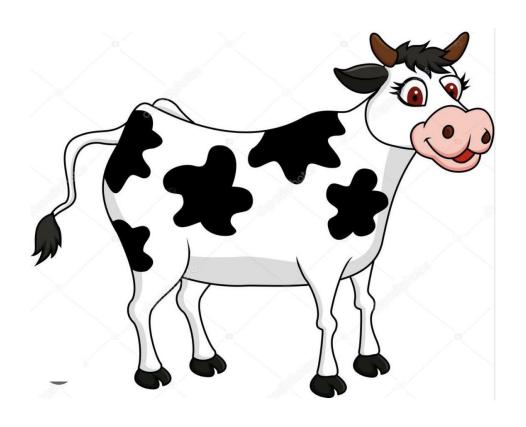
27 years of Bird Flu, Vaccines and Questions

Meryl Nass, MD July 24, 2024







"Control the Food and you **Control the** People"



Food Action Alliance

The Food Action Alliance is a leading multi-stakeholder platform for scaling food systems innovation and impact, by mobilizing collective action, partnerships, and investments in leading national food systems strategies and flagship initiatives that demonstrate the best of what is possible in food systems transformation.

"With ~828 million people suffering from hunger, and food production being a huge contributor to climate change and biodiversity loss, there is an urgent need to transform prevailing food systems."

HPAI in Great Britain since 1959

Outbreaks in poultry

- -1959 H5N1
- -1963 H7N3
- -1979 H7N7
- -1991 H5N1
- -2007 H5N1 x 2

- Incidents in wild and other birds
 - -2005 H5N1 Q
 - -2006 H5N1
 - -2008 H5N1

Outbreak of Avian Influenza A(H5N1) Virus Infection in Hong Kong in 1997 •••

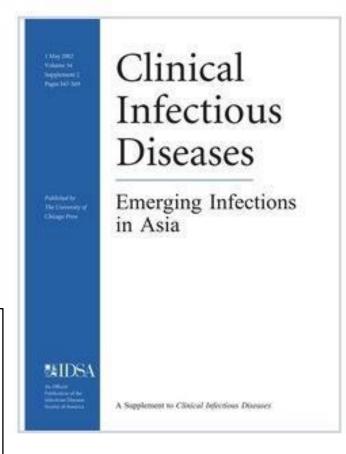
Paul K. S. Chan M

Clinical Infectious Diseases, Volume 34, Issue Supplement_2, May 2002, Pages S58–S64,

https://doi.org/10.1086/338820

Published: 01 May 2002

The first outbreak of avian influenza A(H5N1) virus in humans occurred in Hong Kong in 1997. Infection was confirmed in 18 individuals, 6 of whom died. Infections were acquired by humans directly from chickens, without the involvement of an intermediate host. The outbreak was halted by a territory-wide slaughter of more than 1.5 million chickens at the end of December 1997. The clinical spectrum of H5N1 infection ranges from asymptomatic infection to fatal pneumonitis and multiple organ failure.



There are many Influenza A viruses that affect many animals and people. They are named based on the type of hemagglutinin and neuraminidase enzymes they possess

Current Human Influenza A viruses

- H1N1
- H3N2

Current Influenza A viruses in birds. Those highlighted can infect humans

- H5N1
- H5N8
- H7N3
- H7N9
- H9N2 etc.

"High Pathogenicity" Avian Influenza (HPAI) currently refers to strains designated high pathogenicity in chickens, not humans or other animals

2004: Prototype vaccines

Dr Alan Hay, director of the World Influenza Centre in London, said the prototype vaccine was made at St. Jude Children's Research Hospital in Memphis, Tennessee and by the U.K.'s <u>National Institute for</u> Biological Standards and Control, labs that collaborate with the WHO on animal influenza virus. Hay said there were still a number of obstacles before last year's prototype vaccine could be wheeled out to protect Asian populations against H5N1. "There is the consideration that these viruses may be viewed as genetically modified organisms, and so some countries may take a more lenient view of that than other countries," he said.

Old bird flu vaccine may do the trick

Richard Ingham AFP

Scientists hope they can wheel out a bird flu vaccine already being developed to curb the latest outbreak in Vietnam. But they don't know if the current virus strain is similar enough to earlier strains, on which the vaccine is based.

U.K. and U.S. scientists working for the World Health Organization (WHO) last year readied a potential vaccine against the H5N1 strain of avian influenza virus, just two months after the disease hit Hong Kong.

Labs in Hong Kong and Tokyo are now unravelling the genetic sequence of the flu virus that has now struck Vietnam see if it is similar to the virus in last's year brief outbreak.

"If we are lucky, in the best-case scenario, the viruses will be found by the end of this week to be very similar, which means we will already have a prototype vaccine," said Dr Klaus Stoehr, head of WHO's global influenza program.

The prototype has already passed basic tests to ensure it is safety and effective in chickens, which are the hosts for the disease, and among ferrets, as a lab substitute for humans. Tuesday, 20 January 2004



This sick child is one of nine people thought to have the bird flu at Vietnam's national hospital of pediatrics in Hanoi (Reuters/Kham)

Avian Flu Still Spreading, Experts Warn - 2004-02-26

https://www.voanews.com/a/a-13-a-2004-02-26-41-avian-67487242/282001.html

- About 100 million birds have already died or been slaughtered in the battle against the disease, which has also infected 32 people and killed more than 20.
- The bird flu first crossed into humans in 1997 in Hong Kong then killing six of the 18 people it infected.
- Several weeks ago the government banned live chicken imports from mainland China when outbreaks were discovered across the country.
- Poultry retailers and distributors went on strike Thursday to protest the government ban, saying it was damaging consumer confidence and crippling their businesses.

2004



> N Engl J Med. 2004 Mar 18;350(12):1179-88. doi: 10.1056/NEJMoa040419. Epub 2004 Feb 25.

Avian influenza A (H5N1) in 10 patients in Vietnam

Tinh Hien Tran ¹, Thanh Liem Nguyen, Thi Dung Nguyen, Thi San Luong, Phuong Mai Pham, van Vinh Chau Nguyen, Thi Suu Pham, Cong Dong Vo, Thi Quynh Mai Le, Thi Thi Ngo, Bach Khoa Dao, Phuc Phat Le, Thanh Truong Nguyen, Thuy Long Hoang, Viet Tung Cao, Truong Giang Le, Dac Tho Nguyen, Hong Nga Le, Kim Tien Nguyen, Hoang San Le, Van Tuan Le, Dolecek Christiane, Tan Thanh Tran, de Jong Menno, Constance Schultsz, Peter Cheng, Wilina Lim, Peter Horby, Jeremy Farrar;

World Health Organization International Avian Influenza Investigative Team

Who raised the alarm about Bird Flu in 2004?

- * Jeremy Farrar
- * Jeremy Farrar's wife
- * Peter Horby, who
 Farrar (Wellcome Trust)
 funded to conduct the
 HCQ overdose trial in the
 UK with 400 deaths
 * The W.H.O.

Conclusions: Influenza A (H5N1) infection, characterized by fever, respiratory symptoms, and lymphopenia, carries a high risk of death. Although in all 10 cases the infection appears to have been acquired directly from infected poultry the potential exists for genetic reassortment with human influenzaviruses and the evolution of human-to-human transmission. Containment of influenza A (H5N1) in poultry throughout Asia is therefore urgently required.

> J Wildl Dis. 2012 Jul;48(3):669-75. doi: 10.7589/0090-3558-48.3.669.

Surveillance of avian influenza viruses in migratory birds in Egypt, 2003-09

Atef Soliman ¹, Magdi Saad, Emad Elassal, Ehab Amir, Chantal Plathonoff, Verina Bahgat, Maha El-Badry, Lu'ay S Ahmed, Mostafa Fouda, Mohammed Gamaleldin, Nahed Abd-Elal Mohamed, Stephanie Salyer, Claire Cornelius, Robert Barthel

Affiliations - collapse

Affiliation

- 1 US Naval Medical Research Unit Number 3, 3A Imtidad Ramses St., Abassia, Cairo, Egypt. atef.soliman.ctr.eg@med.navy.mil
- During September 2003-February 2009, the US Naval Medical Research Unit Number 3, Cairo, Egypt, in collaboration with the Egyptian Ministry of Environment, obtained cloacal swabs from 7,894 migratory birds captured or shot by hunters in different geographic areas in Egypt.
- Of the 7,894 samples, 745 (9.4%) were positive for the influenza A matrix gene
- No major die-offs or sick migratory birds were detected during the study.

https://pubmed.ncbi.nlm.nih.gov/22740532/

How do you give experimental vaccines quickly to an entire population?

- 1. EUA (Emergency Use Authorization)
 OR
- 2. Mock-up or Pre-pandemic vaccine scam: you create a prototype vaccine that will never be used, but you generate all the required paperwork, and you put it through the motions of a licensing process and issue a license. Later, you grandfather in a pandemic vaccineon the basis of this sham license.



- Pandemic influenza vaccines need to be specifically developed against the strain of virus causing the pandemic. Because the strain of flu virus causing a pandemic is not known before a pandemic is imminent, pandemic influenza vaccines can only be prepared once a pandemic has started and the exact strain of flu virus responsible can be identified.
- Pandemic preparedness vaccines can be authorised but not marketed before an influenza pandemic.
- In the event of a pandemic, once the virus strain causing the pandemic is identified, the manufacturer can include this strain in the authorised pandemic preparedness vaccine and apply for the vaccine to be authorised as a 'final' **pandemic vaccine**.
- The zoonotic flu vaccines currently available contain the virus strain A/H5N1 (bird flu) because health experts believe that this strain could cause a future flu pandemic and is responsible for recurrent outbreaks.

https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/pandemic-influenza/vaccines-pandemic-influenza

[Pandemic influenza vaccines. Concepts, European



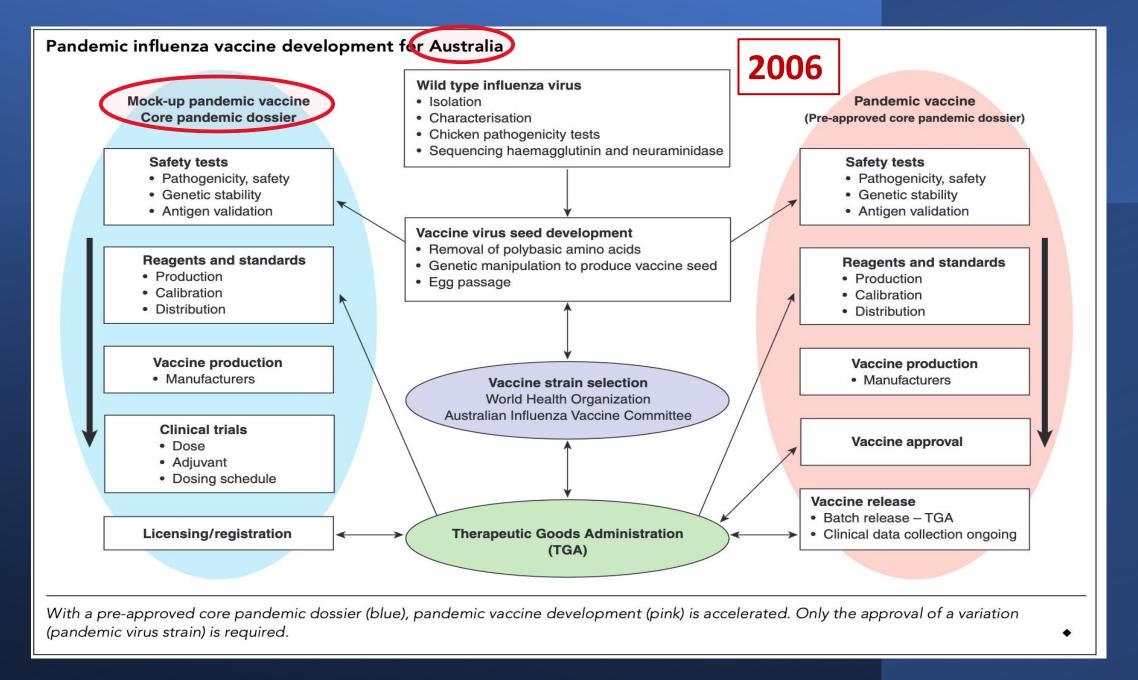
mock-up licenses, and acceptance criteria]

Began in 2003

"The concept of identifying appropriate scientific and regulatory principles to ensure rapid availability of pandemic influenza vaccines when needed were already developed starting in the year 2003. These principles allowed licensing of three so-called mock-up vaccines far ahead of any real presenting pandemic event. Those licenses (Marketing Authorizations) were immediately adapted to the novel H1N1 strain shortly after its identification in April 2009 ensuring that as early as September 2009 large parts of the German as well as of the EU population had access to licensed products which had undergone sufficient evaluation before first use in humans. In contrast, for pandemic vaccine without a previously licensed mock-up version it generally took twice as much time to accumulate data supporting the granting of a Marketing Authorization."

Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2010 Dec; 53 (12): 1242-9.

https://pubmed.ncbi.nlm.nih.gov/21161474/



Current and next generation influenza vaccines: Formulation and production strategies

Peter C. Soema ab, Ronald Kompier c, Jean-Pierre Amorij A, Gideon F.A. Kersten b

- "In addition to H1N1 vaccines, several pandemic H5N1 mock-up vaccines have been currently licensed. Mock-up vaccines are developed to generate a registration dossier, which can subsequently be used for the licensing of an actual pandemic vaccine after inclusion of a pandemic vaccine strain. This could speed up the regulatory approval process in case of a pandemic."
- "Nonetheless, extra care should be given to the safety profile when combining powerful adjuvant with <u>complex protein</u> vaccines such as WIV, split, virosomal or subunit influenza vaccines, since the induction of broad antibody responses increases the <u>risk of cross-reactivity with self-proteins</u>.
- European Journal of Pharmaceutics and Biopharmaceutics Volume 94, August **2015**, Pages 251-263

https://www.sciencedirect.com/science/article/pii/S0939641115002556

... But the concept of mock-up vaccines is irreparably flawed

- 2009: "Once the mock-up had received registration (in this case the H5N1 containing vaccine), licensing of the real pandemic vaccine (in this case Pandemrix) was cut down to five days (4).
- Analogy, however, in this case has a very weak evidence base. In 2008 the American National Vaccine Advisory Committee (NVAC) report "The role of adjuvants and new technologies" stated "antigen/adjuvant combination is vaccine specific and no data are available currently that would allow an extrapolation to another antigen or even to the same formulation given by a different route" (5).
- WHO in its 2007 guidance stated that "Because of the inherent variability in the assay systems used to measure immune responses, it is unwise to directly compare results from different studies (6).
- This view was still held in 2013, when WHO (7) warned that "an adjuvant-mediated enhancement of the immune response to one vaccine antigen, as a rule, cannot be extrapolated to the enhancement of the immune response to another antigen."
- The EMA 2005 Guideline also stresses the uncertainties of novel adjuvant use: "Unpredictability of adjuvant effects in humans results from a complex interplay between such factors as route of administration, antigen dose and the nature of the antigen. For this reason, a final safety evaluation of the newly developed vaccine formulation can only be conducted on the basis of clinical trials" (8)." https://www.bmj.com/content/362/bmj.k3948/rr-22

Heterosubtypic immunity: a false justification for vaccinating before a pandemic to provide a "pre" booster dose

Catherine J. Luke, ... Kanta Subbarao, in <u>Vaccines (Sixth Edition)</u>, 2013 [Ethics anyone?]

"Immunity elicited by infection with an influenza A virus that provides protection against infection by a virus from another HA or NA subtype is referred to as heterosubtypic immunity. This phenomenon was first proposed after the 1957 pandemic, when adults may have had some protection against the pandemic H2N2 strain as a result of previous influenza infection with an H1N1 virus. 197,198 Heterosubtypic immunity has been reported in animal models, 199-202 but evidence of the phenomenon occurring in humans is weak. Given that vaccination with LAIV is known to elicit a broad range of immune responses against conserved influenza virus proteins (see "Immunogenicity of LAIV", earlier), it is possible that LAIV may confer heterosubtypic immunity. One study was designed to address the impact of heterosubtypic immunity induced by LAIV in children.²⁰³ Children with preexisting HAI titers against either H1N1 or H3N2 viruses were challenged with a monovalent LAIV of the other subtype, and the ability of prior immunity to restrict the replication of the vaccine virus was sought as evidence of heterosubtypic immunity. Regardless of prior seropositivity, infection rates were equivalent, suggesting that LAIV did not induce heterosubtypic immunity. Larger population-based studies are underway to determine whether robust heterosubtypic immunity exists in humans."



2007

+MF59

EU approves Novartis's (mock-up) pandemic vaccine

Robert Roos, May 9, 2007

Topics: Avian Influenza (Bird Flu), Influenza Vaccines, Pandemic Influenza



May 9, 2007 CIDRAP News) – The European Union (EU) this week approved a "mock-up" influenza vaccine made by Novartis to permit a faster start on vaccine production in the event of a flu pandemic.

When the World Health Organization (WHO) declares a flu pandemic, the vaccine, called Focetria, will be adapted to contain the pandemic virus, the Swiss-based drug company announced yesterday. The vaccine will not be manufactured until a pandemic is declared.

The European Medicines Agency's (EMEA's) Committee for Medicinal Products for Human Use (CHMP) recommended approval of Focetria on Feb 22. A CHMP statement on that date said the vaccine was based on a 2004 strain of H5N1 avian flu from Vietnam.

The vaccine contains Novartis's proprietary adjuvant MF59 an immune-boosting chemical, which can

US Licenses H5N1 Sanofi bird flu vaccine 2007

https://www.news.sanofi.us/press-releases?item=137063. **EGG-BASED, UNADJUVANTED**







FDA Licenses First U.S. Vaccine for Humans Against Avian Influenza sanofi pasteur receives first U.S. license for a vaccine against avian influenza in humans marking an important milestone in pandemic preparedness

Swiftwater, Pa., and Lyon, France, April 17, 2007 – Sanofi pasteur, the vaccines division of the sanofi-aventis Group, announced today that the U.S. Food and Drug Administration (FDA) has licensed its H5N1 vaccine, the first avian influenza vaccine for humans in the U.S. Sanofi pasteur, in collaboration with the National Institutes of Health, submitted a Biologics License Application to the FDA for this H5N1 vaccine. The licensure serves as a first key step in achieving the government's goal of stockpiling vaccine intended to protect those who are at increased risk of exposure to the H5N1 influenza virus contained in the vaccine during the early stages of a pandemic.



NEW YORK POST

LATEST IN US NEWS



Crazed woman who threw acid at stranger's face in NYC subway...



Dem se Republ commit

US NEWS

lowa declares state of emergency over bird flu outbreak

By Associated Press

Published May 2, 2015, 2:31 p.m. ET

2015

Iowa Governor Terry Branstad declared a state of emergency on Friday due to a rapidly expanding avian flu outbreak, saying the entire state was at risk from the spread of the disease.

The announcement, which gives authorities powers to enforce preventative measures, was made soon after state agriculture officials announced four new poultry farms had initially tested positive for the virus.

Iowa, the top egg-producing state in the United States, is the third state to declare a state of emergency because of the viral outbreak, which either has led or will lead to the extermination of up to 21 million chickens and turkeys nationwide.

Minnesota and Wisconsin declared states of emergency in April.

How a terrifying narrative gets created



US NEWS













Scientists say an apocalyptic bird flu could wipe out half of humanity

By Paula Froelich

Published May 30, 2020 Updated May 30, 2020, 4:23 p.m. ET

2022

the guardian org About this content Sophie Kevany Fri 9 Dec 2022 08.54 EST

https://www.theguardian.com/enviro nment/2022/dec/09/avian-flu-hasled-to-the-killing-of-140m-farmedbirds-since-last-october

Avian flu has led to the killing of 140m farmed birds since last October

Culls and compensation have cost hundreds of millions of pounds in the US, UK and Europe, with current outbreak predicted to worsen



 ☐ Footage taken by animal charity Essere Animali in Italy appeared to show live chickens being

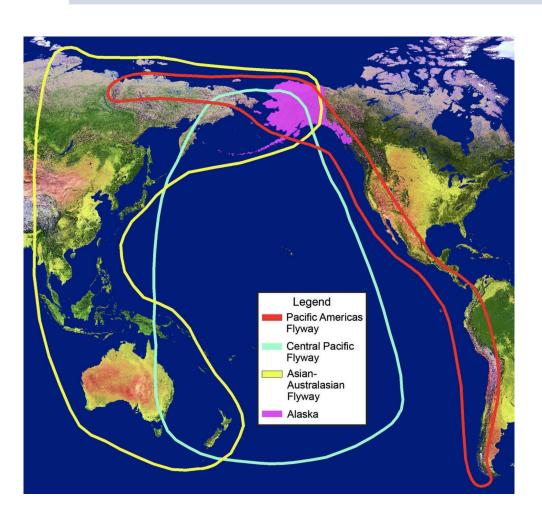


The Bird Flu Enigma

- No one has gotten the virus from cooking or eating cooked poultry
- No one has gotten the virus from eggs
- No one has gotten the virus from milk or dairy products, and FDA has found NO live virus in milk—and failed to investigate an infected raw milk situation
- No one has gotten the virus from eating beef
- It is unlikely you can wipe out the disease by culling animals since it is in the wild bird and mammal populations—spillover from them, or not?
- Are we wiping out flocks that would develop immunity?
- WHY HAVE OVER 500 MILLION CHICKENS, DUCKS AND TURKEYS BEEN CULLED, OFTEN INHUMANELY, IN A VAIN ATTEMPT TO STOP THE VIRUS?

2018

Wild Bird migrations from the US gov't Geological Survey



- "Wild birds, in particular certain species of waterfowl and shorebirds, are considered to be the natural reservoirs for avian influenza viruses.
- These subtypes that naturally occur in wild species usually cause little or no disease.
- In domestic birds, however, some AI viruses can be more pathogenic and mutation or recombination of a virus acquired from wild birds can increase disease potential."

https://www.usgs.gov/centers/nwhc/science/avian-influenza

As of July 19, 4 H5N1 human cases from cows, 7 human cases from chickens: no one hospitalized or died, EVER, in USA. The humans got conjunctivitis and/or a cold

	Wild Birds Detected	Poultry Affected	Dairy Herds Affected	
	9,552 as of 7/18/2024 Full Report >	100,405,876 as of 7/18/2024 Full Report >	163 as of 7/18/2024 I <u>Full Report ></u>	

https://www.cdc.gov/bird-flu/situation-summary/index.html

Jurisdictions with Bird Flu in Wild Birds	States with Outbreaks in Poultry	States with Outbreaks in Dairy Cows
50	48	13

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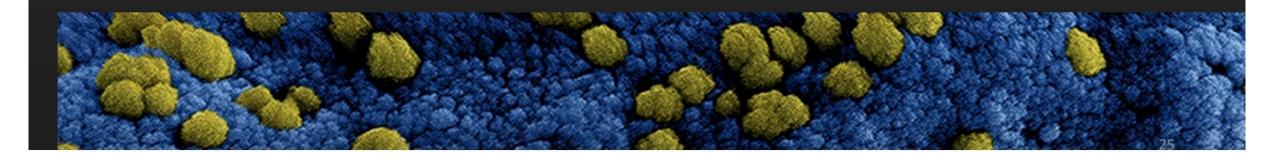
HOME > NEWS > SCIENCEINSIDER > U.S. HALTS FUNDING FOR NEW RISKY VIRUS STUDIES, CALLS FOR VOLUNTARY MORATORIUM

SCIENCEINSIDER BIOLOGY

U.S. halts funding for new risky virus studies, calls for voluntary moratorium

No grants for flu, SARS, or MERS while government pursues 1-year risk analysis

17 OCT 2014 · BY JOCELYN KAISER, DAVID MALAKOFF



careers commentary journals > Science

EXCLUSIVE: Controversial experiments that could make bird flu more risky poised to resume

Two "gain of function" projects halted more than 4 years ago have passed new U.S. review process



2019

"In 2011, Fouchier and Kawaoka alarmed the world by revealing they had separately modified the deadly avian H5N1 influenza virus so that it spread between ferrets.

Advocates of such gain of function (GOF) studies say they can help public health experts better understand how viruses might spread and plan for pandemics. But by enabling the bird virus to more easily spread among mammals, the experiments also raised fears that the pathogen could jump to humans. And critics of the work worried that such a souped-up virus could spark a pandemic if it escaped from a lab or was intentionally released by a bioterrorist. After extensive discussion about whether the two studies should even be published (they ultimately were) and a voluntary moratorium by the two labs, the experiments resumed in 2013 under new U.S. oversight rules."

"Kawaoka's grant is the same one on H5N1 that was paused in 2014."

https://www.science.org/content/article/exclusive-controversial-experiments-make-bird-flu-more -risky-poised-resume

This GOF research on bird flu, paid for by the US government, has gone on since at least 2011.

Why are we, the world's citizens, still putting up with this?

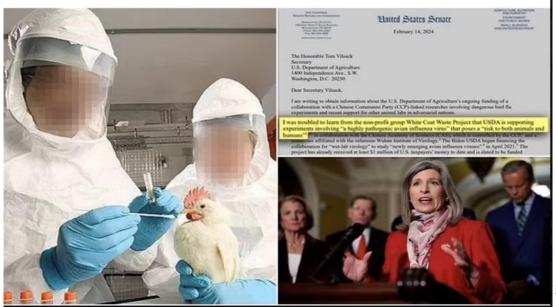
Feb 2024



REVEALED: US is collaborating with Chinese scientists to make bird flu strains more infectious and deadly as part of \$1m project - despite fears similar tests unleashed Covid

By Alexa Lardieri U.S. Deputy Health Editor Dailymail.Com

18:35 EDT 15 Feb 2024, updated 14:43 EDT 16 Feb 2024



Congress of the United States

Washington, DC 20515

April 12, 2024

The Honorable Tom Vilsack Secretary U.S. Department of Agriculture 1400 Independence Ave. SW Washington, DC 20250

Dear Secretary Vilsack,

We are disturbed by recent reports about the U.S. Department of Agriculture's (USDA) collaboration with the Chinese Communist Party (CCP)-linked Chinese Academy of Sciences (CAS) on bird flu research. This research, funded by American taxpayers, could potentially generate dangerous new lab-created virus strains that threaten our national security and public health.¹

https://www.ars.usda.gov/research/project/?accnNo=439621



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Co

Exotic & Emerging Avian Viral Diseases Research: Athens, GA

Research Y People Y USNPRC Y Research Units at USNPRC Y

ARS Home » Southeast Area » Athens, Georgia » U.S. National Poultry Research Center » Exotic & Emerging Avian Viral I Research » Research » Research Project #439621

Project Team

Kapczynski, Darrell

Related National Programs

Animal Health (103)

Research Project: US-UK-China Collab: Predictive phylogenetics for evolutionary and transmission dynamics of newly emerging avian influenza viruses

Location: Exotic & Emerging Avian Viral Diseases Research

Project Number: 6040-32000-081-008-I

Project Type: Interagency Reimbursable Agreement

Start Date: Apr 1, 2021 End Date: Mar 31, 2026

Former CDC Director, virologist Robert Redfield, MD said he would be able to make a GOF bird flu in weeks to months



Camus @ @newstart_2024 · 4h

Bird flu engineered to infect humans could be lab-produced 'in months,' former CDC Director says

Bioengineered bird flu souped up via gain-of-function lab work could be developed in a shockingly short period of time, former CDC Director Robert Redfield told News Nation recently:...

Show more





CEPI was announced in Davos in 2017 by Bill Gates and Jeremy Farrar.

CEPI received \$1.95 billion in 2022 alone.

https://static.cepi.net/downloads/2023-12/CEPI-Annu al-Progress-Report-2022.pdf

The 2023 report highlights how the world could deliver future pandemic-beating vaccines in 100 Days and outlines five key areas of innovation that are needed to contribute to accelerated development of vaccines: 1. pre-existing prototype vaccines for representative pathogens



Building the narrative: Implying we are not prepared, but we could "pull the trigger" and start vaccinating **April 2024**



The Observer Bird flu

'The issue is when to pull the trigger': how prepared are we for human bird flu?

The H5N1 virus has been devastating bird populations, and is now infecting mammals too. Is human-to-human transmission next? And are we ready for another pandemic?



Marks confident in bird flu vaccine stockpile

April 2024

By DAVID LIM and LAUREN GARDNER | 04/02/2024 12:00 PM EDT



Dr. Peter Marks, the FDA's top vaccine regulator, said Monday he's confident the U.S. stockpile of avian flu-specific vaccines would work well if deployed. The remarks came the same day the CDC confirmed that a Texas dairy worker fell ill with bird flu.

"We believe that, if we needed to, they would be reasonably good matches," Marks said at the World Vaccine Congress in Washington,

Whether the federal government would activate new vaccine production depends on how the situation unfolds, Marks indicated.

"... there's probably a pretty low threshold to pull the trigger here," he said. "This is one case we're a little luckier because it's a pathogen that we know. We know what this is and what we have in the freezer, so to speak. We have a little bit of a leg up on at least getting started."

But at the conference, Dr. Luciana Borio, a former FDA official, questioned the vaccines' potency "I'm not as confident as Dr. Marks," she said after his remarks.

https://www.politico.com/newsletters/prescription-pulse/2024/04/02/marks-confident-in-bird-flu-vaccine-stockpile-00150008



- 1. The pharmaceutical company Moderna already has a bird flu mRNA vaccine in Phase 1/2 early-stage human testing. In a statement, Moderna confirmed that "we are in discussions with the U.S. government on advancing our pandemic flu candidate."
- 2. Similar work has been going on at **Pfizer**. Company researchers in December gave human volunteers an **mRNA vaccine against a bird flu strain that's similar to** but not exactly the same as the one in cows. Since then, researchers have performed a lab experiment exposing blood samples from those volunteers to the strain seen in dairy farms, and saw a "notable increases in antibody responses," Pfizer said in a statement.
- 3. As for the vaccine for cows, Penn immunologist Scott Hensley worked with mRNA pioneer and Nobel laureate Drew Weissman to produce the experimental doses. Hensley said that vaccine is similar to the Moderna one for people.

Moderna receives \$176 million from BARDA for mRNA influenza vaccines

July 2, 2024

- * "The U.S. government already has stockpiles of H5 vaccines made by manufacturers including CSL Segirus and Sanofi."
- * "The company has already been working on mRNA-based pandemic vaccines, specifically targeting H5 and H7 avian influenza viruses.... Previous research has shown that H5 viruses are poorly immunogenic in people and vaccination requires two doses to induce what is thought to be a protective response."
- * "The H5 virus targeted in the **Moderna vaccine used in the Phase 1/2 trial** was an **H5N8,** a cousin of H5N1, the virus spreading in dairy cattle in the United States... The Seqirus H5 vaccine in the <u>National Pre-Pandemic Influenza Vaccine Stockpile</u> also targets that H5N8 virus."

"CSL Seqirus, a Proud Champion of Pandemic Preparedness, Signs an Agreement with the European Commission to Provide **Pre-Pandemic**Vaccines to the EU"

- CSL Seqirus to provide 665,000 pre-pandemic (zoonotic) vaccines to support fifteen EU and EEA Member States.
- Outbreaks of highly pathogenic avian influenza (HPAI) viruses in birds and poultry have been reported in Europe.
- The decision by the Health Emergency Preparedness and Response Authority (HERA) demonstrates their commitment to support Member States' pandemic preparedness in the face of these outbreaks.

"Under the terms of the agreement, CSL Seqirus will deliver 665,000 doses of pre-pandemic vaccine that is well-matched to the H5 of the currently circulating H5N1 strain, to fifteen EU and EEA Member States, as well as the "Union Civil Protection Mechanism" (rescEU). In addition, the 4-year contract includes an option for participating authorities to purchase up to an additional 40 million doses of the pre-pandemic vaccine over the life of the contract."

https://newsroom.csl.com/2024-06-11-CSL-Seqirus,-a-Proud-Champion-of-Pandemic-Preparedness,-Signs-an-Agreement-with-the-European-Commission-to-Provide-Pre-Pandemic-Vaccines-to-the-EU

BARDA partners with GSK and CSL Seqirus to manufacture and assess the safety, immunogenicity of pandemic influenza vaccine candidates

WEB ANNOUNCEMENT





BARDA is continuing partnerships with industry collaborators GSK and CSL Seqirus to manufacture investigational lots of influenza A/Astrakhan/3212/2020 (H5N8) virus vaccine and clinically assess the safety, immunogenicity, and dose-sparing ability of adjuvants in combination with the manufactured vaccine candidates.

The U.S. Department of Health and Human Services (HHS) continuously monitors pandemic risk in order to be ready to respond to the threats posed by novel and zoonotic influenza viruses. Within BARDA's Division of Influenza and Emerging Infectious Diseases (IEID), the National Pre-pandemic Influenza Vaccine Stockpile (NPIVS) provides preparedness for influenza pandemics and maintains stockpiles of influenza vaccine antigens and adjuvants. The IEID Division collaborates closely with federal and interagency partners and performs risk assessments to identify and evaluate potential pandemic influenza virus threats.

51 FDA Approved Medical Countermeasures Backed by BARDA

BY GLOBAL BIODEFENSE STAFF - JANUARY 12, 2020



How dangerous is bird flu? Must test be performed in high containment labs?

Either it is deadly or it isn't. Right now it isn't.

So strict regulations for handling bid flu were relaxed.

US relaxes regulations for labs handling bird flu samples to ease virus response

By Julie Steenhuysen

May 14, 2024 5:15 PM EDT · Updated 8 days ago









Purchase Licensing Rights [3]

CHICAGO, May 14 (Reuters) - U.S. government officials have temporarily relaxed strict guidelines on how public health laboratories and healthcare facilities handle, store and transport H5N1 bird flu samples, which are considered high-risk pathogens, in response to the recent spread of the virus to dairy cattle.

The revised guidance, which has not been previously reported, came at the request of the Association of Public Health Laboratories (APHL), which represents state and local labs that monitor and detect public

USA's Bird Flu Vaccines: DANGER!!!

- Home / Vaccines, Blood & Biologics / Vaccines / H5N1 Influenza Virus Vaccine, manufactured by Sanofi Pasteur, Inc. Questions and Answe

H5N1 Influenza Virus Vaccine, manufactured by Sanofi Pasteur, Inc. Questions and Answers

Why didn't the clinical trial include more people?

FDA recognizes that a limited number of people were studied in the clinical trial. The study was designed by the National Institutes of Health (NIH) as an exploratory study to look at the amount of antibodies generated in people from various doses. Because the results showed promise for providing protection against the H5N1 influenza virus and helping with national preparedness for influenza pandemic, Sanofi Pasteur submitted a Biologics License Application to FDA.

https://public4.pagefreezer.com/browse/FDA/06-02-2023T10:15/

https://www.fda.gov/vaccines-blood-biologics/vaccines/h5n1-influenza-virus-vaccine-manufactured-sanofi-pasteur-inc-questions-and-answers

2007—1st H5N1 vax licensed

illnesses. A total number of 103 subjects mean age: 39.4 years; age range 18 through 64 years;

53.4 % female, race: 81.6% White, 10.7% Black or African American, and 7.8% Asian) received

an intramuscular injection of an investigational vaccine formulation of A/Vietnam/1203/2004

(H5N1, clade 1) containing 90 µg hemagglutinin and no preservative, followed by another

injection of the same dose approximately 28 days later. Forty-eight (48) subjects received 0.5 mL

https://www.fda.gov/media/74534/download?attachment

sanofi pasteur Influenza Virus Vaccine, H5N1

- Four serious adverse events (SAEs), all considered unrelated to vaccine, occurred after
- 2 vaccination including one death and three other SAEs (one each: menorrhagia, cerebrovascular

3 event, and breast cancer).

Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted



GSK—2nd licensed 2013

STN#: 125419

Proper Name: Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted

Tradename: N/A

Manufacturer: ID Biomedical Corporation of Quebec

Indication ASO3-adjuvanted

• For active immunization for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine. Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is approved for use in persons (6 months and older) at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.

Content current as of:

11/14/2019

Regulated Product(s)

Biologics Vaccines

Q-Pan (GSK) label

https://www.fda.gov/media/87479/download?attachment

"SAEs were reported for 0.5% of recipients of (H5N1) Virus Monovalent Vaccine, Adjuvanted (n = 3,422) and for 0.3% of placebo recipients (n = 1,139) through Day 42 (21 days following the second dose of vaccine or placebo).

During the approximately one-year safety follow-up (Day 364), SAEs were reported for 3.3% of 125 recipients of (H5N1) Virus Monovalent Vaccine, Adjuvanted and for 4.1% of placebo recipients.

The following SAEs reported through Day 182 in subjects who received (H5N1)Virus Monovalent Vaccine, Adjuvanted are noted due to a temporal association with vaccination or because no alternative plausible causes for the event were identified: cerebral vascular accidents on Day 1 and Day 9 following the second vaccine dose (1 subject), pulmonary embolism (1 subject) on Day 21 following the first vaccine dose, and corneal transplant rejection (1 subject) 18 years post transplant on Day 103 following the second vaccine dose.

The following additional SAEs reported through Day 364 are noted because they were reported exclusively in subjects who received (H5N1) Virus Monovalent Vaccine, Adjuvanted and because no alternative plausible causes were identified: convulsion (3 subjects), on Days 35, 252, and 346 and thyroid cancer (3 subjects) on Days 21, 29, and 223.

Potential Immune-Mediated Diseases: Based on a pre-specified list of events, $\frac{14 \text{ new onset}}{\text{potential immune-mediated diseases}}$ were reported through Day 364, for 13 subjects ($\frac{0.4\%}{\text{ombule}}$) who received (H5N1) Virus Monovalent Vaccine, Adjuvanted (n = 3,422). An additional event was reported for $\frac{1}{\text{ombule}}$ subject (0.09%) who received saline placebo (n = 1,139)."

Q-Pan (Sanofi) Monovalent for children approved 2016

11.2 Risk-Benefit Summary and Assessment

- * "The immune response leads to a statistically significant rise in HI antibody titer, a surrogate endpoint for influenza vaccine effectiveness based upon seasonal influenza data.
- * The safety data in the pediatric population of this and closely related vaccines suggest that there are similar rates of immune-mediated adverse events in study vaccine and control populations. The pediatric clinical trial safety database is not large enough to evaluate reliably rare adverse events such as autoimmune events.
- * Given the high degree of morbidity and mortality associated with H5N1 disease, plans to have the government stockpile and control the use of Q-Pan H5N1, no plans for GSK to market the vaccine, and the restricted usage in persons at increased risk of exposure to H5N1 or during a pandemic results in an overall favorable risk/benefit profile for Q-Pan H5N1."

So, since avian flu is deadly it is okay to license a vaccine for it regardless of danger—Nass analysis

https://www.fda.gov/media/100316/download?attachment

AUDENZ (Influenza A (H5N1) Monovalent Vaccine, MF59-Adjuvanted).

Sequirus—3'd H5N1 vaccine licensed, 2020

- "SAE rates among adults 65 years of age and older were 10.5% in subjects administered AUDENZ and 15.3% in subjects who received placebo. Fatal SAEs included 11 (0.5%) AUDENZ recipients and 1 (0.1%) placebo recipients. No SAEs were assessed as being related to AUDENZ."
- "A total of 8 (2.5%) children 6 months through 17 years of age in the safety population (N=326) experienced SAEs during the study. SAEs consisted of events typical for a pediatric population and were assessed as unrelated to study vaccine. No deaths were reported during the study."
- Manufactured by: Seqirus Inc., 475 Green Oaks Parkway, Holly Springs, NC 27540

https://www.fda.gov/media/135020/download



← Home / Vaccines, Blood & Biologics / Vaccines / Vaccines Licensed for Use in the United States

3 H5N1 Vaccines Licensed for Use in the **United States**

https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states

Influenza Virus Vaccine, H5N1 (for National Stockpile)	No Trade Name
Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted	No Trade Name
Influenza A (H5N1) Monovalent Vaccine, Adjuvanted	AUDENZ

US: licensed H5N1 and unlicensed* H5N8 vaccines

- Sanofi Licensed for adults in 2007 with 103 subjects
- GSK -- Q-pan, Licensed for adults in 2013 and for children over 6 months in 2016. ASO3 adjuvant.
- CSL Sequirus -- Audenz, Licensed for adults in 2020,
 MF59 adjuvant

- * CSL Sequirus contract for H5N8 vaccine and a Phase 2 trial in 2022, MF59 adjuvant
- * Sanofi factory being built in 2023 for ? pandemic vaccines
- * Moderna contract for H5N8 mRNA vaccine 2024



June 2014

N.C. Novartis Site Is First Cell-Based Flu Vaccine Facility in the Country

Novartis selling Holly Springs vaccine plant in \$275M deal

Oct. 2014

BY JOHN MURAWSKI - **JMURAWSKI@NEWSOBSERVER.COM**UPDATED OCTOBER 28, 2014 4:58 AM

"Novartis created its vaccine unit out of its buyout of Chiron in 2006, but the Swiss drugmaker just hasn't been able to gain much traction with it. What the unit does have is the vaccine plant in Holly Springs. Novartis has received about \$500 million in support from the U.S. government for the Holly Springs plant as part of a program that gives the government say over production in the event of a pandemic. The facility in 2012 was approved by the FDA for a new process to manufacture its seasonal flu vaccine based on animal cell cultures that it says cuts weeks off production times. Novartis says the joint investment in the technology and plant is about \$1 billion."

https://www.fiercepharma.com/supply-chain/rumored-novartis-merck-asset-swap-has-interesting-manufactur ing-implications

What went wrong?

"Sanofi Pasteur, which makes the largest share of seasonal flu vaccine in the United States and which received an HHS contract for cell-based vaccine development in 2005, says it is sticking with the traditional egg-based production." **2009**

https://www.cidrap.umn.edu/h1n1-2009-pandemic-influenza/novartis-unveils-us-cell-based-flu-vaccine-plantional egg-based production.



Sanofi Breaks Ground on State-of-the-Art Facility in Swiftwater for Sustainable Production of Pandemic Flu Vaccines

Bridgewater, NJ, April 4, 2023. Sanofi and the Biomedical Advanced Research and Development Authority (BARDA), part of the Administration for Strategic Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), celebrated today the groundbreaking of a new, state-of-the-art formulation and filling facility at Sanofi's Swiftwater site in Pennsylvania.

The new formulation and filling facility will be a two-story building complete with current Good Manufacturing Practices (cGMP) formulation, filling, and support areas. The filler will be capable of filling syringe and vials using isolator barrier technology and single use technology for flexibility. This manufacturing facility represents one of three significant manufacturing investments made at the site, supported by federal funds, as part of a contract awarded earlier on December 5, 2019 by BARDA to increase domestic production capabilities for recombinant pandemic influenza vaccines.

https://www.news.sanofi.us/2023-04-04-Sanofi-Breaks-Ground-on-State-of-the-Art-Facility-in-Swiftwater-for-Sust ainable-Production-of-Pandemic-Flu-Vaccines



July 19, 2024. Sequirus H5N8 vaccine, MDCK cell culture-derived, Holly Springs, NC

- "The provisional CPT code is effective for use on the condition the **H5N8** Influenza virus vaccine candidates receive emergency use authorization from the U.S. Food and Drug Administration.
- For quick reference, the new product code assigned to H5N8 influenza virus vaccines is: 90695 Influenza virus vaccine, H5N8, derived from cell cultures, adjuvanted for intramuscular use
- The new CPT code for H5N8 influenza virus vaccines should be used with one of the following administration codes.
- For children (through 18 years of age) the administration codes are: 90460, 90461 (for additional doses)
- For adults the administration codes are: 90471, 90472 (for additional doses)..."

https://www.ama-assn.org/press-center/press-releases/ama-announces-cpt-update-avian-influenza-vaccines

Member

A pre-pandemic vaccine for a virus not currently infecting humans in Europe has been rolled out

"There are no active cases in humans or in cattle in the EU, as of early June according to the European Centre for Disease Prevention and Control (ECDC)."

EU to secure 40 million avian flu vaccines for 15 countries - officials

By Julia Payne

June 10, 2024 7:47 AM EDT · Updated 7 days ago





https://www.reuters.com/business/healthcare-pharmaceuticals/eu-sec ure-40-million-avian-flu-vaccines-15-countries-officials-2024-06-10/

Avian influenza in Finland in 2024

https://www.ruokavirasto.fi/en/animals/animalhealth-and-diseases/animaldiseases/poultry/avian-influenza/avianinfluenza-in-finland/

As of June 12,
 Finland has detected only ONE bird with H5N1 virus during all of 2024, no cows and no people

Table of the HPAI cases in birds detected in Finland in 2024

Case number	Date of detection	Location where the disease was found	Bird species	Avian influenza
1	3.6.2024 (found 24.1.2024)	Helsinki	Northern goshawk	highly pathogenic H5N1

More information



Avian influenza cases in Finland 2016-2023

Page last updated 6/12/2024

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One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland June 20, 2024

Hanna Nohynek 1 and Otto Matias Helve 1

- "The rationale was the precautionary principle, i.e. to provide protection via immunisation to enable continued fur farming in Finland."
- "Risk groups to whom the Finnish national public health institute recommends vaccination with the MF59-adjuvanted avian influenza vaccine
 - Persons in contact with farmed fur animals;
 - Persons in contact with poultry;
 - Persons handling sick or dead animals or cleaning the related facilities;
 - Persons in charge of ringing birds;
 - Person taking care of birds in animal care facilities;
 - Persons working with birds in bird or livestock farms;
 - Veterinarians working in the public sector;
 - Laboratory personnel working with testing of avian influenza;
 - Close contacts of confirmed or suspected human avian influenza cases."
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11191420/

One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland

June 20, 2024

Hanna Nohynek ¹ and Otto Matias Helve ¹



- Surveillance for the A(H5N8) vaccine safety will be passive.
- "The fact that an MF59-adjuvanted vaccine has never been used in the national immunisation programme in Finland before may raise questions..."
- There are also questions on the degree and duration of protection the vaccine will provide.
- This issue must be evaluated within a framework which considers the intricate interplay between the environment, animals, and humans [18]. Recognising this interconnectedness and the vast array of environmental impacts of human activity is crucial, and our protective measures should consider the overarching goal of maintaining and enhancing planetary health.—Let's create a "One Health" justification to explain why we are vaccinating because it makes no sense otherwise
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11191420/

Summary of risk management plan for Zoonotic Influenza Vaccine Seqirus (aH5N1)

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

The so-called risk minimization measures include only the package insert, and no plan to collect safety data on patients given the vaccine

https://www.ema.europa.e u/en/documents/rmp-sum mary/zoonotic-influenza-va ccine-seqirus-epar-risk-ma nagement-plan-summary en.pdf

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

Not applicable. There are no safety studies imposed as condition of the marketing authorisation (category 1), or as a specific obligation in the context of a conditional marketing authorisation or a marketing authorisation under exceptional circumstances (category 2) or required by the competent authority (category 3).

II.C.2 Other studies in post-authorisation development plan

Not applicable.

Wrap-Up

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2504708/

2007

- Furthermore, there is no evidence that a human pandemic or even an epidemic has been caused by any previous HPAI virus reported in poultry for more than 125 years.
- None of the last 4 pandemics is known to have been temporally associated with a poultry or wild bird epizootic, leaving no historical data to support the possibility that poultry are capable of serving as intermediate hosts in pandemic development.

JAMA. Author manuscript; available in PMC 2008 Aug 11.

Published in final edited form as:

JAMA. 2007 May 2; 297(18): 2025-2027.

doi: 10.1001/jama.297.18.2025

The Next Influenza Pandemic: Can It Be Predicted?

Jeffery K. Taubenberger, MD, PhD, David M. Morens, MD, and Anthony S. Fauci, MD

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The publisher's final edited version of this article is available at JAMA

Although most experts believe another influenza pandemic will occur, it is difficult to predict when or where it will appear or how severe it will be. Neither is there agreement about the subtype of the next pandemic influenza virus. However, the continuing spread of H5N1 highly pathogenic avian influenza A (HPAI) among poultry on several continents, associated with an increasing number of severe and fatal human infections, has raised the pandemic stakes. Genetically and antigenically divergent H5N1 HPAI strains appeared in 1997 and have been spreading globally since 2003. To date, epizootics in approximately 60 countries have caused a reported 291 human cases with 172 deaths.

Although overshadowed by H5N1, at least 8 other poultry epizootics have recently occurred, some involving human infections and, uncommonly, human deaths. H5N1 epizootics are unique, however, in causing mortality in wild birds, occasional infections in mammals, severe human infections, and in rare instances possible human—to—human transmission.

58

PMCID: PMC2504708

NIHMSID: NIHMS54790

PMID: 17488968

H7N9 Avian Influenza A Virus and the Perpetual Challenge of Potential Human Pandemicity 2013

Authors: David M. Morens, Jeffery K. Taubenberger Anthony S. Fauci Authors INFO & AFFILIATIONS

- In the 2003 Netherlands H7N7 outbreak, the majority of infected humans had conjunctivitis alone
- From the 1940s, if not earlier (32), until the 1970s, a well-adapted H7N7 virus was widely enzootic in horses and seems also to have caused uncommon and mild spillover infections in humans
- Since the 1970s, the equine H7N7 virus has become extinct or at least virtually undetectable by surveillance
- LPAI H7N7 viruses have also caused fatal outbreaks in seals (marine mammals) without stable adaptation and have been associated with spillover seal-to-human infections
- In 94 years of virologic surveillance, we have never seen a poultry-adapted influenza virus cause widespread human transmission

Things to remember

- 1. There are multiple bird flu viruses, but their relative roles in killing wild birds and poultry are unclear and the role of wild birds as an H5N1 reservoir is questionable.
- In Egypt, between 2003 and 2009, US Navy scientists found that 10% of healthy birds were positive for an influenza A (bird flu) virus
- 3. Information on how many chickens actually died from bird flu vs testing positive vs were in a chicken house being culled is withheld from the public
- 4. Under 500 humans are said to have died from H5N1 bird flu, around the world, since 1997
- 5. US-paid scientists have been making bird flu viruses more contagious, more deadly and more infectious for humans since at least 2011.
- 6. At least 2 licensed bird flu vaccines may be deadly; what about the rest?
- 7. Jeremy Farrar has stoked fear of bird flu viruses for 20 years, along with others. This seems to have been part of a plan, for which his projects are now cashing in.
- 8. Jeremy Farrar with Bill Gates initiated CEPI to collect billions in donations and make vaccines for emerging pathogens like bird flu, expanding their charities.

(continued)

- 9. Wellcome and BMGF helped sponsor scientists who performed GOF research on bird flu
- 10. Jeremy Farrar is now the Chief Scientist at WHO, pushing for globalizing the use of unlicensed, fast-tracked vaccines with no liability in drafts of the IHR and pandemic treaty
- 11. The WHO's Director-General, who is guided by Farrar, said, I think it's time to be more aggressive in pushing back on anti-vaxxers" a month ago.
- 12. Chickens are being vaccinated in China; Cows are being given mRNA vaccines for bird flu experimentally in the US and vaccines are tentatively being given to humans in Finland and the US.
- The Finland vaccines may be a prototype, designed to gather data to enable the use of other vaccines employing the same "platform," using low-paid workers as guinea pigs
- 14. It is almost a certainty that multiple countries possess strains of lab-derived bird flu that will be deadly to humans. Whether they will quickly mutate into non-virulent forms is in question. Were prototype viruses tested in ferrets, the human model? In humans?
- 15. Why are poultry being culled? Are cows next? Is this virus control or food control? Testing farmers and consumers to see what they will tolerate?



