

Role of Vaccines in Controlling High Pathogenic Avian Influenza (HPAI)

Dr. Suresh K. Mittal, DVM, PhD
Distinguished Professor of Virology
Department of Comparative Pathobiology
College of Veterinary Medicine
Purdue University



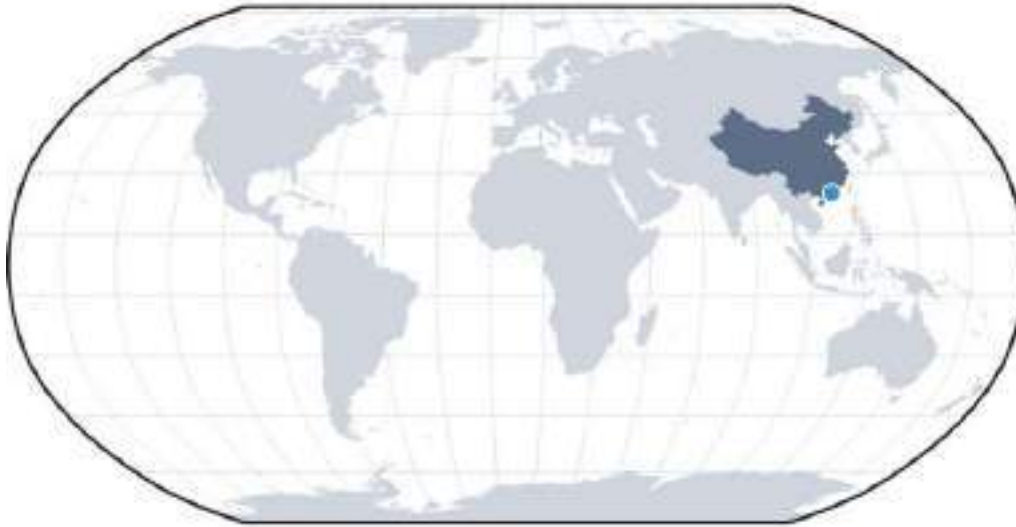
Geographical distribution of HPAI H5 viruses sampled in birds and mammals between 1996 and 2024

● Mammal ● Human

Number of sequences

● 150 ● 100 ● 50 ● 20 ● 10 ● 1

1996–1999



2000–2013



2014–2019



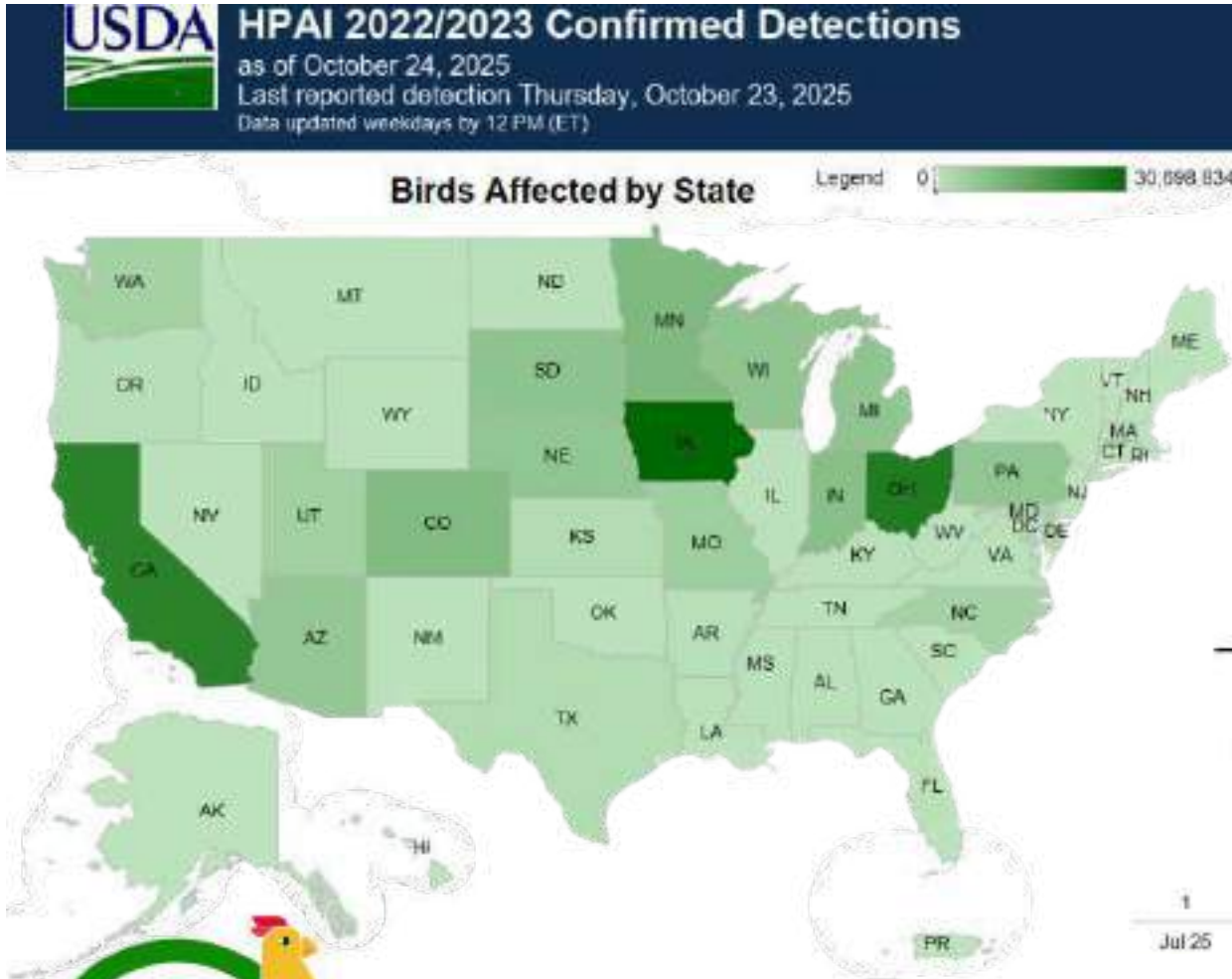
2020–2024



Nature volume 637, pages304–313 (2025)



Influenza H5N1 outbreak in US: Poultry



HPAI has been detected in a total of **1,796 flocks** (836 commercial flocks and 960 backyard flocks) – **50 states + 1 territory**.
 Loss of **182.07 million** birds since the start of the outbreak February 2022 (Loss ~ **US \$3 billion**).

Outbreak Situation Last 30 Days

64 Confirmed Flocks

Flocks tested and confirmed having HPAI

Commercial Flocks

33

Backyard Flocks

31

Birds Affected*

6.56M

*Number of birds on confirmed infected premises.

Detections by Month

Bars reflect most recent 4 months.

Commercial Flocks



Backyard Flocks



Birds Affected*



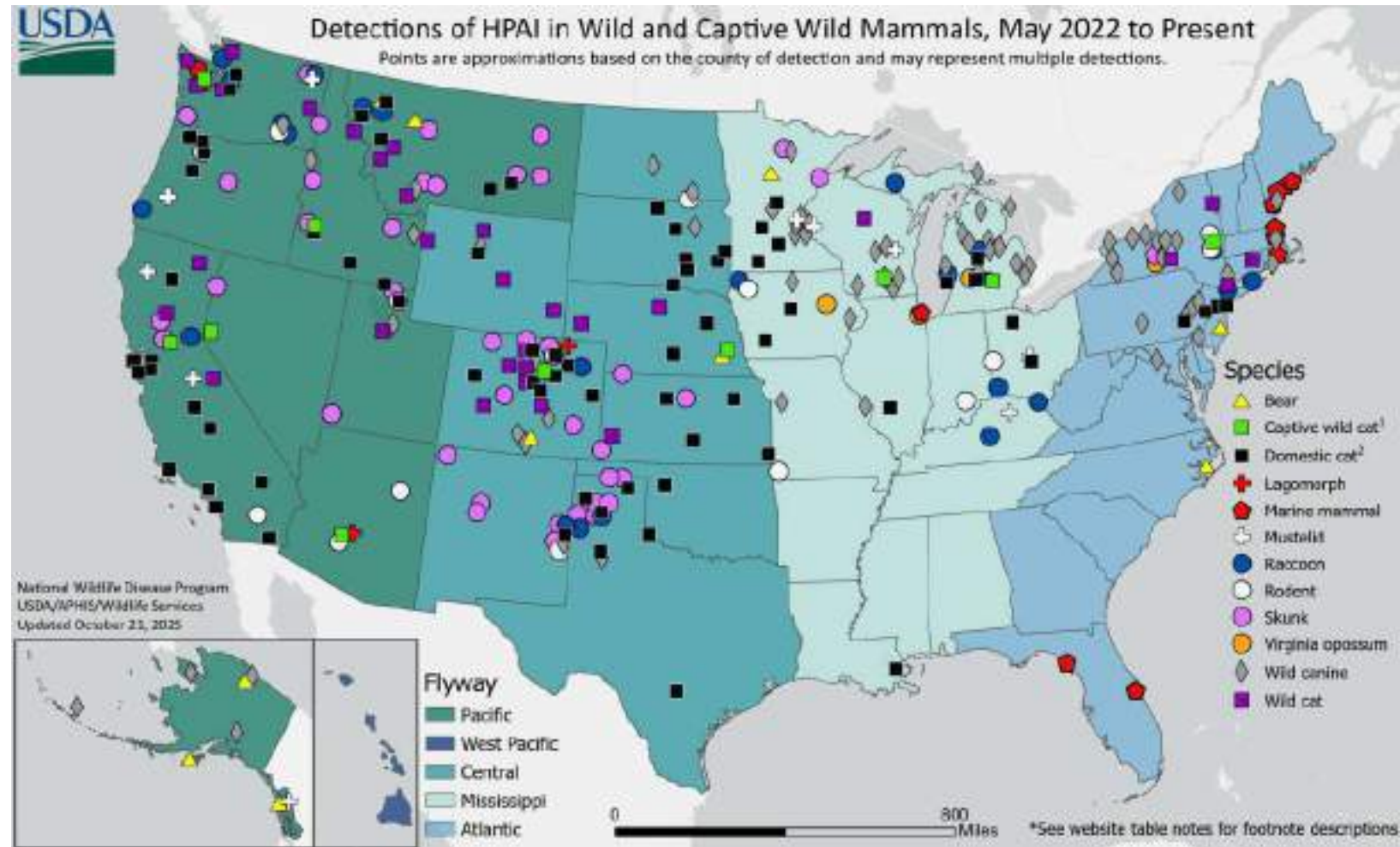
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APHIS,USDA



Influenza H5N1 outbreak in US: Wild and captive mammals



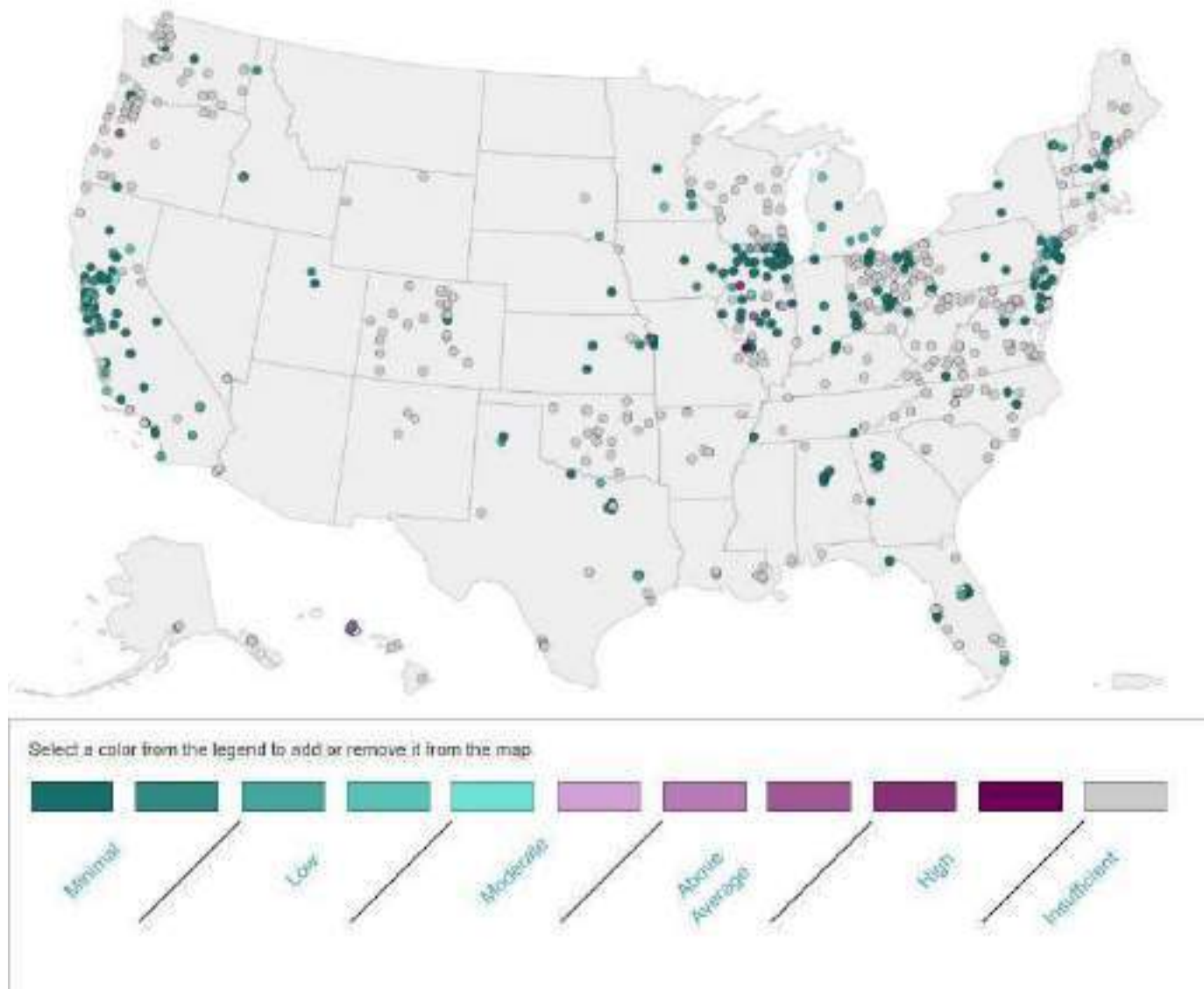
APHIS, USDA

>37 mammalian species infected including cats, foxes, skunks, sea lions, minks, and harbor seals.



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'High' Wastewater Sites and H5 Detections



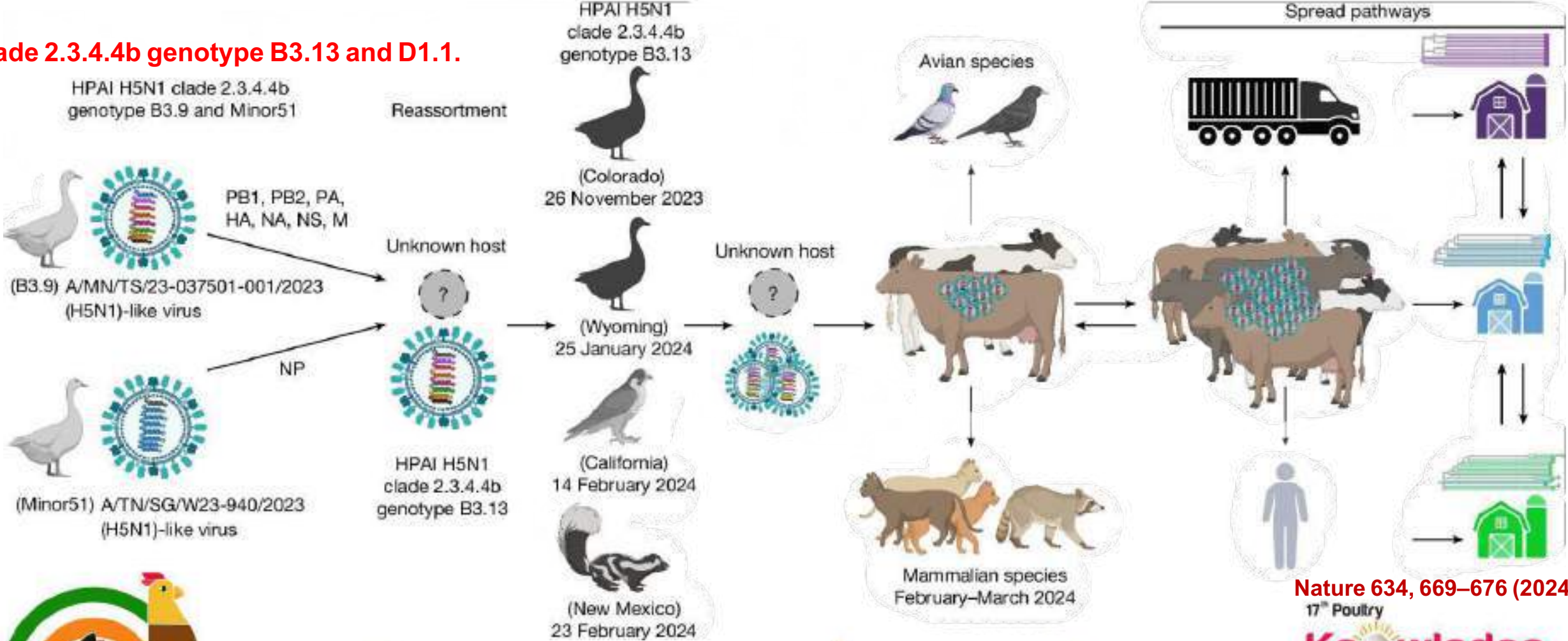
Data from June 2, 2024 – June,15, 2024

Developed Levels for Influenza A Virus in Wastewater

- Influenza A Virus Level metric
- Compare current level to levels at the same site during the 2023-2024 influenza season
- Flag ≥ 80 th percentile as "high"
- Outreach to state/local partners in "high" areas, as well as notifying state, local, and federal partners

Spillover and spread of the HPAI H5N1 into dairy cattle

Clade 2.3.4.4b genotype B3.13 and D1.1.



Nature 634, 669–676 (2024)

17th Poultry Knowledge Day 25 NOVEMBER



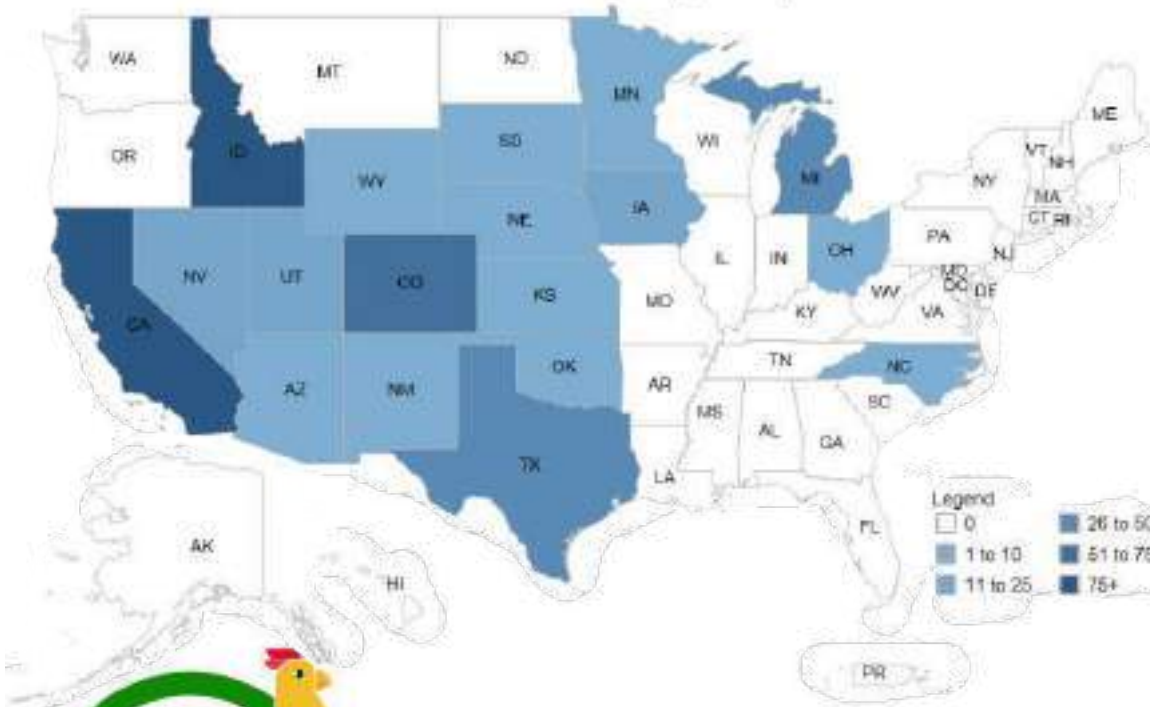
Influenza H5N1 outbreak in US: Cattle

USDA **HPAI Confirmed Cases in Livestock Herds**
Reporting period: March 25, 2024 through October 24, 2025
Last reported new confirmed case: Friday, October 10, 2025
Data updated weekdays by 12pm Eastern

Situational Update

In the Total Outbreak, in Cattle, there were:
1,081 Confirmed Cases in 18 States

Number of Confirmed Cases in Cattle by State, Total Outbreak



(APHIS,USDA)

Clinical signs: A/H5N1 replicates in the mammary gland; mastitis, massive drop in milk production (20 – 100%), and milk with abnormal yellowish colostrum-like color, thick and sometimes curdled consistency and limited respiratory signs. Common in multiparous cows during middle to late lactation.
Transmission: Possibly through contaminated milking machines.



Nature 634, 669–676 (2024)

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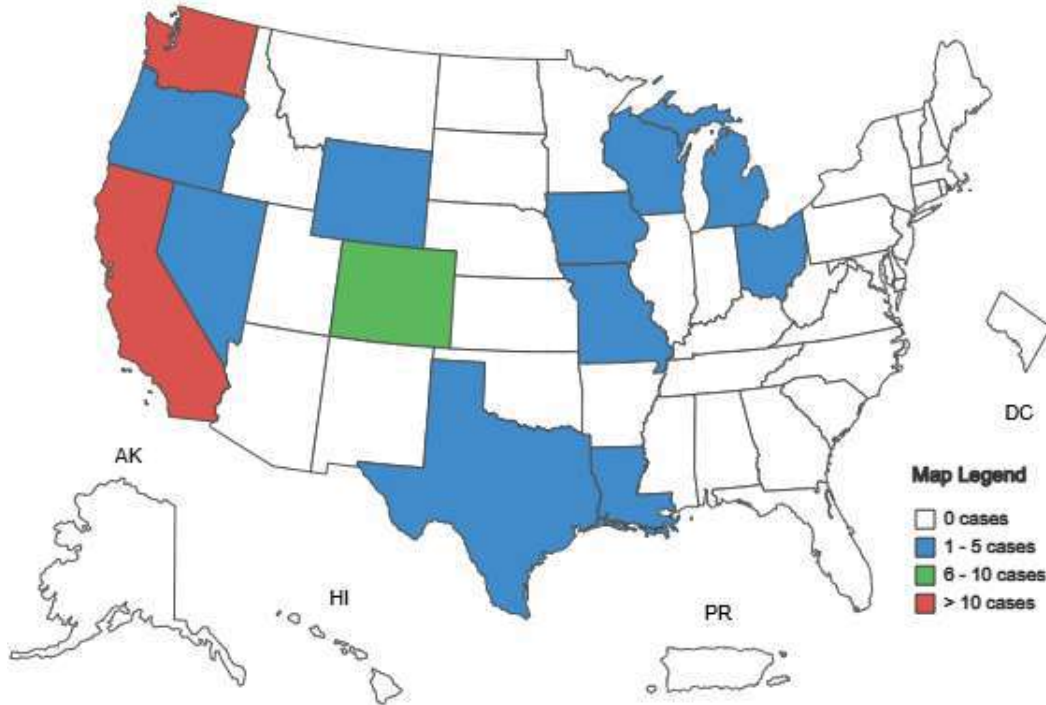


Influenza H5N1 outbreak in US : Human cases



70 confirmed cases and 1 death

Cases By State, H5 Season (H5)



Exposure Associated with Commercial agriculture and Related Operations

State	Dairy Herds (Cattle)	Poultry Farms and Culling Operations	Other Animal Exposure	Exposure Source Unknown	State Total
California	36	0	0	2	38
Colorado	1	9	0	0	10
Iowa	0	1	0	0	1
Louisiana	0	0	1	0	1
Michigan	2	0	0	0	2
Missouri	0	0	0	1	1
Nevada	1	0	0	0	1
Ohio	0	1	0	0	1
Oregon	0	1	0	0	1
Texas	1	0	0	0	1
Washington	0	11	0	0	11
Wisconsin	0	1	0	0	1
Wyoming	0	0	1	0	1
Total	41	24	2	3	70

https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html

Most cases have been directly linked to workers having contact with affected cattle or poultry farms, and clinical signs include conjunctivitis and conjunctival hemorrhage. No reports of human-to-human transmission.



HPAI: Preventive Measures for the Poultry Industry

- Biosecurity
- Hygiene and disinfection
- Quarantine of new birds
- Monitoring flocks
- Disease surveillance
- Depopulation and disinfection of the premises
- Set up of quarantine zones
- Vaccination (As a supportive measure)



HPAI: Potential Reasons of Vaccine Hesitancy

- Generation of mutants due to immune pressure
- Masking of clinical symptoms leading to silent transmission
- International trade barriers
- Logistical challenges of immunizing birds
- Change in biosecurity perception
- Vaccine efficacy



HPAI: Potential Advantages of Vaccine Use

- Reduces the incidence of infection
- Reduces shedding of viruses from infected birds
- Reduces the risk of transmission to other poultry and humans
- Reduced risk of spillover to wild animals



Zoetis Receives Conditional License from USDA for Avian Influenza Vaccine, H5N2 Subtype, Killed Virus, for Chickens

- Contains the following avian influenza virus isolate:
- **rgH5N2** - (A/turkey/Indiana/22-003707-003/2022 H5; A/chicken/Egypt/D5490B/2012 N2; PR8 backbone).
- For vaccination of chickens 3 weeks of age or older.

Zoetis - Zoetis Receives Conditional License from USDA for Avian Influenza Vaccine, H5N2 Subtype, Killed Virus, for Chickens



nature biotechnology

News in Brief | Published: 14 April 2025

USDA conditionally approves H5N1 poultry vaccine

Nature Biotechnology 43, 461 (2025) | [Cite this article](#)

3227 Accesses | 1 Citations | 49 Altmetric | [Metrics](#)

The US Department of Agriculture (USDA) has given a conditional approval to animal healthcare company Zoetis for an updated vaccine to protect poultry against the H5N1 bird flu strain. The Zoetis vaccine contains a killed version of an H5N2 variant that the company designed to work against currently circulating variants of the H5N1 virus.

The avian influenza has been spreading in dairy cow and poultry farms in the United States, causing at least several dozen infections in humans and one death. Although vaccination can help control the virus spread, the US government has long resisted its use, unlike those of China, Mexico, Egypt and France, where poultry are vaccinated against avian flu. So far, highly pathogenic influenza viruses have been eliminated from affected flocks by euthanasia. But this strategy has failed to eradicate the H5N1 viruses of the clade 2.3.4.4b that has been circulating in the country since February 2022.

Nature Biotechnology, 43, 461 (2025)



Highly Pathogenic Avian Influenza (HPAI) Poultry Innovation Grand Challenge Funding Opportunity

Last Modified: July 17, 2025

APHIS is announcing the availability of funding to support the new comprehensive strategy to curb highly pathogenic avian influenza (HPAI), protect the U.S. poultry industry, and lower egg prices.

Through this opportunity, APHIS is investing up to \$100 million to support projects in the following priority topics:

- Develop novel vaccines to protect poultry from HPAI
- Develop novel therapeutics to address HPAI in poultry
- Conduct research to further understand avian influenza in poultry and to improve response strategies

APPLICATION DEADLINE:

May 19, 2025 at 11:59 PM ET

OPPORTUNITY NUMBER:

USDA-APHIS-10025-VSSP0000-25-0015

OPPORTUNITY TYPE:

Cooperative Agreement or Interagency Agreement

CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER:

10.025, Plant and Animal Disease, Pest Control, and Animal Care

(APHIS,USDA)



USDA announces \$100M funding opportunity in fight against avian influenza

Biosecurity, therapeutics, research, and potential vaccine candidates of interest

By Malinda Larkin and R. Scott Nolen

Published on April 18, 2025

More than 168 million poultry in the U.S. have been affected with highly pathogenic avian influenza (HPAI, more specifically avian influenza type A H5N1) since February 2022, including in backyard and commercial flocks, according to [the U.S. Department of Agriculture's \(USDA\) Animal and Plant Health Inspection Service \(APHIS\)](#).

In late February, Ag Secretary Brooke Rollins announced [a five-pronged \\$1 billion approach](#) to combat avian flu and reduce egg prices, including efforts to explore vaccine use, therapeutics, and other strategies to protect poultry and reduce depopulation. Then the USDA, under the Trump administration, held its first call on March 11 with state officials and industry stakeholders to discuss surveillance, potential therapeutics and vaccination strategy, and logistics.

On March 20, the USDA, in consultation with the U.S. Department of Health and Human Services (HHS), the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA) [announced initial plans for a funding opportunity](#) to explore prevention, therapeutics, research, and potential vaccine candidates. The USDA will invest up to \$100 million in these projects, which it hopes will identify and foster innovative solutions to fight H5N1 and directly support America's farmers and ranchers.

<https://www.avma.org/news/usda-announces-100m-funding-opportunity-fight-against-avian-influenza>



Countries that have Pursued H5N1 Vaccination in Poultry

- China
- France
- Mexico
- Egypt
- Vietnam
- Indonesia
- Bangladesh



Commonly used HPAI vaccines

Inactivated vaccine

- Nobilis® Influenza H5N2 – Merck
- MEFLUVAC™ H5N8 – Kemin
- Vaxigen Flu H5N8clado 2.3.4.4 - Avimex



<https://www.kemin.com/eu/en/markets/vaccines/products/mefluvac-h5n8>



Vectored vaccine:

Herpesvirus of turkeys (HVT) vector

- VAXXITEK® HVT+IBD+H5 - Boehringer Ingelheim
- Vectormune® AI - Ceva Biovac
- INNOVAX®-ND-H – Merck

Newcastle disease vector

- KNewH5® - Avimex



<https://avimex.com.mx/productos/aves/vaxigen-k-newh5>

DNA vaccine

- ExactVax – Huvepharma

Recombinant vaccine

- Volvac B.E.S.T.® AI +ND – Boehringer Ingelheim



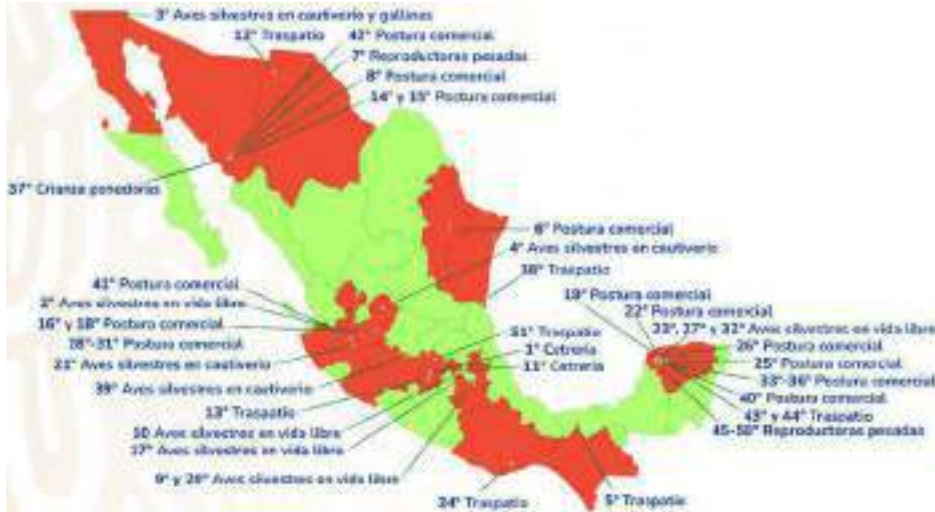
www.hafshejan-co.com/veterinary/wp-content/uploads/2020/09/Brochure-Volvac-BEST-AI-ND-2.pdf

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HPAI vaccination and outcomes:

Poultry industry: 557 million birds
Last H5N1 outbreak: October 2022

Mexico



Vaccines used:

- Volvac BEST® AI + ND KV (Boehringer Ingelheim)
- Vaxigen Flu H5N8 Clade 2.3.4.4 (Avimex)
 - 201.65 million doses were delivered following the outbreak .
 - Mexico has also vaccinated poultry against the H5N2 strain of bird flu back in 1994 and the H7N3 strain in 2012.

Vaccine efficacy:

- Seroconversion and seroprotection ~80 %.
- Reduced virus shedding by birds.
- Reverse genetics vaccine performed better than the inactivated vaccines.

Outcomes:

- There was a reduction in number of outbreaks with no new outbreaks being reported for more than a month.
- Sporadic recurrences were reported due to reintroduction of virus by migratory birds.
- Virus remains enzootic in certain regions.
- Low vaccine efficacy – antigenic mismatch.
- Vaccination alone was insufficient without strict biosecurity, surveillance, and movement control.

	Cases	Exposed	Sick	Dead	Eliminated
Commercial	29	5,667,765	1,670,418	350,126	4,961,689*
Backyard	8	12,745	7,554	1,673	11,095
Wild	14	300,685	217	211	150
Total	51	5,981,195	1,678,189	352,010	4,972,934



rr-americas.woah.org/app/uploads/2023/02/109_experiencia-en-mexico-iaap-omsa_eng.pdf

GMPC TOP, 3(1), 29 (2023)
Vaccine: X, 26, 100709 (2025)



HPAI vaccination and outcomes:

France

France launched a nationwide preventive duck vaccination campaign in October 2023

In France: 40 millions of poultry culled 2016-2023, 1 642 million euros of compensation

2016-2017 : H5N8 HPAI

488 flocks affected mainly ducks in south-west of France- 4.5 millions of poultry culled

2020-2021 : H5N8 HPAI

492 flocks affected mainly ducks in south-west of France - 3.3 millions of poultry culled

2021-2022 : H5N1 HPAI

1377 flocks affected mainly duck production areas - 22 millions of poultry culled

2022-2023 : H5N1 HPAI

402 flocks affected - 10 millions of poultry culled

Vaccines used:

- Volvac B.E.S.T. ® AI+ND (Boehringer Ingelheim)
- CEVA RESPONS AI H5 (Ceva Animal Health): Self-amplifying mRNA vaccine

Over 80 million doses (2023-2025) administered (33 million Volvac, 27 million CEVA).

Outcomes:

- Dramatic outbreak reduction: Only 11 outbreaks in 2023-2024 A and 19 outbreaks in 2024-2025 as of August 2025.
- 314–756 outbreaks were averted in 2023–2024, representing a 96%–99% reduction in epizootic size, likely attributable to vaccination.
- Estimated total cost - €105 million for 60 million ducks, far lower than the €1.4 billion that the HPAI crisis cost France in 2021-2022.

Emerg Infect Dis, 31(7),1468-1471 (2025)

rr-asia.woaah.org/app/uploads/2025/10/S2.08_Grasland-France_HPAI_vaccination.pdf

<https://www.poultryworld.net/health-nutrition/health/one-year-of-avian-influenza-vaccination-in-france>



HPAI vaccination and outcomes:

Egypt was the first African country to report H5N1 in February 2006 and began vaccination in 2006

Egypt

HPAI H5 in Egypt

Year	Farm	backyard	LBM	Nursery	Slaughter houses	Export	Frozen	customs	Total
2017	25	123	82						230
2018	23	41	29	1					94
2019	20	23	42						85
2020	19	11	36			1			67
2021	11	2	56				1		70
2022	6	3	61		1			1	72
2023	6	6	47						59
2024	2	2	30						34

LBM-Live bird markets

rr-middleeast.wuah.org/app/uploads/2025/01/6-Current-situation-ME-2024-Egypt.pdf

Vaccines used:

More than 20 vaccines have been used including inactivated, vectored and recombinant vaccines.

Vaccine efficacy:

Low vaccine efficacy in the field due to maternal antibodies, vaccine strain mismatch, poor vaccine coverage, variable vaccination protocols and quality control issues with some commercial vaccines

Outcomes:

- Vaccination provided some individual bird protection but failed to achieve population-level disease control.
- Vaccines failed to prevent virus shedding - continued circulation and silent transmission
- Sole focus on vaccination without adequate surveillance, biosecurity, and outbreak investigation 80% (24 million USD) of the available HPAI control budget to vaccination since program launch.
- As of 2024, Egypt has both H5N1 and H5N8 co-circulating.

Emerg Infect Dis.,22(3),379-388 (2016)

Egypt. J Vet Med Res,12(2), 1285 (2025)

Proc Natl Acad Sci U S A.,107(24),11044-49 (2010)

J Mol Genet Med, 3(2), 198-204 (2009)

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Influenza vaccination in wild birds

Safety and Immunogenicity of Poultry Vaccine for Protecting Critically Endangered Avian Species against Highly Pathogenic Avian Influenza Virus, United States

Todd E. Katzner, Ashleigh V. Blackford, Mary Donahue, Samantha E.J. Gibbs, Julianna Lench, Michael Martin, Tonie E. Rocke, J. Jeffrey Root, Darrel Styles, Sunny Cooper, Kristin Dean, Zachary Dvornicky-Raymond, Dominique Keller, Carlos Sanchez, Brett Dunlap, Thomas Grier, Michael P. Jones, Gregory Nitzel, Erin Patrick, Maureen Purcell, Aaron J. Specht, David L. Suarez



- California condors are **critically endangered**, population ≈ 560 birds.
- In 2023, HPAI outbreak >21 birds ($\approx 18\%$ of the subpopulation) died.

Vaccine: Inactivated vaccine (1057.R1 serial 590088) (rgH5N1) (Zoetis Inc., Parsippany, NJ)

Regimen: Either prime-boost regimen (2-vaccine) - 0.5 mL on day 0 and day 21 subcutaneous or 1-vaccine regimen of 1.0 mL on day 0 subcutaneous.

Outcome: All vaccinated vultures and 80% of vaccinated condors showed maximum measured antibody response within the published range associated with survival of vaccinated and virally challenged chickens.



Emerg Infect Dis, 31(6),1131-1139 (2025)

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HPAI Comprehensive Control Strategy

- Vaccination with regular vaccine updates to match circulating strains
- Strict biosecurity
- Hygiene and disinfection
- Surveillance

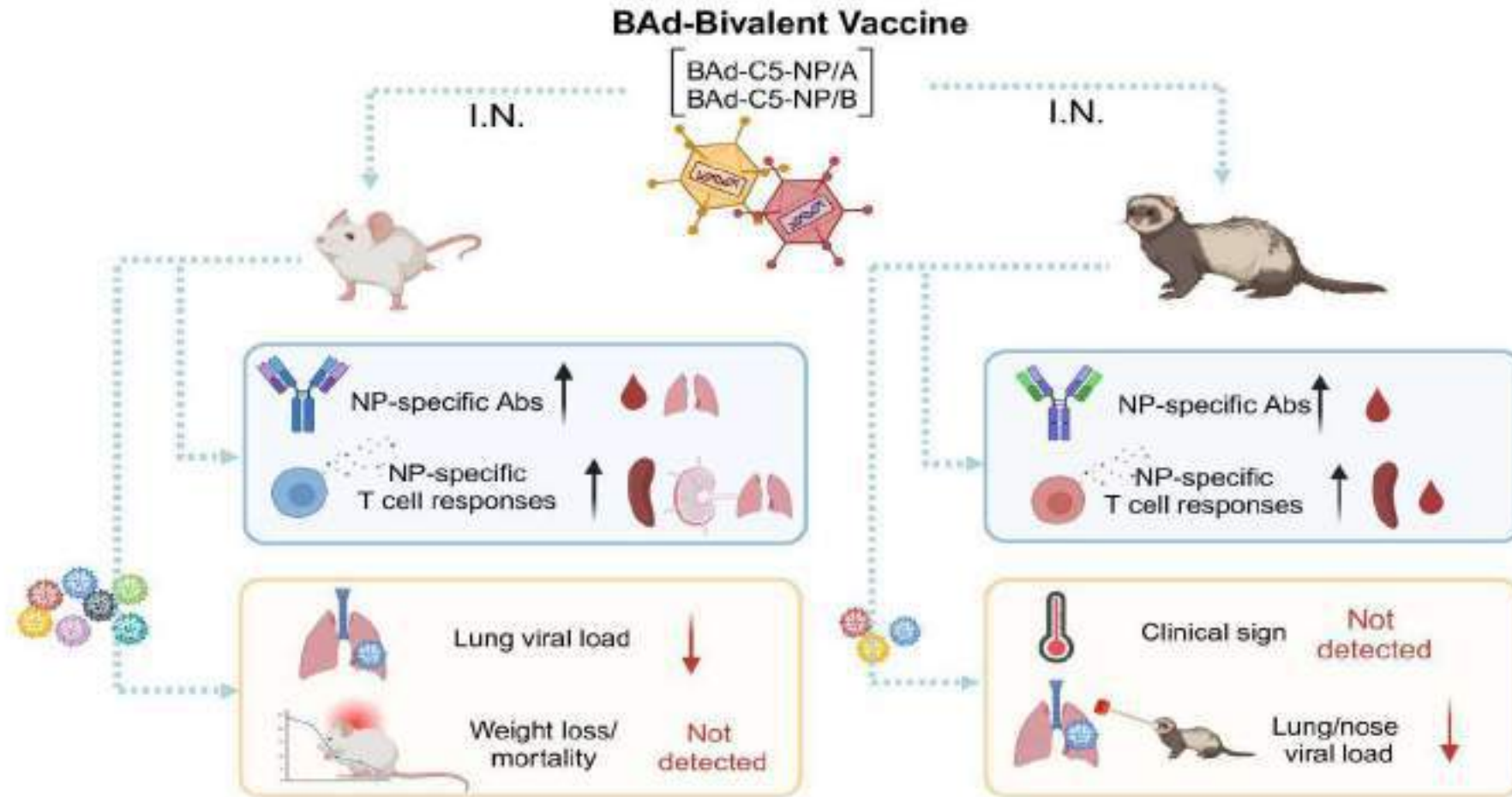


HPAI: Challenges for the Indian Poultry Industry, Administrators and Decision Makers

- Effectiveness of the current measures
- Antigenic drift will happen regardless of India's decision in favor of or against vaccination
- Control of unauthorized vaccine use by the Indian poultry farmers
- Lessons learnt from the U.S. experience
- Significant investment by the U.S. in developing better HPAI vaccines
- Play a dominant or dormant role in HPAI control strategies

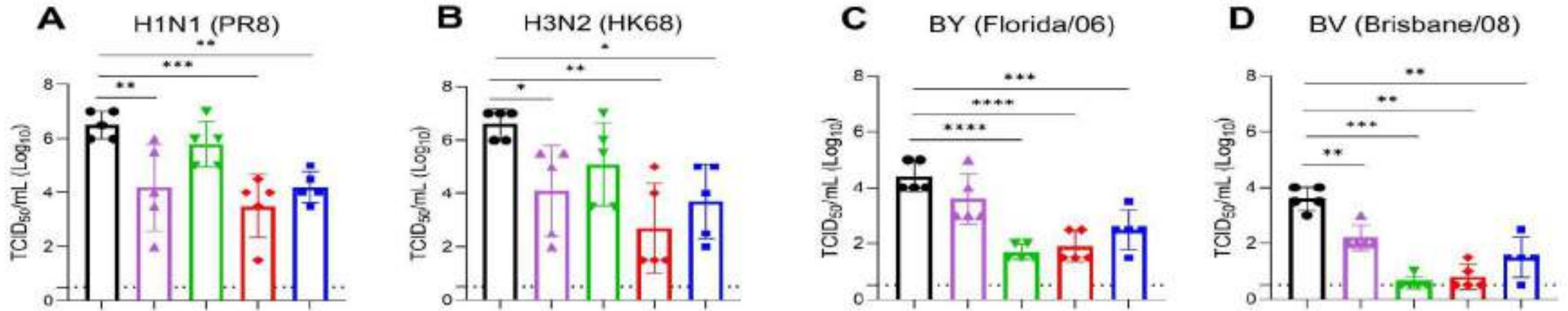


Bovine Adenoviral Vector-based Universal Influenza Vaccine

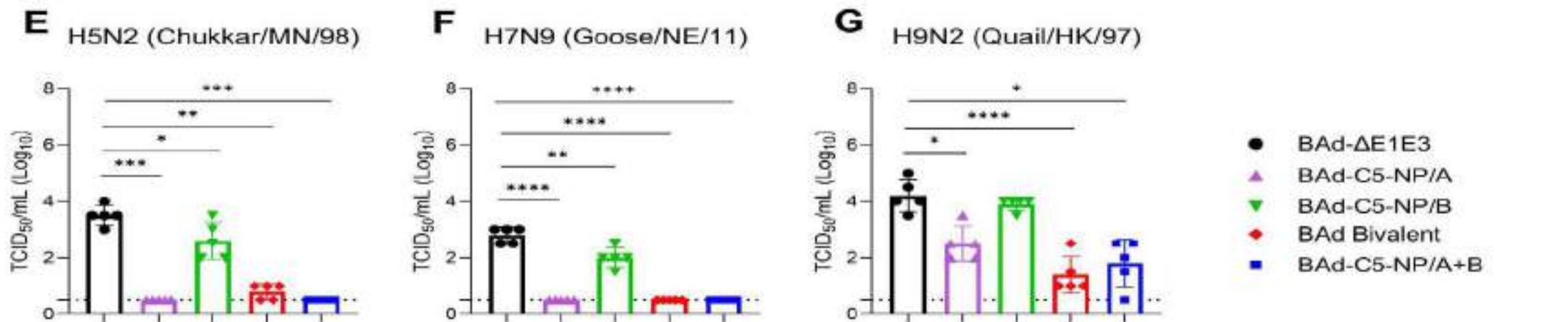


Lung Virus Titers: Protection Efficacy against H1, H3, H5, H7, H9, & Influenza B in Mice

Seasonal influenza viruses



Avian influenza viruses



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THANK YOU



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