior population immunity such a flu strain could have devastating consequences, including high death rates and increased hospitalizations.

IV. WHAT WE KNOW ABOUT THE H5N1 VIRUS

Virus Biology

There are two distinct types of influenza viruses that cause annual seasonal influenza outbreaks in humans - A and B[37,38]. H5N1 avian flu is a highly pathogenic influenza A virus. Influenza A viruses are further classified into subtypes based on 2 surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA); there are 16 HA and 9 NA subtypes circulating in birds[39]. Subtypes are named by combining the H and N numbers – e.g., A(H1N1), A(H3N2), and so on[40]. Several influenza A subtypes have previously caused human epidemics - H1, H2, H3 and N1 and N2[41]. The first known human infections of H5N1 were identified in 1997 (18 cases with 6 fatalities in Hong Kong)[42]. The two surface glycoproteins – HA and NA – play balanced, complimentary roles in the life cycle of the flu virus. HA and NA bind to host cell receptors containing sialic acid residues. HA initiates the entry of the virus into the host cell and NA helps new virus bud from infected host cells, after it has replicated[43].

Characteristics of both the H5N1 virus and the host animal influence avian flu infection dynamics. The current H5N1 clade 2.3.4.4b circulating globally has resulted in high death rates in wild birds and poultry as the virus preferentially binds to abundant a2,3-linked sialic acid receptors in the respiratory and intestinal tracts of waterfowl and poultry[44]. With mutations in the HA and polymerase subunits that improve the ability to enter the host cells and to replicate, the current circulating H5N1 virus has a wide host range with cross species infection in wildlife and domestic animals[37]. There is evidence of a2,3 receptors in the mammary glands of dairy cattle which could explain the infection and replication in mammary glands of cattle and the unprecedented outbreak in dairy cattle in the US[45], which is thought to primarily transmit cow-to-cow through using the same milking devices.

One of the main factors limiting transmission to humans is receptor binding. The HA of human flu viruses have a strong preference for a2,6 receptors found on human cells, while avian flu virus HA prefer a2,3 receptors found on avian epithelia[39]. However, avian preferred a2,3 receptors can be found in the human lower respiratory tract and in the human eye, whereas human a2,6 receptors are more plentiful in the human upper respiratory tract[46]. At least one study has shown that human gut tissues express SA receptors with avian flu preferred a2,3 linkages[47].

H5N1 is considered to be among the most pathogenic of the avian flu viruses with associated high mortality rates in birds and mammals, including humans[37]. The H5N1 virus could adapt to infect people more easily and to spread among human populations through mutations, such as in the polymerase enzyme needed to replicate the virus or in the HA portion so it could attach more easily to human cells[48]. Evolving mutations in HA and NA can also lead to "antigenic drift and shift" rendering vaccines and anti-virals less effective[49]. Of concern is a recent study using lab-based structural analysis and binding assays which showed that a single mutation could switch bovine H5 HA to be receptive to human-type receptors[50]. Cats infected by H5N1 have showed infection in multiple organs and widespread co-expression of sialic acid a-2,6 and a-2,3 receptors, suggesting cats could also serve as mixing vessels[51], similar to what has been observed in swine[52].

Animal Infection

As noted earlier in the text, most of the currently circulating H5N1 viruses described since 2020 belong to clade 2.3.4.4b[15]. Since 2022, H5N1 has been detected in more than 200 mammals, including dairy cattle in the US[16,26]. H5N1 is impacting a greater and ever-increasing number of mammal species than seen with previous circulating strains of H5N1 prior to 2020 and has proved capable of leading to massive deaths (including of more than 20,000 South American sea lions), raising concern for species at risk[53]. The current panzootic H5N1 clade 2.3.4.4b has expanded to new geographic regions and continents, including to North and South America, and recently found in multiple avian species and two seal species the Antarctic Region[54] as well as seals near Resolute Bay, Nunavut[55].

It is likely that close contact with and eating infected birds is the most common source of infection for mammals, with H5N1 infection disproportionately affecting scavenging and carnivorous animals[53]. Avian reservoirs, such as aquatic bird species, maintain H5N1 virus and transmit to other birds, poultry, swine, fur animals and other mammals[56]. Stressors related to ecosystem changes, and intensified farming practices may be contributing to the vulnerability of a wider array of animals to avian flu. Symptoms of H5N1 infection in mammals reportedly include runny nose, high fever, respiratory distress, hemorrhage, and neurological symptoms[37]. H5N1 infection can lead to both neurologic and/or respiratory effects in mammals, as seen for example in tigers, mink, sea lions, among others, suggesting an ability to invade neural tissue (neurotropism) in mammals, similar to birds[53]. Mammal-to-mammal transmission of H5N1 may have occurred, for example in American sea lions, tigers and farmed minks, and warrants further investigation[53]. A ferret study showed that a recent mammal H5N1 avian flu strain and an H5N1 virus strain from an infected Texas dairy worker had low, but increased ability to transmit by air compared to older H5N1 strains[57].

Importantly, prevention against an avian flu pandemic includes reducing spillover of infection within and between animals and people which requires characterization of the virus and ongoing close monitoring of wildlife as well as commercial farms[58]. Furthermore, mutations in the current circulating H5N1 virus are aligned with an increased risk of human infection[56] emphasizing the importance of biosecurity measures to contain H5N1 viral spread and the need to assess ongoing genetic changes in the virus[58].

Human Infection

Even though the current H5N1 outbreak is a panzootic event primarily affecting animals, sporadic human cases have been slowly increasing since 2021[26]. Contact with sick poultry is a major source of human infection. In the recent H5N1 outbreak in the US, close contact with infected dairy cattle has been linked to more than half of the approximately 60 sporadic human cases. The 2024 human cases show no evidence to-date of sustained human-to-human transmission of H5N1[3], yet limited human-to-human spread cannot be entirely ruled out for cases where no source of exposure was identified.

As described above, the distribution of receptors in the human upper and lower respiratory tract may help explain why humans are not readily infected by H5N1, as the lungs are not as accessible to airborne virus; when avian flu strains do infect the human lung, acute respiratory distress and a severe and rapidly progressive pneumonia may result with high case fatality rates[41]. The a2,3-linked sialic acid receptors, present in the lower respiratory tract of humans[39,41,46] are also present on the conjunctiva of the eye[59], likely explaining the recent human H5N1 cases with only ocular involvement. The lack of a2,3-linked sialic acid receptors in the upper respiratory tract and tissues surrounding the eye explains why these infections don't spread beyond the eye, despite the tear ducts being contiguous with the respiratory tract.

A response to a pathogen can vary widely and is influenced by variable characteristics of the virus and the host (i.e. animal or person infected). The virus biology and pathogenicity as well as the site of infection, route and scale of exposure, virulence, and transmissibility influence the degree of illness[39]. Host characteristics include degree of previous exposure, and demographic factors, such as age, underlying illness, and obesity[60]. Understanding the immune response and susceptibility to flu infection and severity of illness is complex. The first influenza virus infection or "immune imprinting", influences subsequent infections and vaccinations as well as "immune memory"[61]. H1N1 and H5N1 viruses share the same neuraminidase subtype, N1. There is evidence that H1N1 neuraminidase antibodies cross-react with H5N1 viruses[62]. A recent serum study showed high titers of NA-inhibiting antibodies to clade 2.3.4.4b in 97% of serum samples collected in 2020 while low titers were found before 2009 H1N1 exposure, suggesting that there may be some existing protective immunity for people previously exposed to, or vaccinated for H1N1, such as from the 2009 H1N1 outbreak[63],[42]. Earlier data have shown that children and young adults may be more susceptible than other age groups to severe illness from an H5N1 infection[64], which could be related to a lack of previous exposure to N1. Ongoing epidemiological regional assessments can provide insight into risk assessment and response as the H5N1 clade 2.3.4.4b virus evolves[65].

Medical Countermeasures for People

Influenza viruses, including H5N1, continually change, and are "predictably unpredictable". H5N1 virus mutations over time can affect the severity of illness, how easily the virus spreads within and between animals and humans and the effectiveness of medical countermeasures used to diagnose and treat and infection – that is, vaccines, therapeutics and tests. Our ability to fight H5N1 influenza is currently limited.

Vaccines

The constantly evolving nature of influenza viruses requires frequent reformulation of influenza vaccines[49],[66]. As of February 2024, there were three H5N1 clade 2.3.4.4b candidate vaccine viruses (CVV) listed by the World Health Organization[67]. Canada has agreements with several national and international vaccine manufacturers and under these agreements, the pandemic influenza vaccine production process would be initiated in response to a pandemic influenza declaration by the World Health Organization[68]. However, time would be needed to tailor the vaccine to a specific virulent pandemic strain and production technology capacity would be required to scale-up manufacturing with logistical capabilities in place to distribute them. Some countries, such as the US, have stockpiled prepandemic CVV[69], as they may offer partial protection. Different vaccine platforms merit investigation as well as expanded manufacturing capacity along with talent and supportive skills. There is a limited ability for making avian flu egg-based vaccines without impeding seasonal influenza vaccine production and few of these facilities reside in Canada. It is worth noting that there is a global egg shortage[70]. Other platforms, including cell-based vaccines, recombinant and mRNA vaccines hold promise for avian influenza vaccines[42].

Health Canada has authorized three pandemic influenza vaccines that can be updated to counter new strains: Arepanrix and Foclivia (developed using H5N1) and Panenza (developed using H1N1). As of December 2024, one vaccine targeting the updated H5N1 strain was under review[71].

Antivirals

There have been four classes of antivirals approved for pandemic or seasonal flu. These include adamantanes (amantadine, rimantadine), nucleoside analogues (favipiravir), neuraminidase inhibitors (oseltamivir, zanamivir, peramivir, laninamivir), and cap-dependent endonuclease (CEN) inhibitors (baloxavir marboxil – BXM)[38,56]. Adamantanes are not recommended as a monotherapy for avian flu due to resistance[56,72]. At least one case of H5N1 drug resistance to oseltamivir known as Tamiflu has been reported; drug resistance in H5N1 isolates from neuraminidase treated patients should be monitored[73]. There are also small molecule inhibitors which do not target the neuraminidase or polymerase protein approved in some countries and studies would be required to determine effectiveness for avian flu. Monoclonal antibodies (mAbs) are another treatment possibility and an area of preclinical development[56]. New flu antivirals are also in development[74].

Antivirals have been approved in Canada for the treatment of seasonal flu, while there are no antivirals approved by Health Canada specifically targeting the treatment or prophylaxis of avian H5 influenza. Off-label use of these drugs for avian H5 influenza is regulated at the provincial and territorial levels. Scientific research on available and upcoming antivirals is important for preparedness, and, as above, there remain uncertainties about the efficacy of existing therapeutics to treat H5N1 illness[42]. To illustrate, changes in N1 subtype viruses could reduce oseltamivir (Tamiflu) susceptibility, raising concern for the emergence of antiviral-resistant variants and the possibility of similar resistance developing for other antiviral drugs.

Tests

Rapid detection of avian flu is essential for overall situational awareness to inform response, as well as for the timely and appropriate treatment. Antivirals are important treatments for individuals infected or exposed to H5N1, but timely and accurate testing is essential so antivirals can be started as soon as possible; delay reduces effectiveness. A recent review of detection techniques for H5N1 described serological, immunological, molecular biology, genetic and biosensor technology with varying associated sensitivity and specificity[75]. While there are excellent laboratory-based tests that can distinguish H5N1, including assays like ELISA and RT-PCR, rapid tests that can be used on site (in homes, on farms, in the field, etc.) are lacking.

Health Canada has received no applications for rapid tests related to avian flu, and the currently licensed influenza tests cannot distinguish between infection with seasonal influenza or novel influenza A.

Medical Countermeasures for Animals

There is no treatment for H5N1 virus in animals and sick cows typically recover within 2 weeks[76]. The mass culling of infected poultry and biosecurity measures are the two main control strategies to prevent and reduce spread of H5N1 in animals[77], each with economic burden and mental health impact.

While the World Organization for Animal Health has recommended vaccination as part of an avian flu control measure strategy, vaccination of animals remains controversial[78]. In addition to fear of international trade restriction, concerns include that animal vaccination against avian flu could hide subclinical infections or lead to more virulent avian flu virus strains through recombination and genetic assortment with circulating field strains[78]. However, some countries vaccinate poultry flocks against avian flu, including China, Hong Kong, Indonesia, Mexico, Vietnam and France[79]. A recent systematic review demonstrated vaccine efficacy in poultry against avian flu mortality ranging from 78% to 97%[77]. Like the US, Canada does not currently vaccinate commercial livestock or poultry against avian flu and is currently exploring the use of vaccination as an additional tool. For example, Canada has a Highly Pathogenic Avian Influenza Vaccination Task Force examining the development and implementation of vaccination for avian flu in Canada and there are two H5N1 vaccine candidates for use in dairy cows in field trials underway in the US[80,81].

V. A ONE HEALTH APPROACH

The evolution of avian flu and the related degree of harm it can cause to animal species and humans is influenced by interactions within and between animals, humans and ecosystems. A long view to limit the impact of avian flu on animal, human and environmental health requires taking a One Health approach supporting the Quadripartite One Health Joint Plan of Action (2022-2026)[82]. One Health is described as "An integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent".

Lessons from the COVID-19 global pandemic illustrate the complexity of actions required to promote and protect human health during a global pandemic. Layering on animal and environmental health adds even more complexity, considering spillover of infection at the margins, harm to animals, ecosystems, biodiversity and species at risk, as well as environmental stressors. Key areas requiring research and action are at the intersecting margins of human, animal, and environmental health; examples are described in Table 1.

Table 1: One Health Approach and Avian Influenza

Human/Environment Margin	Human/Animal Margin	Animal/Environment Margin
Human activity creating environmental stressors	Avian flu virus transmission within and between wild and domestic animals	Environmental stressors influencing animal avian flu virus genomic evolution
Wildlife health and welfare	Animal to human and human to animal transmission	Avian flu infection impacts on ecosystems, biodiversity, and species at risk
Environmental contamination as reservoirs of human avian flu infection	Medical countermeasures for people and animals	Animal and environmental avian flu viral contamination as reservoirs of animal avian flu infection
Wastewater sampling	Resilient health systems	

This composite landscape requires multidisciplinary and multisectoral approaches with integrated systems, as well as effective governance models for timely information sharing, and adaptive, collaborative actions. An effective One Health approach demands early and strong multisectoral coordination and collaboration between public health and animal sectors, with clear lines of responsibility[27].

VI. ENHANCING READINESS THROUGH SCIENCE AND RESEARCH

Scientific evidence is required to make effective decisions for limiting spread and preventing or treating illness and efficiently mitigating economic impact. An integrated One Health approach requires aligning research activities to address gaps in rapid detection; continuing to protect agrifood, ecosystems and wildlife; and preventing, treating and managing avian flu in animals and people.

At present, many knowledge gaps need to be addressed to enhance prevention and response to avian flu outbreaks. For example, knowledge of the modes by which the H5N1 virus is transmitted within and across species is incomplete. Similarly, potential animal and environmental reservoirs of infection remain uncertain. Much also needs to be elucidated with respect to basic virus biology and pathogenicity, meaning how infection leads to disease of varying severity in different species.

Additionally, host characteristics that modulate susceptibility to infection and disease severity including immunity conferred by prior infection or vaccination to other avian flu viruses needs to be better understood. On the other hand, controlling infection and managing outbreaks requires the development of medical and non-medical interventions including rapid tests, effective vaccines and therapies as well as evidence-informed protective behaviours and infection control measures.

Table 2 below provides an overview of the key knowledge needs as well as science and data gaps within each one that need to be prioritized to enhance preparedness and response to avian flu outbreaks and epidemics. Given the current context, focus should be on H5N1. Ultimately a similar approach can be adopted to manage other avian flu viruses and strains over time.

Table 2: Key Knowledge Needs and Priority Gaps*

H5N1 is the current priority, eventually considering H7, as well as other emergent subtypes and strains

Key Knowledge Need	Priority Gap
1. Transmission pathways	• Predominant mode(s) and relative contribution of transmission between and across animal species e.g., close contact with an infected host, contaminated environments, scavenged meat, airborne, surface contact, bodily fluids, waterborne, reservoirs, etc. and which animal species require more focussed surveillance • Virus half-life on surfaces, biologic samples, air, etc., the importance of which depending on the mode of transmission being addressed
2. Virus Biology and Pathogenicity	• Evolving H5N1 biology and genomics, selection pressures • Viability and pathogenicity of potential reassortants (e.g. mixing of seasonal flu with avian flu strains to develop a new human strain) • Host-pathogen interactions that can determine susceptibility and pathogenicity beyond sequence-based analysis • How the virus causes disease - infective dose, permissive factors, viral evolution
3. Rapid detection	• Accurate and rapidly accessible PCR/molecular tests for both diagnosis and surveillance • Affordable, highly sensitive, point of care rapid tests that are deployable in the community • Field and laboratory monitoring for situational awareness data collection
4. Host Characterization	• Extent of infection and magnitude of impact on wild animals, including animals hunted for food, e.g., through host susceptibility testing • Animal host characteristics that increase susceptibility to avian flu infection • Host susceptibility testing • How the virus enters the host, receptor locations in animals and humans and tissue distribution • Clinical presentation and prognosis
5. Immunity and Immunology	• Pre-existing immunity from previous exposure to other influenza viruses including the 2009 H1N1 outbreak and seasonal influenza, particularly the N-1 subtype • Understanding immune response and immunopathology to evolving and reassortment strains • Tests to measure H5N1 antibodies
6. Infection Prevention and Control	• Preventive and innovative interventions and biosecurity measures where animals are kept and transported to reduce virus exposure, e.g. ventilation, filtration, sterilization, personal protective equipment. • Methods of humane depopulation • Vaccination strategies
7. Tools and Medical Countermeasures	• Focused research and development for effective, targeted animal and human vaccines • Therapeutics, antivirals, diagnostics and vaccines for animals and humans • Integrated systems and platforms for expanded surveillance to support early detection • Manufacturing at scale for cross-cutting access to medical countermeasures.
8. Socio-behavioural and Risk Communication	• Effective protective behaviour and biosecurity practices in physical environments. • Effectively targeted risk communication and approaches to reduce infection and protect livelihoods

VII. SCIENCE ROADMAP AND ACTION PLAN FOR AVIAN FLU MANAGEMENT

The *Science Roadmap and Action Plan for Avian Flu Management* (the Roadmap) is meant to serve as a guide for an integrated and multidisciplinary approach to avian flu research and development in Canada. A One Health approach is recommended. The Roadmap and its priority actions should be regularly reviewed as the situation evolves, especially in the event of sustained H5N1 human-to-human transmission.

The Roadmap consists of three cross-cutting, horizontal objectives, five principles, and four pathway goals with related priority scientific actions. It calls for cross-sectoral collaboration and coordination, including at national and international levels.

CROSS-CUTTING OBJECTIVES

1. Rapid avian flu virus detection for timely response and effective risk assessment
2. Protection of agrifood safety, eco-systems, and wildlife health
3. Prevention, treatment and management of H5N1 infection and illness in animals and people

PRINCIPLES

1. Evidence-informed decision-making
2. Open and secure science, research and data
3. Trust, excellence and equity
4. Societal harm reduction
5. Respectful engagement and collaboration with at-risk communities

PATHWAY GOALS

The Roadmap follows three pathway goals to help achieve the target outcomes, each with associated priority scientific actions, currently at various stages of development:

1. Monitoring avian flu virus spread and understand the virus and its threats
2. Mitigating avian flu impact on the environment, animals and humans
3. Enhancing avian flu pandemic prevention, readiness and response.

To be successful, the *Science Roadmap and Action Plan for Avian Flu Management* must be accompanied by actions in the fourth pathway, "Strengthen supportive platforms and systems" with stable funding mechanisms that enable integrated approaches and collaborations.

Table 3: At a Glance - Science Roadmap and Action Plan for Avian Flu Management

Science Roadmap and Action Plan for Avian Flu Management	
Cross-Cutting Objectives	
• Rapid avian flu virus detection for timely response and risk assessment • Continued protection of agrifood, wildlife and eco-systems • Prevention, treatment and management of avian flu infection and illness in animals and people	
Pathway Goals	**Recommended Priority Scientific Actions**
Pathway #1 **Monitor Avian Flu Virus Spread and Understand the Virus and its Threats**	1. Data and situational awareness 2. Risk assessment 3. Pathogenicity and virus biology 4. Modes of transmission
Pathway #2 **Mitigate Avian Flu Impact on the Environment, Animals and Humans**	5. Strengthen virus detection and monitoring 6. Limit animal spread 7. Reduce spillover and infection in people
Pathway #3 **Enhance Avian Flu Pandemic Prevention, Readiness and Response**	8. Deploy effective medical countermeasures for people and animals 9. Adopt prevention and preparedness strategies 10. Protect vulnerable populations and promote occupational health and safety 11. Minimize impact on society
Pathway #4 **Strengthen Supportive Platforms and Systems**	12. Effective monitoring systems, laboratory and testing capacity. 13. Integrated one health partnerships, networks and governance models, leveraging current capabilities 14. Open and secure science and data platforms

Recommended Avian Flu Priority Scientific Actions and Sub-Actions by Pathway:

1. **Data and Situational Awareness**

   1.1. Monitor changes in avian flu viruses in birds and non-human mammals to detect mutations that may affect disease severity across species, including through enhanced observational and experimental data gathering.

   1.2. Enhance data capture of animals currently affected in Canada, especially of priority migratory birds, susceptible animals and species at risk, including live animal sampling and serological data.

   1.3. Improve the range of diagnostic tests for avian flu and subtypes for a broad range of situations, environments and species. This includes point of care rapid tests for animals and humans.

   1.4. Determine the effectiveness of different sampling methodologies in various species and environments, such as blood sampling for serology or fecal fluid, tissue and carcass sampling, among other.

   1.5. Enhance laboratory and testing capacity including for wastewater testing and sequencing.

2. **Risk Assessment**

   2.1. Proactively ensure thatepidemiological, clinical, demographic and genomic data are available publicly in real time and over the long-term to promote trust and support research and evidence informed decisions.

   2.2. Test the use of space-based and artificial intelligence technologies to augment early warning systems.

   2.3. Conduct research on avian flu viral strains to estimate both the emergence and impact risks, applying the Influenza Risk Assessment Tool (IRAT) and the Tool for Influenza Pandemic Risk Assessment (TIPRA) to investigate viral properties, human population attributes, and epidemiology in animal hosts[83,84,85].

   2.4. Conduct data analysis and scenario modelling on likelihood of widespread avian flu outbreaks in animals and humans and effectiveness of prevention/mitigation measures, while communicating risk assessments publicly and directly to professional and high-risk communities.

3. **Pathogenicity and Virus Biology**

   3.1. Elucidate avian flu virus biology and host-pathogen interactions, including viral evolution, factors affecting infectivity, reproduction, biologic fitness and the relationship of viral load to disease presentation.

   3.1.1. Advance *in vitro* and *in vivo* experimental disease and transmission models.

   3.1.2. Apply computational biology and genomic epidemiology to understand how genetic variants influence disease.

   3.2. Identify key host characteristics and virus interactions that determine species susceptibility to the evolving virus. This includes assessing the affinity of host cell receptors.

   3.3. Increase understanding of the biological characteristics and disease presentation of avian flu viruses in humans and other species, particularly for H5N1 clade 2.3.4.4b and the impact of infection on organs and biological systems.

4. **Modes of Transmission**

   4.1. Investigate avian flu transmission pathways within and across species. This includes domestic and wild birds, mammals (including marine mammals), domestic and wild ruminants, swine, companion animals, and humans (particularly between wild birds and animals on farms).

   4.2. Study the ability of the avian flu virus to survive and transmit on surfaces, in water, through air, and in biologic fluids and systems, including human saliva, and gastrointestinal fluids.

   4.3. Maintain food safety.

   4.3.1. Study potential risks and impacts of avian flu on hunting and traditional foods, working with Indigenous partners.

   4.3.2. Study possible infectivity of some agrifood products, such as raw milk cheeses.

   4.3.3. Assess potential avian flu risks from feeding animal products and byproducts such as food waste to other animals, including pets (e.g. raw pet food, fish food).

   4.3.4. Evaluate the effectiveness of food grade cleaning agents on the inactivation of avian influenza virus and virus survival on food contact surfaces.

PATHWAY #2 MITIGATE AVIAN FLU IMPACT ON THE ENVIRONMENT, ANIMALS AND HUMANS

5. Strengthen Virus Detection and Monitoring

5.1. Expand wastewater surveillance as an early warning signal for increased avian flu infection in vulnerable environments and communities across Canada, including remote and rural locations.

5.2. Develop targeted surveillance of potential bridging species, adjusting to include other species as new evidence emerges (live, harvested, sick and dead animals).

5.2.1. Identify and characterize host range of key wild birds and other animals that are potential bridging species that may act as vectors of infection, including animals hunted for food.

5.2.2. Carry out whole genome sequencing of as many virus isolates as possible to investigate localized clusters of infection and where particular wild bird species may play an important role in disease circulation.

5.3. Monitor long-term trends in avian flu dynamics.

5.3.1. Increase coordinated approaches and necessary data linkages to determine spread, changes in virus distribution and markers of viral evolution linking data to case information, genomic and transmission studies.

5.3.2. Support phylogenetic studies to assess viral evolution in host species.

5.3.3. Evaluate past exposure of wildlife to H5N1 and other influenza viruses through serological testing and enhance understanding of pre-existing immunity.

5.3.4. Design/advise on effective and scalable surveillance methods to optimize the detection and characterization of avian influenza viruses in wild birds across seasons and in all North American flyways.

5.3.5. Enhance research opportunities and sampling for avian influenza as they arise for dead or harvested animals, including marine mammals[86].

5.3.6. Enhance wild bird and mammal surveillance to determine potential avian flu exposure in wildlife species in national parks, national marine conservation areas and national historic sites in Canada.

6. Limit Animal Spread

6.1. Evaluate the factors that contribute to environmental contamination, persistence, and avian flu virus transmissibility. This includes viral transmission within and between birds and wild and domesticated animals, as well as ongoing spread within infected animal populations and beyond (e.g. bird to cow and subsequent cow to cow, etc.)

6.1.1. Develop experimental *in vitro* and *in vivo* models for known and potential hosts.

6.1.2. Investigate water as a potential reservoir that could sustain the virus.

6.1.3. Examine effects of human activity, such as deforestation and other environmental stressors on increased susceptibility of wildlife to avian flu.

6.2. Evaluate methods for animal carcass monitoring and disposal to effectively contain spread.

6.3. Design, evaluate and promote innovative tools and approaches for biosecurity and infection prevention and control, considering the differing context of farms, and human activities therein.

6.4. Develop tests/assays to facilitate the differentiation of infected and vaccinated animals.

7. Reduce Spillover and Infection in People

7.1. Minimize infectious disease transmission at the animal-human interface on and between farms, including monitoring poultry and cattle, as well as swine which are potential "mixing vessels" capable of generating pandemic influenza strains.

7.1.1. Assess effectiveness of PPE and decontamination practices in different contexts, as evidence on the predominant modes of avian flu transmission evolves.

7.1.2. Develop evidence-based recommendations to enhance protective behaviour, such as wearing appropriate PPE and isolating when infected, among others.

7.1.3. Develop and communicate avian flu infection prevention and control, as well as farmed animal biosecurity best practices in a targeted and context sensitive manner.

7.2. Enhance understanding of human infection and illness associated with avian flu viruses, such as clinical presentation, susceptibility and pathophysiology. This includes virologic, immunologic, genomic and epidemiologic characteristics.

7.2.1. Analyze the potential of immunity acquired from previous influenza virus exposure (e.g. 2009 H1N1) to protect against avian flu-induced human disease.

7.2.2. Conduct antibody (serology) testing in human populations potentially exposed to animals infected with avian flu. This includes exposure to infected wild, domestic and farmed animals such as migratory birds infected with avian flu, especially geese and ducks (waterfowl hunters, indigenous hunters, researchers), and individuals at higher risk, such as veterinarians and farm workers, especially individuals working in cattle milking parlours.

7.3. Engage in open dialogue with higher risk populations to inform research, prevention and response needs. This includes producers, animal and wildlife workers; agricultural sector workers; fur industry; hunters and trappers; and, Indigenous communities relying on traditional foods, among other.

7.4. Conduct behavioural science studies to inform risk communication and medical and non-medical prevention approaches.

PATHWAY #3 ENHANCE AVIAN FLU PANDEMIC PREVENTION, READINESS AND RESPONSE

8. **Deploy Effective Medical Countermeasures for People and Animals (tests, vaccines, and therapeutics).**

8.1. Urgently develop an H5N1 medical countermeasures research and development action plan, considering the latest scientific evidence on the effectiveness of available therapeutics and vaccines against the current clade, and the lack of rapid diagnostic tests.

8.1.1. Align medical countermeasure research and development across diagnostics, therapeutics and vaccines for H5N1, consistent with the goals of the 100 Days Mission[87].

8.1.2. Support research into the development of universal flu therapeutics and vaccines for animals and people.

8.2. Use innovative platforms and technologies, such as artificial intelligence, to accelerate medical countermeasure development, e.g. mapping virus evolution, increased infectivity or pathology and ability to evade acquired immunity.

8.3. Develop functional serology assays for humans and animals that can be used rapidly to detect exposure to novel subtypes of avian flu viruses that may not yet be well characterized.

8.4. Develop prototype candidate vaccine viruses (CVV) using various technologies that can be scaled up by manufacturers to produce an effective H5N1 flu vaccine.

8.5. Evaluate feasibility and effectiveness of animal vaccination along with criteria or guiding principles for vaccinating priority animal species.

8.6. Expand the knowledge of avian flu animal vaccine development in Canada and how the immune system responds to vaccines in poultry, cattle, swine, goats, and susceptible companion animals, such as dogs and cats.

9. **Adopt Prevention and Preparedness Strategies**

9.1. Map and assess current avian flu emergency response capabilities in Canada.

9.2. Link avian flu stockpile requirements to mission critical research needs, including for avian flu diagnostics, vaccines and therapeutics, leveraging Canada's Biomanufacturing and Life Sciences Strategy (BLSS).

9.3. Develop, validate, and stockpile reagents for conducting high priority influenza research.

9.4. Identify and address regulatory and procedural barriers to a rapid and early avian flu response.

9.4.1. Streamline regulatory, clinical trial, and research ethics review processes within and between jurisdictions as part of pandemic preparedness to protect animal and public health across the life course.

9.4.2. Ensure emergency data sharing and material transfer agreement protocols are in place.

10. **Protect Vulnerable Populations and Promote Occupational Health and Safety**

10.1. Set-up monitoring studies in at-risk environments, including for occupational exposure, ideally through longitudinal cohort studies. This will shed light on exposure routes, and how to limit human spread.

10.2. Prioritize vaccination for at-risk individuals, updating guidance as the evidence evolves, including on vaccine effectiveness against specific viral clades.

10.3. Enhance safe and secure work practices, including infection prevention and control strategies based on prevalent modes of transmission.

10.4. Develop evidence-based measures to protect the health of at-risk individuals and limit ongoing transmission. This includes for such activities as removal of infected animal carcasses.

10.5. Proactively establish implementation science mechanisms to integrate research and care as the situation evolves; this will ensure that acute and chronic health impacts resulting from avian flu infection are readily captured, studied and effectively treated.

10.6. Develop and implement evidence-based approaches to address mental health issues in individuals involved with culling animals, including vets, farmers and their families, among others.

11. Minimize Impact on Society

11.1. Conduct and leverage behavioural science studies for effective communication to individuals and communities at-risk so they are empowered to make evidence-informed choices about avian flu protective behaviour and response, including related to food, health and economic options.

11.2. Promote science literacy and proactively mitigate and address threats posed by misinformation, highlighting scientific action that reduces the health and economic impact of vaccine preventable diseases between and during pandemics.

11.3. Build health system resilience in the event of a rapid rise in human avian flu cases. This includes awareness, human resources and infrastructure for testing, vaccination, and treatment.

11.4. Determine and address socioeconomic impacts over the short and longer term.

11.4.1. Study the impact of policy levers such as taxation measures or compensation programs, among others, on availability of testing data for scenario planning, risk assessment and decision making, considering socio-economic factors.

11.4.2. As part of the scientific approach, identify and meaningfully engage (including in different languages) with communities vulnerable to H5N1 impact, taking steps to understand local perspectives and avoid worsening existing inequities.

PATHWAY #4 ENHANCE SUPPORTIVE PLATFORMS AND SYSTEMS

12. **Enhance effective monitoring systems, laboratory and testing capacity** for surge capacity readiness and avian flu surveillance networks. This includes assessment of the current capacity for avian flu research in containment environments in Canada and ways to streamline related processes during a pandemic response, while upholding research security.

13. **Establish integrated one health partnerships, networks and governance models, leveraging current capabilities.** This includes bringing together academic as well as private and public sectors, in-line with the recommendations of the Chief Science Advisor of Canada report on *Strengthening the Use of Science for Emergency Management in Canada*[88] and the *Report of the Expert Panel for the Review of the Federal Approach to Pandemic Science Advice and Research Coordination*[89].

13.1. Develop a Canadian pandemic readiness science and research framework as part of a broader pandemic preparedness planning strategy, modelled after this avian flu framework.

13.2. Foster avian flu collaborative models, networks and partnerships with other countries, such as the US given the shared North American Plan for Animal and Pandemic Influenza[90], and with international funders and regulatory bodies.

14. **Uphold open and secure science and data platforms.** This includes open data and sample sharing practices within collaborative networks and systems, while maintaining research ethics, safety and research security.

14.1. Ensure that genome sequences with complete metadata on sequencing and assembly are rapidly shared and stored on public databases to support phylogenetic analysis and other avian flu research.

14.2. As a top priority, ensure data and sample sharing agreements and protocols are proactively in place with security cleared researchers and organizations to facilitate research and development of medical countermeasures, support biobanks and robust biobanking networks, as appropriate.

14.3. Develop dynamic modelling platforms and ensure the availability of timely data to inform policy, considering health and food security, as well as socioeconomic needs.

VIII. HOW TO USE THE ROADMAP

This Roadmap is meant to serve as a guide for collaborative avian flu scientific action to optimize the interconnected health and well-being of humans, animals and the environment. It addresses the four essential elements that underpin effective emergency preparedness and response goals, namely data; fundamental knowledge of virus-host interactions; medical countermeasures tools and products; and methods and platforms, including effective ways to communicate.

Given the large and growing number of birds and mammals affected by H5N1, and the steady rise of human H5N1 cases globally, there is a sense of urgency to address the many persisting knowledge gaps. Specific current and future efforts can be "mapped" by partners against the framework to amplify research synergies, address persistent gaps, and streamline collective efforts. Partners include Canadian federal departments and agencies, provincial, territorial and international governments, along with academic, not for profit (e.g. Canadian Wildlife Health Cooperative) and private sectors including farming.

IX. CONCLUSION

The flu virus is notoriously difficult to predict given its ability to mutate, but the unprecedented panzootic spread of H5N1 is heightening the need for preparedness and response[91,92].

Implementing the *Science Roadmap and Action Plan for Avian Flu Management* will improve avian flu virus detection for timely response and risk assessment, protect the agrifood sector, and improve the prevention, treatment and management of avian flu infection and illness in animals and people in Canada.

As an evolving virus with a relatively new circulating H5N1 clade, a broader basis of fundamental knowledge of the virus biology and how it interacts with hosts is essential for effective avian flu prevention and management. There is a pressing need to improve the understanding of predominant transmission pathways, including through bridging species capable of contributing to widespread outbreaks in animals and people. Early containment mitigates impact. We must also make targeted efforts to study the extent and role of prior avian flu immunity in humans and animals to understand how severe an outbreak could be.

Protocols and methods for data and sample sharing need to be in place now. Front-end development of functional serology assays to detect exposure to viruses that are not well characterized should be an immediate priority. With the large-scale outbreak in the US and on some poultry farms in Canada, farm biosecurity measures in Canada must be enhanced to keep avian flu away from animals, property and people. Health system resilience and readiness including health care worker training and awareness, and support for priority populations who are most likely to be exposed to avian flu virus, would help mitigate the potential health and social impact of avian flu. Regulatory and procedural barriers to a rapid and early avian flu response need to be identified and quickly addressed.

For an effective response, research efforts that are part of an overall avian flu medical countermeasures strategy are required to accelerate the development, use and accessibility of avian flu tests, vaccines, and therapeutics. Testing capability is urgently needed that can rapidly differentiate between seasonal flu, COVID-19 and highly pathogenic flu strains and sub-types. Avian flu rapid tests at home and in the field for animals and people are essential for early detection, situational awareness and timely treatment. Evolving research to develop and deploy well matched avian flu candidate vaccine viruses (CVV) is also key. Avian flu stockpile requirements need to inform mission critical research, including for avian flu diagnostics, vaccines and therapeutics, leveraging *Canada's Biomanufacturing and Life Sciences Strategy* (BLSS).

Implementing the Roadmap will enhance integration across sectors, reduce fragmentation and minimize gaps, effectively operationalizing a One Health approach. Advancing the 14 recommended priority scientific actions and sub-actions will require collaboration, coordination and data sharing among many partners. This includes within and between Canadian federal departments and agencies, such as the Canadian Food Inspection Agency, the Public Health Agency of Canada, Health Canada, Environment and Climate Change Canada, Health Emergency Readiness Canada, Parks Canada, Department of Fisheries and Oceans, Indigenous Services Canada, among others listed in Annex 1. In this regard, it is commendable that the Public Health Agency of Canada and the Canadian Food Inspection Agency have proactively mobilized and sought input from external scientific experts taking a One Health approach to avian flu from the outset. Importantly, partners also extend to provincial, territorial and international levels of government and institutions, producers in the agrifood sector, academic centres and experts as well as other non-governmental and private partners.

X. ACKNOWLEDGEMENTS

XI. ANNEX I: FEDERAL ORGANIZATIONS IN CANADA IMPLICATED IN THE AVIAN FLU RESPONSE[93]

- **The Canadian Food Inspection Agency** (CFIA) is mandated to take the lead role in responding to animal health emergencies and has developed many detailed plans and procedures in collaboration with the Public Health Agency of Canada (PHAC), WHO and others. The CFIA is the primary agency responsible for prevention, preparation and response to an animal influenza outbreak, supported by PS. The CFIA has collaborative agreements with federal and provincial government partners that outline roles and responsibilities prior to and during an animal influenza outbreak.

- **Environment and Climate Change Canada** (ECCC): The identification of risks associated with outbreaks in wildlife and the overall health of wildlife is the collective responsibility of both federal and provincial/territorial departments, ministries, and agencies as well as through academic partnerships (particularly the Canadian Wildlife Health Cooperative). ECCC is the lead federal organization responsible for the conservation and protection of migratory birds and animals listed under the Species at Risk Act (SARA).

- **Fisheries and Oceans Canada** (DFO): Provides scientific expertise and advice on marine mammals to other agencies, permitting around possession and hunting of marine mammals, facilitating sample collection and testing of wild marine mammals, promoting the reporting of marine mammal mortality events, coordinating responses to marine mammals in distress.

- **Parks Canada Agency** (PC): responds to detections in wildlife in national parks, national marine conservations areas and reserves, supporting ECCC and provincial and territorial responses. Provides information to the public visiting parks, including information on human-wildlife interactions.

- **Agriculture and Agri-Food Canada** (AAFC): Connecting to the agriculture sector, national and local industry, as well as FPT governments, provides programs, services and support to industry for the impacts of the outbreak response. Promotes and supporting biosecurity best practices within the agricultural sector.

- **The Public Health Agency of Canada** (PHAC): monitors the international and domestic influenza situation and has developed The Canadian Pandemic Influenza Plan for the Health Sector in collaboration with provincial/territorial representatives. PHAC is the primary federal agency addressing pandemic influenza preparedness and response, supported by PS and Health Canada. PHAC also engages and coordinates efforts among domestic and international health partners. The IHR National Focal Point for Canada is in the Centre for Emergency Preparedness and Response within PHAC.

- **Health Canada** (HC): is responsible for ensuring regulatory preparedness, including accelerated approval of a pandemic influenza vaccine; and spearheading federal workplace health initiatives. Health Canada also provides risk assessment to support food safety investigations and minimize public health risks from the consumption of contaminated foods.

- **Indigenous Services Canada** (ISC): is responsible for supporting preparedness and response efforts in First Nations on reserve and Inuit communities.

- **Health Emergency Readiness Canada** (HERC): is a recently created special operating agency within Innovation, Science, and Economic Development (ISED), supported by Health Canada and the Public Health Agency of Canada. It is focused on ensuring that Canada can respond to health emergencies by supporting the development and production of medical countermeasures (MCMs), including vaccines, therapeutics, and diagnostic tools. The Agency helps grow the Canadian life sciences and biomanufacturing ecosystem and strengthens international partnerships.

- **National Research Council Canada** (NRC): The NRC is responsible for undertaking, assisting or promoting scientific and industrial research in fields of importance to Canada. This includes providing vital scientific and technological services to the research and industrial communities, establishing, operating and maintaining a national science library, and publishing and selling or otherwise distributing such scientific and technical information.

- **Canadian Institutes of Health Research** (CIHR): As the federal funding agency responsible for investing in health research, and situated within the Health Portfolio, CIHR plays a central role in supporting a coordinated and prioritized research response to pandemic threats. Through the Centre for Research on Pandemic Preparedness and Health Emergencies (CRPPHE) and its scientific institutes, CIHR works to ensure that Canada has an emergency-ready health research system.

- **Public Safety Canada** (PS): is the federal department that coordinates the overall federal government's domestic response efforts and provides support to government and key national players in responding to events of national significance. Within PS, the Government Operations Centre (GOC) operates around the clock as a mechanism to communicate and coordinate with federal, provincial and territorial emergency operations centers.

- **The Department of Foreign Affairs and International Trade** (DFAIT): is responsible for the coordination of Canada's international response, including international efforts to contain the spread of a pandemic virus; communicating with foreign governments and international organizations; and managing foreign offers of assistance. DFAIT is also responsible for providing travel advice and responding to the consular needs of Canadians in distress.

- **Innovation, Science and Economic Development** (ISED): works in partnership with the members of the Innovation, Science and Economic Development Portfolio to leverage resources and exploit synergies in several specific areas, including innovation through science and technology. ISED leads Canada's Biomanufacturing and Life Science Strategy which aims to improve Canada's long-term pandemic resilience and promote growth in the domestic life-sciences sector.

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