

Avian influenza A(H5Nx): Public health knowledge gaps and research needs

September, 2025
Public Health Agency of Canada



La version française est également disponible sous le titre : Grippe aviaire A(H5Nx) : Lacunes dans les connaissances en matière de santé publique et besoins de recherche

Suggested citation: Public Health Agency of Canada. Avian Influenza A(H5Nx) public health knowledge gaps and research needs. Ottawa, ON: Public Health Agency of Canada; 2025.

To obtain additional information, please contact:

Public Health Agency of Canada

Email: emerging.science-sciences.emergentes@phac-aspc.gc.ca

This publication can be made available in alternative formats upon request.

© His Majesty the King in Right of Canada, as represented by the Minister of Health, 2025

Publication date: September 2025

This publication may only be reproduced for personal or internal use without permission if the source is fully acknowledged.

Cat.: HP5-266/2025E-PDF

ISBN: 978-0-660-78650-6

Pub.: 250208

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

Contents

Introduction	4
Building science and research capacity using a One Health approach	6
PHAC science integration and coordination for preparedness and response .	7
PHAC science and surveillance activities for preparedness and response	8
Prioritized knowledge gaps and research needs.....	12
Theme 1: Virus biology and epidemiology	14
Theme 2: Methods and tools to advance public health action.	19
Theme 3: Evidence-based interventions.	21
Appendices	30
Methods	30
Key sources consulted.....	31
Definitions	33
Footnote A.....	34
References.....	34

Introduction

The circulation of clade 2.3.4.4b strains of the avian influenza A(H5N1) virus has led to widespread outbreaks among domestic and wild birds, as well as some wild and domestic mammals, across Europe, North, Central and South America - including across Canada. [Government authorities in Canada are currently responding to the outbreak of avian influenza A\(H5N1\) in farmed birds and wildlife across Canada.](#) While A(H5N1) is a subtype of influenza viruses that mainly infects birds, and some mammals, it has been found in rare and sporadic [human cases](#) in several countries, including the United States (U.S.) and Canada. There is no current evidence of human-to-human transmission to date.

In March 2024 in the U.S., A(H5N1) genotype B3.13 was detected in dairy cows and milk for the first time and has since resulted in multi-state transmission among dairy cattle with spillover to poultry farms. [Reference 1](#) Since April 2024, several human cases of A(H5N1) in U.S. dairy and poultry workers have been reported. [Reference 2](#) Most of the human infections in the U.S. have been with genotype B3.13, and mild in severity. There has been one fatal human case infected with genotype D1.1, with reported exposure to sick and dead birds in backyard flocks. Additional spillover events were detected in early 2025 in Nevada and Arizona U.S., each with the detection of unique strains of influenza A(H5N1) genotype D1.1 in dairy cattle, with subsequent transmission to a dairy worker in Nevada.

As of August 2025 in Canada, there has been one reported [human case of domestically acquired A\(H5N1\) genotype D1.1](#), detected in British Columbia. While the source of infection for this case is unknown, A(H5N1) genotype D1.1 continues to be the most prevalent genotype circulating in Canada, with wild birds and poultry most impacted. There has been no detection of genotype B3.13 in any wild or domestic animals or humans in Canada. There has been [no detection of A\(H5N1\) in dairy cattle, or in pasteurized or raw \(unpasteurized\) milk.](#) The overall [risk of avian influenza A\(H5N1\) clade 2.3.4.4b to the Canadian population](#) remains low; however, those with higher-level exposure to infected animals are at increased risk.

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

The Public Health Agency of Canada's (PHAC) role includes preventing and controlling infectious diseases; and preparing and responding to health emergencies. This applies to assessing the human health risk of avian influenza, and engaging in risk-appropriate prevention, preparedness, and response activities. Integrating emerging science, including the identification of knowledge gaps and priorities, throughout PHAC surveillance, preparedness and response activities supports an evidence-informed approach.

PHAC leads a collaborative approach with consideration for One Health perspectives to identify and synthesize priority knowledge gaps and research needs. These were originally developed in 2024, and updated in 2025, by synthesizing diverse inputs from PHAC, federal partners, and extramural scientists and researchers participating in the [PHAC Expert Panel on Avian Influenza A\(H5Nx\)](#). The updated gaps presented below align with the broader federal science agenda, and support the 2025 '[Managing Avian Flu Science Roadmap and Action Plan](#)' developed by the Office of the Chief Science Advisor of Canada. Additionally, the gaps are complementary to the '[Highly pathogenic avian influenza \(HPAI\) science and research priorities](#)' identified by the Canadian Food Inspection Agency (CFIA) in 2024. See [Appendices](#) for details on key sources consulted, and the methods used to identify the knowledge gaps and research priorities.

To catalyze knowledge generation on immediate research needs related to current outbreaks of avian influenza A(H5N1), the Canadian Institutes of Health Research (CIHR) in collaboration with federal and provincial partners invests in research that will help Canada prevent, prepare for, respond to and recover from outbreaks of avian influenza A(H5N1); [funding \\$5.2M for 35 research projects in 2024-25](#), with plans for additional [team grants totaling \\$4.5M](#) to support interdisciplinary research on Avian Influenza beginning 2026.

Related efforts to ensure Canada's readiness for future pandemics are funded through the Canadian Biomedical Research Fund and the Biosciences Research Infrastructure Fund (CBRF-BRIF). An initial [investment of \\$10M enabled the creation of five research hubs](#) led by universities across Canada who will partner with public, private and non-profit organizations

across the biomanufacturing and life sciences sector ([stage 1](#)) to accelerate the research and development of life-saving vaccines and therapeutics. An additional \$570M in funding is supporting research, talent development, and research infrastructure projects being completed through the hubs ([stage 2](#)), which includes research that will both directly and indirectly inform avian influenza A(H5Nx) knowledge gaps and research needs.

Building science and research capacity using a One Health approach

In Canada, there is a need to understand baseline domestic research strengths, and bolster preparedness and response for A(H5Nx), by leveraging knowledge and science capacity gained from the COVID-19 pandemic. A One Health approach can enable conditions for interdisciplinary research at the animal-human-environment interface.

Mechanisms for, and enablers of, science and research in this area include but are not limited to:

- Building system linkages and integrating data across surveillance systems at the human-animal-environment interface
- Developing One Health research collaborations
- Leveraging existing research and surveillance networks related to influenza, wastewater monitoring, modelling, laboratories, and pandemic preparedness
- Sharing data, including genomics data, biological materials and developing standard protocols

Avian influenza A(H5N1) is considered both a human and animal pathogen [Reference 3](#) and therefore, laboratory facilities must have the appropriate licensing in place in order to acquire this virus under the following legislative and regulatory frameworks:

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- [*Human Pathogens and Toxins Act*](#) and its regulations. It is a Risk Group 3 security sensitive biological agent and regulated by PHAC.
- [*Health of Animals Act*](#) and its regulations. It is a Risk Group 3 foreign animal disease pathogen of concern and regulated by CFIA.

PHAC science integration and coordination for preparedness and response

PHAC routinely works in close collaboration with domestic and international public health system counterparts, including Government of Canada departments and agencies, and provincial and territorial public health authorities, to coordinate and advance science and surveillance activities on emerging public health threats. Avian influenza response is supported by existing and dedicated federal, provincial, and territorial (FPT) governance mechanisms, including the FPT Senior Leader's Committee on HPAI, which convenes the Committee of the Chief Medical Officers of Health, the Committee of the Chief Veterinary Officers, and supporting bodies.

PHAC participates as a member of the:

- [Canadian Institutes for Health Research Centre for Research on Pandemic Preparedness and Health Emergencies Steering Committee](#) to influence research funding priorities associated with emerging public health threats, including A(H5N1).
- [Biomanufacturing and Life Sciences Strategy](#) governance to coordinate research and development activities related to vaccines, therapeutics, and diagnostics.
- Canadian Food Inspection Agency's [Highly Pathogenic Avian Influenza Vaccination Task Force](#) to discuss and inform the potential use of animal vaccination in Canada.

Domestically, PHAC also convenes and participates in the following mechanisms for scientific collaboration:

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- [Canadian Public Health Laboratory Network](#) to assure an integrated public health laboratory network response to infectious diseases that encompasses One Health.
- [Emerging Infectious Disease Modelling Initiative](#) network to strengthen collaborative efforts among the academic community and all relevant stakeholders to conduct and coordinate infectious diseases modelling.
- Pan-Canadian Wastewater Monitoring Network to share emerging science and best practices, coordinate studies and testing sites, and improve methods and approaches to detect H5 viruses in wastewater.
- Multi-Agency Steering Committee for Public Health Risks Associated with Avian Influenza A(H5N1) in Canada to describe, anticipate or estimate public health risks, develop recommended actions, and explore future outcomes of risk.
- [Expert Panel on Avian Influenza A\(H5Nx\) in Canada](#) to ensure the best available science advice and identification of knowledge gaps in an ongoing way.

More broadly, the FPT Pandemic Preparedness Task Group (under the Communicable and Infectious Disease Steering Committee) has been stood up to support partnerships on pandemic preparedness initiatives and progress on shared pandemic preparedness actions to strengthen our collective approach to readiness for future pandemics.

PHAC science and surveillance activities for preparedness and response

PHAC's National Microbiology Laboratory (NML) is a World Health Organization (WHO) National Influenza Centre and collaborates extensively with the CFIA National Centre for Foreign Animal Disease laboratory, a designated reference laboratory by the World Organisation for Animal Health for avian influenza. The Containment Level 3 and 4 facilities of these laboratories are leading-edge and uniquely equipped to conduct research

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

studies to characterize the A(H5Nx) virus, model virulence and transmissibility and assess medical countermeasures including antivirals and vaccines. The NML supports human diagnostic testing and research for avian influenza virus including:

- **Diagnosis:** providing enhanced reference/diagnostic services for emerging influenza viruses. Developing and providing recommendations on diagnostic test protocols for provincial and territorial partners to enable decentralized testing. For areas without established testing, NML can provide rapid testing support if and when needed. The molecular assays used at the NML to detect the H5 subtype are able to detect the currently circulating 2.3.4.4b HA clade of A(H5N1).
- **Capacity building:** The NML works closely with provinces and territories to support a decentralized testing approach and most provincial public health labs are able to rapidly detect any human cases of A(H5N1), including the new clade. Testing is decentralized and supported by NML through the provision of ongoing recommendations on diagnostic protocols, supply of control reagents, and annual distribution of proficiency tests which includes an assessment of the capabilities to detect and subtype H5N1 avian influenza virus, including the HA.
- **Viral surveillance:** conducting whole genome sequencing and viral characterization to monitor viral evolution, detect new and emerging strains, assess medical countermeasures, and virus relatedness to the candidate H5 vaccines.
- **Research:** development of animal models, transmission studies, vaccine studies and in vivo evaluation of known and novel antivirals. This includes in-progress testing of newly emerging influenza A(H5N1) and A(H5N5) viruses in ferrets and mice. Additional research is focused on identifying molecular determinants of virulence and transmissibility in emerging strains and implementation of functional assays to identify and characterize viruses with altered biological properties that may

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

influence their capacity to infect humans. This includes evaluating the role of wastewater monitoring as an indicator for surveillance, given that it currently cannot distinguish between the source of the virus (animal vs. human).

Horizontal science and national surveillance initiatives mobilized by PHAC for A(H5N1) include:

- Identifying general knowledge gaps and research needs, as well as specific research priorities (for example, the [National Advisory Committee on Immunization's preliminary guidance on human vaccination against avian influenza in a non-pandemic context identifies research priorities to inform vaccine guidance](#)).
- Leading collaborative human surveillance activities:
 - Providing [national case definitions](#). Provincial/Territorial (PT) public health authorities are required to report confirmed and probable human cases of A(H5N1) to PHAC within 24 hours. Confirmed human cases of A(H5N1) are notifiable under the International Health Regulations (2005).
 - Providing a [protocol for enhanced human surveillance of avian influenza A\(H5N1\) on farms in Canada](#) to support local public health authorities in the event of human infection or unusual exposure scenarios on Canadian farms with infected poultry and livestock.
 - Detecting and monitoring avian influenza cases in humans using multiple approaches (e.g., syndromic surveillance ([FluWatchers](#)), laboratory testing and typing, hospitalization data, outbreak reporting, event-based surveillance).
 - Monitoring, assessing, and supporting integration of One Health avian influenza surveillance through human, animal (wildlife and domestic animals) and environmental data sources.

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Monitoring public information sources to detect and communicate information about potential public health threats worldwide – including avian influenza cases in humans and animals – through the Global Public Health Intelligence Network.
- Deploying field epidemiologists at the request of jurisdictions to support surveillance activities as needed.
- Modelling: working with other government departments and modelling networks to model bird migration into Canada and transmission among wildlife to understand the potential risk of transmission to humans.
- Conducting [rapid risk assessments](#) and [pandemic risk scenario analyses](#) to identify emerging threats, develop recommendations, explore possible risk outcomes, and describe, anticipate or estimate public health risks.
- Conducting and commissioning knowledge syntheses and evidence profiles to address emerging questions by compiling and assessing the best available published scientific literature. This work will help inform future updates to technical guidance documents to ensure they remain evidence informed.
- Conducting qualitative behavioural science research with key at-risk populations to better understand how PHAC might effectively connect with and communicate information to these groups, improve trust, and encourage safe public health behaviours.
- Evaluation of the efficacy and effectiveness of any non-pandemic H5 vaccines, authorized in Canada, in preventing acute respiratory illness, outpatient visits, hospitalization, Intensive Care Unit admission, and death associated with A(H5N1).
- Establishing the PHAC Expert Roster Platform, with an initial call-out to [identify expertise in HPAI A\(H5N1\) across Canada](#).

Prioritized knowledge gaps and research needs

Emergence of novel pathogens or re-emergence of concerning pathogens occurs periodically, and PHAC, along with its partners in Canada and abroad, are consistently monitoring for unusual or concerning trends. Avian influenza A(H5N1) activity has been documented in humans since 1997. Recent human cases have been mainly due to exposure to infected poultry or dairy cattle and their environments, with no current evidence of human-to-human transmission. The recent development of more extensive presence of A(H5N1) in wild birds, poultry and mammals requires additional science and surveillance activities in order to better understand the potential threat to human health. To that end, PHAC is presenting below, the current research priorities that will support ongoing risk assessment and responses.

While governmental agencies, provincial/territorial authorities, communities, and academic researchers are actively pursuing answers to several of the gaps presented, there remains significant opportunity for further science and research activities to address these, and other, knowledge gaps by One Health partners. Strategies to address these knowledge gaps and research needs may be achieved through a diversity of approaches. The knowledge gaps and research needs identified in this document are not intended to privilege specific methodological approaches or research designs. Knowledge gaps are grouped by key thematic areas. Interdependencies between knowledge generating activities, and the capacity or feasibility to address the gaps, are not described in this document. The knowledge gaps identified are relevant to public health from a One Health perspective. The list of knowledge gaps does not constitute an exhaustive list of all science and research needs related to A(H5Nx).

There are several considerations informing the next phase of integrated preparedness and risk assessment activities. Influenza A(H5N1) is primarily affecting animals at this time, with sporadic cases identified in humans, mostly linked with exposures to infected animals. There has been an increase

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

in scientific and public health actions domestically and globally since PHAC initially published research priorities in June 2024.

Given this context, addressing the following scientific priorities are of greatest immediate urgency to advance federal One Health preparedness and response goals of preventing animal-to-animal and animal-to-human spread, and the containment goal of preventing human-to-human transmission:

1. **Continued innovation in detection, surveillance methods, data science, modelling and molecular characterization** of A(H5Nx) at the human-animal interface, and the development, use and assessment of point-of-care diagnostics in both humans and animals.
2. Research to understand the safety, immunogenicity and effectiveness of **human vaccines and other immunizing agents against avian influenza**.
3. Research to understand the safety and effectiveness of **antivirals and other therapeutics; mechanisms to reduce the emergence of antiviral resistance**; and research to support the development of **novel medical countermeasures**.
4. **Explore social and behavioural factors** shaping trust, acceptability and effectiveness of public health measures, medical interventions, and One Health interventions; and other factors that influence human interactions with animals.

The priorities above are being addressed across departments in the Government of Canada with their partners. Some of the identified gaps fall within the mandated responsibilities of federal and provincial/territorial government partners, particularly those involving core public health laboratory and surveillance functions. However, meaningful progress will depend on strong collaboration across disciplines, sectors, and jurisdictions. Coordinated efforts are needed to reduce administrative and logistical barriers and to

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

support the sharing of data, samples, protocols, and evidence syntheses – both domestically and internationally – to foster innovation using a One Health approach.

Science and research must be integrated into outbreak simulations and preparedness exercises, and these activities can benefit from implementation science (including program evaluation) to identify best practices and effective methods.

Researchers and scientists across disciplines and domains are encouraged to engage early and co-develop science activities with impacted communities, such as people at higher risk of exposure to infected animals, to facilitate receptivity of proposed actions, and promote integration of diverse perspectives. This includes prioritizing equity-informed, culturally appropriate and community-led approaches with populations, including First Nations, Inuit, and Métis communities. Incorporating Sex and Gender Based Plus considerations in the design, conduct, analysis, and interpretation of studies can also be applied as part of a broader equity lens in science and research activities.

A comprehensive list of knowledge gaps follows below; many of which would only become relevant in the context of a large-scale spillover event to humans, or significant human-to-human transmission. Those marked with footnote "a" were most consistently assessed as being timely priorities. These reflect ongoing uncertainties, knowledge or evidence gaps highlighted in the literature and from expert advice; are critical to improving our assessment of risk related to spillover into humans; are activities best initiated in the current preparedness phase; and are aligned with federal A(H5Nx) priorities.

Theme 1: Virus biology and epidemiology.

Sub-theme: Pathogen identification, characterization, and description of avian influenza A(H5Nx).

Characterize the biology and behaviour of avian influenza A(H5Nx) viruses in animals and humans to inform assessment and mitigation of risk of transmission to humans. ^a

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Are circulating viruses in birds and non-human mammals, including ruminants, evolving such that A(H5Nx) infectiousness, transmissibility, virulence, disease severity and progression, and immunity, are impacted? [a](#)
- What viral genomic markers and phenotyping of currently circulating strains are associated with increased potential for infectiousness, virulence, disease severity, and direct mammal-to-mammal spread? [a](#)
- What is the virus survivability in different environments as influenced by the complex relationship of biological, physical and environmental factors?
- What are the risks and consequences of reassortment between A(H5Nx) and other endemic influenza viruses in other species, including swine and humans? [a](#)
- What is the risk of A(H5Nx) transmission between livestock on affected farms, and to companion animals and other domestic species? [a](#)
- What is the degree of virus shedding by infected hosts, and the duration of shedding, incubation and infectious period? [a](#)
- How does the virus gain entry and replicate in humans? [a](#)

Understand virological and genomic factors (including reassortment and viral evolution) that may impact the ability of the viruses to infect and cause disease in humans. [a](#)

- What genomic markers indicate potential impacts on human health or sustained human-to-human transmission (e.g., infectiousness, transmissibility, virulence, disease severity and progression, immunity, and susceptibility to antivirals and medical countermeasures)? [a](#)
- What is the pathogenicity and transmissibility of circulating A(H5Nx) strains and what implications does it have on risk to human health? [a](#)

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Develop and use various animal models to elucidate species specific risks, pathology, tissue tropism, viral distribution, primary replication sites following various routes of exposure. [a](#)
- What is the immunopathology of disease and are there immunomodulatory targets that are druggable? [a](#)

Understand innate and adaptive immunity to influenza A(H5Nx) in humans, including antigen/antibody and cellular immune responses to infection, treatment, and vaccination; and antigenic cross reactivity with other influenza viruses. [a](#)

- What is the antigenic cross reactivity between A(H5Nx) and other influenza viruses (from infection or vaccination)? [a](#)
- What are the correlates and duration of seroprotection for A(H5Nx)? [a](#)
- What is the immune response in individuals with mild or asymptomatic A(H5Nx) infection? [a](#)
- What are the host response characteristics in wildlife (avian and mammalian hosts) that experience severe disease vs sub-clinical infection, including in remote areas?

Sub-theme: Epidemiology and surveillance.

Describe the epidemiology (e.g., incidence, prevalence, case severity, populations at increased risk, mortality rate) of avian influenza and A(H5Nx) via surveillance, and testing activities at the human-animal-environment interface (e.g., in wild birds, wild mammals, and domestic animals) and for scenarios where human-to-human transmission may occur. [a](#)

- What are the frequency, distribution, and characteristics of symptomatic and asymptomatic A(H5Nx) infection in wild birds, wild mammals, domestic animals, and feral cat colonies, including modes of

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

transmission, incubation and infectious periods, clinical presentation, and severity? ^a

- How can integrated wildlife, agricultural, and domestic animal surveillance systems be combined to identify geographical areas and settings with increased risk of human exposure? ^a
- What are the risk factors for human infection with A(H5Nx) and populations at highest risk? ^a
- What are the types of human interactions with animals that increase risk of human exposure (e.g., interaction with agricultural animals such as poultry, dairy cattle, and swine; other animals including companion animals; contaminated animal products, or their environments) and implications for preventive public health guidance? ^a
- How does the risk of infection vary by mode of transmission to humans (e.g., exposure to companion animals, consumption of raw meat, eggs, cheese, or milk and milk products, and contact with fomites including contaminated farming equipment)? ^a
- What is the clinical presentation, spectrum of disease severity, and course of infection (including long lasting impacts) of A(H5Nx) infections in known human cases? ^a

Define factors relating to the susceptibility and transmission parameters of different birds, mammals, and humans to avian influenza A(H5Nx) viruses (e.g., clinical signs, incubation period, contagious period, virus shedding) to understand the potential risk to and impact on human health. ^a

- In different species of mammals and birds, what clinical host and virological factors are associated with increased susceptibility to influenza A(H5Nx) infection in humans? How do these differ across species? ^a

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- What are the modes of transmission (e.g., fomites, aerosol, direct contact) of A(H5Nx) within and between species? [a](#)
- What factors contribute to spillover events from one species to the next, including from mammals or birds to humans? [a](#)
- How do animal (commercial, domestic or wildlife) control/containment measures and animal vaccination strategies modify human health risk? [a](#)
- How does A(H5Nx) transmission to or between companion animals and other domestic animals affect human health risk? [a](#)
- How does clinical presentation of A(H5Nx) infection in other species relate to presentation in humans?

Improve the understanding and monitor key epidemiological parameters and genomic epidemiology of influenza A(H5Nx) infections in humans (e.g., sequencing data, mutation monitoring, epidemiological metrics for reported human cases domestically and globally). [a](#)

- What is the prevalence, mortality rates, and geographic distribution of influenza A(H5Nx) cases, clusters and outbreaks in humans, including an understanding of asymptomatic infections? [a](#)
- What is the incubation period, infectious period and reproductive rate of A(H5Nx) in humans? [a](#)
- How does the sequencing data vary within and between genotypes and HA clades; and between vaccine strains, regional, and international comparators? [a](#)

Assess sero-epidemiology in different populations including groups at higher risk of occupational or recreational exposure to infected animals (e.g., poultry or livestock workers and residents on these farms, slaughterhouse and processing plant workers, workers who transport

livestock, wildlife officers, researchers, or rehabilitators, veterinarians and veterinary technicians, hunters and trappers, people who process wild game or birds for food, non-commercial farm operators or hobbyists [e.g., people with backyard flocks, exhibition farms] those living in rural/remote and Northern settings, contacts of cases).^a

- What is the level of population immunity in high-risk groups and in the general population?^a
- How does pre-existing anti-N1 immunity affect clinical presentation (e.g., attenuated illness), modulate risk assessment, or result in subsequent adaptation or viral transmission?^a
- What is the assessed immunity of to A(H5Nx) in high-risk occupational groups and/or other at-risk communities (e.g., poultry or livestock farmers, hunters, those who work at zoos, and wildlife care rehabilitation workers, municipal and parks employees, hunters/trappers, those living in rural/remote settings, contacts of cases)?

Theme 2: Methods and tools to advance public health action.

Sub-theme: Detection and diagnosis.

Enhanced and targeted surveillance (e.g., wastewater, serosurveys) for early detection of animal and human cases in populations at increased risk of exposure.^a

- What is the level of under-detection of mild and sub-clinical human infections? How could this enhance our understanding of avian and/or animal exposures associated with asymptomatic or mild infections?^a
- Explore the challenges and potential use for wastewater surveillance for early detection of animal and human influenza, including sample detection in proximity to at-risk premises and leverage genomic analyses to differentiate between high and low pathogenicity avian influenza.

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- What are the barriers to participation of high-risk populations in enhanced surveillance, including in occupational and industry settings? What are effective strategies to overcome these barriers? ^a

Design, implement, and evaluate point of care testing (e.g., molecular, genomic, serological and/or antigen detection) for rapid detection. ^a

- What is the effectiveness of genomic, molecular and/or serological methods for rapid detection of novel influenza viruses/strains/clades?

Understand the range of testing modalities, their effectiveness and accessibility.

- In addition to diagnostic tests - used where evidence of symptoms/illness is/are present, do we have screening tests available that could be used to test asymptomatic animals and humans - that are highly sensitive and specific?
- What new diagnostic assays need to be developed (e.g., to differentiate between antibodies produced due to an infection from those produced due to vaccination)?
- Develop and support the refinement of sensitive and specific serologic assay to enable the detection of asymptomatic infection in exposed groups.
- What is the best testing strategy for individuals presenting with non-respiratory symptoms (e.g., conjunctival versus nasopharyngeal swabs)?

Sub-theme: Modelling.

Undertake predictive modelling to better understand disease dynamics, risk scenarios, and to inform resource allocation and response timelines.

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- What are the potential pandemic risk scenarios associated with human-to-human transmission, considering environmental factors such as weather, population displacement, and community housing (e.g., arrival of asylum seekers)?
- In the event of human-to-human transmission, what is the risk of continued transmission and importation of human cases, estimates of disease severity and transmission parameters (e.g., reproduction number and generation time), and the effectiveness of interventions including available antiviral treatments?
- What is the potential impact of pharmaceutical (i.e., pre-exposure prophylaxis, post-exposure prophylaxis and treatment) and non-pharmaceutical health interventions on A(H5Nx) epidemiology and other societal impacts?
- Forecast health system capacity for managing human cases of A(H5Nx), including pan-Canadian healthcare demand for various medical countermeasures (e.g., drugs, diagnostics, personal protective equipment (PPE), medical devices), including impact of imported cases
- What is the available economic modelling of interventions to prevent mammal-to-human and human-to-human transmission?
- How can artificial intelligence support modelling for risk assessment?

Theme 3: Evidence-based interventions.

Sub-theme: Pharmaceutical public health interventions: therapeutics.

Assess and understand the safety, effectiveness, for antivirals and other therapeutics in the prevention (pre-exposure and post-exposure) and treatment of human A(H5Nx) infection. ^a

- What existing therapeutics approved for use in humans can be repurposed for use against A(H5Nx) infection (e.g., antivirals, immunomodulators, monoclonal antibodies)? ^a

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Support the development of novel therapeutics (e.g., antivirals, immunotherapies, or monoclonal antibodies) for preventing and treating human A(H5Nx) infection. [a](#)
- What is the comparative effectiveness and safety (including adverse events, drug interactions, warnings, precautions, contra-indications and potential for teratogenicity) of different therapeutics used against human A(H5Nx) infection in healthy individuals of all ages, pregnant individuals, and those with co-morbidities? [a](#)
- What are the effectiveness and safety (including adverse events, drug interactions, warnings, precautions, contra-indications and potential for teratogenicity) of different combination therapies for the treatment of serious infection (e.g., in individuals who are ventilated) or refractory infection (e.g., individuals who are ventilated)? [a](#)
- What are the most effective and equitable antiviral distribution and implementation strategies, including in remote areas?
- What is the effectiveness and safety of combining vaccines and therapeutics in the treatment and prevention of A(H5Nx) infection? This includes understanding potential synergistic or antagonistic effects between different therapeutics and vaccines.
- What is the effectiveness of different dosages of approved antivirals or other therapeutics (e.g., frequency of administration and duration of treatment) in different patient populations (e.g., in the intensive care units, obesity, older population, pediatrics)? [a](#)
- What factors affect individuals' decisions to seek medical care, use prescribed treatments, and adhere to their therapeutic regimen? [a](#)
- Evaluate costs, shelf-life, storage requirements, available dosages and formulations, as they relate to stockpiling decisions for antivirals and other therapeutics. [a](#)

Evaluate mechanisms to reduce the emergence of A(H5Nx) resistance to antivirals. [a](#)

- What are effective mechanisms to reduce the emergence of A(H5Nx) antiviral resistance? [a](#)
- What is the value of combination therapy in reducing the likelihood of emerging resistance? [a](#)
- Can sequencing capacity be leveraged to support surveillance for emerging resistance (e.g., sequencing of samples from patients receiving prophylactic/therapeutic antivirals)? [a](#)
- Are there novel broad-spectrum therapeutics (antivirals or immunotherapies) in development that are effective against multiple strains and also provide a higher genetic barrier to resistance? How effective and safe are they? [a](#)

Sub-theme: Pharmaceutical public health interventions: vaccines and other immunizing agents.**Further understand the safety, immunogenicity, and effectiveness of human vaccines against avian influenza (HVAI) for preventing infection and attenuating severe illness. [a](#)**

- Pre-authorization immunogenicity and safety data for strain-updated HVAI. [a](#)
- Post-authorization effectiveness, safety, and immunogenicity data on including the duration of protection and/or the duration of the immune response. [a](#)
 - What is the safety, immunogenicity, and effectiveness of HVAI in special populations; in large populations or in populations not included in clinical trials (e.g., children, older adults, pregnant individuals, immunocompromised individuals)? [a](#)

Public Health Agency of Canada - Avian Influenza A(H5Nx):
Public Health Knowledge Gaps and Research Needs 2025

- What is the effectiveness of different dose strategies (dose schedule, number of doses, sparing strategies)?^a
 - Efficacy/effectiveness and immunogenicity after 1 dose of HVAI?
 - Is there a need for and optimal timing for a second dose of HVAI?
 - Is dose-sparing possible given that inactivated avian influenza virus vaccines have historically demonstrated poor immunogenicity and required high antigen content and/or adjuvant?
 - Is dose priming with a different, but related, avian influenza vaccine effective due to reliance on high antigen content/adjuvants?
 - Safety and immunogenicity of concurrent administration with other vaccines?
- What is the breadth of immune response conferred by the vaccines, including:
 - Are there interactions between seasonal influenza vaccines and HVAI vaccines?
 - What is the contribution of pre-existing or cross-protective immunity from seasonal influenza vaccines and/or infections or other heterologous avian influenza A(H5N1) strains?^a
 - What are the impacts of cross-protective immunity on the safety and efficacy of HVAI?
- Understanding the role of the neuraminidase glycoprotein in providing protection across all circulating neuraminidase subtypes and genotypes.

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Characterization of viral evolution following the implementation of vaccination (e.g., vaccine escape).
- Research into influenza immunization that offer broader strain protection and/or longer duration of protection, including novel vaccine platforms (or other immunizing agents). [a](#)
- Given the risk of highly pathogenic avian influenza viruses being embryo-lethal, can the A(H5Nx) virus strains of interest be propagated efficiently in eggs to create vaccines in bulk quantities? If not, are there any antigen-like strains that could be propagated more efficiently?
 - What is the anticipated impact on vaccine effectiveness due to pivoting to a related strain?
 - What is the threshold for making the switch in strain propagation?
- Which vaccine platforms are best suited for protection against influenza A(H5Nx)? What are the comparative safety, immunogenicity, efficacy and effectiveness profiles of different human A(H5Nx) vaccines?
- What adjuvants for influenza vaccines will enhance the immunogenicity and efficacy against A(H5Nx) viruses?

Explore considerations for vaccine implementation and intervention strategies, in different populations. [a](#)

- What is the anticipated demand of HVAI? [a](#)
- What are the mechanisms to support vaccine uptake/confidence (e.g., ease of administration, minimizing pain)?
- What is the acceptability of HVAI if offered to key populations? [a](#)

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- What is the feasibility of targeting HVAI programs for key populations, including costs and opportunity costs of implementing potential HVAI programs?
- What is the effectiveness of various vaccination implementation strategies (e.g., universal vaccination, targeted to high-risk groups and populations with a high burden of disease concentration, pre- or post-exposure, ring vaccination, etc.)?

Sub-theme: Non-pharmaceutical public health interventions.

Evaluate whether protective measures and interventions such as the use of personal protective equipment (PPE), ventilation/air filtration, and cleaning/disinfection impact transmission and risk of infection among exposed persons. ^a

- How do ventilation and air filtration impact A(H5Nx) transmission in high-exposure occupational settings for humans?
- How effective and acceptable are various types of PPE, when used as recommended, against zoonotic A(H5Nx) transmission in high-risk occupational settings? Can novel types of PPE be developed that would be easier to use? ^a
- What are the most critical factors to consider when selecting appropriate PPE for individuals working in environments with potential exposure and for use in special populations?
- What are the most effective disinfectants for eliminating the virus from various surfaces?
- Are there any novel technologies or approaches being developed to enhance the efficacy of protection, cleaning, and/or disinfection methods?

Sub-theme: Behavioural and social sciences.

Describe the behavioural factors influencing human interactions with different types of animals and geographic and cultural variation in human-animal contacts. ^a

- How do those living in Canada interact with, and what is the exposure level to, animals at a higher risk of A(H5Nx) exposure/infection?
- What are the specific behavioural risk factors and considerations associated with companion animals (e.g., cats)? ^a
- What are the behavioural, cultural, socioeconomic, climate change, geographical, land-use (or planning) factors at the community level that can increase spillover potential, including among Indigenous communities?
- What are the challenges, concerns, and needs of the public, and specifically Indigenous communities, to inform the development of appropriate guidance and improve knowledge translation on A(H5Nx) infection prevention and control?

Understand factors affecting adherence to preventative One Health interventions and public health measures to reduce exposure to A(H5Nx) and how they influence transmission rates. ^a

- What are the barriers/facilitators of personal protective equipment adherence among humans at risk of exposure (e.g., poultry or livestock farmers, hunters, veterinarians, animal care staff, those who work at zoos, and wildlife care rehabilitation workers, municipal and parks employees, hunters/trappers, those living in rural/remote settings), and how can uptake be improved? ^a
- What are the barriers/facilitators to biosecurity and emergency response adherence among animal health sectors (e.g., poultry farms, livestock farms, others)? ^a

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- How do we most effectively engage populations at increased risk of exposure to A(H5Nx) viruses to achieve adherence with risk mitigation measures? [a](#)
- What are the barriers/facilitators to testing/participation in surveillance among humans at risk of exposure, and how can uptake be improved? [a](#)
- Among humans at risk of exposure (e.g., poultry or livestock farmers, hunters, veterinarians, animal care staff, those who work at zoos, and wildlife care rehabilitation workers, municipal and parks employees, hunters/trappers, those living in rural/remote settings) what are the barriers/facilitators to the following: a) immunization with seasonal human influenza vaccine; b) immunization with a HVAI; and, c) acceptance of antiviral prophylaxis? [a](#)
- What are the knowledge, attitudes and beliefs of populations at increased risk of exposure to A(H5Nx) viruses? The general population? [a](#)
- What is the acceptability in key populations and the general population for medical countermeasures; public health measures; and interventions at the human-animal-environment interface for avian influenza? [a](#)

Define the risk factors (including but not limited to medical, social, and behavioural), associated with A(H5Nx) to inform risk communication, public health guidance and interventions. [a](#)

- What factors contribute to lack of trust in public health authorities in the animal/wildlife sectors? What factors contribute to lack of trust in public health authorities among Indigenous communities reliant on country foods, hunting/trapping?
- What factors contribute to the potential for misinformation and disinformation associated with varying A(H5Nx) risk scenarios? [a](#)

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- Evaluate the types of information (e.g., scientific evidence and economic factors) that influence public health decision-making by policy makers, communities, and individuals during health emergencies.
- How can we support community level preparedness for avian influenza in equity seeking populations?

Appendices

Methods

A list of knowledge gaps was developed in 2024 by synthesizing diverse inputs (see Key Sources detailed below).

Knowledge gaps were then validated by PHAC and extramural scientists and researchers participating in the [PHAC Expert Panel on Avian Influenza A\(H5Nx\)](#). The validation process resulted in a high degree of concurrence amongst experts on key public health criteria, including:

- Relevance to phase of emergency: initiation of research to address the gap was deemed appropriate during preparedness and response phases.
- Relevance to pandemic preparedness: addressing the gap would be generalizable to broader pandemic preparedness beyond A(H5Nx).
- Impact on dimensions of risk assessment: addressing the gap would impact public health decision-making and action impacting risk of sporadic or widespread A(H5Nx) human-spillover and pandemic.

The methodological objective was not to achieve absolute consensus among all sources and experts consulted, but to identify the priority knowledge gaps and research needs expected to have the greatest relevance to preparedness and response for possible human infection with the current circulating avian influenza virus, and to A(H5Nx) broadly, in Canada.

In the spring of 2025, the A(H5Nx) knowledge gaps and research priorities were reassessed and updated in a phased approach. An extensive review of both internal and external sources (including published scientific reviews) was used to refine the existing gaps within the current context and state of knowledge and add new knowledge gaps identified since 2024. This was followed by re-validation of the expanded list of knowledge gaps in consideration of:

- recent scientific advances;

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- current scientific activities already underway within the Canadian federal government and federally funded extramural research (links found below for reference); and
- additional Canadian sources highlighting A(H5Nx) priorities including the Chief Science Advisor of Canada's Science Roadmap, internal PHAC stock taking efforts, National Advisory Committee on Immunization identified needs, Provincial needs highlighted by the Canadian Council of Medical Officers and Canadian Veterinary officers, and extramural science advice provided via the PHAC Expert Panel on Avian Influenza A(H5Nx).

Priority gaps were validated against the original criteria and were consistently identified as:

- relevant to improving understanding of risk assessment for human spillover, especially in high-exposure groups;
- best addressed through early scientific investigation;
- requiring further research beyond current scientific efforts in place; and
- aligned with federal A(H5Nx) preparedness and response priorities.

Key sources consulted

- [PHAC Pandemic risk scenario analysis update: Influenza A\(H5Nx\) clade 2.3.4.4b virus and related future novel viruses](#) (2024-06-06)
- Archived: [PHAC Rapid risk assessment: Avian influenza A\(H5N1\) clade 2.3.4.4b](#) (2023-07-27)
- [Rapid risk assessment update: Avian influenza A\(H5N1\) clade 2.3.4.4b, public health implications for Canada](#) (2024-11-29)

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- [McMaster Health Forum Living Evidence Profile: Examining what is known about the emergence, transmission, and spectrum of the burden of disease of avian influenza A\(H5Nx\) subtypes](#) (version 7.4, 2024-07-17)
- [McMaster Health Forum Rapid Evidence Profile: Identifying features and impacts of public health strategies that can be used to prevent, reduce and/or mitigate avian influenza spillover to humans](#) (2024-01-12)
- [United Kingdom Health Security Agency technical briefing](#) (2023-07-14)
- [CDC Public Health Science Agenda for Highly Pathogenic Avian Influenza A\(H5N1\) – June 2024](#) (2024-06-24)
- [NIAID Research Agenda for 2024 H5N1 Influenza – May 2025](#) (2024-05-23)
- FDA Research Agenda for 2024 Highly Pathogenic H5N1 Avian Influenza (2024-06-24)
- [WOAH: Global Strategy for the Prevention and Control of High Pathogenicity Avian Influenza \(2024-2033\)](#) (2025-02-19)
- [University of Calgary, Potential for Transmission of Avian Influenza Virus to Humans Associated with handling, Preparing, and Consuming Contaminated Meat, Organs, Eggs, Milk, and other Dairy Products from Infected Animals: A Rapid Evidence Synthesis](#) (2024-10)
- [University of Calgary: Human risk of avian influenza A\(H5N1\) associated with exposure to infected dairy cattle and other livestock](#) (2024-09)
- [McMaster University, Molecular signatures of mammalian adaptation of avian influenza viruses](#) (2024-07-31)

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

- [Rapid response: Preliminary guidance on human vaccination against avian influenza in a non-pandemic context as of December 2024](#) (2025-02-19)
- PHAC H5N1 preparedness, scenarios, stocktaking and action planning documents (including IDVPB Stocktaking Deck). (Internal document)
- Interdepartmental briefing documents from the Canadian Food Inspection Agency and Environment and Climate Change Canada. (Internal document)
- Royal Society of Canada One Health meeting H5N1: Evolving Situation, Evolving Science meeting materials. (Internal document)
- Gaps identified by Council of Chief Medical Officers of Health and Chief Veterinary Officers (FPT Leaders Table). (Internal document)
- [OCSA Managing Avian Flu: A Science Roadmap and Action Plan](#) (2025-02)
- Meeting records of discussion from the [PHAC Expert Panel on Avian Influenza A\(H5Nx\)](#) (and associated summary of science advice received from the panel).
- Meeting notes from the WHO R&D Blueprint Global Consultation: What research is important to prepare and respond to H5N1 influenza outbreaks (2025-03-19). (Internal document)
- [Guidance on human health issues related to avian influenza in Canada \(HHAI\)](#) (2025-07-22)

Definitions

Science: The pursuit and application of knowledge and understanding of the natural and social world following a systematic methodology based on evidence. [Reference 4](#) This includes a continuum of creative and systematic

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

activities directly related to the generation, advancement, dissemination and application of scientific and technological knowledge. In the context of this report, this may include knowledge syntheses, operational/implementation research, applied research, and observational and intervention studies.

Research: Any undertaking intended to extend knowledge through a discipline's inquiry or systematic investigation. [Reference 5](#)

One Health: "an integrated, unifying approach that aims to sustainably balance and optimize the health of humans, animals, plants and ecosystems. It recognizes the health of humans, domestic and wild animals, plants and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development." [Reference 6](#)

Footnote A

Those marked with footnote "a" were most consistently assessed as being timely priorities. These reflect ongoing uncertainties, knowledge or evidence gaps highlighted in the literature and from expert advice; are critical to improving our assessment of risk related to spillover into humans; are activities best initiated in the current preparedness phase; and are aligned with federal A(H5Nx) priorities.

References

Reference 1

Burrough ER, Magstadt DR, Petersen B, Timmermans SJ, Gauger PC, Zhang J, et al. Highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus infection in domestic dairy cattle and cats, United States, 2024. *Emerg Infect Dis.* 2024 Jul [cited 2024 May 13]. <https://doi.org/10.3201/eid3007.240508>

Reference 2

Public Health Agency of Canada - Avian Influenza A(H5Nx): Public Health Knowledge Gaps and Research Needs 2025

Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses updated June 5, 2024. Available from:

<https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-report-06052024.htm> Technical Report: June 2024 Highly Pathogenic Avian Influenza A(H5N1) Viruses | Bird Flu | CDC

Reference 3

Government of Canada. Influenza virus type A: Infectious substances pathogen safety data sheet. Updated 04 October 2023. Available from: [Influenza virus type A: Infectious substances pathogen safety data sheet - Canada.ca](https://www.canada.ca/en/health-canada/services/infectious-diseases/influenza-virus-type-a-infectious-substances-pathogen-safety-data-sheet.html)

Reference 4

Adapted from Science Council. Our definition of science [Internet]. N.d. [cited 2024 May 13]. Available from: <https://sciencecouncil.org/about-science/our-definition-of-science/>

Reference 5

Adapted from Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 2. 2022. [cited 2025 July 28]. Available from: <https://ethics.gc.ca/eng/documents/tcps2-2018-en-interactive-final.pdf> Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022)

Reference 6

Adapted from the One health joint plan of action (2022-2026): working together for the health of humans, animals plants and the environment. Updated 14 October 2022. Available from: [One health joint plan of action \(2022–2026\): working together for the health of humans, animals, plants and the environment.](https://www.onehealth.ca/one-health-joint-plan-of-action-2022-2026)