

Influenza in the One Health Context

Course Number: 588-612-19

Monday, April 8, 2019

FACULTY

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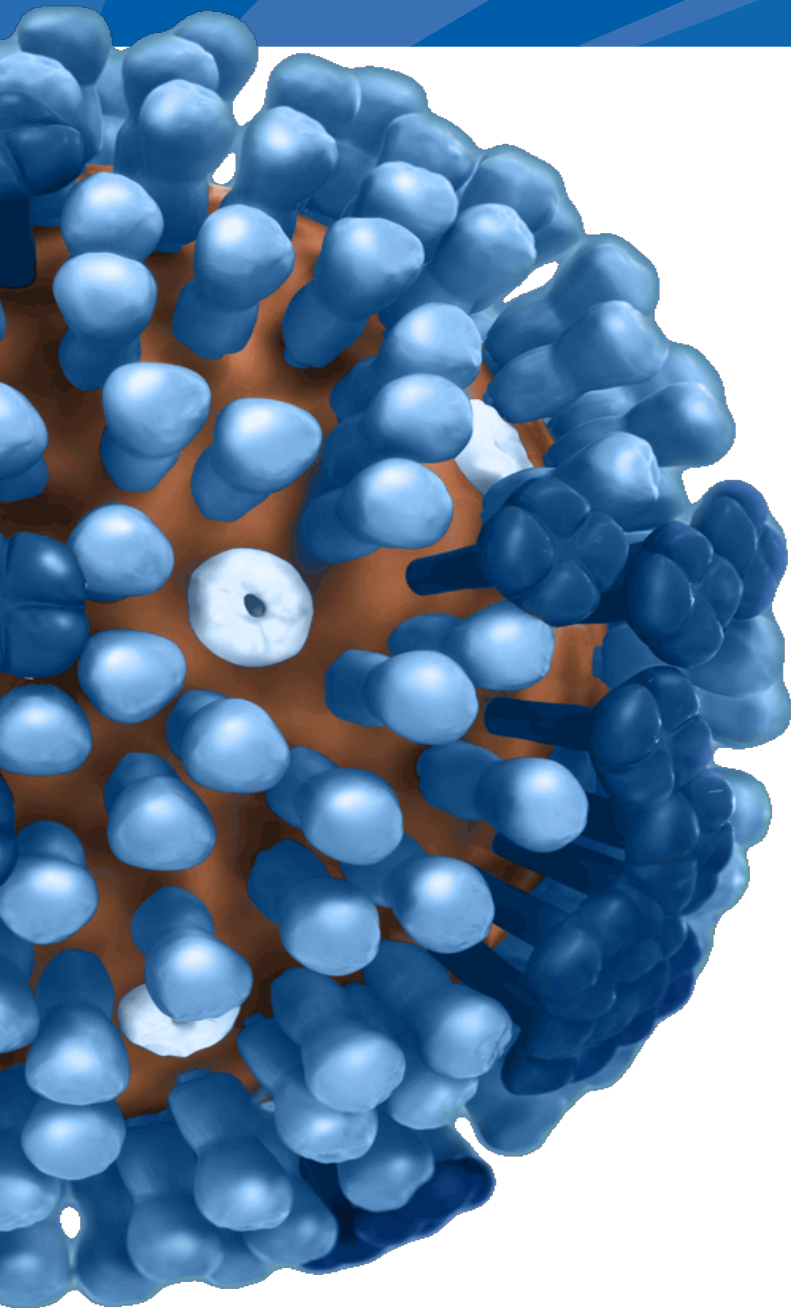
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Analysis. Answers. Action.

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Influenza at the Animal-Human Interface



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Influenza Division
Centers for Disease Control and Prevention

APHL Webinar
08 April 2019



- **What is One Health**
 - Influenza and One Health
 - CDC Influenza Program
 - Influenza Partner Highlights
- **One Health and Influenza**
 - Animal
 - Zoonotic
 - Novel
 - Human
- **Animal Influenza Update**
 - Avian Influenza
 - Swine Influenza
 - Canine Influenza
 - Equine Influenza
- **Pandemic Influenza**
 - Influenza Risk Assessment Tool
 - Candidate Vaccine Viruses
- **Field Experience**
 - Asia Vietnam



Zoonotic Diseases

WORLD HEALTH

- **60%** of pathogens that cause human diseases come from domestic animals or wildlife.
- **75%** of emerging human pathogens are of animal origin.
- **80%** of pathogens that are of concern for bioterrorism originate in animals.



FOOD SECURITY



- **More than 70%** ^[1] additional animal protein will be needed to feed the world by 2050.
- Meanwhile, **more than 20%** of animal production losses in the world are linked to animal diseases.

ENVIRONMENT



Understanding the **connections** between biodiversity, ecosystems and infectious diseases is crucial.

ECONOMY



- Animal diseases pose a direct threat to the **incomes** of rural communities that depend on livestock production.
- **More than 75%** ^[2] of the billion people in the world who live on less than \$2 per day depend on subsistence farming and raising livestock to survive.

^[1] FAO, 2011. World Livestock 2011 - *Livestock in food security*.

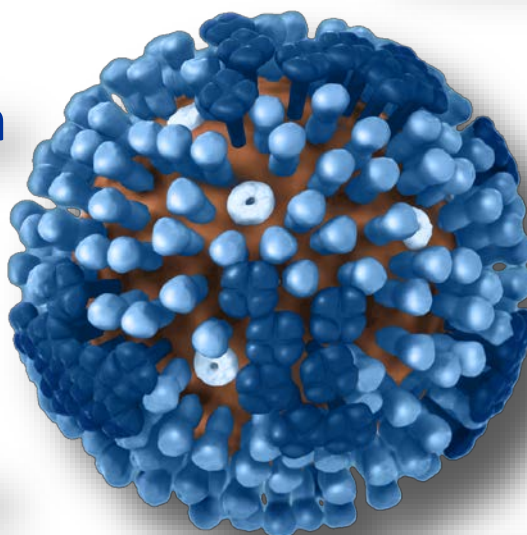
^[2] FAO & OIE, 2015. *Global control and eradication of peste des petits ruminants Investing in veterinary systems, food security and poverty alleviation*.

- **A Tripartite Guide to Addressing Zoonotic Diseases in Countries*** (FAO, OIE, WHO; 2019)
- **One Health is a collaborative, multidisciplinary, and multisectoral approach that can address urgent, ongoing, or potential health threats at the human-animal-environment interface at subnational, national, global, and regional levels.**
- **Tripartite Three Priorities: Animal Influenza, Rabies, Antimicrobial Resistance**





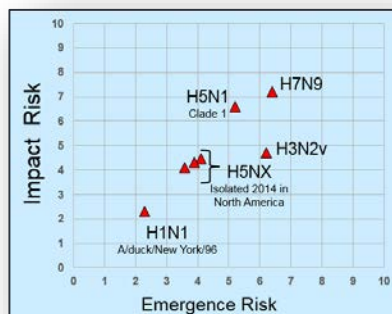
Detection



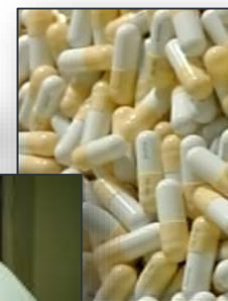
Prevention



Preparedness and Response



Treatment



- **Human seasonal influenza**
 - Large global burden of disease
 - 3-5 million severe cases/year
 - 290,000 – 650,000 deaths/year
- **Influenza is a vaccine-preventable disease**
- **Animal and Zoonotic Influenza**
 - Since 2003, numerous strains of animal influenza viruses have crossed species (zoonosis) and caused occasional illness in humans (novel)
- **Pandemic Influenza**
 - Novel influenza viruses can cause sporadic, unpredictable pandemics
 - 1918 (20-100 million deaths worldwide); 1957; 1968; 2009



U.S. Centers for Disease Control and Prevention



CDC Yearly Lab Work on Flu Viruses

More than 1 million patient specimens are tested in clinical labs participating in CDC domestic disease surveillance.*

About 100,000 specimens are tested in 93 state/local public health labs.

CDC conducts full genetic sequencing on about 7,000 flu viruses each year.

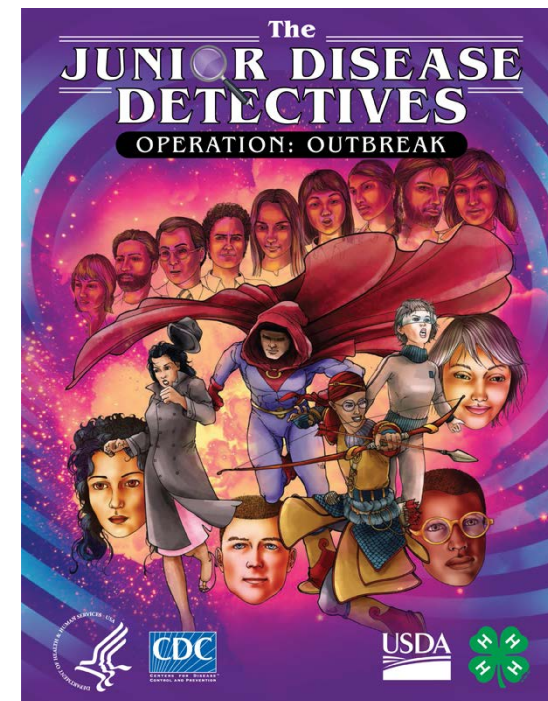
CDC tests about 2,000 flu viruses to determine their immune properties.

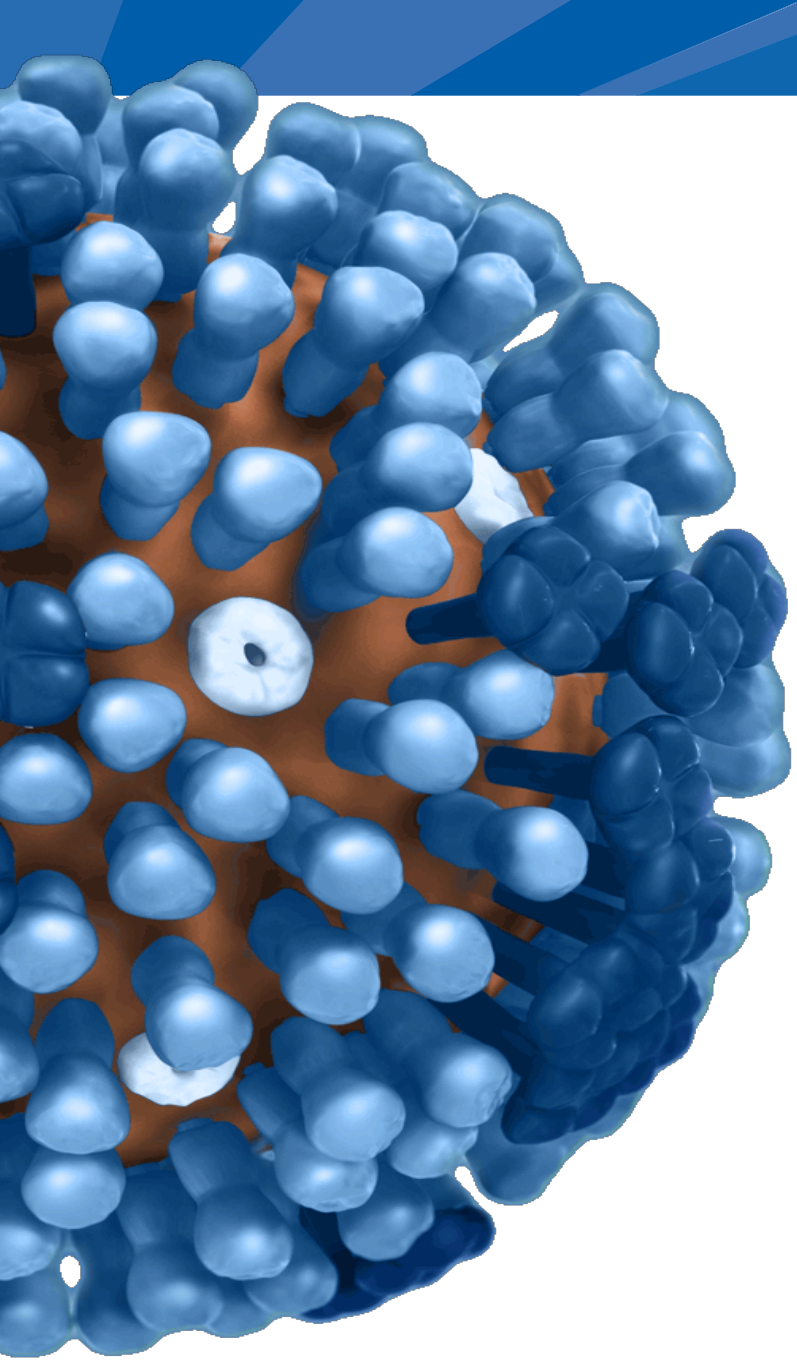
CDC prepares as many as 50 viruses for possible use in vaccine production.



*2017-2018 influenza data as reported by CDC's Influenza Division, National Center for Immunization and Respiratory Diseases (NCIRD)

- **The Junior Disease Detectives: Operation Outbreak Graphic Novel**
- **CDC partnership with USDA and 4-H**
 - Swine and Variant Influenza
 - Public and animal health experts investigate infectious disease outbreaks
 - Zoonotic disease prevention and response through one health efforts
- **CDC partnership with teachers in the Science Ambassador Fellowship**
 - Develop educational activities to accompany the graphic novel
 - Use in middle and high school science, technology, engineering and mathematics (STEM) classrooms





One Health and Influenza

Animal

Zoonotic

Novel

Human



of Influenza A Viruses

Influenza A Viruses

**Animal Influenza (non-human)**

- avian, swine, equine, canine, other animal species
- circulates within species with occasional epizootics
- vaccine available for some species

Reverse Zoonotic (human virus to animal host)

- may or may not sustain transmission in animal host
- potential for virus reassortment events

Cross-Species (animal virus to new animal host)

- may or may not sustain transmission in new animal host
- potential for virus reassortment events

Human Influenza (seasonal)

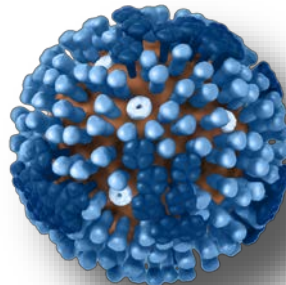
- causes epidemics in people every year
- mild respiratory illness for most, can be severe
- vaccine is best protection

Zoonotic (animal virus to human host)

- Novel (avian or swine to human)
- Variant (swine to human)
- may or may not sustain transmission in human host
- potential for virus reassortment events

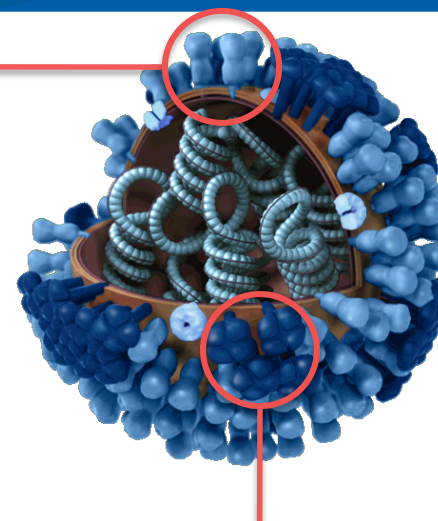
Pandemic (animal-origin virus in human host)

- efficient and sustained human-to-human transmission
- may contain virus gene mixture from multiple hosts
- little to no protection from flu vaccine or prior flu virus infection



Hemagglutinin

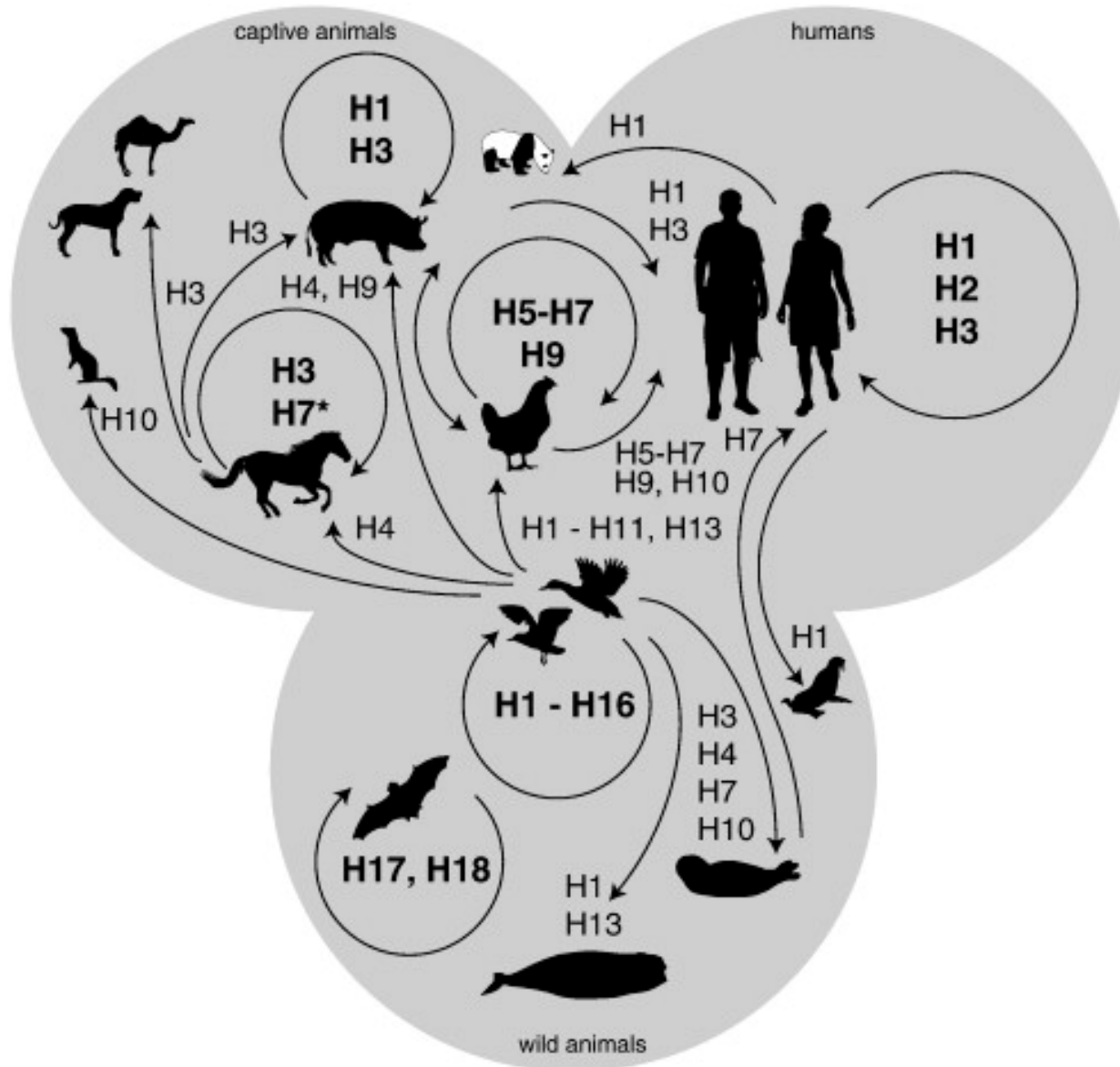
H1			
H2			
H3			 Other Animals
H4			Other Animals
H5			 Other Animals
H6			
H7			 Other Animals
H8			
H9			
H10			
H11			
H12			
H13			
H14			
H15			
H16			
H17			
H18			



Neuraminidase

N1			
N2			
N3			
N4			
N5			
N6			
N7			Other Animals
N8			 Other Animals
N9			
N10			
N11			

Reservoirs and inter-species transmission events of influenza A viruses



- **Subtype of an influenza A virus that is different from currently circulating influenza viruses among humans**
- **Novel subtypes can include H2, H5, H6, H7, H9, H10 (and more)**
- **H1 and H3 subtypes may also be considered novel if originates from a non-human species or a genetic reassortment between animal and human viruses**
- **Pandemics can occur when**
 - **A novel influenza virus emerges, infects humans**
 - **Efficient and sustained spread between people**
 - **Likely no population immunity, no vaccine immediately**

U.S. National Reportable Disease

- Novel Influenza Virus (human infection with animal influenza virus)
- Confirmation at CDC lab
- Investigate case and close contacts with State
- Work with Animal Health Partners (Federal and State) to minimize transmission during animal exhibitions or outbreak responses

Partner with USDA

- USDA monitors avian and swine influenza viruses (monitors animal influenza viruses that affect the food supply, not pets, wild birds, etc)
- Partnership to monitor responders potentially exposed during avian influenza outbreak responses

Weekly Reports on Domestic and Global Activity

- International collaborations in multiple countries
- Avian influenza A H5, H7, H9 viruses
- Human novel influenza virus reports
- Animal Influenza virus outbreaks



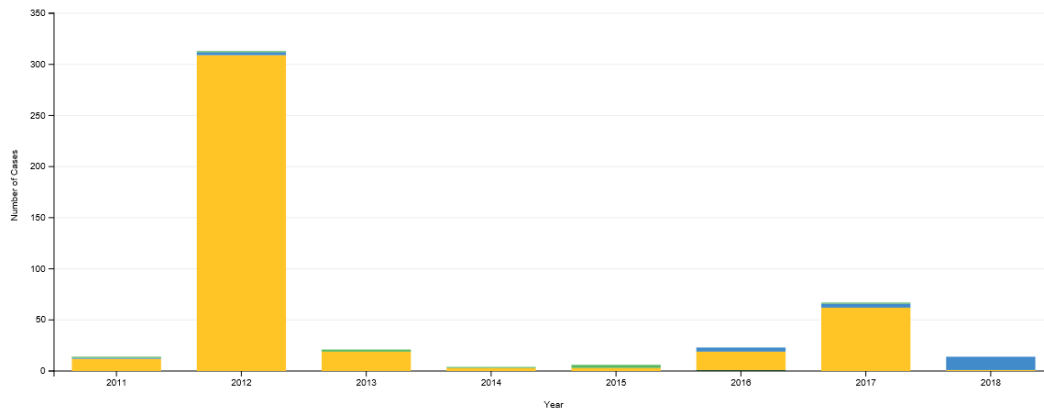
Virologic Characterization

- Novel influenza viruses received from multiple partner sources
- Candidate Vaccine Virus development consideration
- Risk Assessment potential of Animal and Novel Influenza A viruses (IRAT)

FLUVIEW



Cases By Year And Subtype



	2011	2012	2013	2014	2015	2016	2017	2018	Total
Influenza A H1N1v	1	1	2	1	3	0	1	0	9
Influenza A H1N2v	1	3	0	0	0	4	4	13	25
Influenza A H3N2v	12	309	19	3	3	18	62	1	427
Influenza A H7N2	0	0	0	0	0	1	0	0	1
Total	14	313	21	4	6	23	67	14	462

FLUVIEW

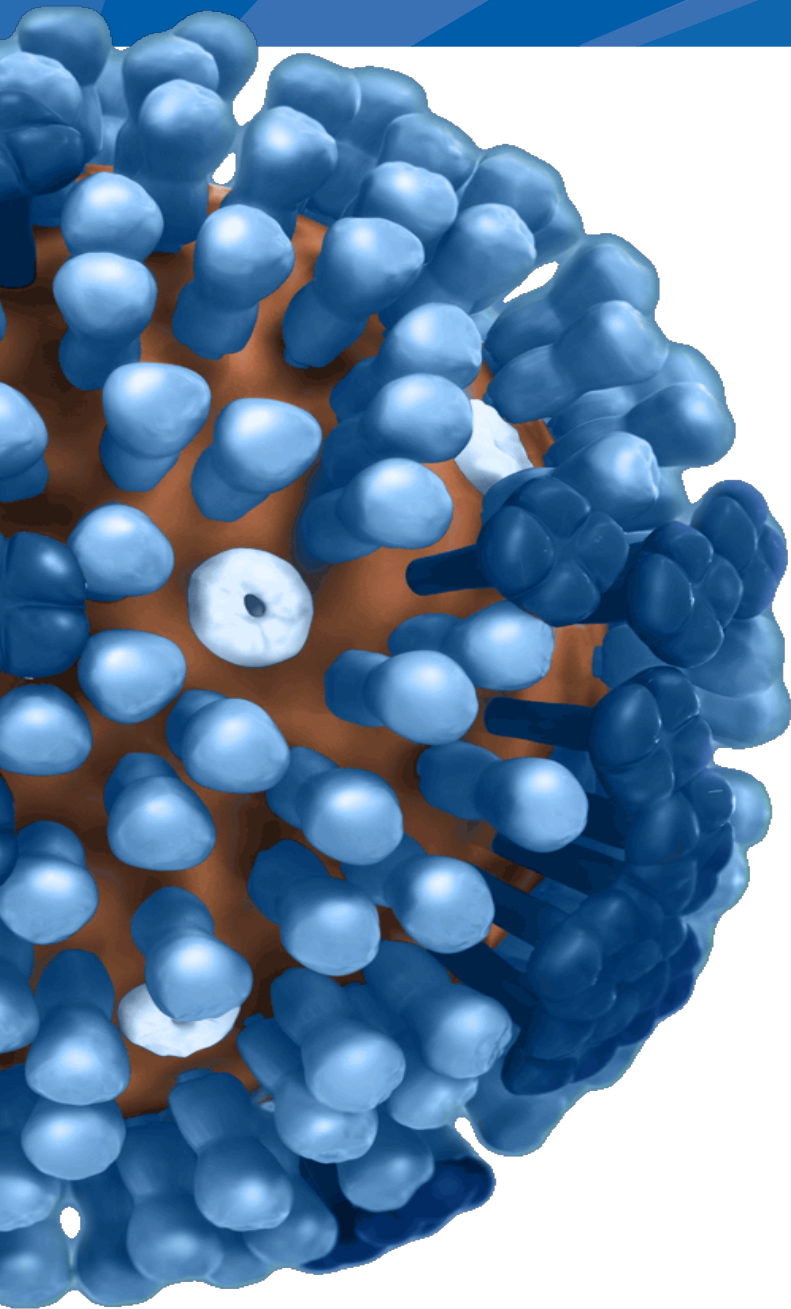


Cases By State, 2018, All Viruses (All Viruses)



14 novel influenza viruses reported to CDC, 2018

- All variant, no avian
- One is A(H3N2)v virus (Indiana [1])
- 13 are A(H1N2)v viruses (California [6], Michigan [3], Ohio [4])



Influenza Update

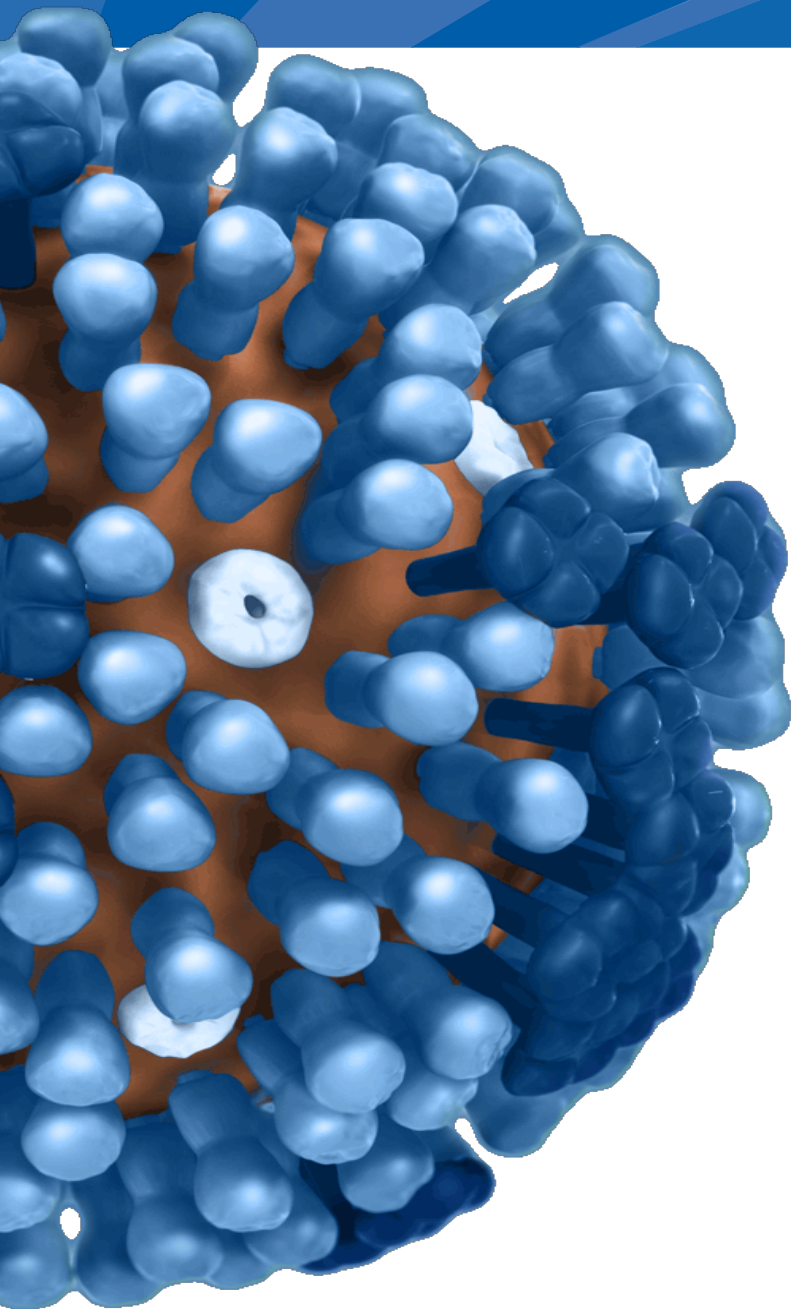
- Avian Influenza
- Swine Influenza
- Canine Influenza
- Equine Influenza



USA, 2018

- **Avian Influenza Virus**
 - LPAI H7N1: 2 poultry outbreaks in 2 states
 - LPAI H5N2: 8 poultry outbreaks in 1 state
 - LPAI H7N3: 3 poultry outbreaks in 1 state
 - No HPAI reported
- **Swine Influenza Virus**
 - IAV-S Surveillance Program (APHIS 2017)
 - about 7600 pooled samples with about 990 (~13%) positive
- **Canine Influenza Virus**
 - Positive CIV samples from 4 states reported by the Canine Influenza Surveillance Network
- **Equine Influenza Virus**
 - No EIV cases reported





Avian Influenza



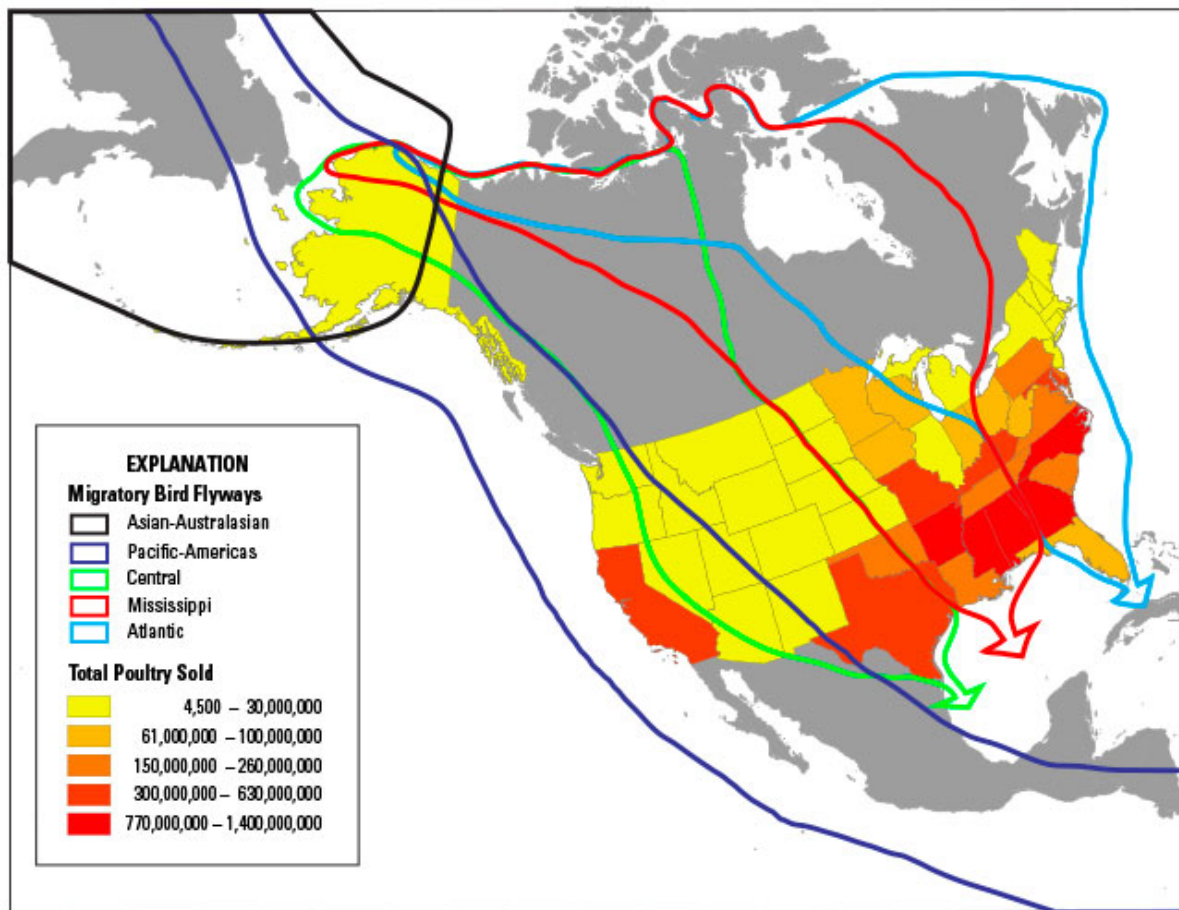
- **Avian influenza A viruses do not normally infect people, but sporadic infections in people have occurred with some avian influenza A viruses**
- **No human infections with HPAI H5 or H7 viruses have been identified in the U.S. to date**
- **Human infections with avian influenza A viruses have most often occurred after contact with infected birds, their secretions or excretions, or their contaminated environment**
- **Three subtypes of avian influenza A viruses are known to infect people (H5, H7 and H9 viruses)**
- **Among these, Asian lineage H5N1 and H7N9 have caused the majority of infections in people**
- **CDC coordinates with USDA and state health departments on appropriate public health measures and works with animal health colleagues to minimize public health risk posed by avian influenza A viruses**



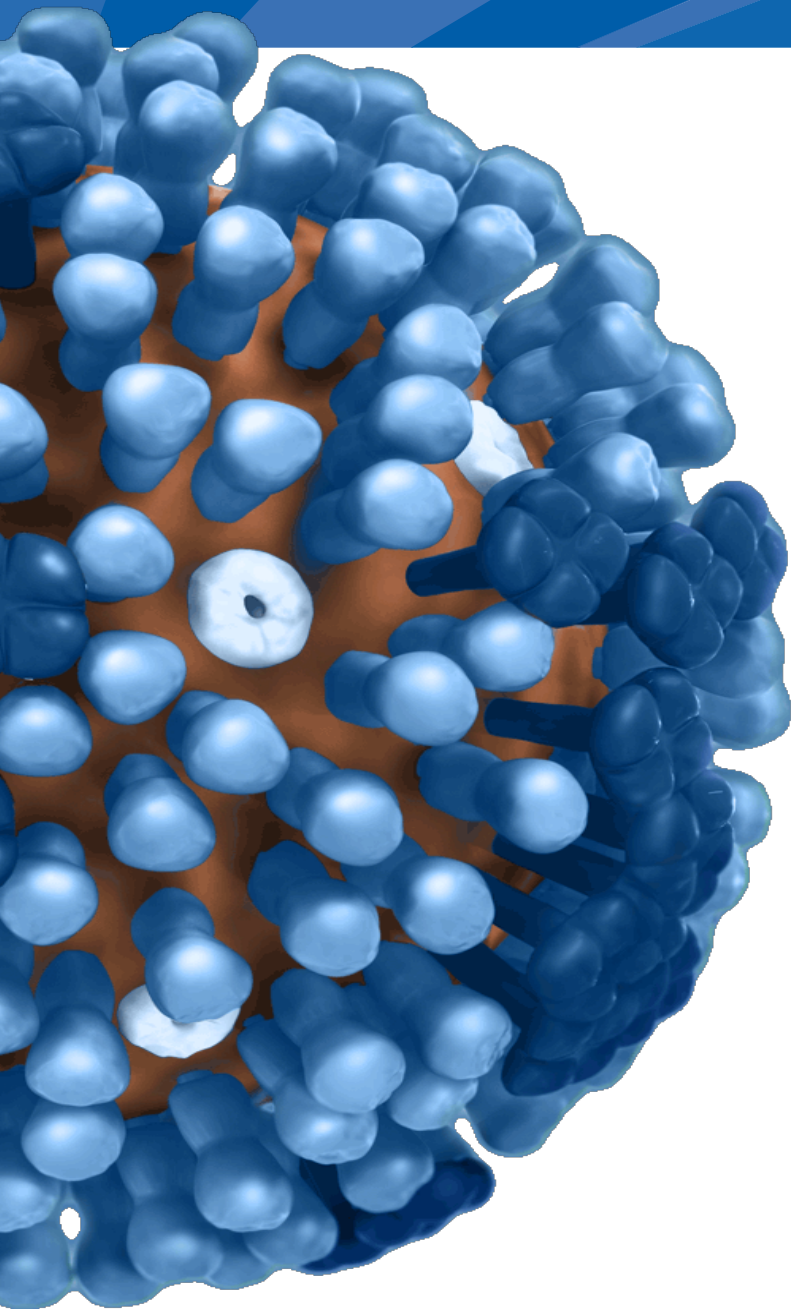


- **Low Pathogenicity Avian Influenza (LPAI)**
 - Poultry are generally asymptomatic
- **High Pathogenicity Avian Influenza (HPAI)**
 - High fatality cause of rapid flock die-off
- **H5 and H7 subtypes reported as HPAI, and H5/H7 LPAI can spontaneously become HPAI**

Carried on Migratory Pathways



- H5 clade 2.3.4.4 first identified in Asia
- Carried by asymptomatic wild waterfowl to North America, North to South
- Identified in wild birds, backyard flocks, commercial poultry
- 2015 domestic poultry and wild bird outbreaks of HPAI H5N1, H5N2, and H5N8 viruses



Swine Influenza



- **Swine influenza virus (SIV or IAV-S)**
 - Causes respiratory symptoms
 - Secondary bacterial infections common
 - Often mild illness; not often fatal
- **Endemic in pig herds**
 - Seroprevalence 50–90%
 - Cause annual epidemics
 - Commercial herds often vaccinated
 - Common subtypes:
 - H1N1, H1N2, H3N2



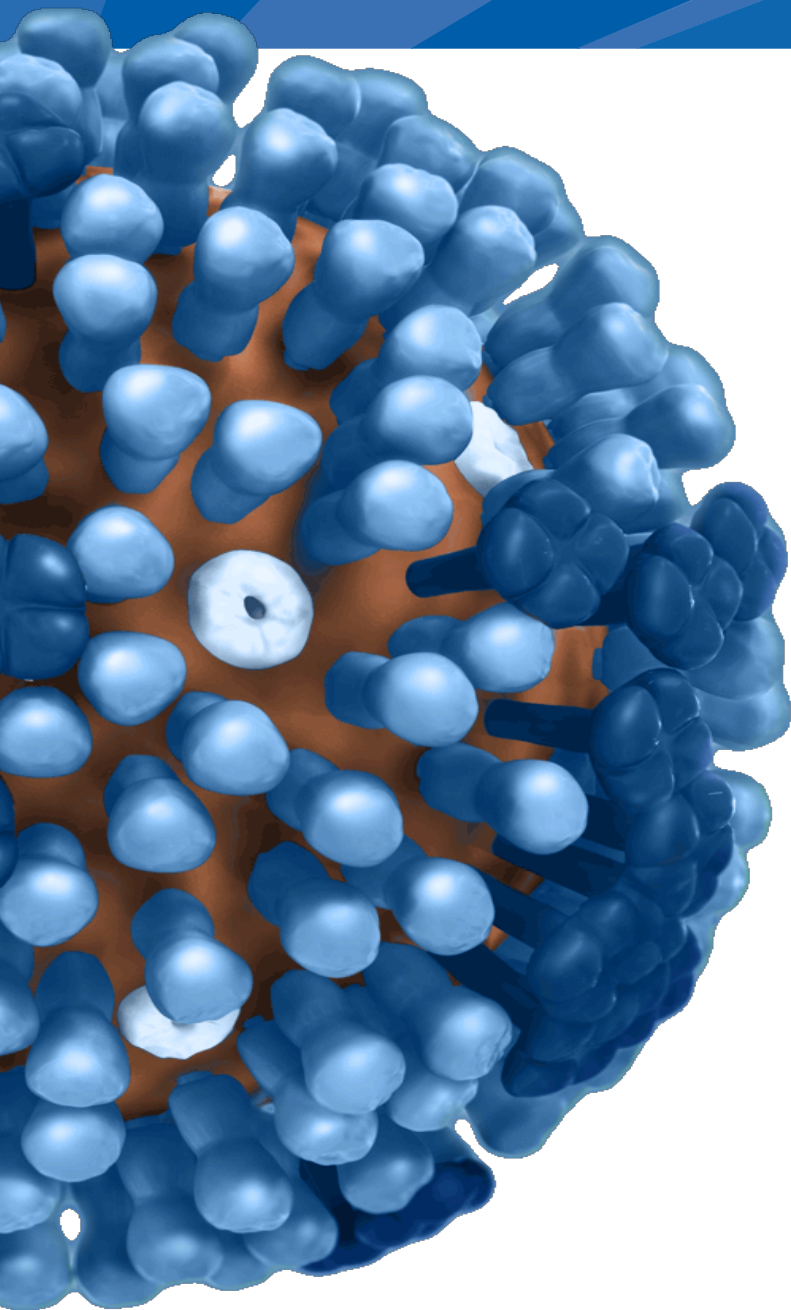
- Swine influenza viruses do not normally infect humans
- When a person is infected with one of these viruses it is called a “variant virus”
 - Denoted by adding the letter “v” to the end of the virus subtype
 - For example, H1N1v, H3N2v, H1N2v
- Clinical characteristics generally consistent with seasonal influenza in people
- Most infections have occurred in children
- Most report direct or indirect exposure to swine
 - Agricultural fair
 - Farm exposure
- Limited transmission from close contact with an infected person has been observed

U.S. DEPARTMENT OF AGRICULTURE
NATIONAL ANIMAL HEALTH
LABORATORY
VETERINARY MEDICAL CENTER
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Canine Influenza

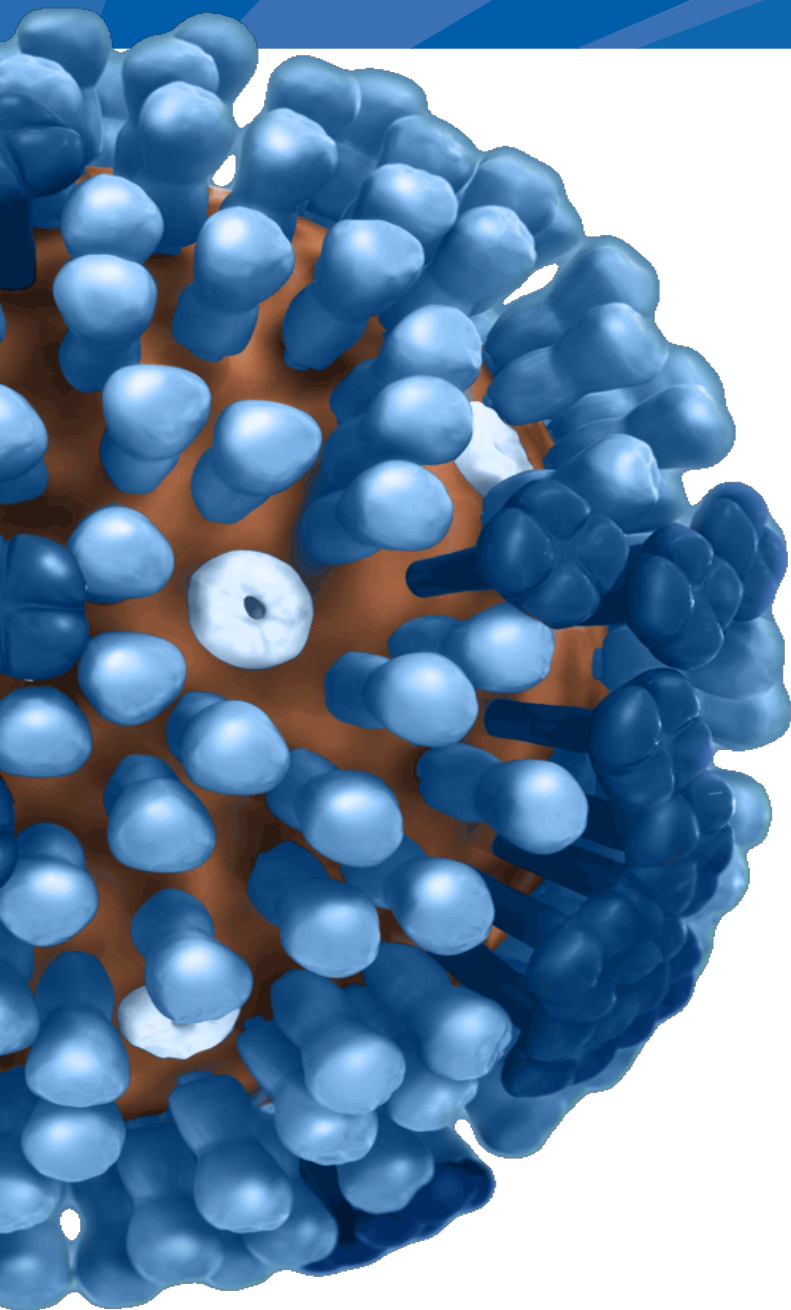


- CIV (canine or dog flu) is now endemic in the US in domestic canines
- Since its first detection in the US in March 2015
 - CIV H3N2*surveillance network has identified 3,523 positive (8%) of 46,600 canine tests in more than 30 states
 - Most states exhibit limited cases, larger outbreaks in a few states including associated with boarding kennels and dog shows
- No known infections in humans
- No known infections in domestic livestock (pigs, cattle, sheep and goats, and poultry)
- Infection in cats





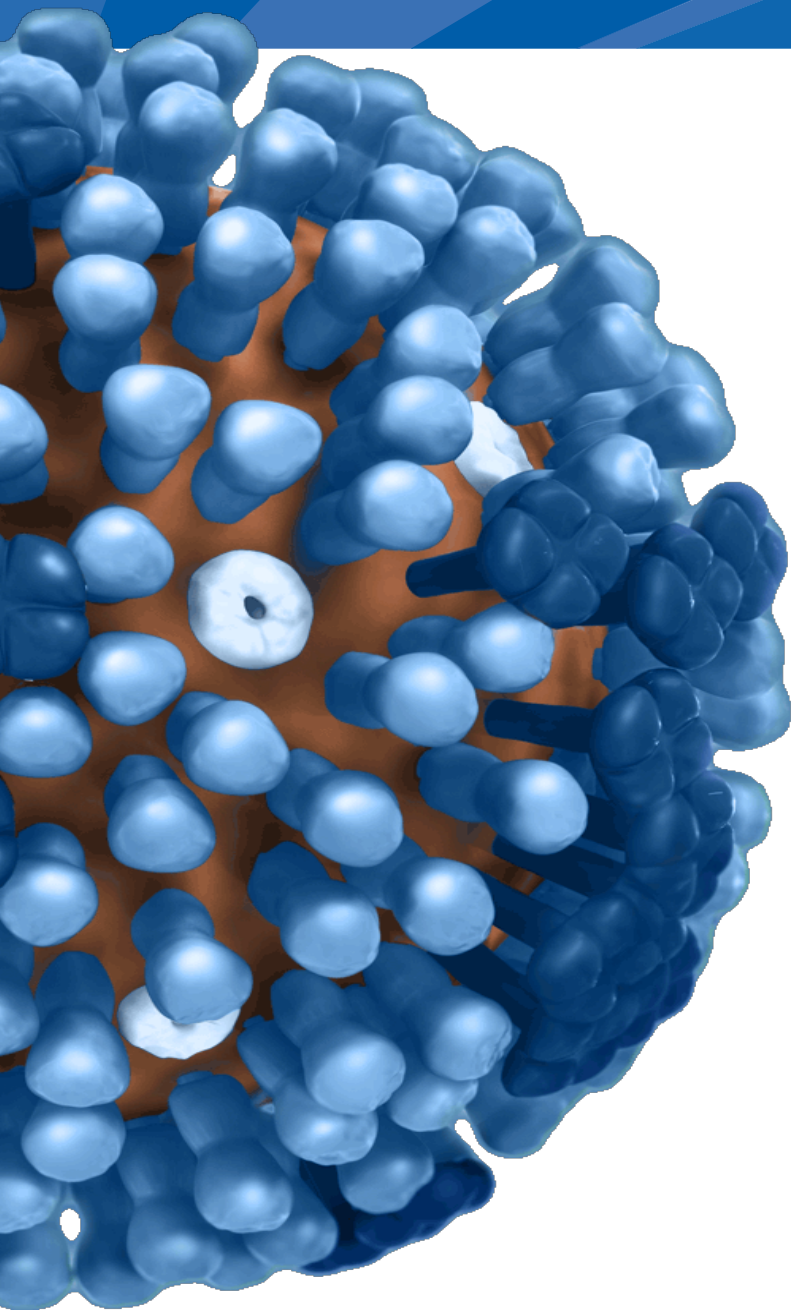
Avian Influenza in Cats



- **2016 outbreak of low pathogenicity avian influenza A(H7N2) virus among cats in animal shelters in New York City**
- **One human infection with H7N2 detected during outbreak, and one infection confirmed retrospectively**
 - Close prolonged unprotected exposure with infected cats at shelter
- **Occasional reports of human, avian, and canine influenza infection in cats**
- **No reports of influenza viruses commonly circulating in cats (no feline influenza virus)**



Equine Influenza



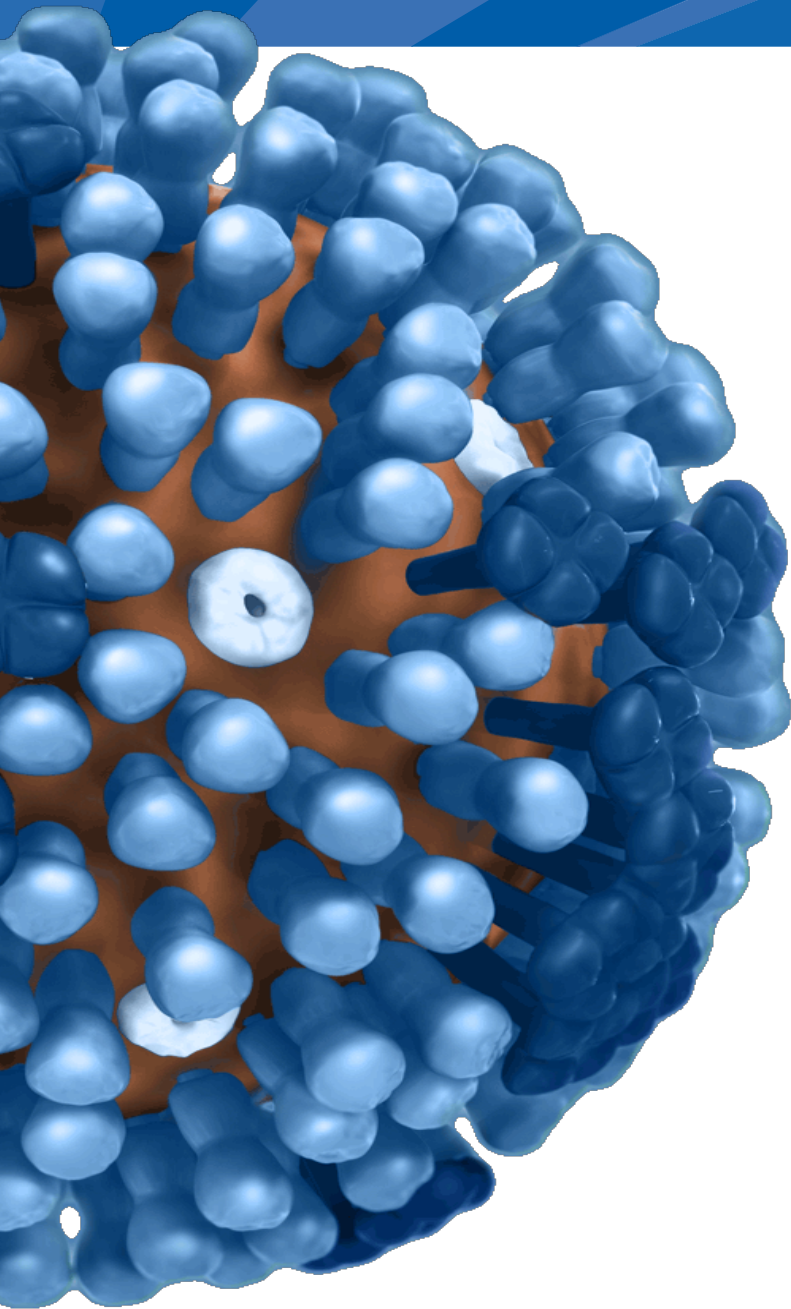
- **EIV (horse flu) is a contagious respiratory disease in horses and other equine**
- **In 2018, the US reported no cases of EIV H3N8**
- **Current 2019 EIV outbreaks in England, France, and other European countries**
- **In the past, a few people in contact with EIV infected horses have developed antibodies to EIV**
- **In the past, a few studies reported human illness following experimental infection with EIV**



2014-2018

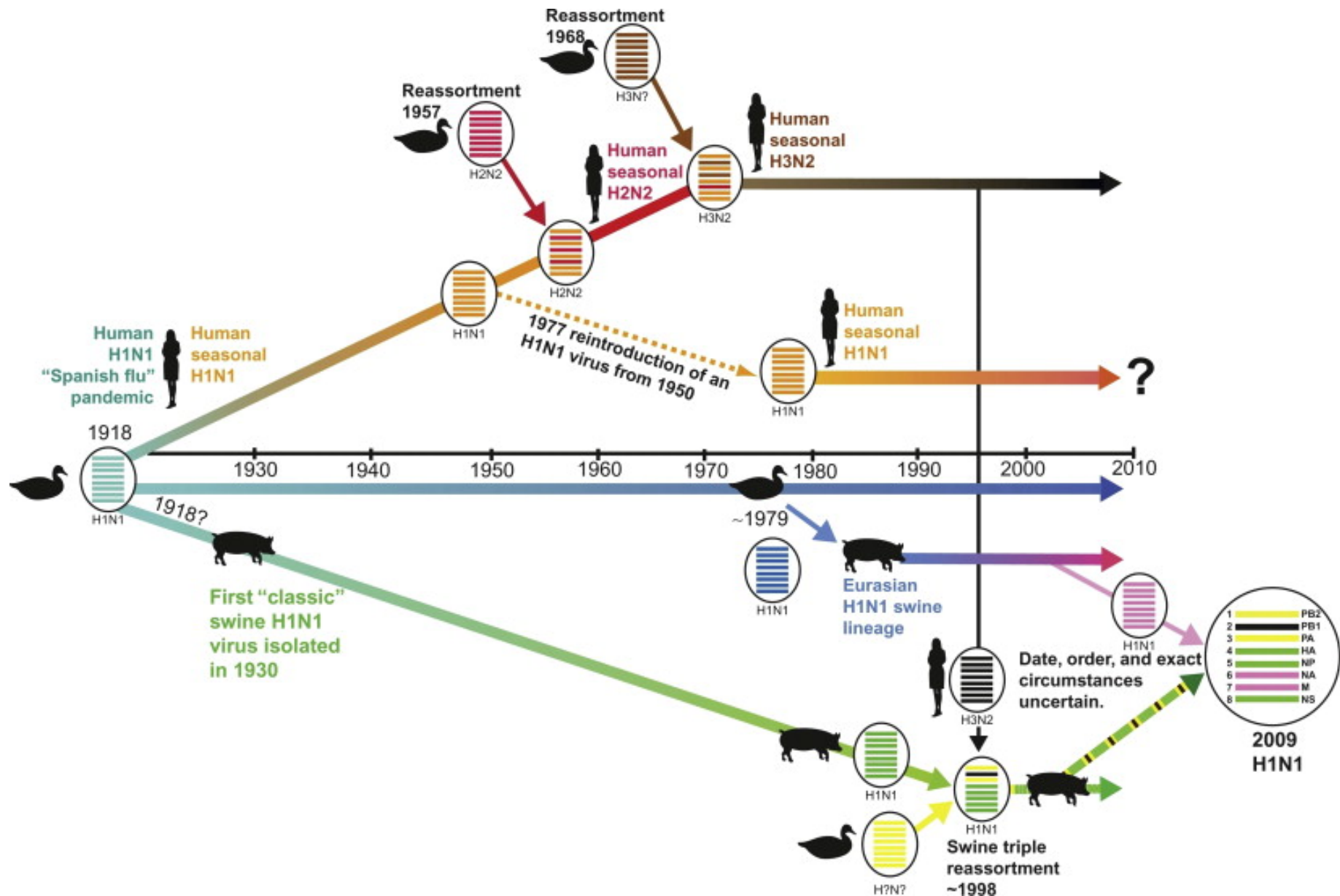
- **North America**
 - **Canada (H5, H5N2, H5N8)**
 - **United States (H5, H5N1, H5N2, H5N8, H7, H7N3, H7N8, H7N9)**
 - **Mexico (H5N2, H7N3)**
- **Central America: none**
- **South America**
 - **Chile (LPAI H7N6, 2017)**
- **Caribbean**
 - **Dominican Republic (LPAI H5N2, 2017)**



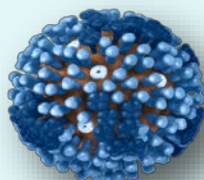


Pandemic Influenza Influenza Risk Assessment Tool Candidate Vaccine Viruses





- Uses 10 scientific criteria to measure potential pandemic risk associated with two scenarios: emergence and public health impact
- These criteria are grouped into three main categories: properties of the virus, attributes of the population, and ecology & epidemiology of the virus at the animal-human interface



Virus

1. **Genomic variation**
2. **Receptor binding**
3. **Transmission in Laboratory animals**
4. **Antivirals and Treatment Options**



Population

5. **Existing Population Immunity**
6. **Disease Severity and Pathogenesis**
7. **Antigenic Relationship to Vaccine Candidates**



Ecology

8. **Global Geographic Distribution**
9. **Infection in Animals, Human Risk of Infection**
10. **Human Infections and Transmission**

Example:

Human Infections (scored on a scale of 1-10)

Scoring by Subject Matter Experts



Low Risk
Score [1-3]

no known human infections

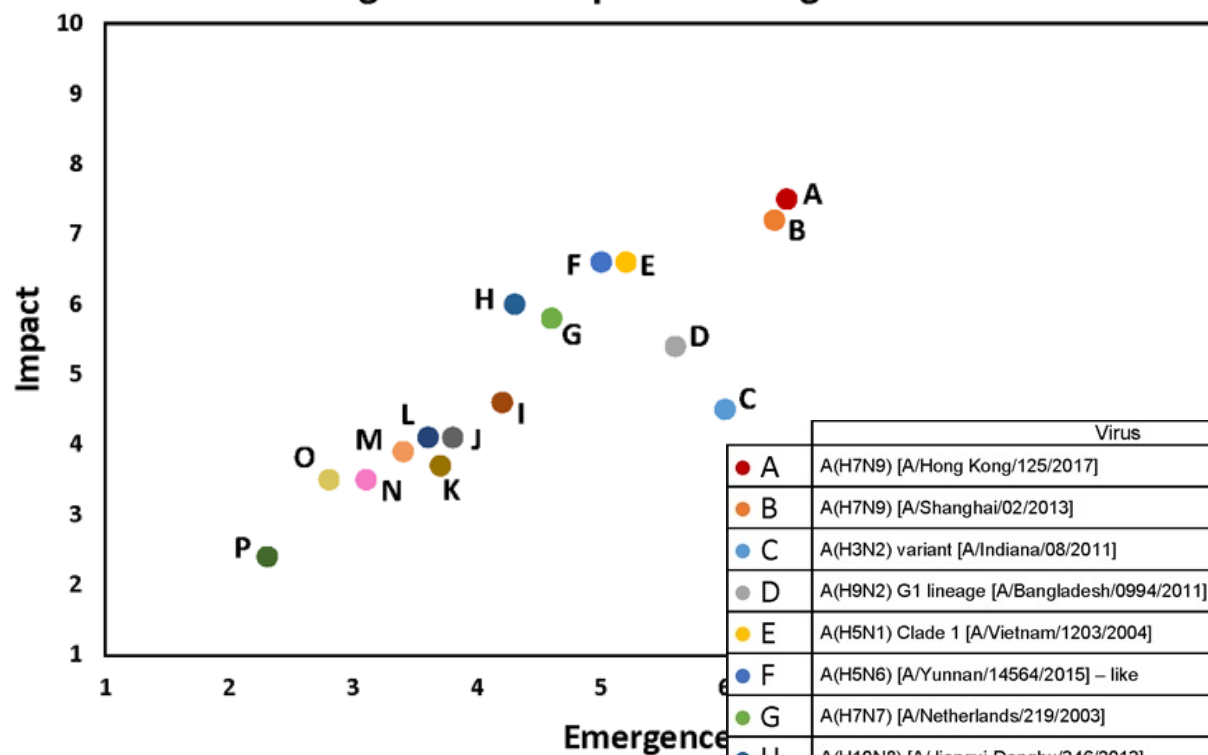
Moderate Risk
Score [4 – 7]

sporadic, isolated human cases
rare human-to-human transmission

High Risk
Score [8 – 10]

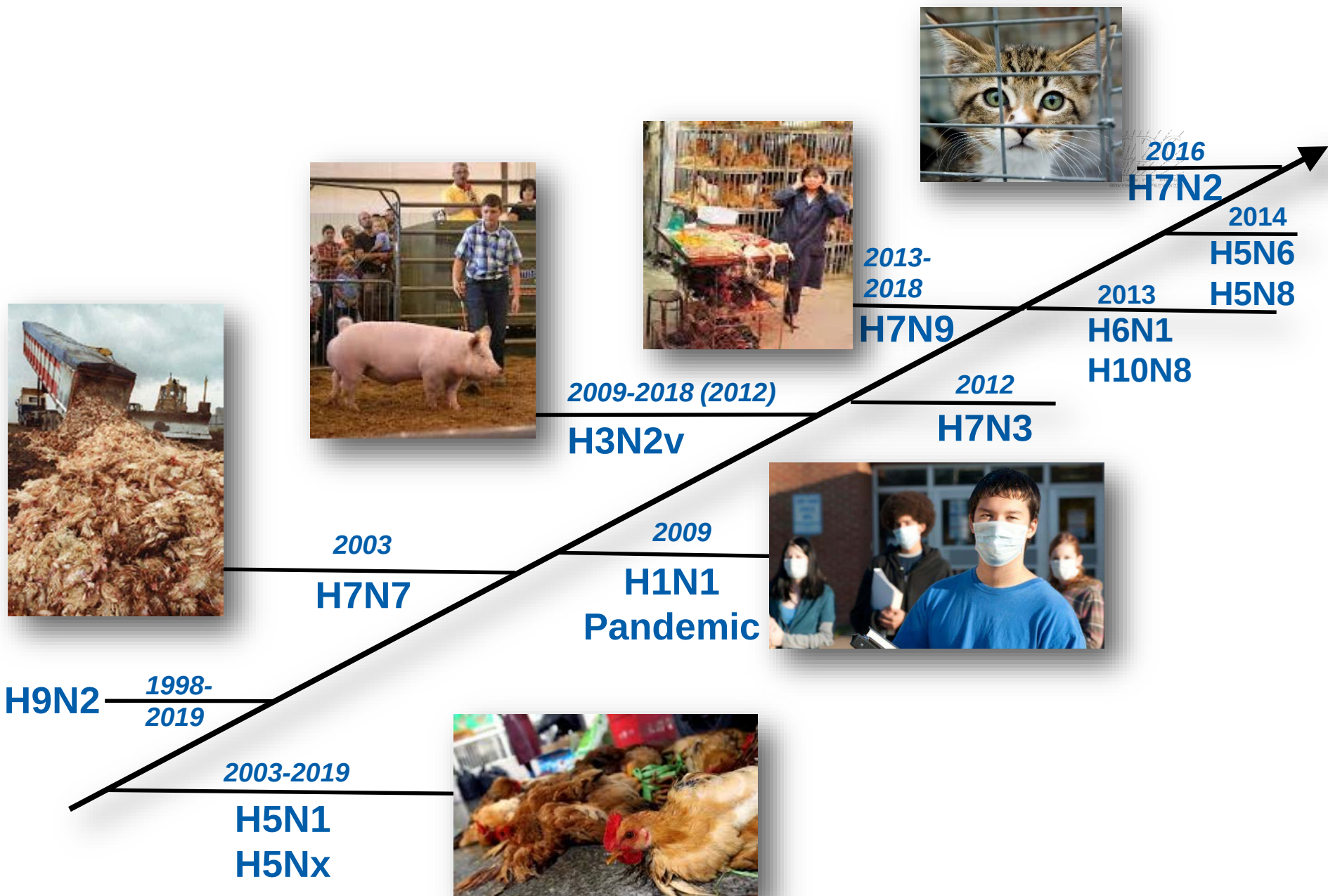
several clusters in multiple
geographic areas

IRAT Emergence and Impact - Average Risk Scores



	Virus	Emergence Score	Impact Score
● A	A(H7N9) [A/Hong Kong/125/2017]	6.5	7.5
● B	A(H7N9) [A/Shanghai/02/2013]	6.4	7.2
● C	A(H3N2) variant [A/Indiana/08/2011]	6.0	4.5
● D	A(H9N2) G1 lineage [A/Bangladesh/0994/2011]	5.6	5.4
● E	A(H5N1) Clade 1 [A/Vietnam/1203/2004]	5.2	6.6
● F	A(H5N6) [A/Yunnan/14564/2015] – like	5.0	6.6
● G	A(H7N7) [A/Netherlands/219/2003]	4.6	5.8
● H	A(H10N8) [A/Jiangxi-Donghu/346/2013]	4.3	6.0
● I	A(H5N8) [A/gyrfalcon/Washington/41088/2014]	4.2	4.6
● J	A(H5N2) [A/Northern pintail/Washington/40964/2014]	3.8	4.1
● K	A(H3N2) [A/canine/Illinois/12191/2015]	3.7	3.7
● L	A(H5N1) [A/American green-winged teal/Washington/1957050/2014]	3.6	4.1
● M	A(H7N8) [A/turkey/Indiana/1573-2/2016]	3.4	3.9
● N	A(H7N9) [A/chicken/Tennessee/17-007431-3/2017]	3.1	3.5
● O	A(H7N9) [A/chicken/Tennessee/17-007147-2/2017]	2.8	3.5
● P	A(H1N1) [A/duck/New York/1996]	2.3	2.4

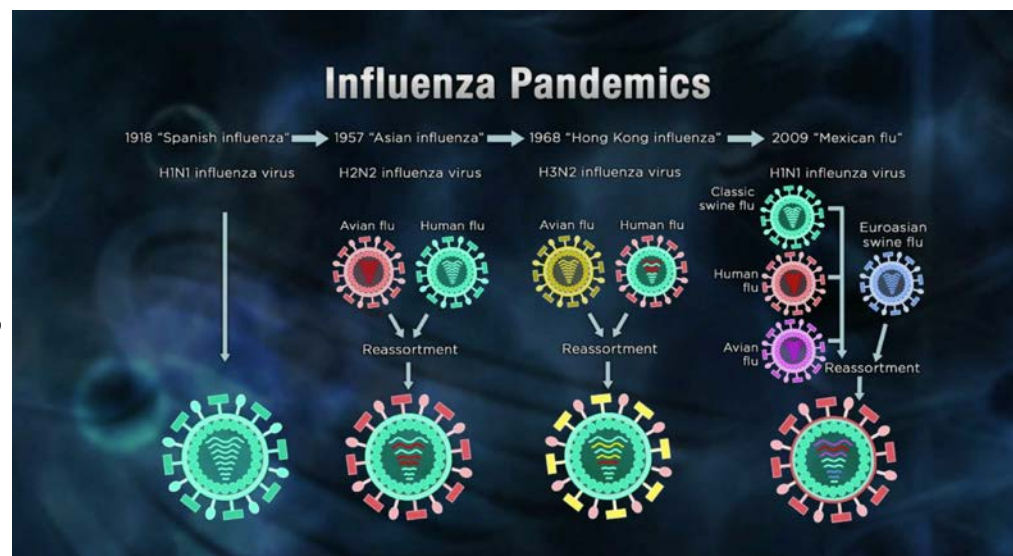
16 animal Influenza viruses assessed - H7N9 in China (A) has highest score since 2013

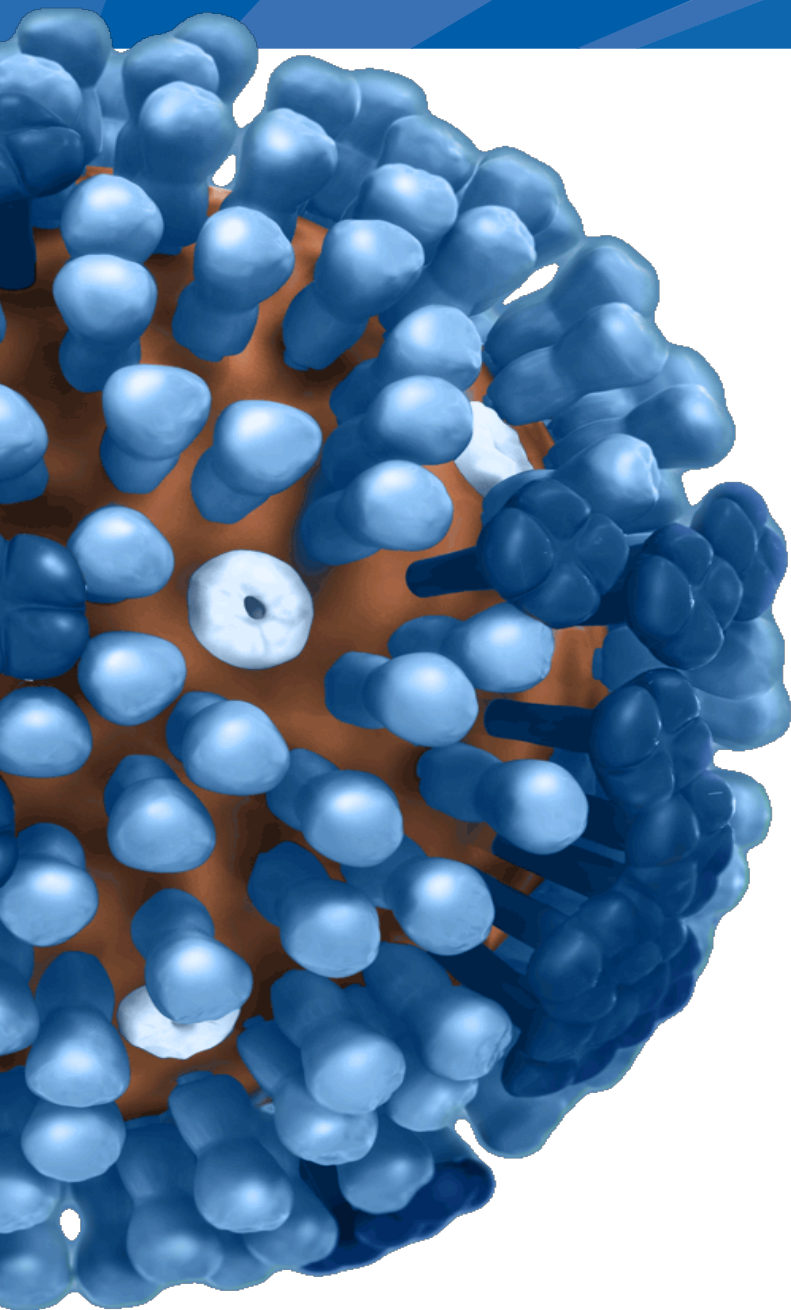


- **Candidate vaccine viruses**
 - Prepared by CDC or another public health partner
 - Can be used by vaccine manufacturers to produce a flu vaccine



- **Pandemic viruses**
 - Eight Segmented Genes
 - Undergo mutations constantly
 - Can be exchanged with genes from other flu viruses





Field Experience Asia Vietnam



Area: 331,210 sq km (127,881 sq mi)
65th country in size
~ size of New Mexico
Length over 1,609 km. (>1,000 mi.)

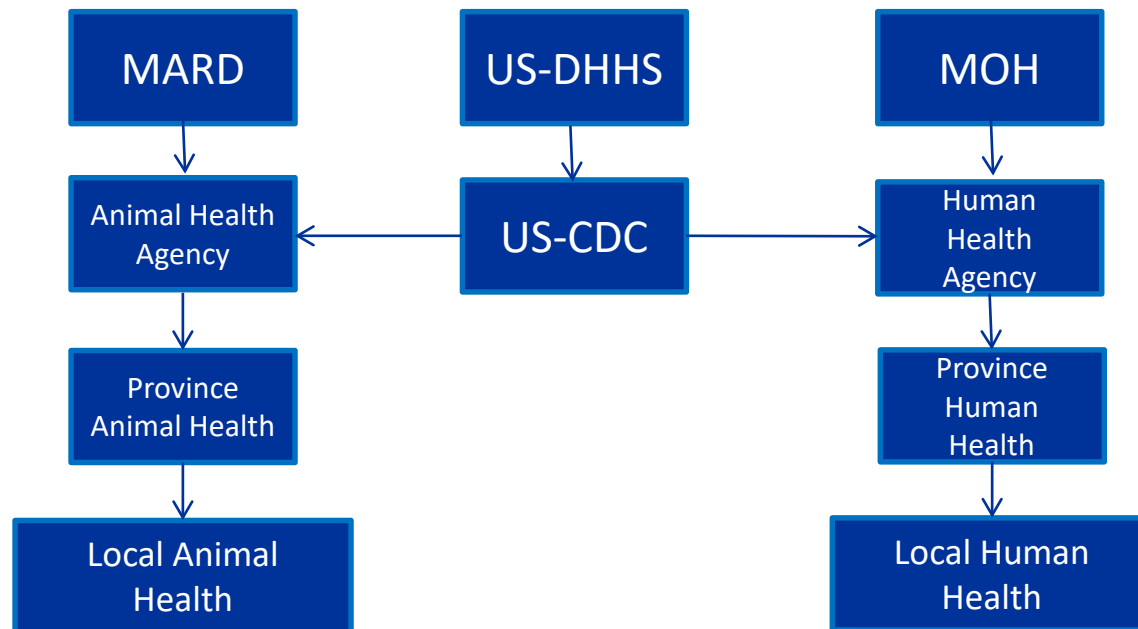
Population (2018): 97 million
15th most populous nation
54 ethnic groups

Terrain: mountainous to coastal delta
63 provinces in 4 geographic regions

Climate: Tropical-South; Monsoon-North



- ❑ Cooperative agreement partnerships
- ❑ One Health surveillance and research of influenza and other zoonotic diseases
- ❑ Provide data and information for more effective strategies and policies for better disease prevention and control



- ❑ **HHS/CDC-MARD/DAH Letter of Intent (April 2010)**
 - Research of Influenza Viruses and other Zoonotic Diseases
- ❑ **MOH/MARD Letter of Agreement (November 2011)**
 - Partnership for Influenza and other Zoonotic Diseases Projects and Activities in Vietnam
- ❑ **USCDC - Vietnam Ministry One Health Cooperative Agreements**
 - MOH 2012 award for joint surveillance & research with MARD
 - MARD 2012 award for joint surveillance & research with MOH



Activities at the Animal-Human Interface in Vietnam

- ❑ **Avian Influenza A/H5N1 human case review**
- ❑ **Avian Influenza A/H5N1 virus evolution studies in poultry and humans**
- ❑ **AHI human, avian and swine influenza virus identification, transmission and evolution studies in people, pigs and poultry**
- ❑ **Identifying endemic avian and swine influenza foci through novel traceback techniques**
- ❑ **Surveillance for Avian Influenza A/H7N9 virus in poultry and in humans, in northern Vietnam provinces**

Outcomes of One Health Collaboration at the Animal-Human Interface in Vietnam

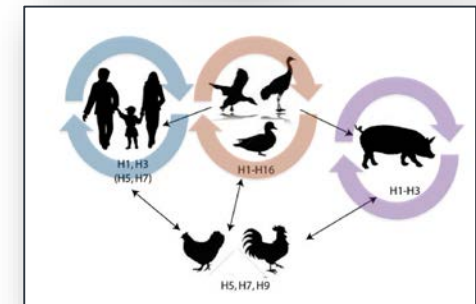
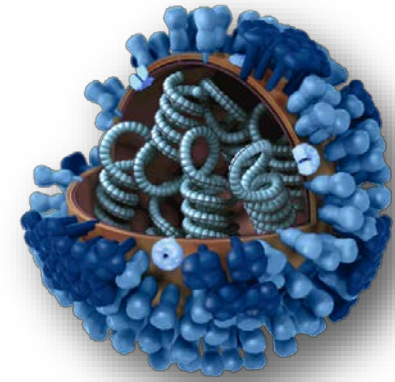
Influenza Division



- ❑ One Health Reports and Recommendations provided to Vietnam MOH and MARD
- ❑ Support and develop policies on human and animal influenza virus prevention and control
- ❑ Identification of human and animal influenza seasons in Vietnam
- ❑ Optimum human seasonal and poultry vaccination times
- ❑ Better understand human and animal influenza virus evolution and transmission risk factors occurring at the animal-human interface in Vietnam and regionally



- Influenza viruses are constantly changing in animals and humans, requiring ongoing surveillance and frequent vaccine virus changes
- Path from animal flu to zoonotic flu to novel flu to pandemic flu is complex and often is the result of multiple virus changes in birds, swine, and humans
- Number of emerging novel influenza viruses is increasing, requiring ongoing laboratory and epidemiologic investigations for risk assessments

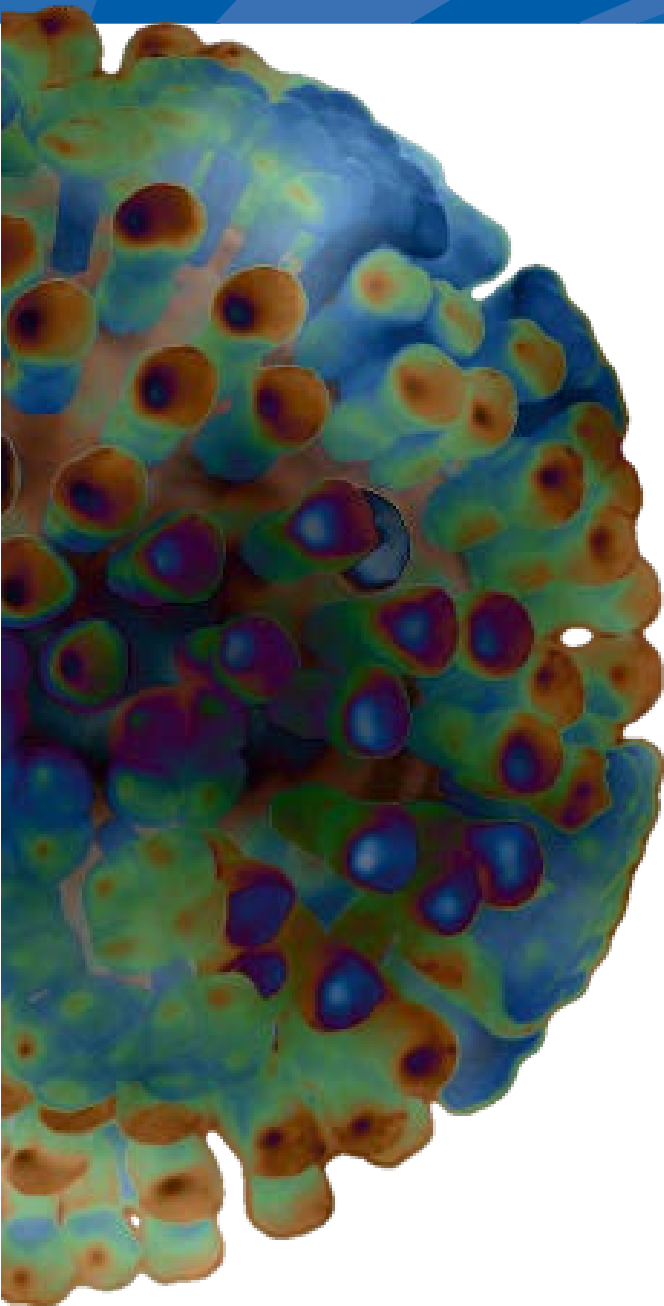


 Virus	1. Genomic variation
	2. Receptor binding
	3. Transmission in Laboratory animals
	4. Antivirals and Treatment Options
 Population	5. Existing Population Immunity
	6. Disease Severity and Pathogenesis
	7. Antigenic Relationship to Vaccine Candidates
 Ecology	8. Global Geographic Distribution
	9. Infection in Animals, Human Risk of Infection
	10. Human Infections and Transmission

Thank You



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and

Emergency Management of Zoonotic Disease Outbreaks

Information and Resources

- ❑ **WHO: Handbook for the assessment of capacities at the human–animal interface;**
 - Second edition related to the Joint External Evaluation Tool International Health Regulations (2005)
 - <http://www.who.int/ihr/publications/9789241511889/en/>
- ❑ **WHO: Handbook for the assessment of capacities at the human-animal interface (2015)**
 - http://www.who.int/ihr/publications/handbook_OMS_OIE/en/
- ❑ **OIE: Planning for Emergencies**
 - <http://www.oie.int/en/solidarity/emergency-management/planning-for-emergencies/>
- ❑ **OIE: Interagency Cooperation for Emergency Management**
 - <http://www.oie.int/en/solidarity/emergency-management/interagency-cooperation-for-emergency-management/>
- ❑ **FAO: Emergency Management Centre for Animal Health**
 - <http://www.fao.org/emergencies/how-we-work/prepare-and-respond/emc-ah/en/>
- ❑ **FAO: Good Emergency Management Practice: The Essentials**
 - <http://www.fao.org/emergencies/resources/documents/resources-detail/en/c/157578/>
- ❑ **CDC: Zoonotic Disease Prioritization**
 - <https://www.cdc.gov/onehealth/global-activities/prioritization.html>
- ❑ **APHIS: Animal Health Emergency Management**
 - <https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/emergency-management>

- **OIE** – World Organization for Animal Health
 - AI: <http://www.oie.int/en/animal-health-in-the-world/avian-influenza-portal/>
 - SI: <http://www.oie.int/en/animal-health-in-the-world/animal-diseases/Swine-influenza/>
 - EI: <http://www.oie.int/en/animal-health-in-the-world/animal-diseases/Equine-influenza/>
- **FAO** – Food and Agriculture Organization of the United Nations
 - AI: <http://www.fao.org/avianflu/en/index.html>
- **WHO** – World Health Organization
 - ZI/HAI: http://www.who.int/influenza/human_animal_interface/en/
- **CDC** – Centers for Disease Control and Prevention
 - Other Flu: https://www.cdc.gov/flu/other_flu.htm
- **APHIS** – Animal and Plant Health Inspection Service (USDA)
 - AI: <https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease>
 - SI: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/swine-disease-information/ct_swine_health_home

- U.S. Department of Homeland Security (DHS), National Response Framework, Third Edition, June 2016 
 - <https://www.fema.gov/media-library/assets/documents/117791>
- U.S. Federal Emergency Management Agency (FEMA), National Disaster Recovery Framework Second Edition, June 2016
 - <https://www.fema.gov/national-disaster-recovery-framework>

- Overall U.S. structure and mechanisms for coordinating and providing support for a Federal response to an incident, including the management of zoonotic disease outbreaks (human and animal)
 - Federal-to-Federal agency support
 - Federal-to-States support
- Provided in the FEMA Emergency Support Functions (ESFs)
 - ESF # 8 (USDHHS) coordinating with
 - ESF # 11 (USDA)
 - <https://www.fema.gov/media-library/assets/documents/25512>

USA Multi-Agency Coordination for Zoonotic Disease Outbreaks (2)

- Emergency Support Function
 - The ESFs provide the structure for coordinating Federal interagency support for a Federal response to an incident.
- ESF # 8 (USDHHS)
 - Public Health and Medical Services provides the mechanism for Federal assistance to supplement local, state, tribal, territorial, and insular area resources in response to a disaster, emergency, or incident that may lead to a public health, medical, behavioral, or human service emergency, including those that have international implications.
- ESF # 11 (USDA)
 - Agriculture and Natural Resources organizes and coordinates Federal support for the protection of the Nation's agricultural and natural and cultural resources during national emergencies.



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