



# **Avian/Pandemic Influenza**

Where We've Been, Where We Are Now,  
Where We're Going

---

**Force Health Protection Conference  
August 2006**

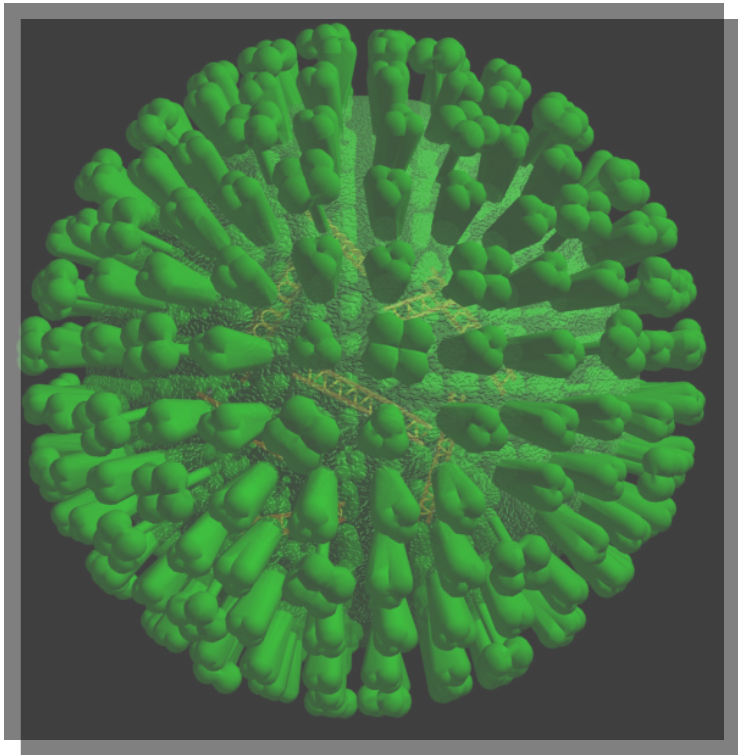
**LTC Wayne Hachey**

Office of the Assistant Secretary of Defense  
(Health Affairs) Force Health Protection and Readiness



# The Influenza A Virus

---



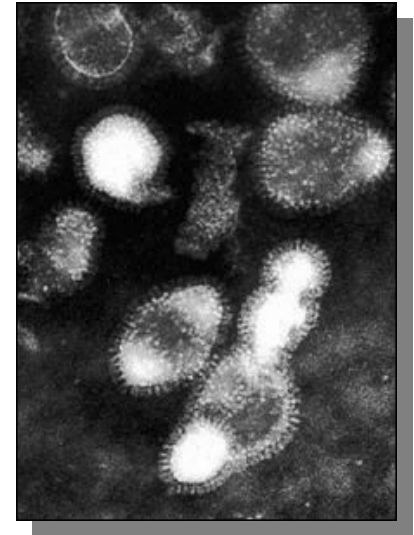
- Typically spherical
  - 50-120 nm diameter
- Single-stranded RNA virus
  - No proof reading
- Genome in 8 segments
- 10 proteins
  - Includes key surface glycoproteins
  - Haemagglutinin (HA)
  - Neuraminidase (NA)



# Influenza A Viruses

---

- High mutation rate
  - Rapid change by antigenic drift and exchange of gene segments (antigenic shift or reassortment)
- Found in a wide variety of avian and mammalian species (human, pigs, horses)
- Waterfowl probably the natural hosts
  - (fowl plague described in 1878)



# Influenza A & People

---

- Yearly outbreak – 36,000 deaths in US
- Pandemic strains with novel surface protein have/can cause significant increases in illness and death
- 1918 Spanish flu was most likely an avian flu that adapted without reassortment.
- Other two pandemics in 1957 & 68 result of reassortment (H2N2 & H3N2)



# Why Worry?

## 1918 Spanish (Kansas) Flu

---

- Duration of pandemic 1918-1920
- Rapid onset. Some died within 24 hours of symptoms
- Secondary pneumonia biggest killer
- Virus seems to have mutated from a less virulent flu experienced earlier in the year



# 1918 Spanish Flu

---

- In the US:
  - 25 million infected
  - 500,000 – 675,000 dead
  - 103 million population (292M in 2004)
  - Only year in 20<sup>th</sup> century U.S. had negative population growth
- World wide:
  - 20 to 50 million dead
  - World population approximately 2 billion (6.3B in 2004)



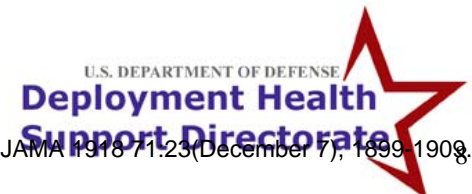
# Previous Impact of a Pandemic on DoD

## **Why DoD Is Concerned**

# The 1918 Pandemic in the U.S. Military

---

- 1<sup>st</sup> wave Jan-Feb 1918 Haskell County Kansas – seeded Camp Funston, Kansas
- 2<sup>nd</sup> wave Start: ~12 September 1918 @ Index epidemic Camp Devens, Massachusetts
- Next 8 days: 11 other major camps
- By end of September: 31 major camps
- By end of October: All major U.S. camps





# September 12 – October 31

---

- 22% caught the flu
- 5.8% of those with flu died
- 17% of those with flu caught pneumonia
- 34% of those with pneumonia died



*Flu ward at Walter Reed Hospital*



# September – October 1918

---

- **Camp Devens: September 1-30**
  - 25% of the camp developed influenza
    - 17% developed pneumonia
    - 35% of those with pneumonia died
- **Camp Dix: mid September - October 31**
  - 20% of the camp developed influenza
    - 18% developed pneumonia
    - 50% of those with pneumonia died



# Military Impact

- 25% of military caught the flu
  - 1 million soldiers
  - Mirrored civilian population
- Flu killed more than bullets
  - 57,460 died of flu vs 50,280 in combat
- War dept. estimated that it lost 8,743,102 days among enlisted men

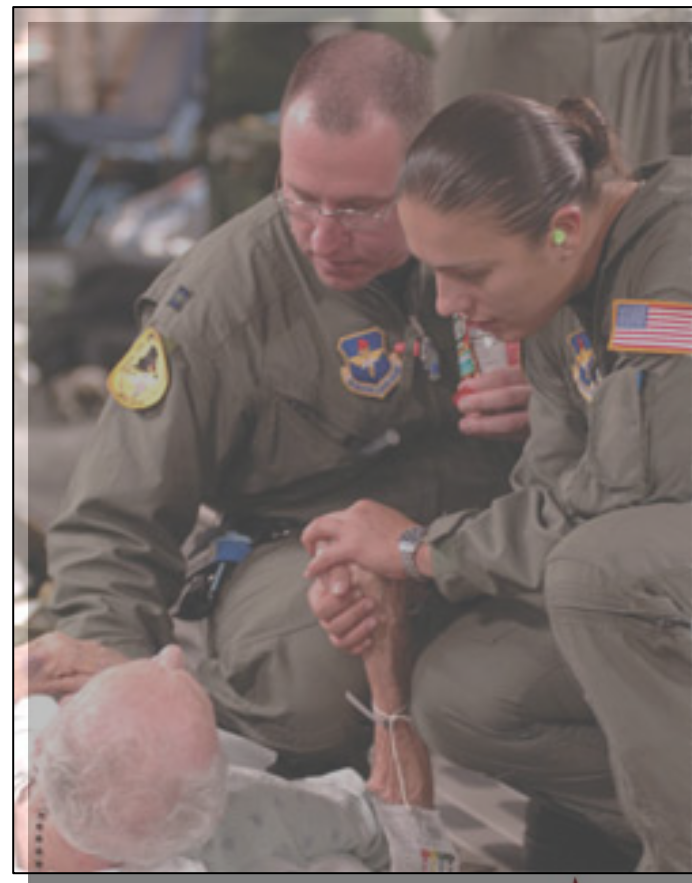


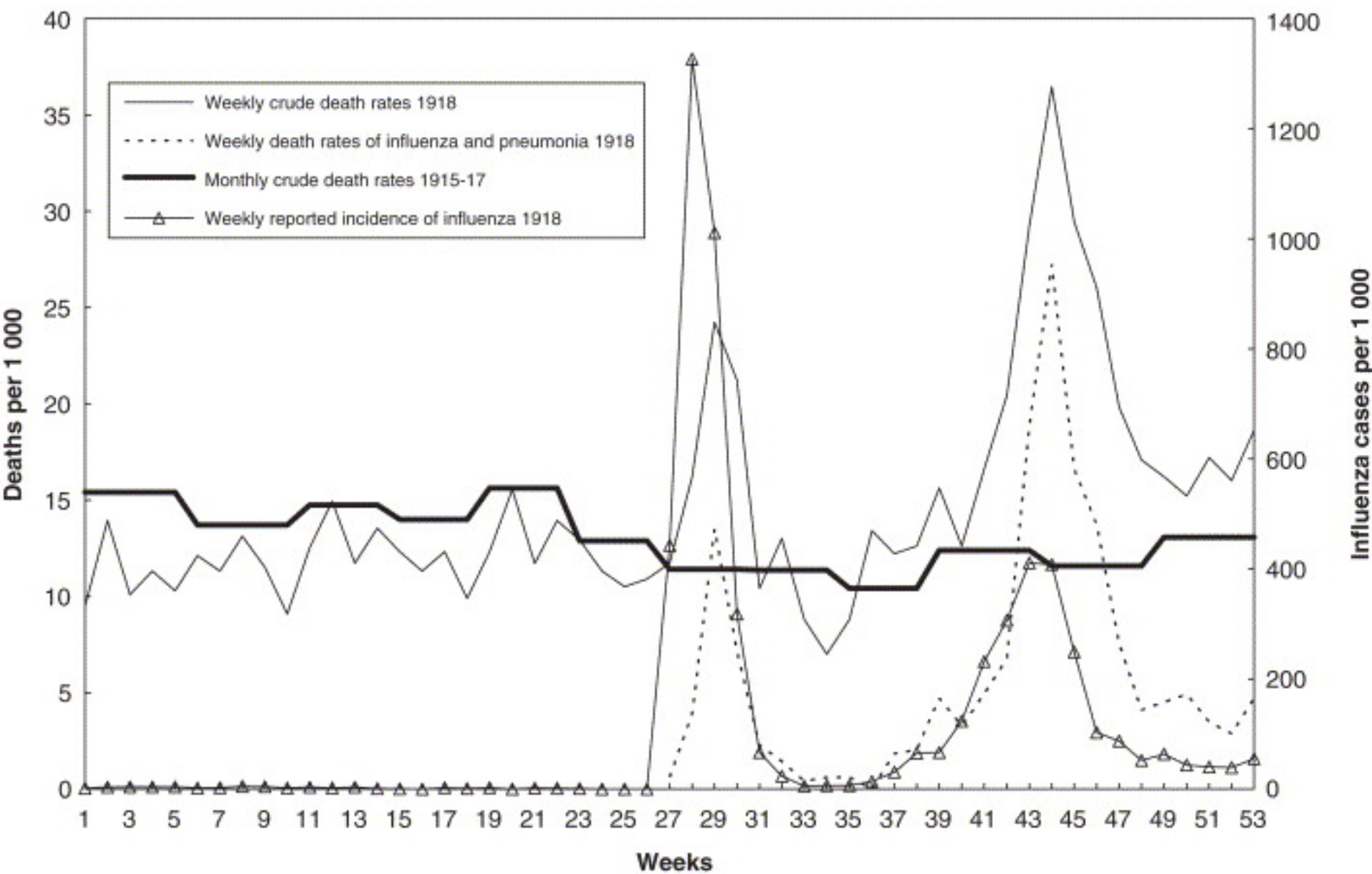
*Soldier receives throat spray  
for Spanish Flu*



# Potential Impact on DoD with the Next Pandemic

- 30-35% attack rate
- 50% seeking care
- 10-20% hospitalization rate
- 40% of workforce out
- Disruption of essential services
- Multiple taskings in the face of decreased manpower
  - National defense
  - Humanitarian relief
  - National response efforts





Weekly crude death rates, incidence rates and death rates from influenza in 1918, and monthly average crude death rates for the years 1915–17 in Kristiania. *Sources:* [Kristiania Sundhetskommision, 1919](#); [Mamelund, 2003a](#).





# Avian Influenza

---

- Diverse group of Influenza A viruses infecting wild and domestic birds
  - can have a low or high pathological disease presentation
- Usually affects avian GI or respiratory tracts
- Usually low path (mild or no symptoms)
- Usually high path is a domestic poultry disease (only H5 or H7)
  - H5N1 is an outlier that is jumping back and forth between wild and domestic birds



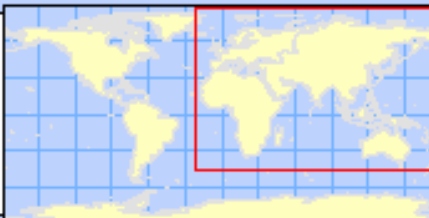
**Is it here yet?**







**NBIC BioStatus**  
**Avian Influenza (H5N1) in Birds**  
**Eastern Hemisphere**



**UNCLASSIFIED**

- Confirmed Bird
- Suspected Bird
- Change from Previous Report



Confirmed animal cases of H5N1 infection have been reported in  
 Afghanistan, Albania, Austria, Azerbaijan, Bosnia-Herzegovina,  
 Bulgaria, Burkina Faso, Cambodia, Cameroon, China, Croatia,  
 Cyprus, Czech Republic, Denmark, Djibouti, Egypt, Ethiopia,  
 France, Georgia, Germany, Greece, Hong Kong, Hungary,  
 India, Indonesia, Iran, Iraq, Israel, Italy, Ivory Coast, Japan, Jordan,  
 Kazakhstan, Laos, Malaysia, Mongolia, Myanmar, Niger, Nigeria,  
 Pakistan, Poland, Romania, Russia, Saudi Arabia, Serbia, Slovakia,  
 Slovenia, South Korea (ROK), Sudan, Sweden, Switzerland,  
 Thailand, Turkey, Ukraine, United Kingdom (Scotland), Vietnam,  
 and the West Bank.

Suspected animal cases of H5N1 infection have been reported in  
 America, Cape Verde, Congo (Democratic Republic), Eritrea,  
 Gabon, Ghana, Ireland, Kazakhstan, Kenya, Lebanon, Mauritania,  
 Moldova, Morocco, Nepal, North Korea, Tajikistan, Uganda, the  
 United Arab Emirates (Dubai), United Kingdom (England) and Yemen.

**UNCLASSIFIED**

produced by: NSTD/HQ  
 date of information: 20060621

# Who to Blame?



# Is There a Pandemic?





# Only If You Have Feathers



# Global H5N1 Situation

---

- 1997 emerged as poultry & human disease
- Remains an avian influenza virus
- 2006 continued spread in poultry
  - 54 countries (Africa, Asia, Europe, Middle East) since 2004
- 2006 continued infections of people
  - 10 countries
  - Remains rare
  - Most infected by direct exposure to infected poultry
  - A minority infected by contact with an infected person



# Is There a Change in the Epidemiology in Poultry or in the Virus ?

---

- Still high mortality in poultry
- Continued geographic spread
- Establishment of endemicity
- Limited data suggest some changes to the virus but not enough to change strains in current animal vaccines





# Has the Epidemiology of H5N1 in Humans Changed?

---

- Increase in geographic location of cases since 2005
- No major changes in age, sex, and clinical characteristics
- Clusters continue to occur
  - In 2005, cluster size 2-3 cases
  - In 2006, cluster size 2-8 per cluster
- Most cases had poultry exposures (OR 29, 3-308)
- Non-sustained human-to-human transmission observed in 2005 and 2006



# Clinical Characteristics

---

- Higher mortality with decreasing age
- All have fever
- Cough, sputum, dyspnea and rhinorrhea frequent
- Thrombocytopenia seen commonly and almost exclusively in pediatric population
- Neutropenia in nearly all pediatric cases and less than 40% of adults
- Most deaths associated with ARDS





# Clusters

---

- Not new – first seen in 1997 in Hong Kong
- Seen in several countries under certain conditions
- Can have different causes
  - Sometimes when multiple persons exposed to infected poultry (products)
  - Sometimes when person(s) in close, intimate contact with an infected person
- Human-to-human transmission that is not sustained is **NOT** a reason to change pandemic alert phase



# Clusters

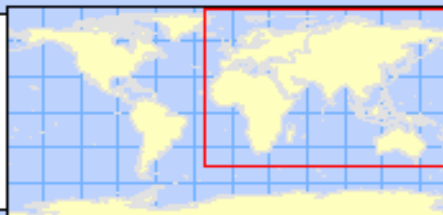
---

- Size
  - Does NOT by itself indicate increased transmissibility
  - Is not criteria for making pandemic phase change
- Critical questions for investigations
  - Is basic cause exposure to bird (products) or human-to-human?
  - If human-to-human did transmission occur because of close, intimate contact?
  - Is the transmission limited or sustained?



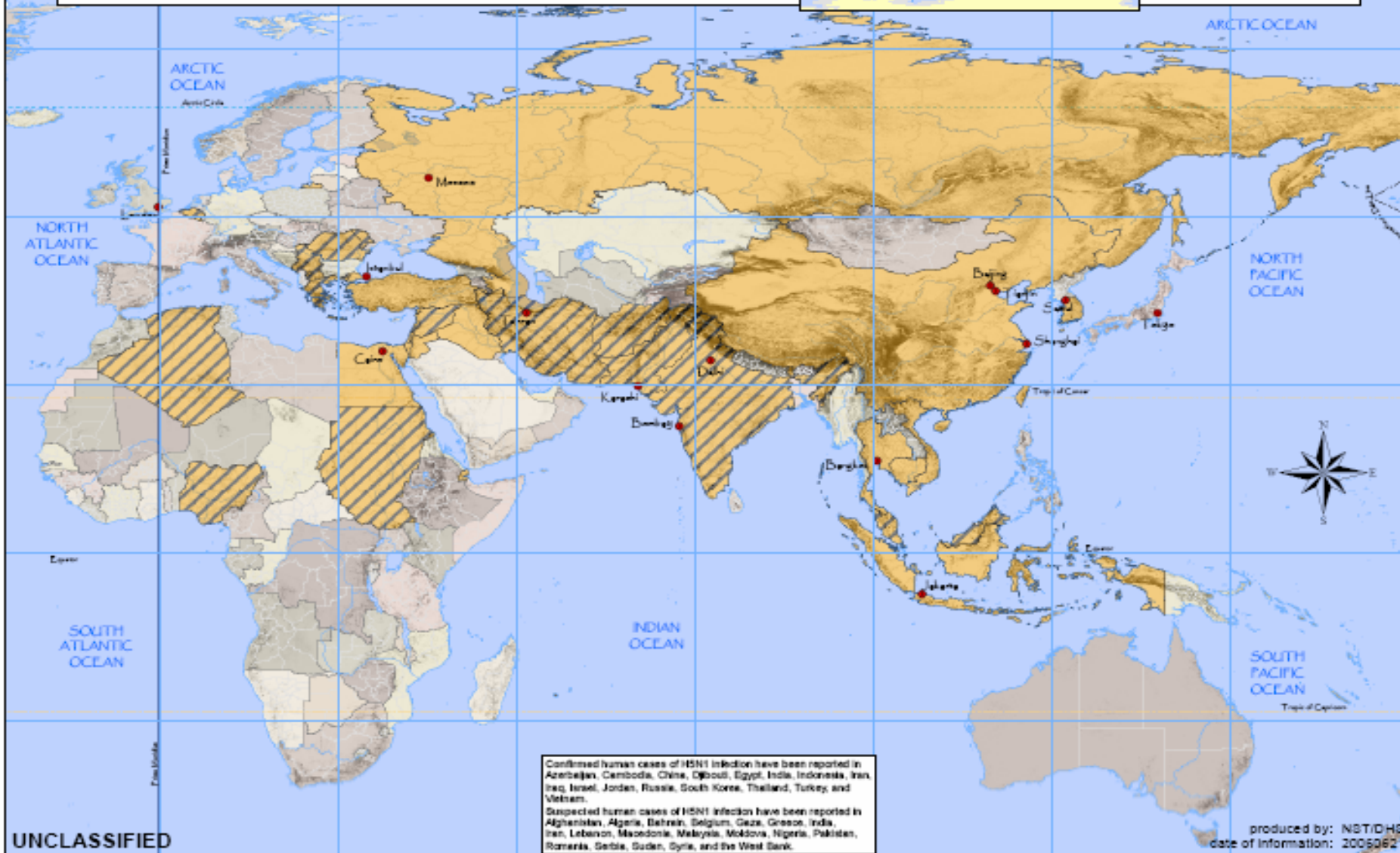


# NBIC BioStatus Avian Influenza (H5N1) in Humans Eastern Hemisphere



UNCLASSIFIED

- Confirmed Human
- Suspected Human
- Change from Previous Report



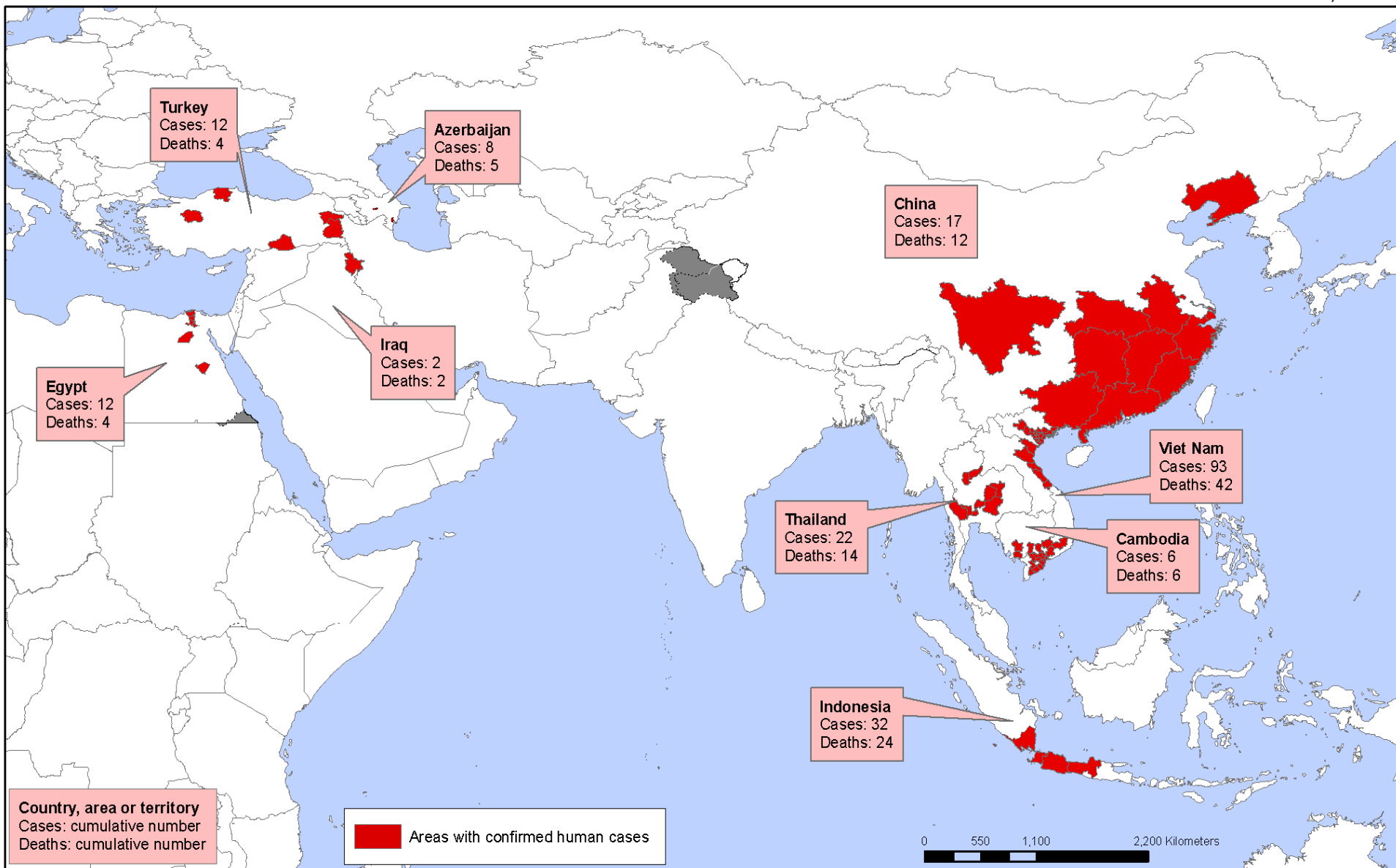
UNCLASSIFIED

# Cumulative Number of Confirmed Human Cases of Avian Influenza Reported to WHO July 4, 2006

Country	2006		Total since 2003	
	Cases	Deaths	Cases	Deaths
Azerbaijan	8	5	8	5
Cambodia	2	2	6	6
China	10	7	18	12
Djibouti	1	0	1	0
Egypt	14	6	14	6
Indonesia	35	29	49	37
Iraq	2	2	2	2
Thailand	0	0	22	14
Turkey	12	4	12	4
Viet Nam	0	0	93	42
<b>Total</b>	<b>85</b>	<b>55</b>	<b>229</b>	<b>131</b>

# Affected areas with confirmed human cases of H5N1 avian influenza since 2003

Status as of 21 April 2006



# Current Threat Containment Problems

---

- 75-80% poultry farms are small backyard operations - limits biosecurity
- Numerous endemic viruses resulting in 50-70% baseline poultry deaths
- Multiple disincentives to report a die-off
  - Fear
  - Distrust
  - Poor or no reimbursement
  - Attachment



# Containment Problems

---

- Uncertain transparency
  - H5N1 has been circulating in China for at least a decade
    - Not reported because information on epidemics of High Path AI were State secrets until 2003
    - Currently one laboratory in China has permission to conduct AI research
  - H5N1 noted in PRC veterinary sources before 1997
  - Improving



# Containment Problems

---

- Many countries lack comprehensive surveillance or response plans
  - Lack short, intermediate or long term plans or needs assessment
  - Poor coordination between Ministries of Agriculture and Health result in inability to assess true capabilities and needs





# U.S. Risk

---

- 3 Million registered fighting cocks in CA
- 9.3 Billion commercial chickens - good biosecurity
- 100 Million chickens in unregulated live bird market – not so good biosecurity
- 60 Million foreign visitors to the US
- 60 Million US visitors to foreign countries
- 400 Million crossings in from Mexico
- Fomite in Viet Nam can be in Boise in two flights



# National Plan Tasks

## HA As Primary Agency

---

1. Open source information sharing
2. Inpatient and outpatient disease surveillance
3. Monitoring health of military forces worldwide
4. Develop/enhance DoD network of overseas infrastructure
5. Refinement of DoD laboratory methods
6. Employ active and passive influenza surveillance in foreign countries
7. Enhance influenza surveillance reporting techniques
8. Provide health statistics on influenza-like illnesses



# National Plan DoD (HA) Tasks

---

9. Conduct medical materiel requirements gap analysis
10. Maintain antiviral and vaccine stockpiles
11. Establish stockpiles of vaccine against H5N1
12. Procure 2.4 million antiviral medications
13. Supply military units/bases with influenza medication
14. Enhance public health response capabilities
15. Ensure DoD hospital access to diagnostic testing
16. Implement infection control campaigns
17. Update risk communication material



# Plans are Nice but You Need Material to Make It Happen

STAR TRIBUNE  
BOOK



# Vaccine

---

- 2.4 Million doses (90ug) purchased
  - 1.7 million available due to vaccine degradation
- Bottled 1.3 million doses
- Following licensure
  - Current concept includes administration beginning at WHO Phase 4.
- Adjuvant trial results anticipated July 2006
- Clade 2 pilot lot commissioned by HHS



# Vietnam 1203 H5N1 Vaccine Safety and Immunogenicity

---

- No severe adverse events
  - Generally well tolerated
- Only those receiving two doses of 90 ug
  - Achieved neutralization antibody titers of 1:40 or greater in > 50% of subjects (54%)
  - Achieved hemagglutination-inhibition titers of 1:40 or greater in > 50% of subjects (58%)



# Cross Reactivity of Vietnam 1203 Vaccine with Clade 1 & 2 Strains

## HEMAGGLUTINATION INHIBITION REACTIONS OF H5 INFLUENZA SPECIMENS

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA							
	VN/1203	VN/30321	VN30408	DK/KP	IND/5	IND/6	DK/HU/15	IND/5-R
1 A/VIETNAM/1203/2004	<u>320</u>	80	320	10	20	10	160	10
2 A/VIETNAM/JPHN30321/2005	80	<u>320</u>	80	160	160	20	40	10
3 A/VIETNAM/HN30408/05	160	40	<u>640</u>	160	20	5	320	10
4 A/DUCK KULON PROGO/BBVET/1X/04	20	40	20	<u>2560</u>	1280	320	80	640
5 A/INDONESIA/5/2005	10	40	10	1280	<u>1280</u>	320	40	320
6 A/INDONESIA/6/2005	10	20	20	1280	1280	<u>640</u>	40	320
7 A/DUCK/HUNANWG/15/04	20	40	40	80	80	10	<u>160</u>	10
8 A/INDONESIA/5/05 X PR/8-R (CDC)	10	40	20	2560	1280	1280	80	<u>320</u>

# Antivirals

## Relenza

---

- Now approved for treatment and prophylaxis
- Still no clinical experience with H5N1
- Contract awarded to Glaxo Smith Kline for \$5.25 million worth of Relenza, or 241,000 treatment courses
  - Anticipated delivery in March 2007
  - Possible partial shipment in mid-2006
- Concern: effectiveness if + viremia





# Antivirals

## Tamiflu

---

- 2.4 million treatment courses prepositioned
  - Revised contract permits use in Phases 3-6
- Purchasing an additional 470,000 treatment courses and preposition at MTF's
  - 470K represents 10% of PAR
  - Facilitate use during initial stages of pandemic and for use during primary zoonotic outbreaks with limited human disease
- Plan to purchase an additional 500K to be added to 2.4 million stockpile



# Tamiflu

- Adult & pediatric formulations – pediatric compounding instructions now available via MILVAX
  - Compounded formulation stable for 45 days
- Anecdotal and animal data demonstrates efficacy and effectiveness for treatment of current H5N1
- Effective in ferrets following viral doses of biblical proportion
- Resistance documented for Type A influenza
  - 0.4% in adults 4% pediatrics
  - Resistant mutation results in virus that is either incapable of or has decreased infectivity



# Additional Resources

---

- PPE
  - Centrally funded
  - Services purchasing to ensure protection for their populations
- Antibiotics
  - Essential list determined by Service ID SME
  - Funding obtained
  - Distribution scheme being formulated



# Containment Measures

---

- Antivirals are not the magic bullet
- Vaccine will be late and in insufficient amounts
- Best measures are non-pharmacologic
  - Sneeze and cough etiquette
  - Hand washing
  - Daily temperature monitoring
  - Social Distancing
    - Tele-commuting if possible
    - Closing schools (keep kids at home)
    - Cancel social gatherings
  - Flu hot lines, triage, early treatment if needed
  - Risk communication



# Modeling

---

- Results of modeling are converging
  - Common findings
    - Interventions have to be early and of sufficient duration
    - Treatment and isolation 1<sup>st</sup> day of symptoms
      - Need rapid diagnostics
    - Close schools & keep kids at home -effective
    - Social distancing - effective
    - Closing borders and work place not effective
    - BONUS: When non-pharmacologic interventions are used antiviral requirement is significantly reduced

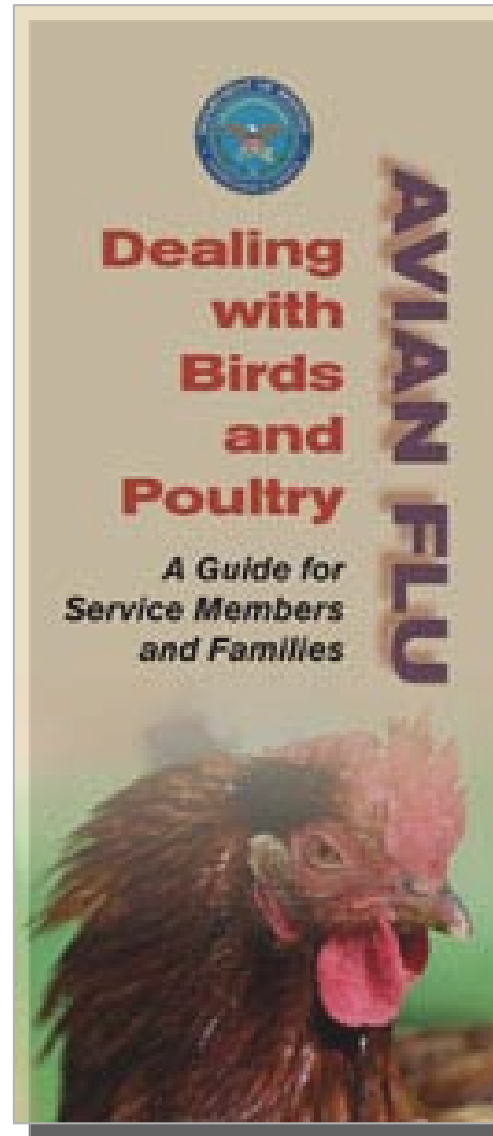


<b>Social Distance Strategy</b>	<b>Peak Infected</b>	<b>Total Infected</b>	<b>Dead</b>
<b>Baseline</b>	<b>1007</b>	<b>5046</b>	<b>463</b>
<b>Close Schools after 10 Sx (99% Compliance), double outside contacts</b>	<b>1064 (-6%)</b>	<b>5746 (-14%)</b>	<b>552 (-19%)</b>
<b>Close Schools after 10 Sx (99% Compliance), keep kids home</b>	<b>30 (97%)</b>	<b>105 (98%)</b>	<b>10 (98%)</b>
<b>Close Schools aft 10 Sx (70% Compliance), keep kids home</b>	<b>64 (94%)</b>	<b>719 (86%)</b>	<b>64 (86%)</b>
<b>Close Schools and Work after 10 Sx (70% Compliance) keep kids home</b>	<b>50 (95%)</b>	<b>413 (92%)</b>	<b>36 (92%)</b>
<b>Adults stay home (99% compliance)</b>	<b>916 (9%)</b>	<b>4728 (6%)</b>	<b>436 (6%)</b>

Extracted from: Local Mitigation Strategies for Pandemic Influenza National Infrastructure Simulation and Analysis Center. Robert J. Glass SAND Number 2005-7955J

# Communication

- Beneficiary Information
  - Web based
  - Printed
    - Prepandemic influenza information sheets
    - Avian (zoonotic) influenza
    - Pandemic influenza





# Communication

---

- Watch board
- <https://fhp.osd.mil/aiWatchboard/index.html>
- Continued evolution
  - Disease status
  - Clinical practice guidelines
    - MHS
    - Operational
  - Policy and guidance





National Response Readiness Status

The Department of Defense  
Force Health Protection  
& Readiness

# Pandemic Influenza

**ALERTS: Pandemic Alert Period Phase 3 - Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.**

Watchboard  
Home

Preparedness &  
Communication

Surveillance &  
Detection

Response &  
Containment

Related Links

- HHS
- CDC
- WHO
- Pandemic Flu
- VA
- USDA
- DoL OSHA
- State Department
- USAID
- DOD GEIS

## Department of Defense Pandemic Flu Stages

Interpandemic Period		National Strategy Goals
<b>Phase 1</b>	No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.	Strengthen influenza pandemic preparedness at the global, regional, national and sub national levels.
<b>Phase 2</b>	No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.	Minimize the risk of transmission to humans; detect and report such transmission rapidly if it occurs.
Pandemic Alert Period		National Strategy Goals
<b>Phase 3</b>	Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.	Ensure rapid characterization of the new virus subtype and early detection, notification and response to additional cases.
<b>Phase 4</b>	Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.	Contain the new virus within limited foci or delay spread to gain time to implement preparedness measures, including vaccine development.
<b>Phase 5</b>	Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).	Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.
Pandemic Period		National Strategy Goals
<b>Phase 6</b>	Increased and sustained transmission in general population.	Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.

More Links



**ALERTS: Pandemic Alert Period Phase 3 - Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.**

## Human Avian Influenza Cases

### Watchboard Home

### Preparedness & Communication

### Surveillance & Detection

### Response & Containment

### Related Links

- HHS
- CDC
- WHO
- Pandemic Flu
- VA
- USDA
- DoL OSHA
- State Department
- USAID
- DoD GEIS

Human Cases Reported for the Week Ending November 18: The World Health Organization (WHO) confirmed five cases, including: in Thailand, an 18-month-old boy from Bangkok; in China, two cases, including a 9-year-old boy from Hunan Province, who recovered, and a 24-year-old female poultry worker who died in Anhui Province; and in Indonesia, two fatalities, a 16-year-old girl and a 20-year-old woman, both from Jakarta. An additional case from Hunan Province, the 12-year-old sister of a confirmed case, was not confirmed by WHO because she died one day after being admitted to the hospital, and was cremated without undergoing testing for H5N1. Her brother was admitted to the hospital the day she died, and received treatment, although no specific information is available. All of the human cases occurred in regions with ongoing poultry outbreaks. All of the victims had contact with sick poultry, including the Bangkok toddler who was playing near them.

Avian Flu Outbreaks	Week Ending Nov. 18, 2005			2005 Cases <sup>1</sup>	2004 Cases <sup>2</sup>
	Location	Date Reported	Probable Source	#Deaths #Cases	#Deaths #Cases
<a href="#">Thailand</a> Bangkok	Nov. 14	chickens	0/1 0/1	1/4	12/17
<a href="#">Vietnam</a>			0/0	23/66 <sup>3</sup>	20/27
<a href="#">Cambodia</a>			0/0	4/4	0/0
<a href="#">Indonesia</a> Jakarta	Nov. 17		2/2 2/2	9/13 <sup>4</sup>	0/0
<a href="#">China</a> Human Province Anhui Province	Nov. 16 Nov. 16	chickens chickens	2/3 <sup>5</sup> 1/2 <sup>5</sup> 1/1	2/3 <sup>5</sup>	0/0
<b>TOTAL</b>			4/6	39/90 <sup>3,4,5</sup>	32/44

<sup>1</sup>The reported cases and deaths are from Mid-December 2004 through November 18, 2005.

<sup>2</sup>The reported cases and deaths are from late-December 2003 through October 2004.

<sup>3</sup>One fatal case from Vietnam in September has not been counted yet by WHO.

<sup>4</sup>Two fatalities from Tangerang in July are included here, but not in the WHO official count.

<sup>5</sup>One fatal case from Human Province is a sister of a confirmed case, but will not be officially confirmed by WHO because she was cremated prior to testing for H5N1.





National Response Readiness Status

To Department Secretary  
Force Health Protection  
& Readiness

# Pandemic Influenza

**ALERTS: Pandemic Alert Period Phase 3 - Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.**

Watchboard  
Home

Preparedness &  
Communication

Surveillance &  
Detection

Response &  
Containment

Related Links

- HHS
- CDC
- WHO
- Pandemic  
Flu
- VA
- USDA
- DoL OSHA
- State  
Department
- USAID
- DOD GEIS

## Preparedness and Communication

### DOD Policy

Department of Defense Influenza Pandemic Preparation and Response Health Policy  
Guidance Final Draft (25 JAN 2006)

Policy for Release of Tamiflu (Osetatmivir) Antiviral Stockpile During an Influenza Pandemic  
Final Draft (10 JAN 2006)

### DOD Interim Guidance

Interim Guidance for Protecting DOD Personnel Involved in Avian Influenza Disease  
Eradication Activities (21 MAR 2006)

