MONTHLY SCIENTIFIC REVIEW ON **AVIAN INFLUENZA A(H5N1)**

EDITION 22 Avril 2025
No. 9

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Situation at a glance

- From 1 January 2003 to 20 January 2025, 964 cases of human infection with avian influenza A(H5N1) viruses and 466 deaths (CFR of 48%) were reported from 24 countries to the WHO. The last case is a 2-year-old boy from Prey Veng Province, Cambodia, who developed symptoms on February 17, 2025. He was hospitalized on February 20 and passed away on February 25, 2025. The child had exposure to chickens in the backyard of his home. (WHO)

- Additionally, 70 human cases of A(H5N1) were recently reported (41 from dairy herds, 24 from poultry farms, 2 from other animal exposure, and 3 with exposure unknown) in 10 states of the USA. **The number of H5N1 human cases reported by the CDC in the United States has remained stable since February 2025**. (CDC) Most recently, three deaths related to bird flu have been reported in Cambodia, along with one in India and another in Mexico

- Following exposure to infected dairy cattle, marking the first documentation of zoonotic transmissions of the A(H5N1) virus from a mammal.

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Scientific articles

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.

This week, discover new insights into H5N1 vaccines, epidemiology, surveillance, and public health risks.

Pathogen characterization

Reverse genetics-derived cattle H5N1 virus from Clade 2.3.4.4b shows enhanced systemic infectivity and pathogenicity than an older Clade 1 H5N1 virus in BALB/c mice.

Na Xiao a, Xiang Yong Oong , Yanxia Chen, Can Li , Howard Chun-Ho Chung , Pui Wang , Zhanhong Ye , Alvin Hiu-Chung Lam , Jianpiao Cai Wenchen Song a Andrew Chak-Yiu Lee , Hin Chu , Kin-Hang Kok , Jasper Fuk-Woo Chan , Shuofeng Yuan, Honglin Chen , Kwok-Yung Yuen , Anna Jin-Xia Zhang

Published in Emerg Microbes Infect in mars 2025

In this study, the authors investigated the viral tissue tropism, histopathological damages, and host immune responses Using both non-lactating and lactating BALB/c mice with a reverse-genetic virus constructed based on A/dairy cattle/Texas/24-008749-003/2024 (Cattle-H5N1) and comparing with an older reference Clade 1 virus, A/Vietnam/1194/2004 virus (VNM1194-H5N1). Cattle-H5N1 was highly lethal in mice (mLD50 = 1.48PFU) with broad tissue tropism and produced higher titer in respiratory tissue and multiple extrapulmonary organs than VNM1194-H5N1. In the lungs, Cattle-H5N1 infection of airway epithelium, type II pneumocytes and CD45+ immune cells were at a higher frequency than those of VNM1194-H5N1-infected mice, resulting in severe epithelial destruction and diffuse alveolar damage accompanied by elevated lung and serum pro-inflammatory cytokine/chemokines. In addition, more suckling mice co-housed with Cattle-H5N1 infected lactating mice were virus-positive (7/30 pups) than VNM1194-H5N1. These findings showed that Cattle-H5N1 is more virulent in mice than VNM1194-H5N1.

Neuraminidase reassortment and oseltamivir resistance in clade 2.3.4.4b A(H5N1) viruses circulating among Canadian poultry, 2024.

Anthony V Signore, Tomy Joseph , Charlene Ranadheera , Cassidy N G Erdelyan , Tamiru N Alkie , Sugandha Raj , Lemarie Pama , Ifeoluwa Ayilara , Tamiko Hisanaga , Oliver Lung , Nathalie Bastien , Yohannes Berhane.

Published in Emerg Microbes Infect in mars 2025.

In this research letter, the authors reported the detection of a clade 2.3.4.4b A(H5N1) reassortant virus with a neuraminidase surface protein derived from a North American lineage low-pathogenic avian influenza virus. This virus caused a widespread and ongoing outbreak across 45 poultry farms in British Columbia, Canada. Isolates from 8 farms reveal a mutation in the neuraminidase protein (H275Y) that is exceptionally rare among clade 2.3.4.4b viruses (present in 0.045% of publicly available clade 2.3.4.4b isolates). NA-H275Y is a well-known marker of resistance to the neuraminidase inhibitor oseltamivir. The authors demonstrated that this substitution maintains its resistance phenotype on the genetic background of H5N1 clade 2.3.4.4b viruses.

Epidemiology

Immune history shapes human antibody responses to H5N1 influenza viruses,

Tyler A. Garretson, Jiaojiao Liu, Shuk Hang Li, Gabrielle Scher, Jefferson J. S. Santos, Glenn Hogan, Marcos Costa Vieira, Colleen Furey, Reilly K. Atkinson, Naiqing Ye, Jordan T. Ort, Kangchon Kim, Kevin A. Hernandez, Theresa Eilola, David C. Schultz, Sara Cherry, Sarah Cobey & Scott E. Hensley.

Published in Nat Med in Mars 2025

The study examines immune responses to H5N1 viruses in 157 individuals born between 1927 and 2016. It reveals that antibody levels against H5N1 are higher in older individuals, suggesting that prior infections with type 1 viruses (H1N1, H2N2) induced immune recognition. In contrast, children, who have not yet been exposed to seasonal viruses, exhibit lower antibody levels. Analysis of responses to an H5N1 vaccine shows that children generate more antibodies after vaccination, whereas older adults already have high antibody levels before vaccination. These results suggest that younger individuals might benefit more from vaccination against H5N1 in the event of a pandemic. The study also highlights the role of anti-stalk antibodies (a conserved part of hemagglutinin) in protection against influenza and underscores the importance of monitoring H5N1 viruses while evaluating

new vaccines tailored to different age groups.

Cross-species and mammal-to-mammal transmission of clade 2.3.4.4b highly pathogenic avian influenza A/H5N1 with PB2 adaptations,

Catalina Pardo-Roa, Martha I. Nelson, Naomi Ariyama, Carolina Aguayo, Leonardo I. Almonacid, Ana S. Gonzalez-Reiche, Gabriela Muñoz, Mauricio Ulloa, Claudia Ávila, Carlos Navarro, Rodolfo Reyes, Pablo N. Castillo-Torres, Christian Mathieu, Ricardo Vergara, Álvaro González, Carmen Gloria González, Hugo Araya, Andrés Castillo, Juan Carlos Torres, Paulo Covarrubias, Patricia Bustos, Harm van Bakel, Jorge Fernández, Rodrigo A. Fasce, Rafael A. Medina.

Published in Nat commun in Mars 2025

The HPAIV H5N1 virus, from lineage 2.3.4.4b, emerged in Chile in late 2022, causing mass mortalities in wild birds, marine mammals, and one human. Genetic analysis showed that Chilean viruses are closely related to those from Peru, suggesting spread along the Pacific coast. Adaptive mutations, such as D701N and Q591K, were detected in marine mammals and humans, and some viruses showed signs of transmission between marine mammals and birds. The outbreak highlighted the rapid spread of the virus through wild bird movements and mammal-to-mammal transmission over thousands of kilometers. Chilean authorities reported thousands of animal deaths, emphasizing the devastating impact on biodiversity. Ongoing surveillance and genetic analysis are essential to assess pandemic risks and better control the virus spread.

Human Cases of Highly Pathogenic Avian Influenza A(H5N1) - California, September-December 2024,

Sophie Zhu, Kathleen Harriman, Caterina Liu, Vit Kraushaar, Cora Hoover, Kyoo Shim, Sharon I Brummitt, Jocelyn Limas, Kathleen Garvey, Jennifer McNary, Nina J Gao, Rahil Ryder, Brandon Stavig, Jeffrey Schapiro, Christina Morales, Debra A Wadford, Holly Howard, James Heffelfinger, Rebecca Campagna, Esmeralda Iniguez-Stevens, Hamed Gharibi, Denise Lopez, Laura Esbenshade, Paula Ptomey, Kavita K Trivedi, Jade A Herrera, Joanna Locke, Nicholas Moss, Paul Rzucidlo, Kimberly Hernandez, Minhphuong Nguyen, Simon Paul, Justin Mateo, Carlos Del Carmen Luna, Yer Chang, Maria Rangel, Keiryl DeLeon, Aisha Masood, Thea Papasozomenos, Payeng Moua, Katie Reinhart, Krista Kniss, C Todd Davis, Marie K Kirby, Erica Pan, Erin L Murray

Published in MMWR Morb Mortal Wkly Rep in Mars 2025

Between September and December 2024, in California, primarily in the Central Valley, 38 human cases of infection with the highly pathogenic avian influenza virus A(H5N1) were identified, including 37 among dairy farm workers exposed to infected cows and one in a child (with unknown exposure). The epidemiological investigation was conducted by local authorities and the CDC through targeted monitoring, including syndromic monitoring of employees, conjunctival, nasal, and pharyngeal sampling, and H5 subtyping tests. Genetic sequence analysis identified clade 2.3.4.4b, genotype B3.13, with no mutations facilitating human-to-human transmission, although partial resistance to baloxavir was detected. The most common symptoms were conjunctivitis (97%), myalgia, and fever. No severe cases or hospitalizations were recorded (all cases were mild). Recommendations include reinforced use of personal protective equipment (e.g., N95 masks), surveillance of exposed workers, administration of oseltamivir, and an interdisciplinary One Health approach to limit the risk of zoonotic transmission and anticipate any concerning viral evolution. The study highlights that no human-to-human transmission has been identified, but continued vigilance is essential.

Surveillance

Novel human-type receptor-binding H5N1 virus in live poultry markets, China,

Feng Wen , Yu Yang , Yong Li , Jinyue Guo , Zhili Li , Lian Liu , Hao Liu , Kun Mei , Limei Qin , Keshan Zhang , Tao Ren , Shujian Huang.

Published in Lancet microbe on in Avril 2025

This correspondence letter reports the identification of a novel H5N1 AIV strain harboring the K193N mutation in the hemagglutinin protein, isolated from a live poultry market in China. This finding raises concerns about the potential for increased human transmissibility of H5N1 viruses in China. These results provide insights into the potential threat posed by H5N1 AIVs with the K193N mutation and highlight the importance of ongoing surveillance and research efforts to prevent pandemic outbreaks.

Vaccination

Intranasal influenza virus-vectored vaccine offers protection against clade 2.3.4.4b H5N1 infection in small animal models, Ying Liu , Shaofeng Deng, Shuang Ren, Rachel Chun-Yee Tam , Siwen Liu , Anna Jinxia Zhang , Kelvin Kai-Wang To , Kwok-Yung Yuen , Honglin Chen, Pui Wang.

Published in Nat commun in Avril 2025

In the context of H5N1 influenza vaccine development, the authors employed a deleted-NS1 live attenuated influenza virus (DelNS1 LAIV) platform to rapidly develop an intranasal vaccine targeting cattle H5N1 and related clade 2.3.4.4b strains, using publicly available sequence data. This platform, previously applied in the development of a COVID-19 vaccine, demonstrated strong potential in preclinical models. A single intranasal dose of the DelNS1-H5N1 vaccine conferred robust protection against lethal challenges with HPAI cattle- and mink-derived H5N1 variants. This protective immunity persisted for up to two months in female mice and male hamsters. The observed immunogenicity was attributed to the potent induction of neutralizing antibodies, mucosal IgA, and T cell responses in mice. Overall, the DelNS1-H5N1 LAIV platform represents a promising candidate for further development as a countermeasure against potential H5N1 outbreaks in humans.

Treatment

Antiviral Susceptibility of Influenza A(H5N1) Clade 2.3.2.1c and 2.3.4.4b Viruses from Humans, 2023-2024, Philippe Noriel Q Pascua, Anton Chesnokov, Ha T Nguyen, Han Di, Juan De La Cruz, Yunho Jang, Andrei A Ivashchenko, Alexandre V Ivachtchenko, Erik A Karlsson, Borann Sar, Chin Savuth, Timothy M Uyeki, Charles Todd Davis, Larisa V Gubareva.

Published in Emerg Infect Dis in Avril 2025

In this study, the authors conducted a comprehensive antiviral susceptibility assessment of H5N1 viruses from clades 2.3.2.1c and 2.3.4.4b isolated from humans in Cambodia, Chile, and the United States during 2023–2024. They assessed the susceptibility of those virus to approved and investigational antiviral drugs. Except for two viruses isolated from Cambodia, all viruses were susceptible to M2 ion channel-blockers in cell culture-based assays. In the neuraminidase inhibition assay, all viruses displayed susceptibility to neuraminidase inhibitor antiviral drugs oseltamivir, zanamivir, peramivir, laninamivir, and AV5080. Oseltamivir was ≈4-fold less potent at inhibiting the neuraminidase activity of clade 2.3.4.4b than clade 2.3.2.1c viruses. All viruses were susceptible to polymerase inhibitors baloxavir and tivoxavir and to polymerase basic 2 inhibitor pimodivir with 50% effective concentrations in low nanomolar ranges.

Baloxavir improves disease outcomes in mice after intranasal or ocular infection with Influenza A virus H5N1-contaminated cow's milk, Jeremy C. Jones, Konstantin Andreev, Thomas P. Fabrizio, Andrew S. Bowman, Elena A. Govorkova & Richard J. Webby.

Published in Nat Microbiol in Mars 2025

In this study, the authors tested the efficacy of US FDA-approved antivirals including the neuraminidase protein NA targeted oseltamivir phosphate (OSE, Tamiflu) and polymerase acidic protein (PA) targeted cap-dependent endonuclease inhibitor active metabolite baloxavir acid (BXA, Xofluza), following lethal oral, intranasal (IN) or ocular inoculation of milk from an A(H5N1)-infected dairy cow. All orally inoculated, non-treated animals succumbed to infection; median survival time (MST) was 4.0 days. MST ranged from 5.0–7.0 days among treated groups. Only high-dose OSE provided longer MST versus non-treated groups. All inoculated, non-treated animals succumbed to infection; MST was 5.0 days. MST ranged from 6–>21 days among treated groups. High-dose OSE and both BXA doses provided longer MST versus non-treated groups, and differences were observed between low and high-dose OSE and between low doses of BXA and OSE. Together this data suggest that better disease outcomes are mediated by BXA than by OSE in IN and ocular infection routes

Public health

Highly Pathogenic Avian Influenza A(H5N1) Virus Stability in Irradiated Raw Milk and Wastewater and on Surfaces, United States,

Franziska Kaiser, Santiago Cardenas, Kwe Claude Yinda, Reshma K Mukesh, Missiani Ochwoto, Shane Gallogly, Arthur Wickenhagen, Kyle Bibby, Emmie de Wit, Dylan Morris, James O Lloyd-Smith, Vincent J Munster

Published in Emerg Infect Dis in Avril 2025

This short communication paper sough to assess the decay rates and corresponding half-lives of H5N1 virus in irradiated raw milk; on polypropylene, stainless steel, and rubber surfaces; and in irradiated wastewater from a treatment plant. The authors found a relatively slow decay in milk, indicating that contaminated milk and fomites pose transmission risks. Although the risk is low, these findings call for caution in milk handling and disposal from infected cattle.

Pathophysiology

Unique immune and other responses of human nasal epithelial cells infected with H5N1 avian influenza virus compared to seasonal human influenza A and B viruses,

Kai Sen Tan, Jing Liu , Anand Kumar Andiappan , Zhe Zhang Ryan Lew , Ting Ting He , Hsiao Hui Ong , Douglas Jie Wen Tay, Zhen Qin Aw , Bowen Yi, Arfah Mohd Fauzi , Thinesshwary Yogarajah , Lee Ching Pei Carmen , Justin Jang Hann Chu , Vincent T Chow , Mookkan Prabakaran, De-Yun Wang

Published in Emerg Microbes Infect in Avril 2025

This comparative study sought to elucidate and compare the differential responses of the nasal epithelium against HPAI infection that may contribute to its pathology, and to identify critical response markers. Human nasal epithelial cells (hNECs) were infected and cultured at the air–liquid interface from multiple healthy donors with clinical isolates of major human seasonal influenza viruses (H1N1, H3N2, influenza B) and HPAI H5N1. The infected cells were subjected to virologic, transcriptomic and secretory protein analyses. While less adapted to infecting the nasal epithelium, HPAI H5N1 elicited unique host responses unlike seasonal influenza. Interestingly, H5N1 infection of hNECs induced responses indicative of subdued antiviral activity (e.g. reduced expression of IFNβ, and inflammasome mediators, IL-1α and IL-1β); decreased wound healing; suppressed re-epithelialization; compromised epithelial barrier integrity; diminished responses to oxidative stress; and increased transmembrane solute and ion carrier gene expression.

Ocular infectivity and replication of a clade 2.3.4.4b A(H5N1) influenza virus associated with human conjunctivitis in a dairy farm worker in the USA: an in-vitro and ferret study,

Jessica A Belser, Joanna A Pulit-Penaloza, Nicole Brock, Xiangjie Sun, Troy J Kieran, Claudia Pappas.

Published in Lancet Microbe in Mars 2025

In this study, the authors aimed to investigate whether the occurrence of ocular complications reported following clade 2.3.4.4b A(H5N1) virus infection was associated with an enhanced capacity of this virus to replicate in mammalian ocular tissue and cause infection following ocular exposure. Primary human nasal and corneal tissue constructs were infected with different Influenza A viruses in vitro. Additionally, ferrets were inoculated by the ocular route with Texas/37 A(H5N1) virus using a liquid inoculum, aerosol inhalation, or ocular-only aerosol exposure to assess pathogenicity and tropism of the virus following different exposure routes. Transmissibility was assessed by placing serologically naive or pre-immune ferrets inoculated by ocular-only aerosol exposure in direct contact with serologically naive ferrets, monitoring pathogenicity in contact animals, and measuring viral titres in nasal washes of both inoculated and contact ferrets. Nasal and corneal tissue constructs supported replication of all IAVs tested. Serologically naive ferrets inoculated by liquid ocular, aerosol inhalation, or aerosol-only ocular routes with Texas/37 virus exhibited a systemic and fatal infection in all animals, transmitting the virus to naive cagemates. By contrast, reduced disease severity following ocular-only aerosol inoculation was observed in animals with pre-existing heterosubtypic immunity. These findings suggests that a clade 2.3.4.4b A(H5N1) virus from the dairy cattle outbreak in the USA, does not appear to possess features indicative of an ocular tropism.

Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

Mexico's fatal H5N1 case involved D1.1 genotype, which has been tied to serious illness

CIDRAP, on Avril 17, 2025

In updates on H5N1 avian flu today, the World Health Organization (WHO) shared new details about Mexico's recent fatal case, the country's first H5N1 infection, along with an updated risk assessment from the WHO and two global animal health groups

Bird flu reinfections at US poultry farms highlight need for vaccines, experts say

The Guardian, on Mars 28, 2025

Scores of poultry operations in the US have been reinfected by bird flu since 2022, costing hundreds of millions of dollars in federal payouts, according to documents obtained by the Guardian.The recurring outbreaks highlight the need for more aggressive prevention, including poultry vaccination and changes to how poultry is farmed, experts say. At least 56 poultry operations, including chicken and turkey farms, in the US have been infected twice by bird flu, according to depopulation and reinfection records from the US Department of Agriculture (USDA).

Au Mexique, une fille de 3 ans meurt de la grippe aviaire H5N1

Le Monde, on Avril 8, 2025

A first death from H5N1 avian influenza has been reported in Mexico, according to the World Health Organization (WHO) on Tuesday, April 8, as confirmed by regional health authorities. The case involved a 3-year-old girl who lived in the state of Coahuila in northern Mexico, they told Agence France-Presse (AFP). She was the first and only reported human case of avian flu in Mexico. The child died as a result of multiple organ failure, explained Coahuila's health secretary, Eliud Aguirre

Grippe aviaire H5N1 : stratégie vaccinale face à d'éventuels cas chez les personnes au contact d'animaux infectés

Haute Autorité de Santé, on Avril 8, 2025

H5N1 avian influenza continues to spread globally, particularly in the United States, where it is affecting multiple animal species and causing infections in individuals who have been in close contact with infected animals. To date, no human-to-human transmission has been observed. At the request of the Ministry of Health, the French National Authority for Health (HAS) has proactively developed recommendations for a vaccination strategy to be implemented in the event of human cases exposed to infected animals in France. The HAS outlines several scenarios and recommends vaccinating individuals exposed to the virus with the prepandemic vaccine developed by the pharmaceutical company Seqirus, particularly in the event of an increase in animal outbreaks and the emergence of severe human cases linked to those outbreaks.

Guidelines and practical information

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

January 2024	Interim Guidance for Employers to Reduce Exposure to Avian Influenza A Viruses for People Working with Animals
August 2024	Practical interim guidance to reduce the risk of infection in people exposed to avian influenza viruses
June 2024	Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations (CDC)
June 2024	Prevention and Antiviral Treatment of Avian Influenza A Viruses in People (CDC)
May 2024	Avis du COVARS du 24 mai 2024 - Point sur la situation liée au virus influenza H5N1 (MESRI)
December 2023	Considerations for emergency vaccination of wild birds against high pathogenicity avian influenza in specific situations (WOAH)
June 2023	Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA (ECDC)
January 2022	Guidelines for the clinical management of severe illness from influenza virus infections (WHO)
December 2021	Avis relatif à la prévention de la transmission à l'homme des virus influenza porcins et aviaires (HCSP)

Fact sheets

Transmission

Influenza A viruses are segmented, negative-sense single-stranded RNA viruses, members of the *Orthomyxoviridae* family. The antigenic diversity of these viruses arises from two surface glycoproteins: **hemagglutinin (HA)** and **neuraminidase (NA).** Combinations of these proteins create numerous influenza subtypes, with currently 18 HA and 11 NA subtypes recognized in the environment. Although avian influenza viruses spread mainly among waterfowl, particularly Anseriformes and Charadriiformes, as well as in other susceptible bird species such as Galliformes. Unlike most other avian influenza viruses, A(H5N1) 2.3.4.4b has infected more than 200 mammal species and they can occasionally infect humans but no sustained human-to-human transmission has been identified.

Diagnosis

Appropriate samples for influenza tests should be rapidly taken and processed from patients with a relevant exposure history within ten days preceding symptom onset. A(H5N1) viruses have been detected in raw milk from infected dairy cows in some locations.

Symptoms

The incubation period for A(H5N1) infection is typically two to five days after the last known exposure. A(H5N1) influenza virus infection can cause a range of diseases in humans, from mild to severe, and in some cases, it can even be fatal. Symptoms are primarily respiratory, including fever, malaise, cough, sore throat, and muscle aches. Other early symptoms may include conjunctivitis and other non-respiratory symptoms. The infection can quickly progress to severe respiratory illness and neurological changes. A(H5N1) virus has also been detected in asymptomatic individuals.

Treatment

Influenza patients should be managed properly to prevent severe illness and death. Patients with laboratory-confirmed should be treated with antiviral medicines like oseltamivir as soon as possible.

Vaccination

Vaccine development leading to the licensure of three H5N1 vaccines - clade 1 and 2.1 - by the FDA and EMA under the trade name Audenz® / Afllunox ®, Preprandix® / Pumarix®, and Foclivia® / Adjupanrix®.

More information

Technological landscape

This section outlines the current pipeline of drug development, clinical trials and technologies aimed at preventing and treating the disease.

VACCINE	**IDCDC-RG71A (Seqirus®)** (A/Astrakhan/3212/2020)	A(H5N8) antigenic prototype 2.3.4.4b Split-inactivated virion, adjuvanted	Restricted use	Developed by CDC, U.S and referenced on WHO GISRS pandemic candidate vaccine pipeline. Successfully passed relevant safety and potency HI testing. Approved by EMA for emergency use in EU/EEA countries since 9 October 2023. Pre-clinical studies have demonstrated that antisera produced against this vaccine is cross-reactive against the currently circulation H5N1 2.3.4.4b from a Texas dairy farm worker. Two phase I/II clinical studies are currently under evaluation in adults, expected to be completed end of 2024 (NCT05874713 and NCT05975840).
	A/Fujian-Sanyuan/21099/2017-like	A(H5N6) antigenic prototype 2.3.4.4b	Restricted use	Developed by CCDC, China and referenced on WHO GISRS pandemic candidate vaccine pipeline. Successfully passed relevant safety and potency HI testing.
	IDCDC-RG78A (A/American wigeon/South Carolina/22-000345-001/2021-like)	A(H5N1) antigenic prototype 2.3.4.4b	Restricted use	Developed by CDC, U.S and referenced on WHO GISRS pandemic candidate vaccine pipeline. Successfully passed relevant safety and potency HI testing.
	NIID-002 (A/Ezo red fox/Hokkaido/1/2022)	A(H5N1) antigenic prototype 2.3.4.4b	Restricted use	Developed by NIID, Japan and referenced on WHO GISRS pandemic candidate vaccine pipeline. Successfully passed relevant safety and potency haemagglutination inhibition testing.
	A/chicken/Ghana/AVL-76321VIR7050-39/2021-like	A(H5N1) antigenic prototype 2.3.4.4b	In development	In development by CDC, U.S. Currently passing relevant safety and potency testing.
	A/chicken/Ghana/20/2015-like	A(H5N1) antigenic prototype 2.3.2.1f	In development	In development by CDC, U.S. Currently passing relevant safety and potency testing.
	Preprandix® / Pumarix® (A/Indonesia/05/2005)	A(H5N1) clade 2.1 Split-inactivated virion, adjuvanted	Restricted use	Contain reactive AS03 adjuvant. Approved by EMA for emergency use in EA/EEA countries since March 2011. LIcensed by the FDA in 2013 and is currently in the U.S. National stockpile for pre-pandemic preparedness. Usable in persons six months of age and older. Generates cross-reactive binding antibodies cross-neutralization titers against H5 clade 2.3.4.4b A/Astrakhan/3212/2020 strain (Khurana et al., 2024).
	Foclivia® / Adjupanrix® (A/VietNam/1194/2004)	A(H5N1) clade 1 Split-inactivated virion, adjuvanted	Restricted use	Developed by Sanofi Pasteur (unadjuvanted), Seqirus (adjuvanted with MF59) or GSK (adjuvanted with AS03) and approved by FDA since September 2016. Vaccines are stored in the U.S. National stockpile for pre-pandemic preparedness. Foclivia® (adjuvanted with MF59) and Adjupanrix® (adjuvanted with AS03) formulation are approved for emergency use in EA/EEA countries in October 2009. Generates cross-reactive binding antibodies cross-neutralization titers against H5 clade 2.3.4.4b A/Astrakhan/3212/2020 strain (Khurana et al., 2024).
	Audenz® / Afllunox ® (A/turkey/Turkey/1/2005)	A(H5N1) 2.2.1 inactivated, monovalent vaccine, adjuvanted	Restricted use	Approved for emergency use in EA/EEA countries in November 2010. Approved by FDA since January 2020 for use in persons six months of age and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine. The license has been renewed in the U.S. on 24 April 2024.
	Panvax®	A(H5N1) Inactivated vaccine, adjuvanted	Restricted use	Developed by CSL Limited and approved by Australia since 2008. The vaccine, given in two doses, was found to be safe and well tolerated among adults aged 18 to 64 and adults older than 64.
	Influenza Virus Vaccine, H5N1 (A/Vietnam/1203/2004)	A(H5N1) clade 1 Inactivated, monovalent vaccine	Restricted use	Developped by Sanofi Pasteur and approved by FDA for emergency use in U.S since 2007. This vaccine is stored in the U.S. National stockpile for pre-pandemic preparedness. Indicated for active immunization of persons 18 through 64 years of age at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.