IQVIA LABORATORIES

Proactive Preparedness for Avian Influenza Virus Pandemic

The value in innovative science and expertise for vaccine development at a faster pace

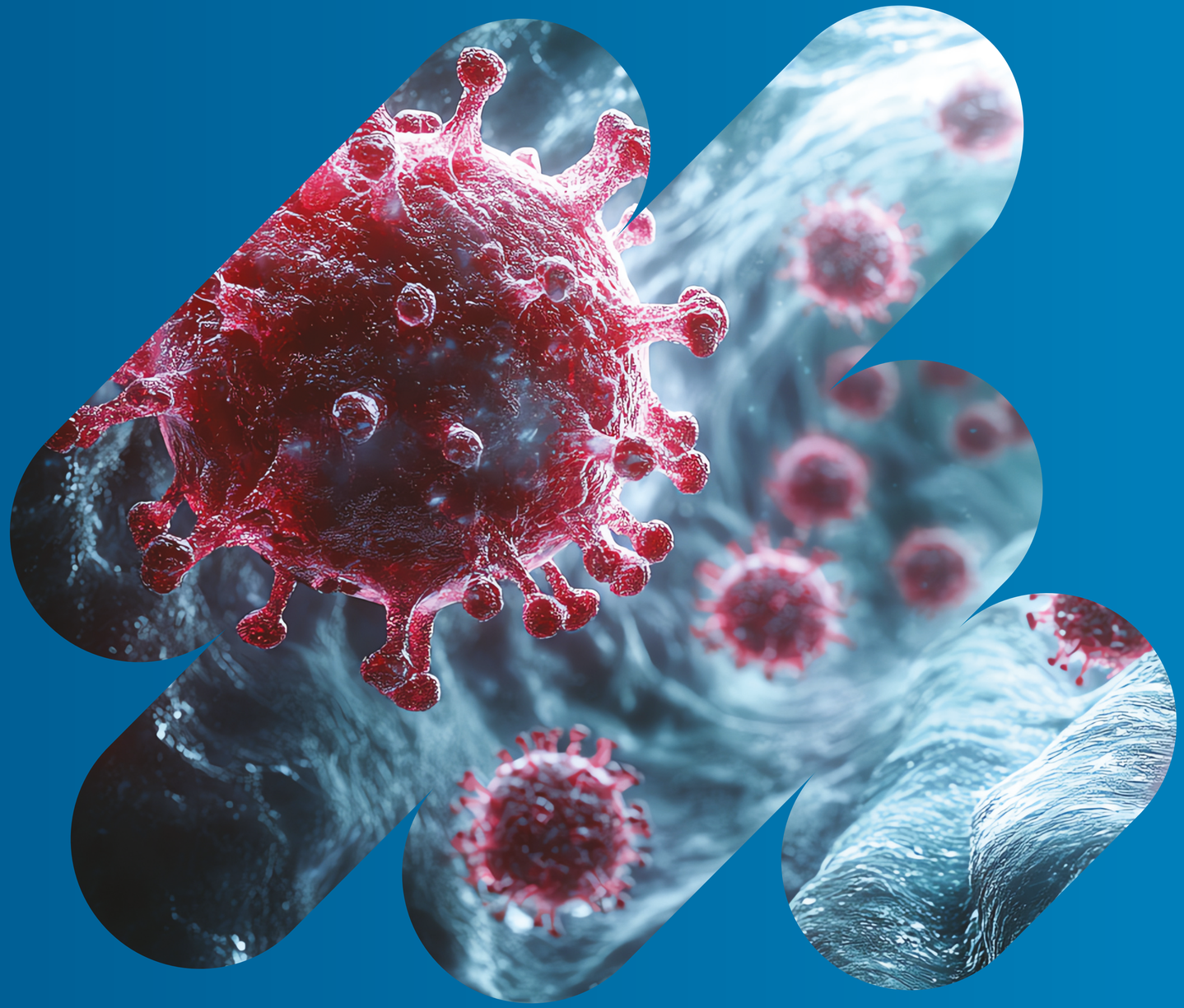

Table of contents

Ongoing global avian influenza pandemic preparedness and protection: Understanding why

H5N1-related health complications:

- Pneumonia
- Respiratory failure
- Acute kidney injury
- Multi-organ failure
- Sepsis
- Meningoencephalitis (inflammation of the brain)

Though avian influenza A (bird flu) typically spreads within animal populations, there is potential for human infection. As recently observed, H5N1, a subtype of avian influenza A, has infected poultry and cows in the U.S., Canada, Cambodia, Australia, China and other countries. If it spreads to humans, moderate disease symptoms can be serious and even life-threatening. Global observations indicate a human mortality rate of approximately 50% from H5N1 infection.

Pandemic influenza outbreaks, including avian influenza A, can occur anywhere at any time and are difficult to prevent, making holistic and proactive outbreak preparedness critical. Why?

- Unlike seasonal influenza, pandemic influenza is a rare event for which there is little pre-existing immunity.
- Because initial signs and symptoms of infection, such as mild fever, cough and muscle aches, are like those of seasonal flu and other respiratory viruses (e.g., COVID-19), individuals may delay medical care, potentially exposing others while contagious.
- To date, more than 500 bird species and 70 mammalian species have been infected with H5N1 across multiple countries globally. The main way to prevent bird flu is to avoid direct contact with infected or dead poultry, cows and other animals. However, typically, testing for H5N1 detection is conducted as multiple flocks or herds within a farming community are infected and symptoms occur, creating room for exposure among farm employees and others in direct contact with these animals.

Currently, the public health risk for humans is low-to-moderate. However, for reasons above, global infectious disease stakeholders, including the World Health Organization, United Nations and the U.S. Centers for Disease Control and Prevention, emphasize the need to thoroughly investigate every occurrence and work to prevent rapid outbreaks through strengthened virus surveillance and related response strategies.

Typically, individuals in direct contact with birds and other animals can determine the need for H5N1 testing in livestock once there are multiple animals affected and potentially in contact with humans. As seen in Figure 1, in the U.S. alone, H5N1 infection among various mammals and birds is expanding, raising concern among global public health stakeholders regarding the risk of virus mutation that allows easier transmission to humans and a pandemic-level scenario.

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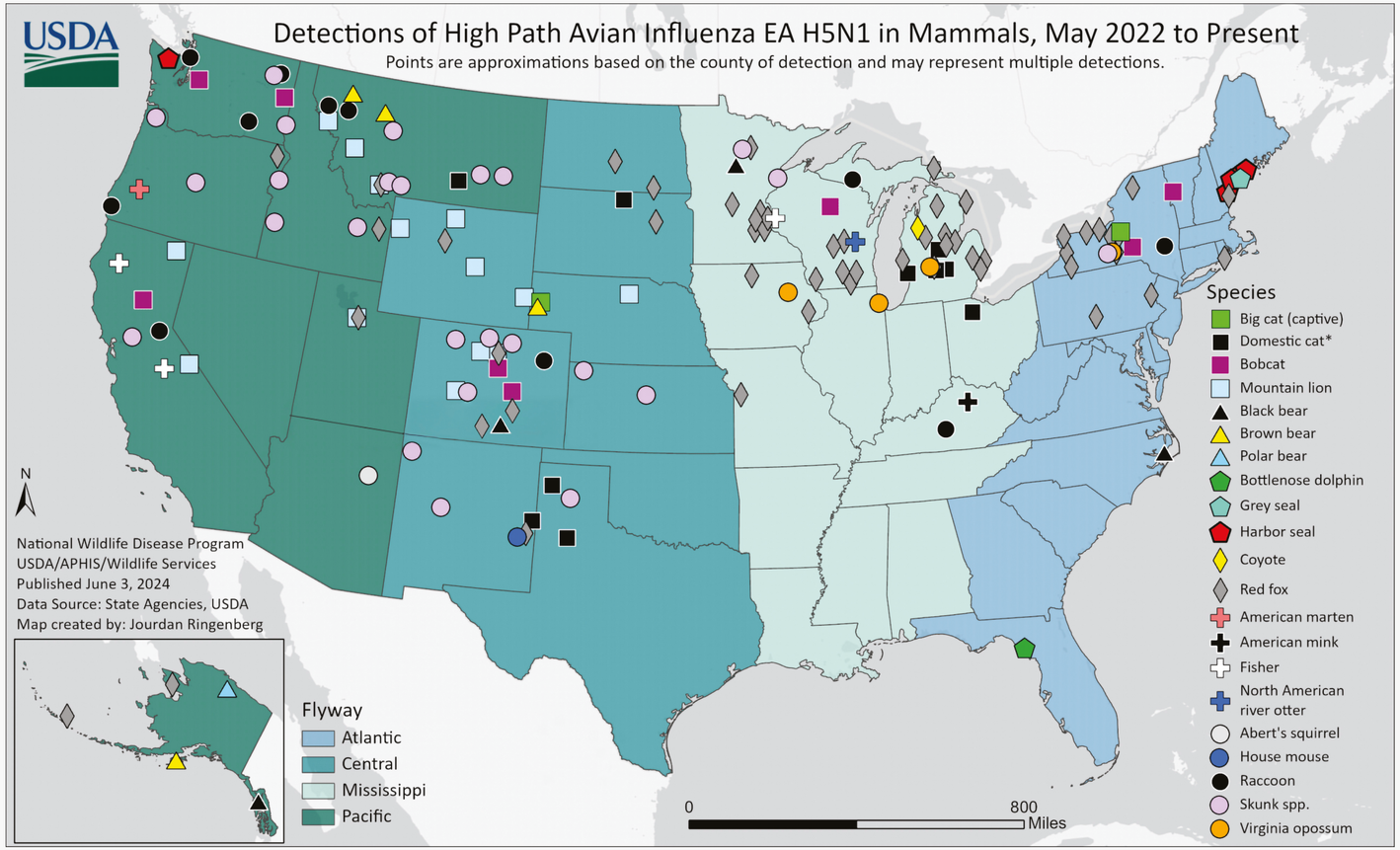
“We must remember … that this (low-to-moderate risk) can change quickly as the virus is evolving, and we must be prepared for such a scenario.”

— Dr. Maria Van Kerkhove, Director of Epidemic and Pandemic Threat Management, WHO



Collaborative virus surveillance and downstream protection efforts: Understanding who

Because we cannot stop or detect avian influenza until it actually occurs in livestock or other animals, it is essential for global infectious disease stakeholders to focus on finding a way to detect the virus and collectively strengthen surveillance efforts worldwide to ensure we're ready for a potential pandemic.

Though vaccinations are an effective way to prevent an avian influenza virus outbreak, attitudes have changed in the six years since COVID-19 cases were first detected and announced, and the ensuing pandemic unfolded. According to scientific literature reviews, there is an undertone of "vaccine fatigue" causing a decreased interest in infectious disease and related vaccine-specific information and education. This fatigue is a viable influencer of how effectively immunity can be maintained in the general population.

However, expert stakeholders maintain the importance of proactively preparing to effectively prevent or fight the next global pandemic, and there were real-world insights and best practices gained from the COVID-19 pandemic. Effective global outbreak preparedness, whether against avian influenza, such as H5N1, or another virus, requires a comprehensive and shared strategic framework focused heavily on deliberate collaborations with key global epidemic preparedness and vaccine development stakeholders.

Within the holistic strategy, who are the key players and how are the moving pieces coming together to better protect those at-risk for serious complications from avian influenza or a similar virus?

Accelerated access to virus strains for evaluation

National government public health experts, such as the CDC and Canada's National Microbiology Laboratory, typically take the lead in closely monitoring virus surveillance to confirm avian influenza infection among animals and spearheading testing and sample collection strategies. From that point, it is a vital part of the strategy to quickly learn more about the virus strain and potential for rapid mutation and transmission.

To get ahead of the potential for a global pandemic, IQVIA Laboratories' Vaccines scientific leadership and team closely collaborates with national government stakeholders, including the Canadian National Microbiology Laboratory, to access secured samples of the specific strain to support the development of effective vaccines and treatments in a timely manner. Experts at IQVIA Laboratories are also in discussion with the CDC to develop a collaborative plan to shift from virus surveillance to vaccine development.

Through ongoing partnerships with leading laboratory network partners in global vaccine protection efforts, including the Coalition for Epidemic Preparedness Innovation, the Bill and Melinda Gates Foundation and the U.K. Health Security Agency, our teams can also ensure access to avian influenza strains for evaluation and potential vaccine development.

Accelerated clinical evidence generation for vaccine validation

In conjunction with national and regional stakeholders, IQVIA Laboratories is supporting CEPI's 100 Days Mission to spearhead faster and more equitable responses to future health emergencies.

Collaborative virus surveillance and downstream protection efforts: Understanding who

IQVIA Laboratories aims to derive meaningful insights from virus surveillance for effective vaccine development via valuable stakeholder collaborations with:

- National government surveillance networks
- Vaccine clinical trial sponsors
- Global and regional public health coalitions
- Non-for-profit organizations

CEPI is relying on IQVIA Laboratories and IQVIA's expertise and resources to implement global clinical research strategies and procedures to rapidly initiate clinical evidence generation regarding vaccines. In the fight against COVID-19, CEPI created a Centralized Laboratory Network in 2020, identifying IQVIA Laboratories and the U.K. HSA as two reference labs to help develop and transfer qualified and validated assays and key reagents necessary for immunogenicity and efficacy evaluation to the Network's labs worldwide. Under the world's largest network of vaccine testing laboratories, it was through an unprecedented level of harmonization and collaboration between stakeholders, including IQVIA Laboratories, that the industry was able to rapidly evaluate, approve and disseminate the most effective vaccine options to respond to the COVID-19 pandemic.

Since the network launched in 2020, the collective efforts have helped assess various vaccine candidates in all stages of development, processing more than 70,000 samples to date.

Additionally, as an integral part of ongoing pandemic preparedness and response efforts, IQVIA Laboratories Global Head of Vaccine Sciences Dr. Luc Gagnon was selected to join CEPI's recently established Global Central Laboratory Network Advisory Council. Dr. Gagnon serves as liaison to help ensure all 18 of the global labs under the CEPI CLN stay engaged in critical decision-making processes regarding global epidemics and public health concerns, including:

- U.K. Medicines and Healthcare products Regulatory Agency
- National Institutes for Food and Drug Control of China
- Uganda Virus Research Institute
- Translational Health Science and Technology Institute of India
- Synexa Life Services, a global provider of biomarker and bioanalytical services.

To lead global epidemic preparedness efforts, it is essential to be fully integrated into the work of stakeholders within the broader healthcare ecosystem. This goes well beyond simply staying in the know of an outbreak and reacting accordingly. It requires maintaining close working relationships with key stakeholders to discuss the finer details. This includes providing strategic guidance and feedback where needed, discussing solutions to overcome scientific and logistical challenges and offering expertise in assay development, validation and use in compliance with regulatory and quality standards in mind.

Fine-tuning the science for effective and timely vaccine protection: Understanding how

Avian influenza strains of interest:

- H5N1 A/Vietnam/1203/2004
- H5N1 A/Indonesia/5/2005
- H5N1 A/turkey/Turkey/1/2005
- H5N1 A/dairy_cattle/Texas/24-008749-001-original/2024|A
- A/American Wigeon/South Carolina/22/2021
- A/Guizhou/1/2013
- A/Cambodia/NPH230032/2023

Virus detection is a critical first step in a holistic global protection strategy, but what next?

The IQVIA Laboratories Vaccines team has more than 25 years of experience in vaccine efficacy and safety evaluation as a partner to industry leading vaccine manufacturers worldwide. In closely monitoring and reviewing avian influence virus surveillance data, including H5N1, from multiple stakeholders over years, our deep bench of cross-functional scientists and clinical experts are ready to qualify strains of interest when needed through a spectrum of advanced lab testing capabilities.

By first securing access to the strain for sequencing, our experts can develop tailored testing tools to further vaccine or anti-viral treatment development faster. With H5N1 virus detection recently in the U.S., Cambodia, Turkey, etc., our deep breadth of experts are proactively qualifying strains and related strength to provide scientific and operational guidance on the potential use of the available vaccine option based off the H5N1 virus strain originating from Indonesia in 2005.

At IQVIA Laboratories Vaccines, experts in protein science, assay development, virology, immunology and vaccines are working hand-in-hand to evaluate the efficacy of the available H5N1 vaccine in response to varying and evolving strains and related mutations. In parallel, the team continues to reach across expert aisles to approach the H5N1 vaccine and/or anti-viral treatment needs with scientific know-how, cutting-edge technology platforms and state-of-the-art laboratories to help develop, quality and validate single and multiplex immunological assays and sample testing to support vaccine development against avian influenza and other potential pandemic threats.

Protein and Science Discovery: Creating a ready-to-respond immunological toolbox

To support avian influenza vaccine development, our Protein Sciences team is equipped to develop and deliver high quality and tailored immunological tools. These include recombinant proteins, antibodies and pseudotype viruses, which are tailored to accelerate discovery and development efforts.

To stay pandemic ready, it is critical to have surrogate assays to assess the response level needed to protect those at-risk. Currently, the team is focused on modifying and/or creating a pseudotype virus based on the current live and recombinant influenza strains of interest to create a hybrid virus, eliminating toxicity found in the strains.

In proactively developing a pandemic-ready vaccine prototype, demonstrating specificity is vital, especially given the potential for multiple

Fine-tuning the science for effective and timely vaccine protection: Understanding how

mutations that allow for quicker spreading. However, as it can be difficult to predict what may be needed during a H5N1 pandemic, the team is focused on developing a broad range of assays that can be adapted quickly to neutralize the virus strain of at hand whether it is the 2005 strain from Indonesia or new H5N1 strains.

Assay Development, Qualification and Validation: Staying versatile and ready with a comprehensive and compliant catalog

With an extensive track record developing, qualifying, validating and transferring tests, our dedicated scientists support vaccine programs, from early development to clinical Phase I-IV. At IQVIA Laboratories, agnostic of modality, the nature of the infectious agent drives our assay development and selection using a wide range of solutions. As such, we maintain flexibility to adapt assays to examine the initial virus but also any variants that may arise, ensuring high assay sensitivity and specificity.

Equally important is to make sure our teams are working to develop assays that are compliant to regulatory authorities guidance and requirements. IQVIA Laboratories assay development, qualification and validation experts are deliberate in closely aligning assays in development to what has been previously approved by the U.S. Food and Drug Administration and other regulatory bodies or can be calibrated to international standards. This helps ensure if or when needed to fight a potential pandemic, regulators can review with reference points in assays currently approved and available for use.

For avian influenza virus testing, maintaining an array of qualified and validated assays (e.g., plasma reduction neutralization, hemagglutination inhibition and enzyme-linked lectin) and recombinant proteins (e.g., neuraminidase) is key to allowing stakeholders to quickly respond to the potential of a pandemic.

Currently, our experts are developing, qualifying and validating serology assays and cell-mediated immunity assays to add to our expanding catalog, staying equipped to assist pharmaceutical stakeholders in rapid vaccine development.

Vaccine Development: Focused on efficacy to respond with quickness and quality

Critical immunological tools and well-established assays are indispensable to the efficient assessment of vaccine candidates. Being able to develop these testing solutions in-house allows our experts worldwide to scale rapidly while offering quality control of batch variations.

To allow for successful movement from vaccine development through clinical evaluation, IQVIA Laboratories Vaccines has integrated advanced platforms to keep steadfast focus on evaluating vaccine and/or anti-viral treatment efficacy, which helps with pandemic preparedness and response. To date, our assays have generated data to support preclinical and clinical studies using mRNA, viral-vector, protein-adjuvant, and plant-derived virus-like particle vaccines.

Using automation, our experts can execute assays with any of the platforms below per individual needs to increase throughout and assay precision:

- Viral functional assays
- Bacterial functional assays
- Ligand binding assays
- Molecular biology
- Cellular mediated immunology assays
- *In vivo* models

Currently, IQVIA Laboratories Vaccines is strategically expanding to provide infectious disease stakeholders with strategic guidance, viable treatment pathways and related expertise and capabilities.

The essential need for global outbreak readiness at a faster pace: Understanding when

In learning from previous outbreaks, including COVID-19, the next global pandemic can happen at any time.

With strategic foresight, IQVIA Laboratories aims to stay ahead of the game and help steer effective vaccine and anti-viral treatment development for the H5N1 virus and any other global threats when needed, collaborating among in-house cross-functional scientists and clinical experts as well as external partners and global epidemic stakeholders. In the times of a potential pandemic, putting the right tools in place quickly without compromising quality is a necessity to ensuring the holistic efforts to protect those at-risk make a stronger impact.

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