Animal & Plant Health Agency

A worldwide overview on the recent multiple incursions of AI viruses in poultry

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APHA-Weybridge

G7 CVOs meeting, Rome 4th October 2017

Disease Impact

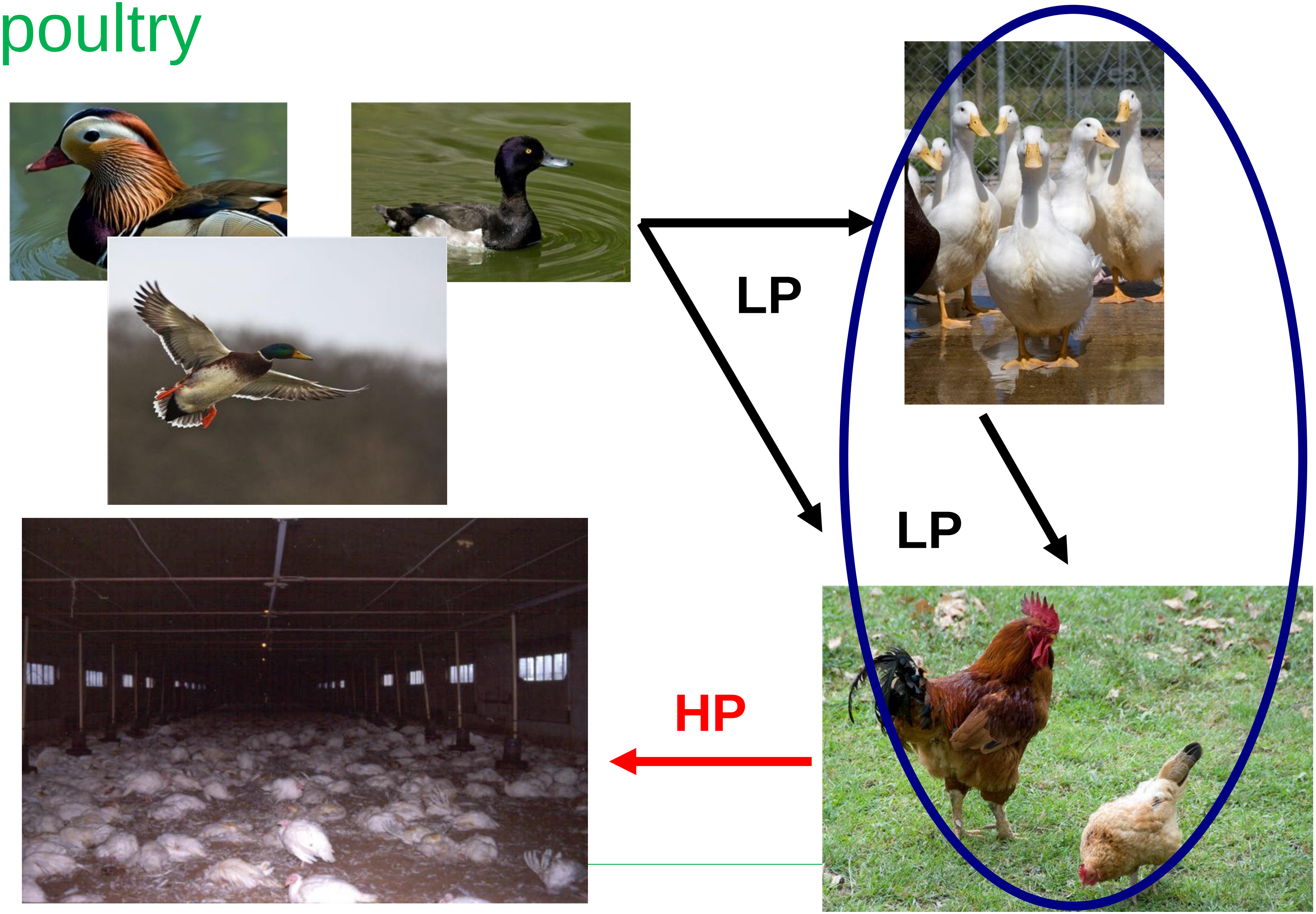
- Increasingly important disease of poultry
  - Societal impact in some developing countries
  - >600? million poultry culled/killed due to H5N1, H5Nx
  - >$25?? billion to global economy
- Global changes in distribution
  - Uncontrolled spread
  - Endemnicity in several countries/regions
  - Emergence of new clades/waves of infection
- Zoonotic infection
  - Implications for pandemic preparedness
- Spread to other host populations

Epidemiology of avian influenza

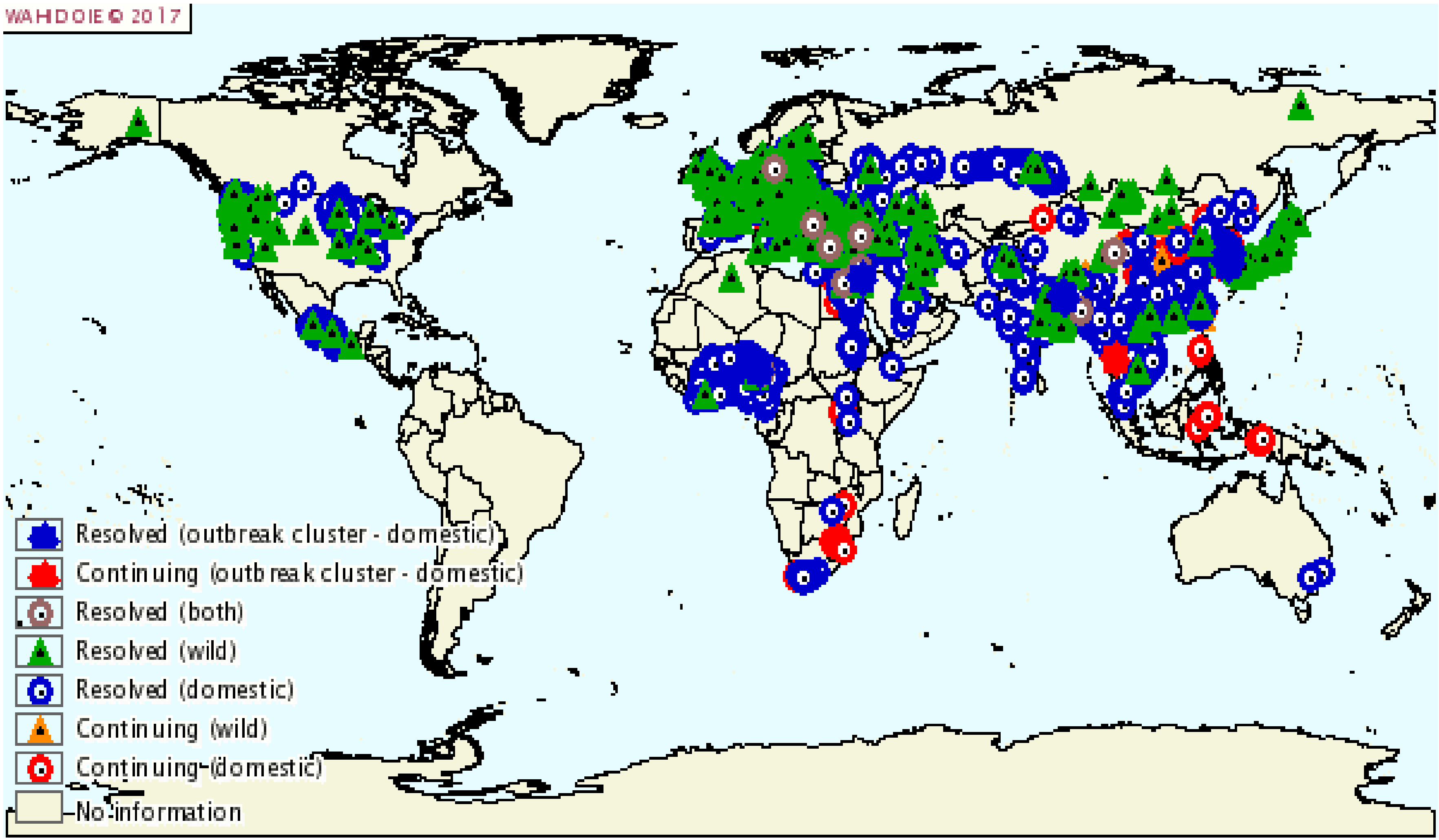
- Conventional
  - wild bird reservoir of LPAI
  - spread to poultry
  - some LPAI viruses mutate to HPAI
- Panzootic LPAI
  - H9N2

- HPAI H5N1, then since 2013 H5N2, H5N3, H5N8…..
  - completely different including wild bird reservoirs

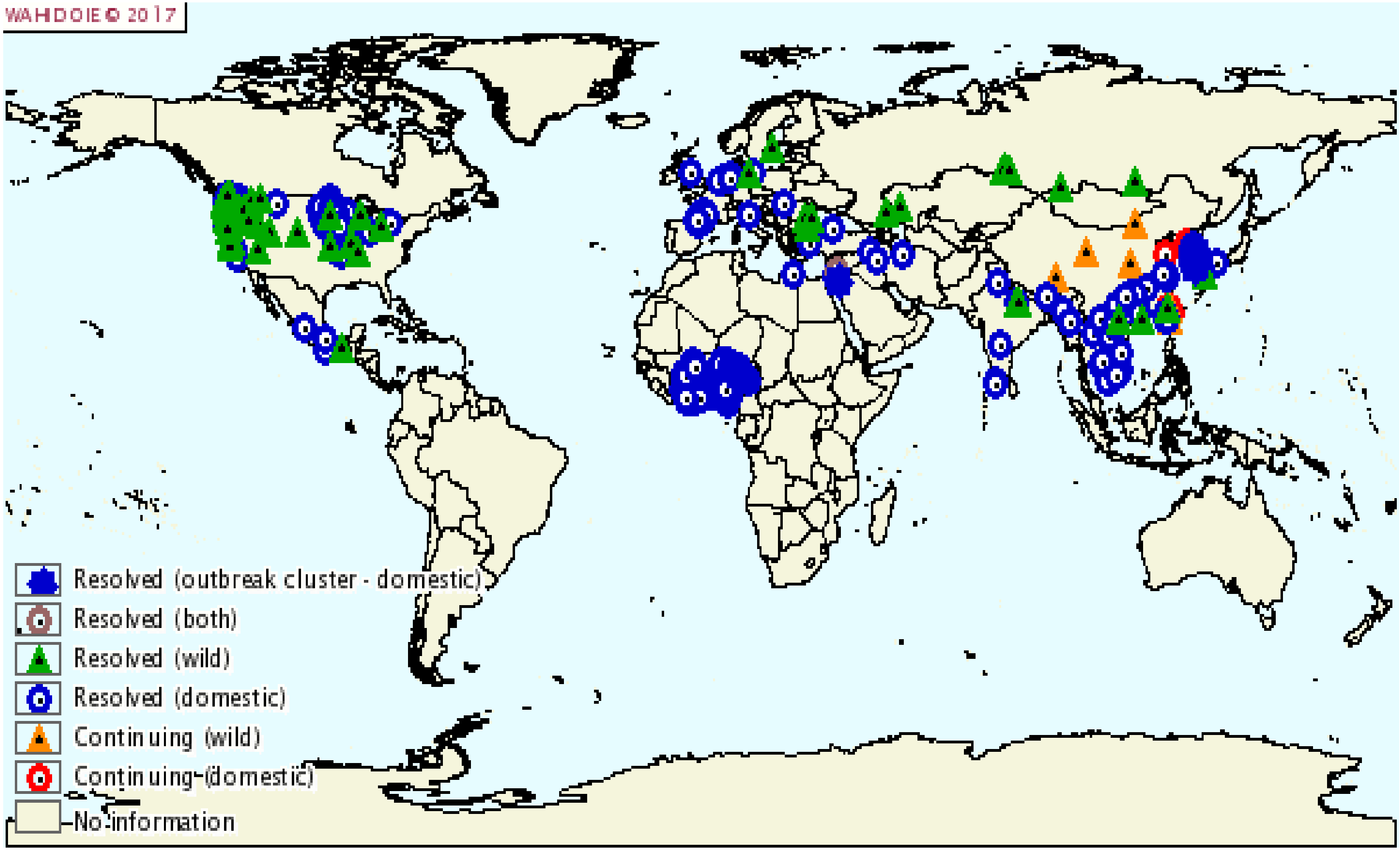
LPNAI (H5 & H7 AIVs) entry into farmed poultry



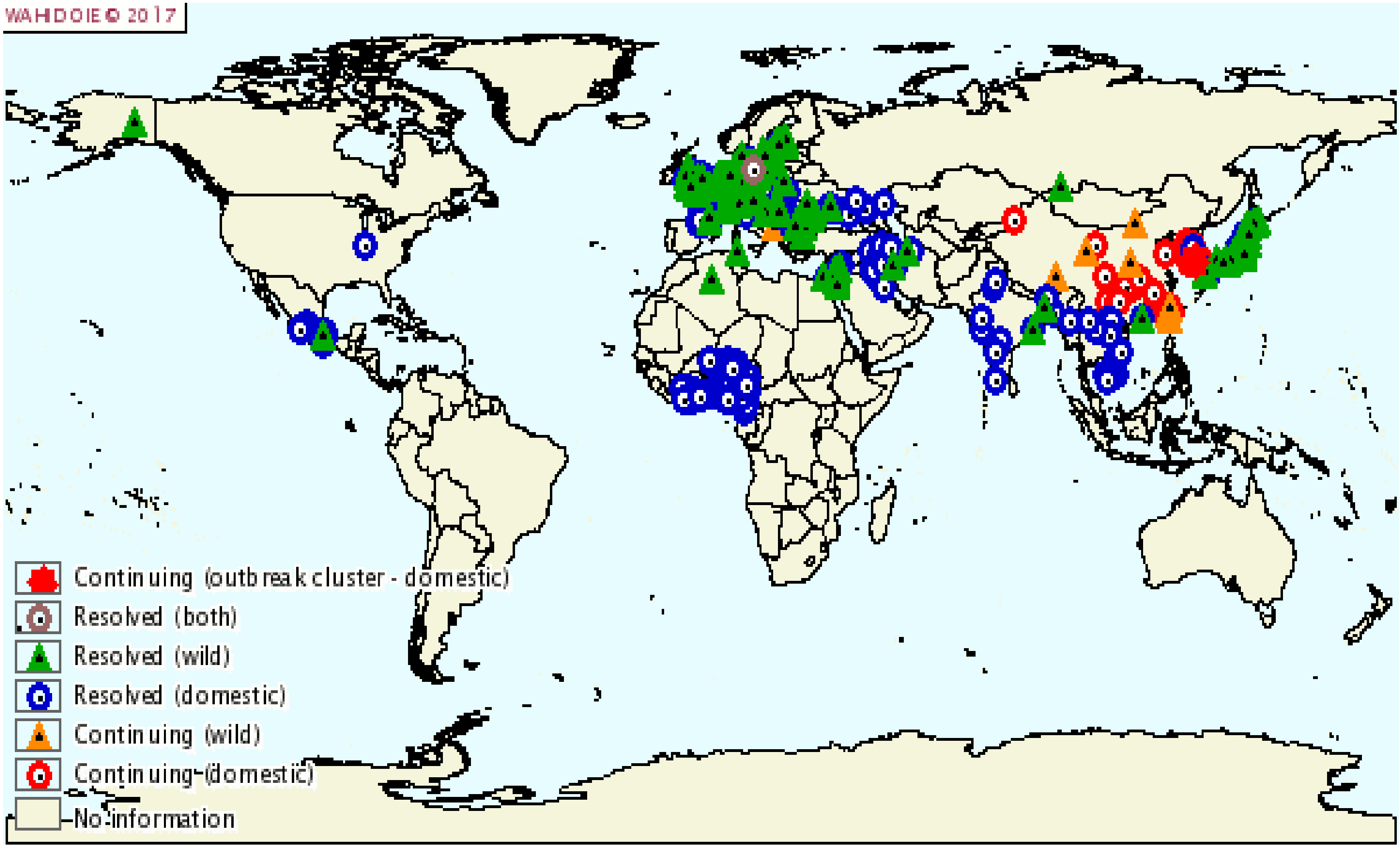
HPAI outbreaks 2005-2017



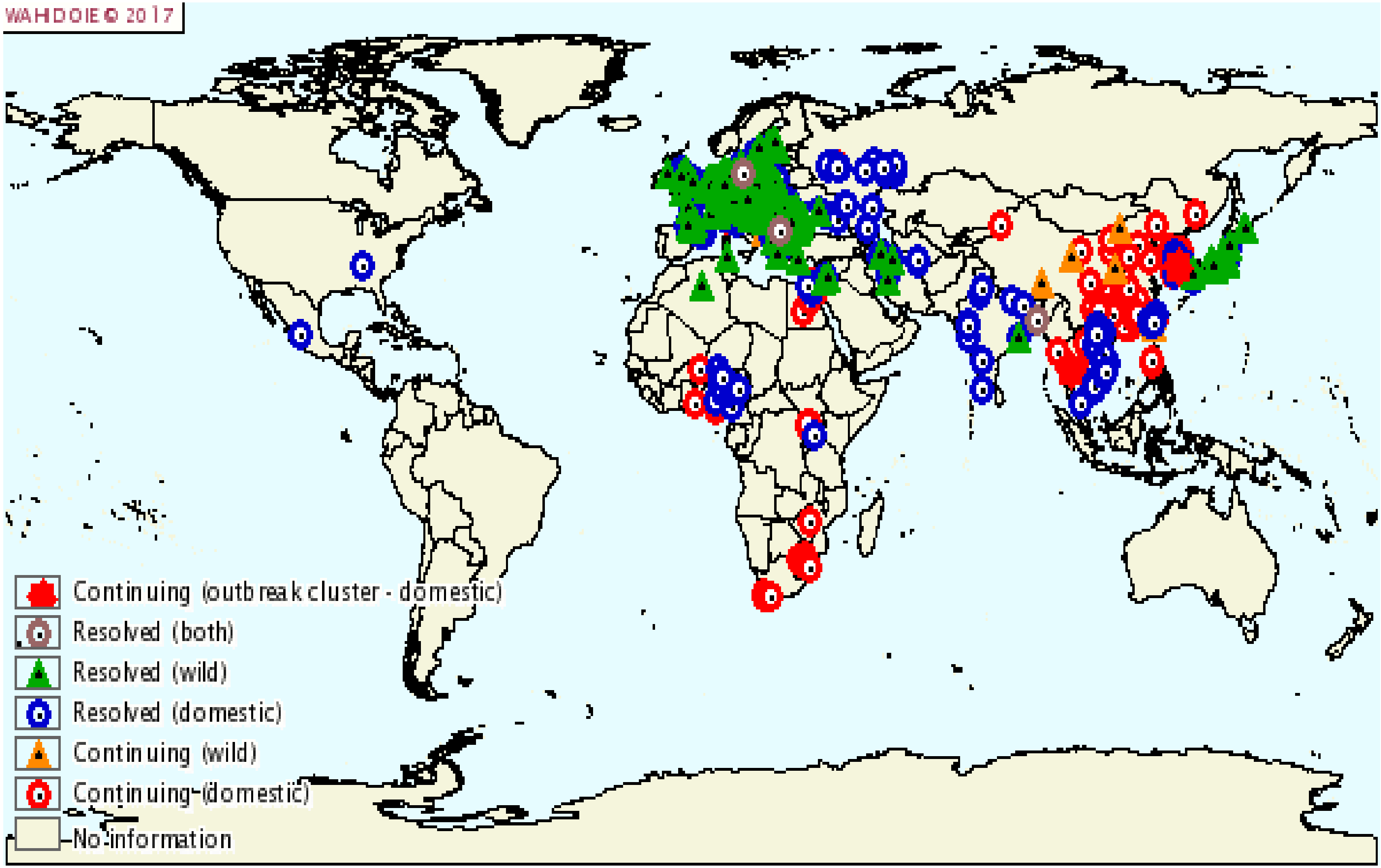
HPAI outbreaks 2015



HPAI outbreaks 2016

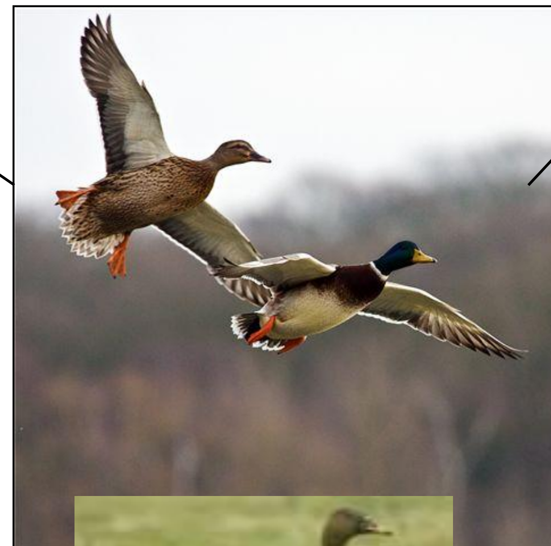


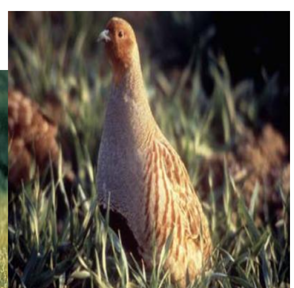
HPAI outbreaks 2017




Primary incursion
YES but NOT always





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EURASIAN H5 HPAI

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HPAI H5N1 ancestral virus

Goose/Guangdong/96

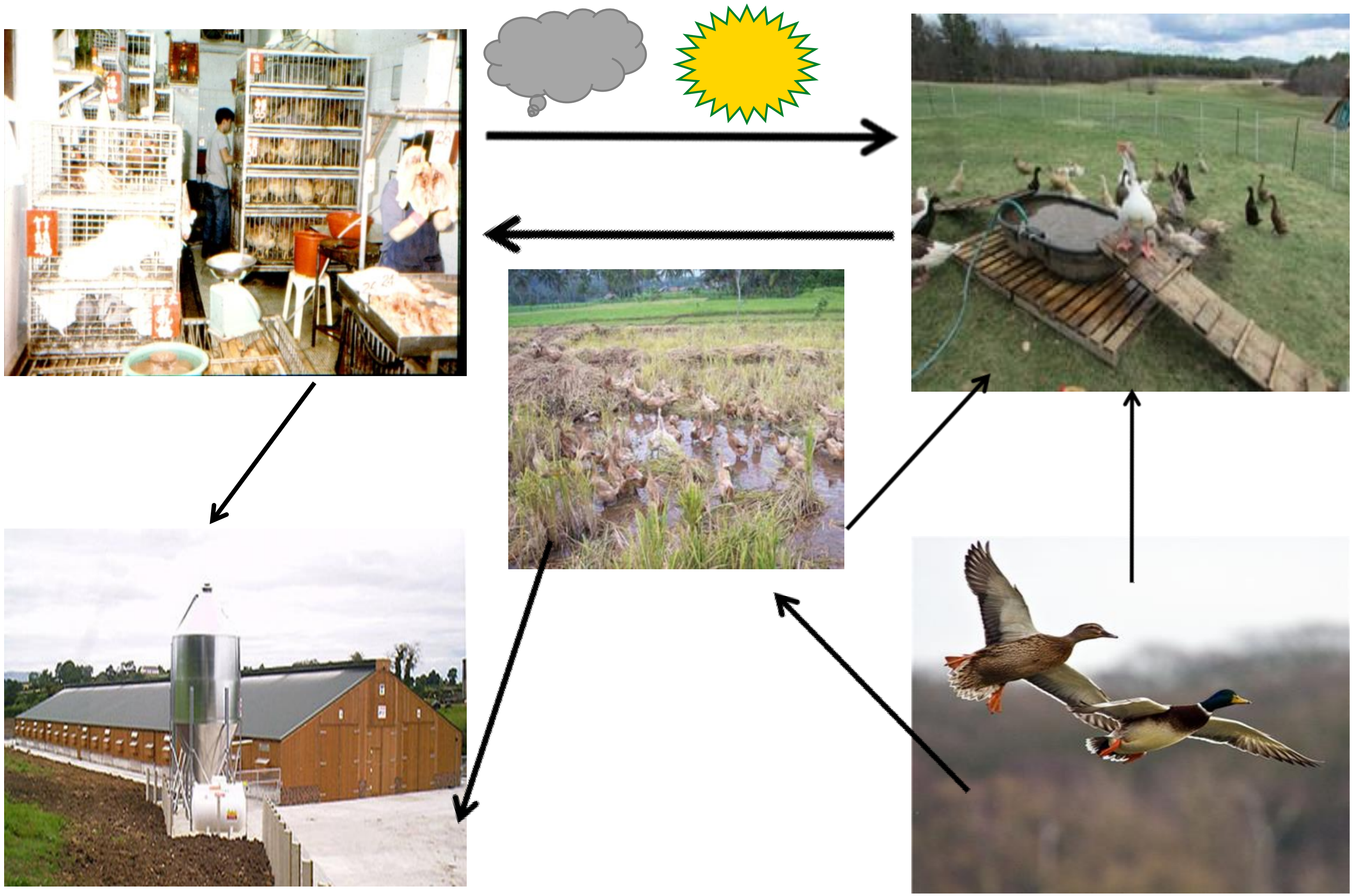
Infection dynamics in poultry -HPAI

LD_{50} (log10)			MID_{50} (log10)		
H5	H7	ND	H5	H7	ND
3.7	4.3	2.5	≤ 3.7	≤ 4.3	<2
<1	2.3	>10	<1	≤ 2.3	nd
2.5	>6.0	>6.0	**<1**	4.1	>6.0

Aldous et al 2010

Aldous et al 2010 Avian Pathol 36:265-73.

Relationship between husbandry/ecosystems for maintenance of HPAI



Epidemiology of HPAI H5 (‘Guangdong-lineage’)

- Waves of infection especially in countries with:
  - extensive trade in live poultry through live bird markets
  - free ranging ducks

- Virus spread through poor biosecurity within the poultry sectors (3 & 4); lack of preventative measures
  - Extensive small holder poultry production

- Maintenance and spread via wild birds

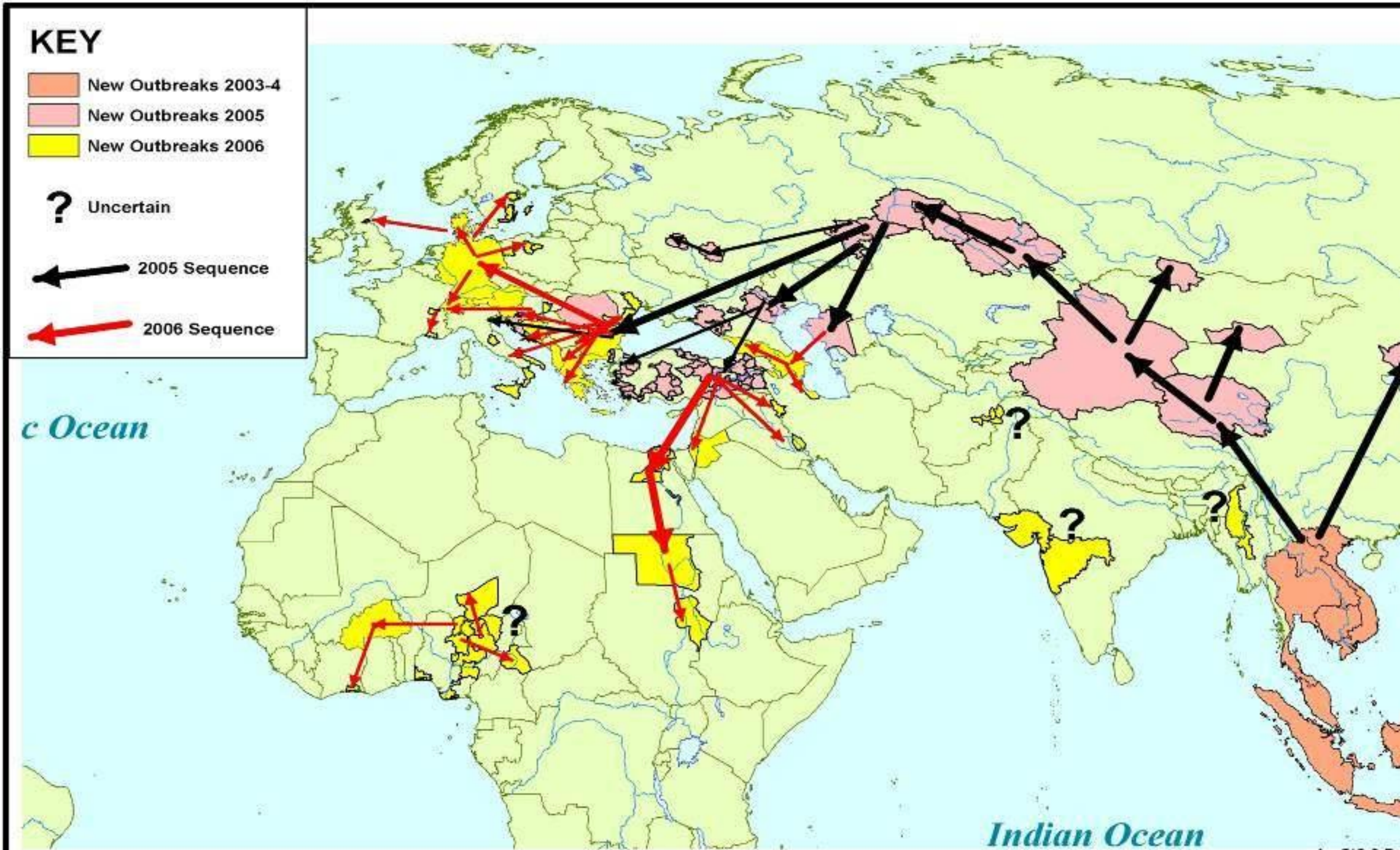
- Virus evolution, changing molecular epidemiology and diversity add complexity
  - Challenges for appropriate vaccination

Multiple waves new strains – virus constantly evolving (Goose/Guangdong lineage)

- Antigenetic change – H or HA
  - Accumulated changes
- Genotypic variation
  - Genetic reassortment
- 1997- H5N1 multiple clades (0, 1, 2, 7)
  - 2.2 spread to Europe/Africa
  - 2.1 spread to Indonesia

- 2009 – H5N1, selection of clades with greater fitness for birds
  - Ie clade 2.3.2.1

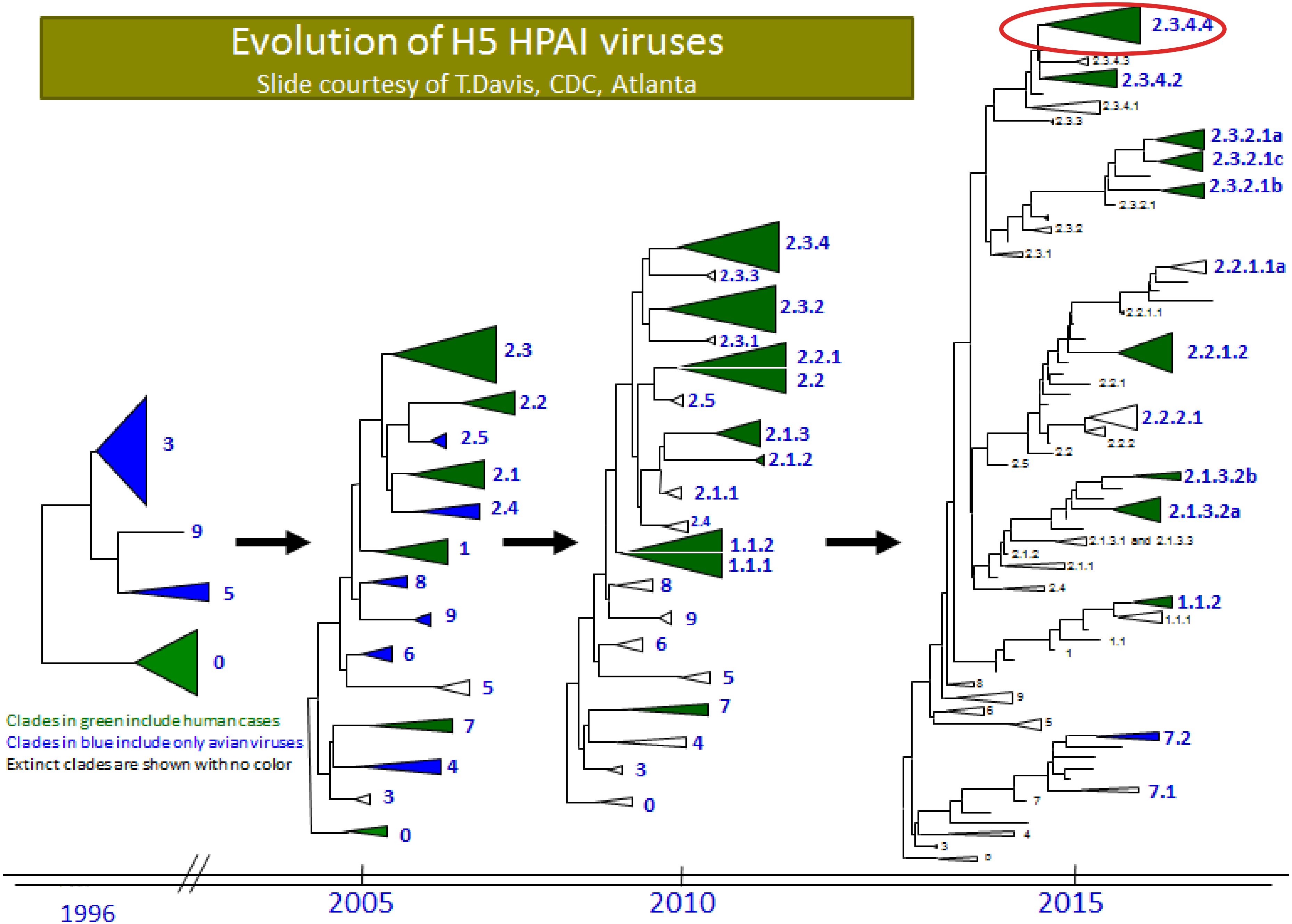
- 2013 – H5N2, H5N8
  - Ie clade 2.3.4.4



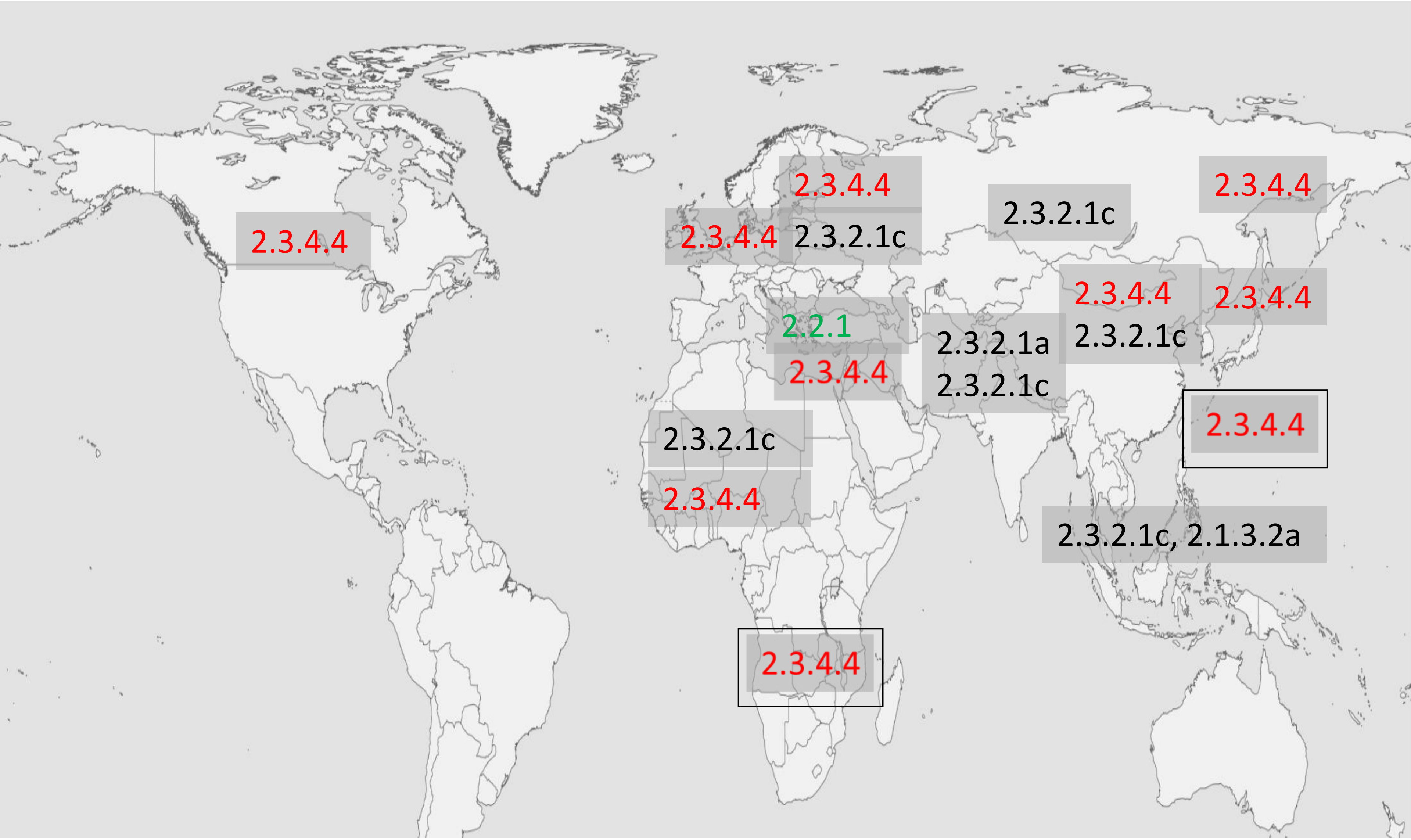
Possible HPAI H5N1 Dispersal Routes (2005 - 2006)
(Note: Arrows indicate apparent sequence of geographic spread over time)

Evolution of H5 HPAI viruses

Slide courtesy of T.Davis, CDC, Atlanta

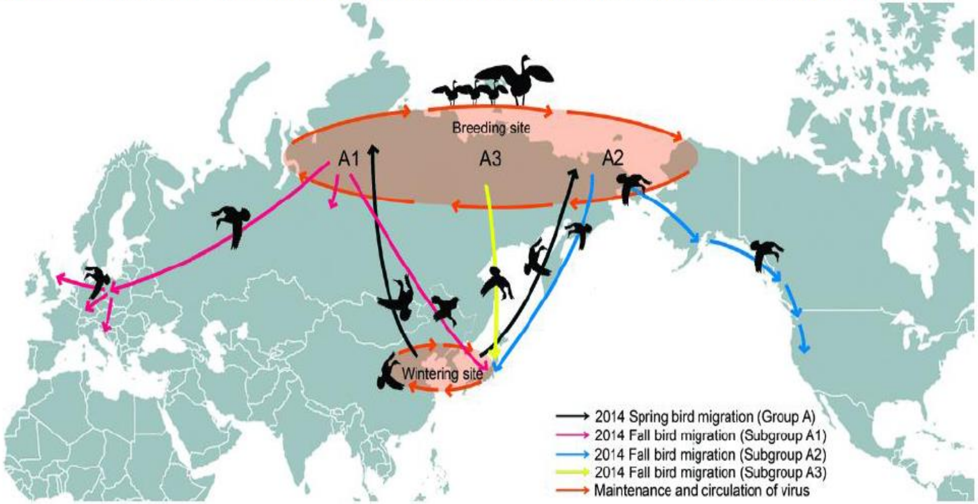


HA Clade of H5 HPAI viruses isolated in October 2014 – August 2017



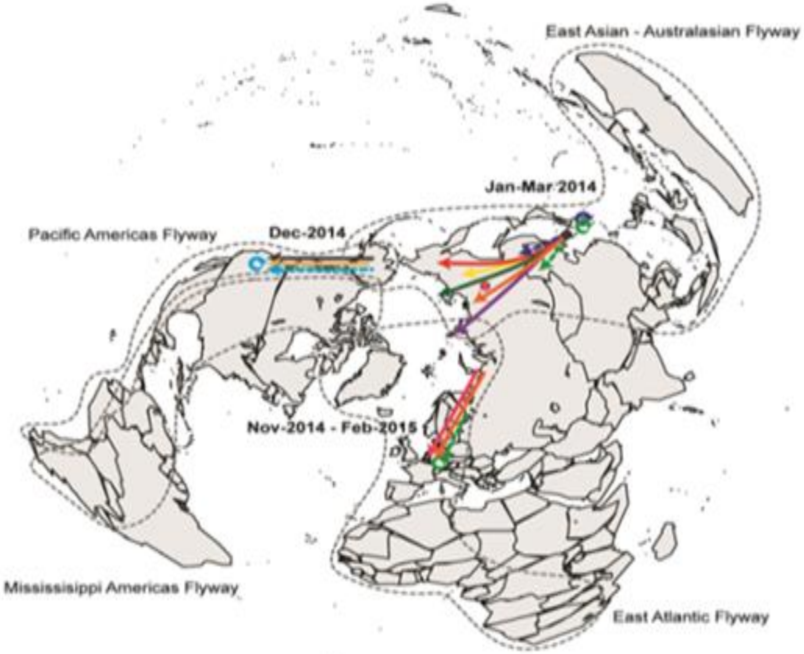
Temporal global spread of related viruses –wild bird mediated

Figure 2. **Indicative transmission** routes of HPAI A(H5N8) through birds migrating into Europe



Journal of Virology, 2015, Jun;89(12):6521-4, doi 10.1128/JVI.00728-15. Reproduced with permission from the American Society for Microbiology

Group A: *comprises Chinese, Russian, South Korean, Japanese, European and North American A(H5N8) 2.3.4.4 viruses representing intercontinental group A;* ***Subgroup A1:*** *composed of A(H5N8) viruses from Europe and Russia from late 2014 and three viruses detected in Japan in December 2014;* ***Subgroup A2:*** *composed of A(H5N8), as well as H5 clade 2.3.4.4 North American HPAIV reassortants (A(H5N2) and A(H5N1))detected in North America starting in late 2014 and a Japanese virus, A/crane/Kagoshima/KU1/2014(H5N8), detected in November 2014;* ***Subgroup A3:*** *composed of A(H5N8) viruses isolated in Japan in December 2014 and Korea in January 2015 [28].*



Role for migratory wild birds in the global spread of avian influenza H5N8 ***Science*** **14 Oct 2016: Vol. 354, Issue 6309, pp. 213-217**

Recent expansion in number of wild bird species affected but similar orders of Aves

Species	Number of events*	%	High Risk Species not detected positive to date in the current epizootic
Mute swan (*Cygnus olor*)	325	20%	Black-necked Grebe (*Podiceps nigricollis*)
Swan spp	253	16%	Bewick's Swan (*Cygnus columbianus*)
Duck spp	140	9%	Barnacle Goose (*Branta leucopsis*)
Unspecified	140	9%	Brent Goose (*Branta bernicla*)
Goose spp.	91	6%	Red-breasted Goose (*Branta ruficollis*)
Gulls spp	84	5%	Gadwall (*Anas strepera*)
Tufted duck (*Aythya fuligula*)	82	5%	Northern Pintail (*Anas acuta*)
Whooper swan (*Cygnus cygnus*)	79	5%	Garganey (*Anas querquedula*)
Common buzzard (*Buteo buteo*)	70	4%	Northern Shoveler (*Anas clypeata*)
Grey heron (*Ardea cinerea*)	45	3%	Marbled Teal (*Marmaronetta angustirostris*)
Mallard (*Anas platyrhynchos*)	41	2%	Smew (*Mergus albellus*)
Herring gull (*Larus argentatus*)	27	2%	Black Kite (*Milvus migrans*)
Black-headed gull (*Chroicocephalus ridibundus*)	23	1%	Red Kite (*Milvus milvus*)
White-tailed eagle (*Haliaeetus albicilla*)	21	1%	Eurasian Marsh Harrier (*Circus aeruginosus*)
Greylag goose (*Anser anser*)	21	1%	Rough-legged Buzzard (*Buteo lagopus*)
Eurasian wigeon (*Anas penelope*)	20	1%	Purple Swamphen (*Porphyrio porphyrio*)
Heron spp.	16	1%	Eurasian Golden Plover (*Pluvialis apricaria*)
Great cormorant (*Phalacrocorax carbo*)	15	1%	Northern Lapwing (*Vanellus vanellus*)
Great crested grebe (*Podiceps cristatus*)	12	1%	Ruff (*Philomachus pugnax*)
Great black-backed gull (*Larus marinus*)	11	1%	Black-tailed Godwit (*Limosa limosa*)
Greater White-fronted Goose (*Anser albifrons albifrons*)	9	1%	
Common pochard (*Aythya farina*)	8	<1%	
Common coot (*Fulica atra*)	8	<1%	
Peregrine falcon (*Falco peregrinus*)	8	<1%	
Canada Goose (*Branta Canadensis*)	5	<1%	
Little grebe (Tachybaptus ruficollis)	4	<1%	
Common magpie (*Pica pica*)	4	<1%	
Lesser white-fronted goose (*Anser erythropus*)	4	<1%	
Owl spp.	4	<1%	
Eurasian teal (*Anas crecca*)	3	<1%	
Hooded crow (*Corvus cornix*)	3	<1%	
White stork (*Ciconia ciconia*)	3	<1%	
Falcon spp	3	<1%	
Hawk spp	3	<1%	
Buzzard spp	2	<1%	
Common gull (*Larus canus*)	2	<1%	
Common moorhen (*Gallinula chloropus*)	2	<1%	
Red-crested pochard (*Netta rufina*)	2	<1%	
Common tern (*Sterna hirundo*)	2	<1%	
Shelduck (*Tadorna tadorna*)	2	<1%	
Song Thrush (*Turdus philomelos*)	2	<1%	
Common Kestrel (*Falco tinnunculus*)	2	<1%	
Wood pigeon (*Columba palumbus*)	2	<1%	
Rook (*Corvus frugilegus*)	2	<1%	
Carrion crow (*Corvus corone*)	1	<1%	
Common eider (*Somateria mollissima*)	1	<1%	
Common goldeneye (*Bucephala clangula*)	1	<1%	
Common raven	1	<1%	
Curlew (Numenius spp.)	1	<1%	
Eagle (spp. unspecified)	1	<1%	
Eurasian Eagle-Owl (*Bubo bubo*)	1	<1%	
Eurasian Sparrowhawk (*Accipiter nisus*)	1	<1%	
Eurasian white fronted goose (*Anser albifrons*)	1	<1%	
Green sandpiper (*Tringa ochropus*)	1	<1%	
Lesser black-backed gull (*Larus fuscus*)	1	<1%	
Wigeon spp.	1	<1%	
Common Blackbird (*Turdus merula*)	1	<1%	
Taiga bean goose (*Anser fabalis*)	1	<1%	
Pink-footed Goose (*Anser brachyrhynchus*)	1	<1%	
Eurasian collared dove (*Streptopelia decaocto*)	1	<1%	
Crested coot (*Fulica cristata*)	1	<1%	

*Note: Several events involved different species; Bird species in bold are on the list of higher risk species

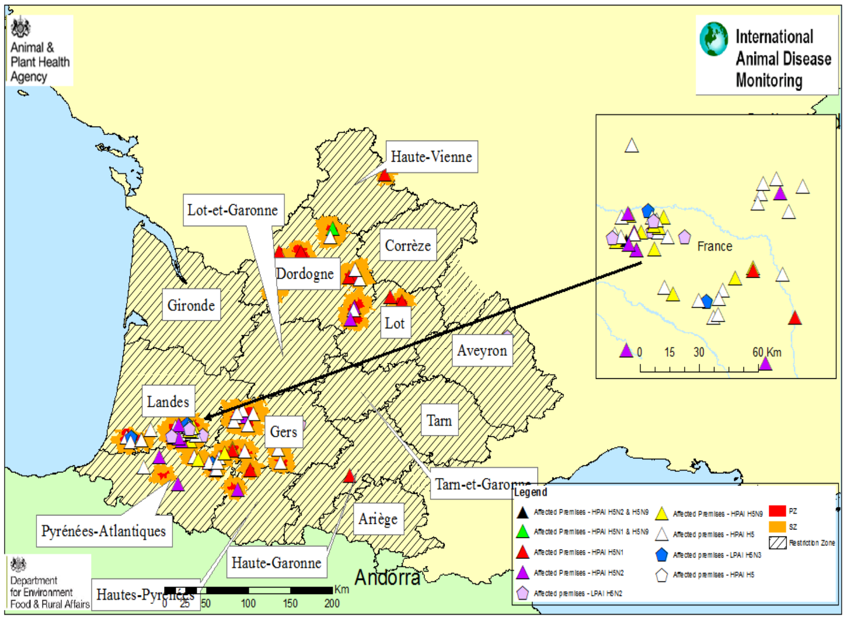
Migratory and non-migratory birds c50 species

Duck sector production and spread of H5 HPAI

Two major epizootics in SW France

2015-16 H5 HPAI 'classical' European

2016-17 H5N8 (clade 2.3.4.4)



Map Prepared by IDM

Date prepared 15/02/2016

H5N1, H5N2 & H5N9 HPAI and H5N2, H5N3 LPAI outbreaks in backyard and commercial poultry
France, November 2015 - February 2016

Absolute Scale 1:3,500,000

Practices of rearing ducks in the Foie Gras industry and conducive for spread of virus!

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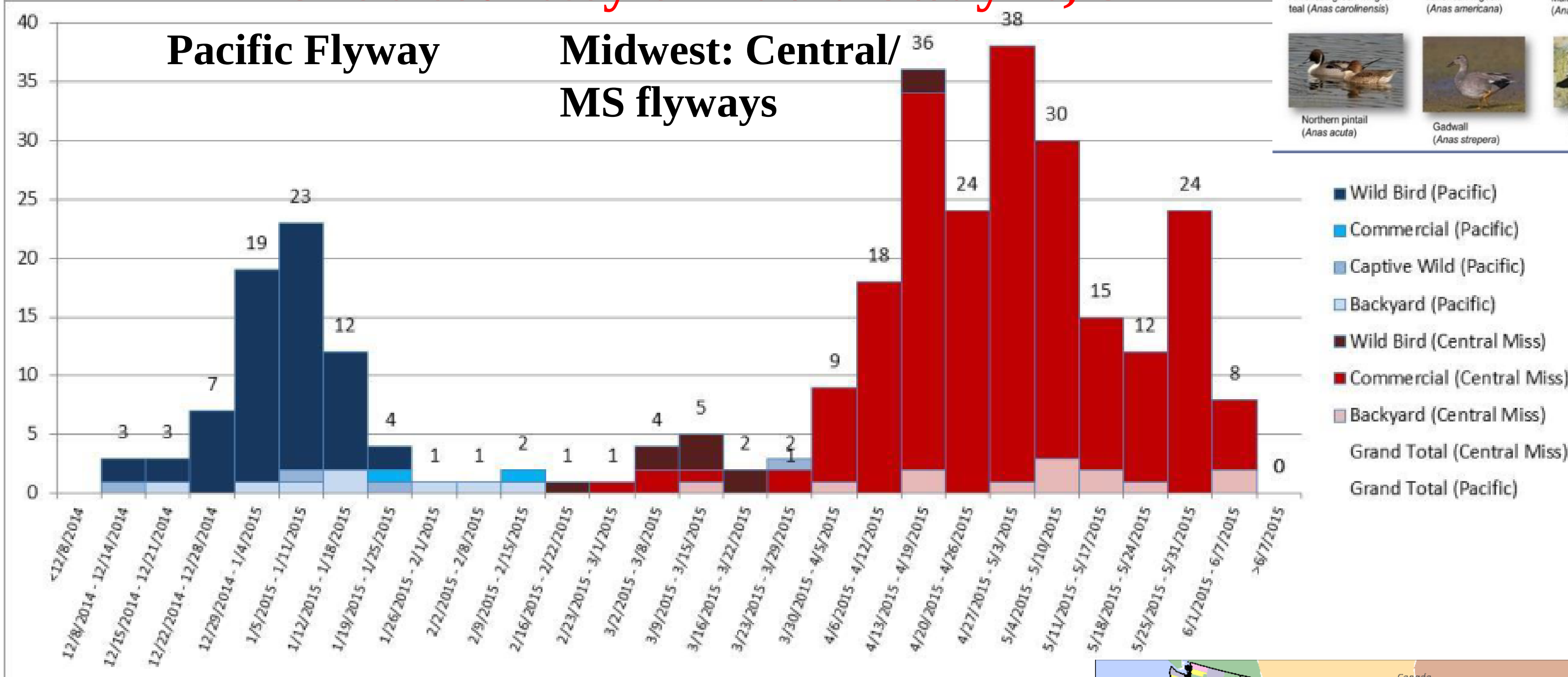
Emergence and spread of clade 2.3.4.4 viruses

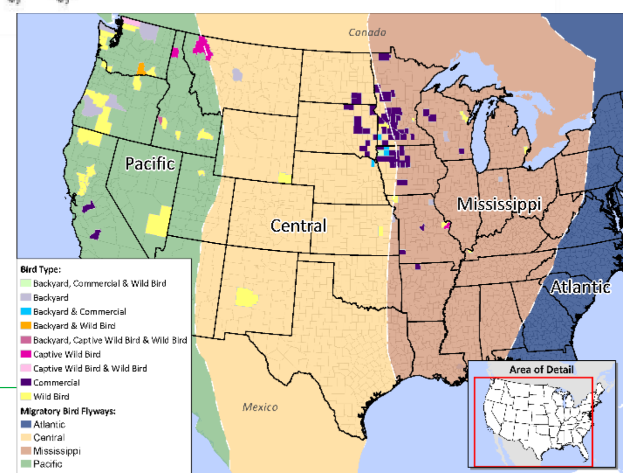
12/8/2014 to 6/17/2015 – H5 HPAIV in wild bird, backyard poultry and commercial poultry

Slide courtesy of David Swayne, SEPRL



311 detections (4 captive WB; 21 backyard; 211 commercial flocks, 75 WB)

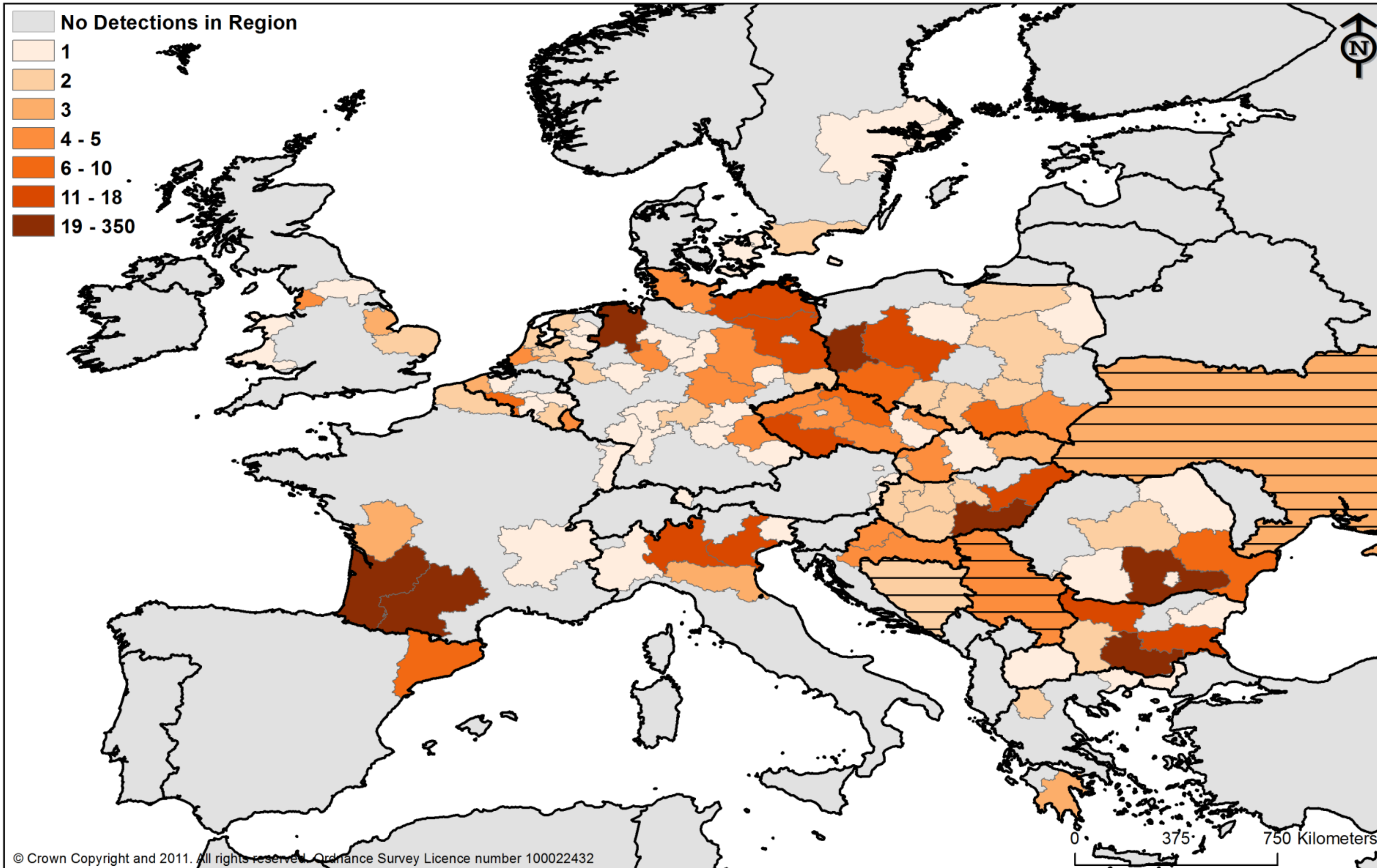
- **21 states affected; 15 states with wild bird cases**
- **50.4m poultry: chickens (~ 43m) > turkeys (~ 7.5m)**
- **Direct cost $1.6b; economy wide $3.3b**
- **Federal taxpayer - $850m (~$200m indemnity, ~$650m response cost)**



H5N8 HPAI epizootic in Europe/Central Asia/Africa 2016-17

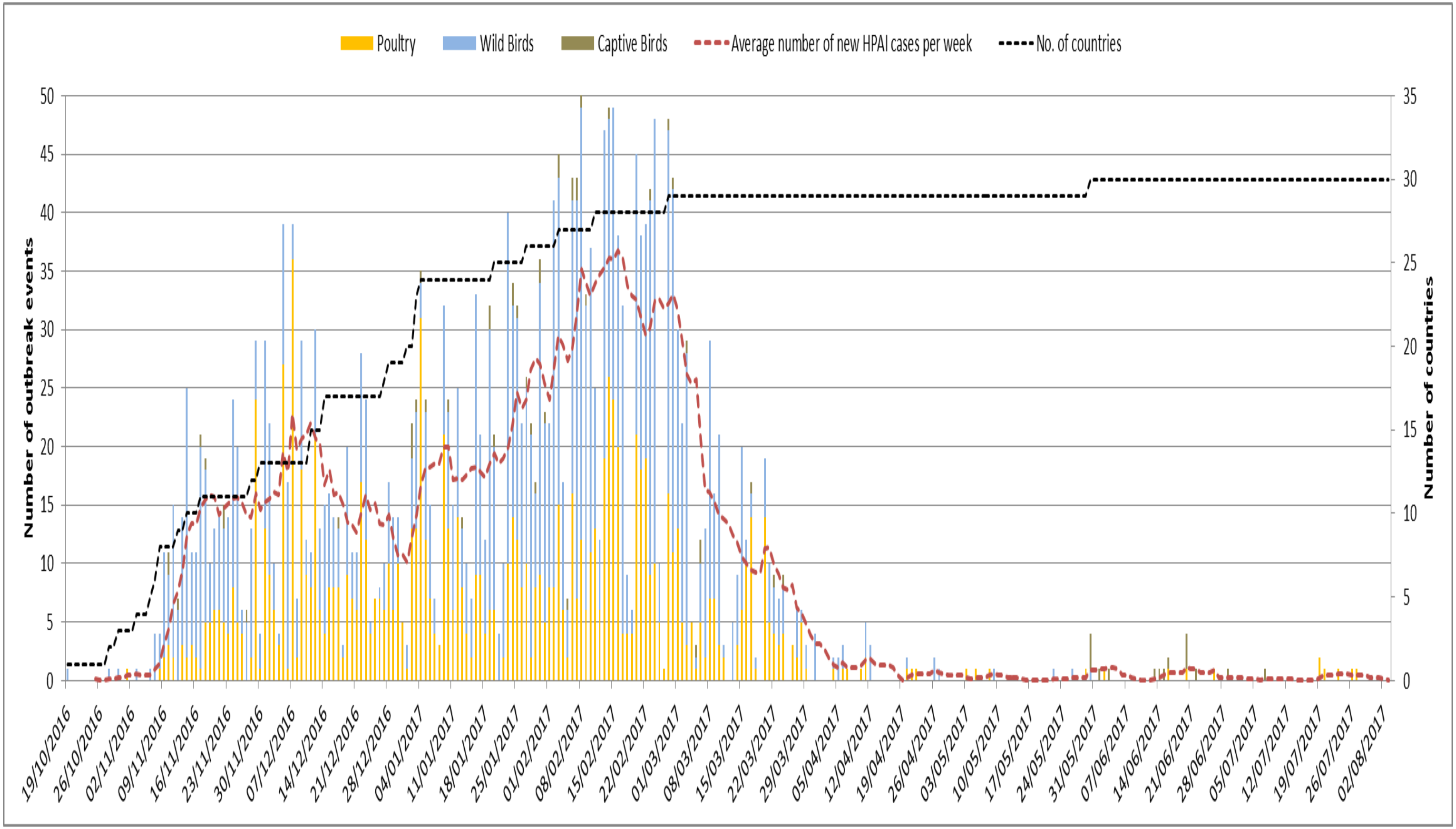
- **2,765 outbreaks/events of H5N8 Highly Pathogenic Avian Influenza have been reported in poultry (1,149), wild birds (1,562) and captive birds (54)** from 29 European countries
- **20 outbreaks/events of H5N5 Highly Pathogenic Avian Influenza have been reported in poultry (5), wild birds (14) and captive birds (1)** from 11 European countries
- Central Asia (Russian Federation, India, Iran, Kazakhstan), Middle East (Kuwait, Israel) and Africa (Egypt, Tunisia, Nigeria, Cameroon, Uganda, DR Congo, Zimbabwe, South Africa)
- Further reassortment in region
  - **H5N5 HPAI in poultry & wild birds** from 7 European countries.
  - H5N6 HPAI in poultry (1) in Greece



CREATOR: EU Reference Laboratory DATE: 12/09/2017	**Detections of H5 HPAI in Poultry and Captive Birds by NUTS2 region between October 2016 and August 2017** *Non-EU countries are marked by a hashed line and report at country level	Animal & Plant Health Agency

European epidemic curve HPAI in domestic and wild birds (source: ADNS data available 19th October 2016 – 3rd August 2017)



Key characteristics of H5N8 epizootics

- Epidemiological patterns
  - Seasonality – wild bird migratory pathways
  - Host populations
  - Secondary spread especially in domestic waterfowl
  - Captive birds and backyard flocks
- Clinical presentation
  - Severe all hosts; no human cases
- Heavy infection pressure
  - Wild birds and environment
- Virus persistence/introduction
  - Fastidious
  - Fomite pathways - multiple
- Virus evolution
  - Limited change in HA
  - Second generation reassortants

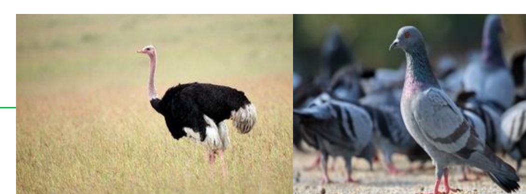
Host susceptibility/infection outcome

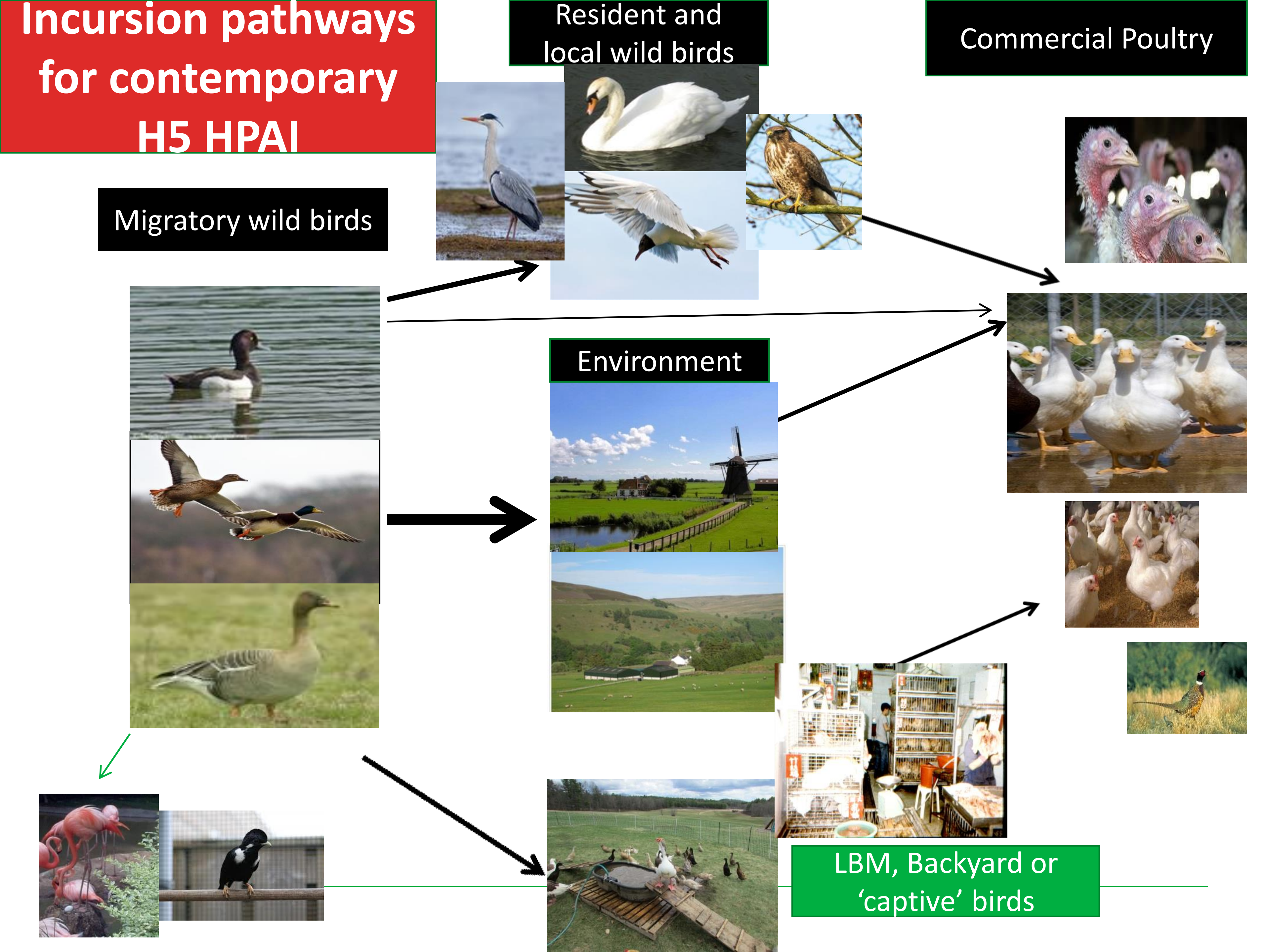
- Galliformes -severe
  - Chickens and turkeys
  - Guinea Fowl

- Galliformes – intermediate
  - Phasianidae

- Domestic anseriformes
  - Severe/moderate
  - Experimental infection of ducks;
    birds recover, seroconvert (APHA unpub)
  - Outdoor birds protective effect of prior
    exposure to heterologous virus

- Others – susceptible
  - Ratites, pigeons




Incursion pathways for contemporary H5 HPAI
Resident and local wild birds
Commercial Poultry
Migratory wild birds
Environment
LBM, Backyard or 'captive' birds

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Spread and maintenance in ducks

Can be more limited in other production systems

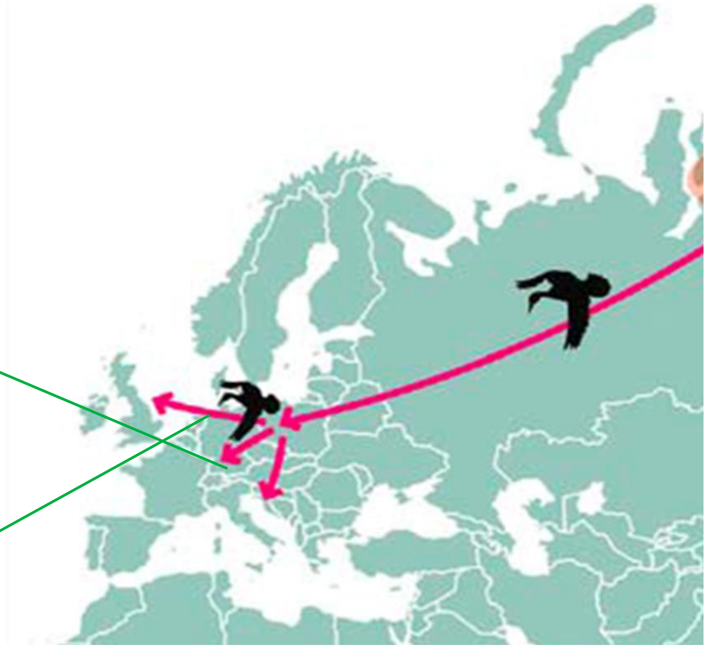
Anseriforme reservoirs?

- H5N8 disease spectrum dependent on age/breed
- Minimum infectious dose less than 2 logs
  - Age dependent
- Shed ~5 logs virus/gram of faeces

- Attentuation of virus for anseriformes as it adapts??

- **Implications for surveillance in both wild and domestic birds**

Phylogeny of the HA gene of H5 HPAI
Europe/Asia/Africa 2016-17



Common ancestral virus to Russian Federation/wild bird/May 2016
TMRCA January 2016

Virus continually evolving/changing – new traits and fitness

Reassortment with LPAI in wild birds: can be all gene segments

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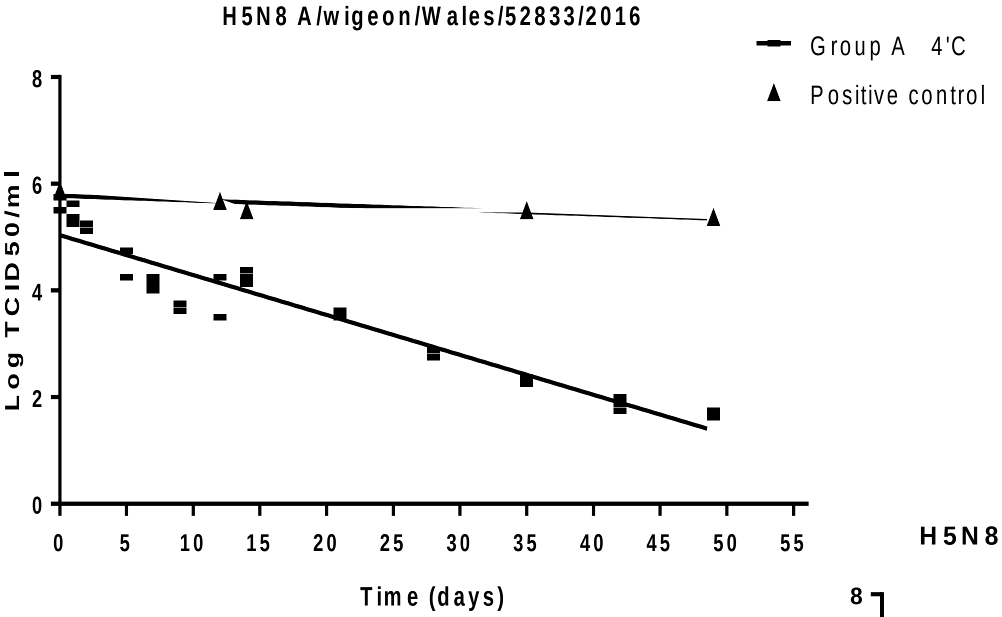
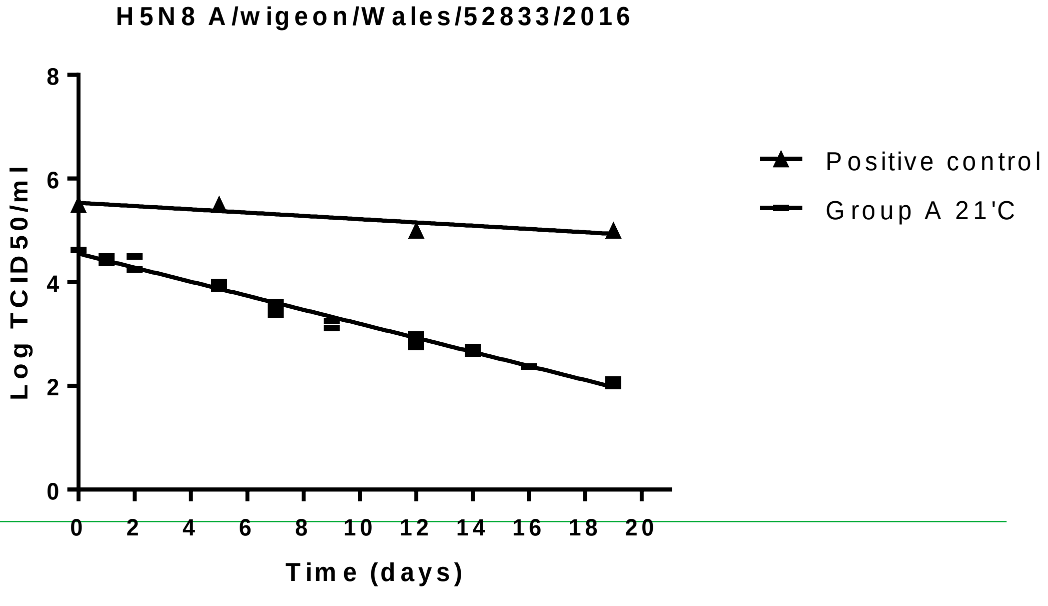
Environmental survival

Key risk factor leading to fomite introduction and maintenance in wild birds

AIV survival and infectivity – H5N8
APHA unpublished prelim data



c48-60 days to reduce below infectious levels for poultry



SURVIVAL KINTETICS OF HPAI IN DIFFERENT SUBSTRATES

D_T value, in days, for log_{10} reduction in virus infectivity over time measured at 4°C and 20°C, standard error mean (SEM)

Virus	H7N1 HPAI				H5N1 HPAI	
Tissue	Muscle		Feather		Muscle	Feather
Host	Chicken	Turkey	Chicken	Turkey	Chicken	Chicken
4'C	9.8 (0.371)	8.7 (0.543)	5.1 (0.538)	8.8 (0.834)	13.1(0.477)	not tested
20'C	5.9 (0.329)	2.8 (0.414)	2.3 (0.769)	2.0 (0.517)	1.6 (0.694)	2.9 (0.607)

Sample matrix DT value in days (unless specified) for log10 reduction in virus infectivity (* half-life in seconds) over time measured at 4°C and 20°C									
Virus	Temp °C	Faeces	Litter	pH5*	pH7.2	pH9	Distilled water	Salted water	UVB Exposed
H7N1	20	0.83	<5min	34.76sec*	18.46	8	21.28	14.42	2.63hrs
	4	3.33	<5min	24.99sec	20.61	12.36	32.66	19.94	not tested
H5N1	20	4.41	<10min	28.74sec*	15.17	3.61	52	52	2.78hrs
	4	12.05	<10min	33.62sec	37.89	40.3	72.81	74.78	not tested
	*half-life in seconds								

Vaccination as a tool for prevention/control Vaccine development for veterinary use

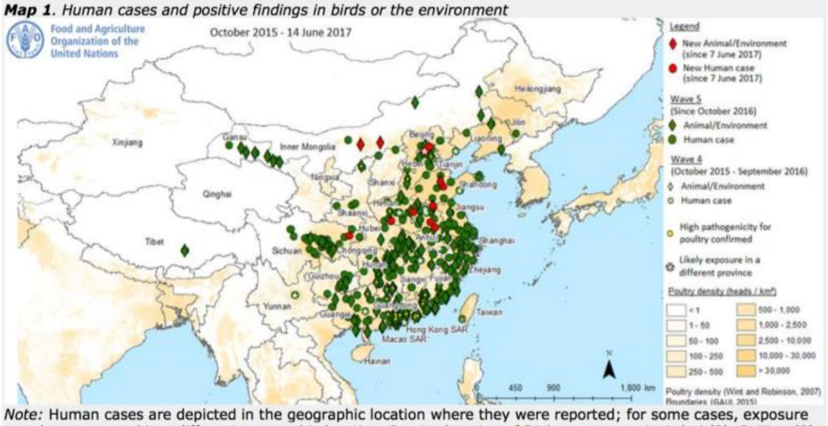
- Although many current vaccines have used few have proven utility against H5 HPAI leading to effective control/eradication
- Lack ease of delivery and efficacy versus a diverse family of viruses
- Innovations in vaccine design have largely not been invested in for AI sufficient for global application
- Target hosts: anseriformes present greatest challenge
- Differentiating Infected from Vaccinated Animals
- Produced in accord with international standards (OIE)

- Other approaches genetic resistance in poultry lines??

Other threat viruses: H7N9?

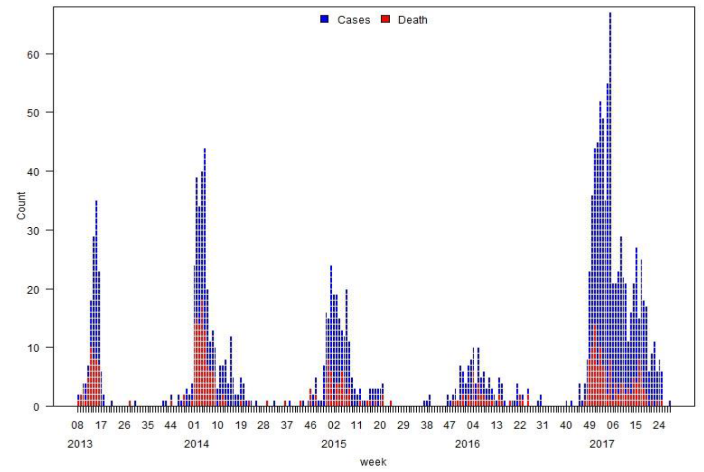
- H7N9: exists in LP and HP form in China but worrying changes in disease pattern – vaccination being applied
  - Currently lacks capability to infect migratory waterfowl but spread via humans a real risk
  - Major zoonotic risk
  - Global travel in people (returning travellers from Far East/Africa stay off poultry farms!)??
  - How long before these viruses are detected beyond China?

***Map 1**. Human cases and positive findings in birds or the environment*



Note: Human cases are depicted in the geographic location where they were reported; for some cases, exposure may have occurred in a different geographic location. Precise location of 24 human cases in Anhui (2), Beijing (2), Guangdong (1), Guangxi (1), Hebei (3), Hunan (1), Hubei (2), Jiangsu (1), Jiangxi (6), Sichuan (2) and Zhejiang (3) Provinces are currently not known, these cases are therefore not shown on the map.

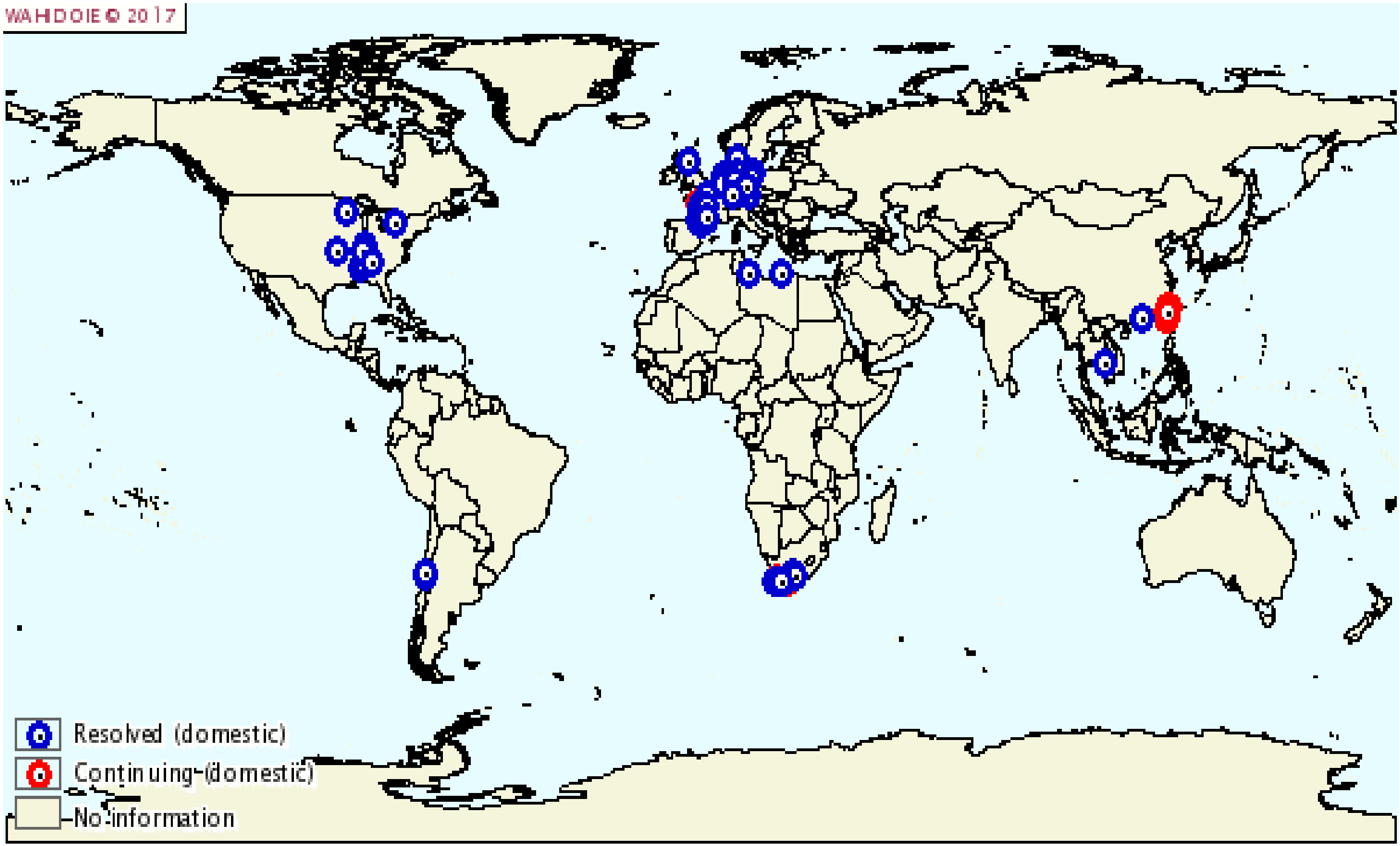
Number of confirmed human H7N9 cases and deaths, as reported to WHO by week, as of 2017-7-24



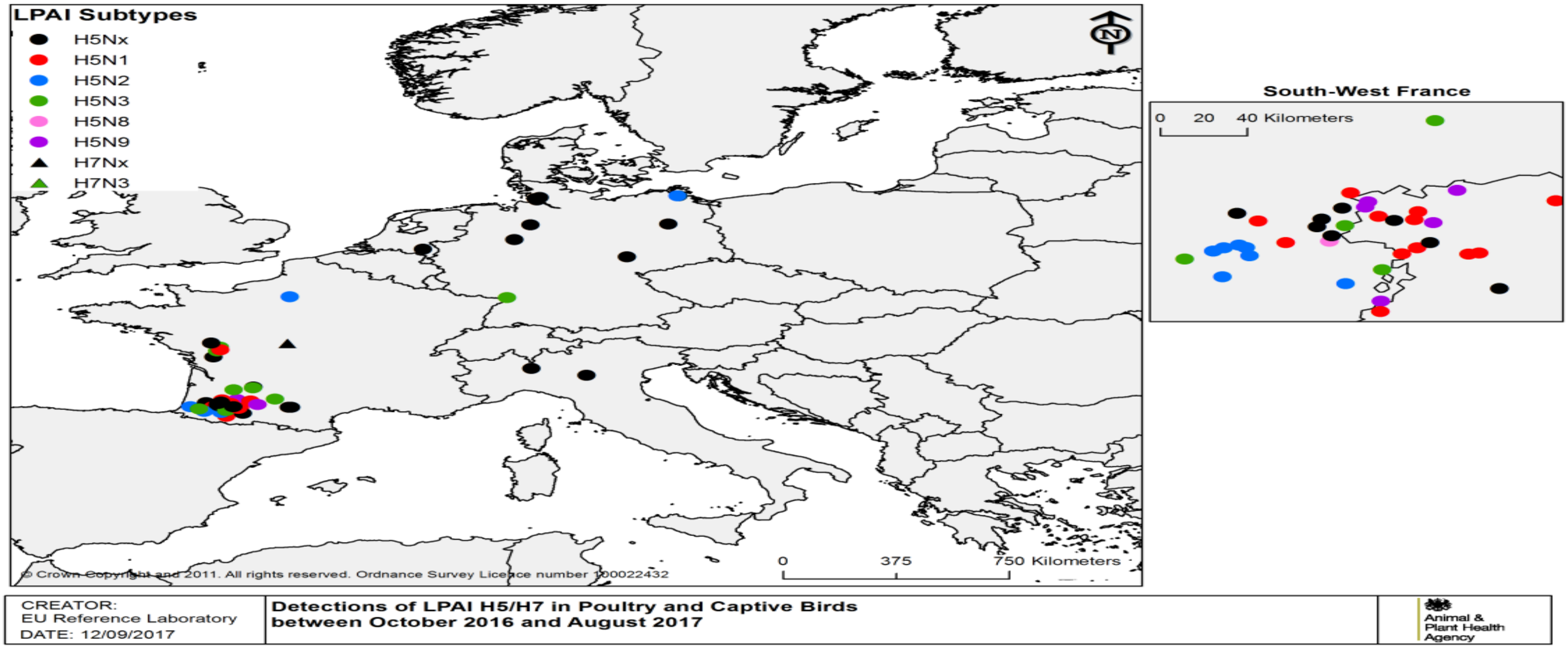
Other HPAI 2016-17

- Mexico H7N3
- Italy H7N7
- USA
  - H7N8 (2016)
  - H7N9 (2017)

H5/H7 LPAI 2016-2017



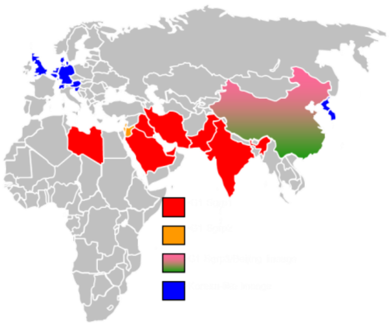
Active surveillance for LPAI – consequences!

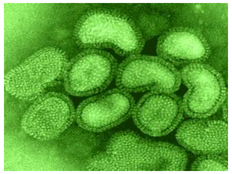


Is surveillance for LPAI, its consequences via interventions and impacts ie trade still fit for purpose. Is risk mitigated for HPAI??

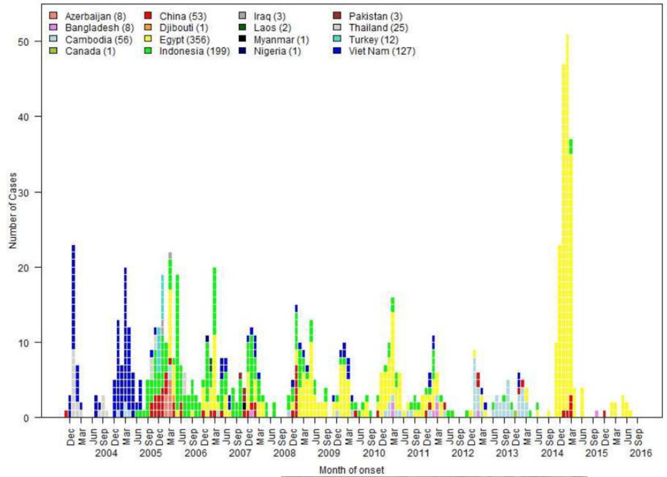
H9N2 is ubiquitous throughout the world

- Often the most frequently detected influenza subtype in chickens
  - Wide spectra of disease signs
  - Economic impact on production
  - New epizootics in Europe, Africa, Asia
  - Subject to control through vaccination in many countries
- Cocirculation with H5 HPAI
  - Attenuation of clinical presentation

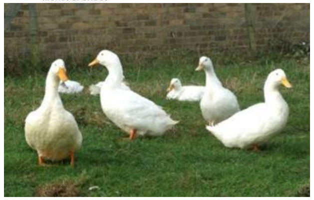




Zoonotic avian influenza



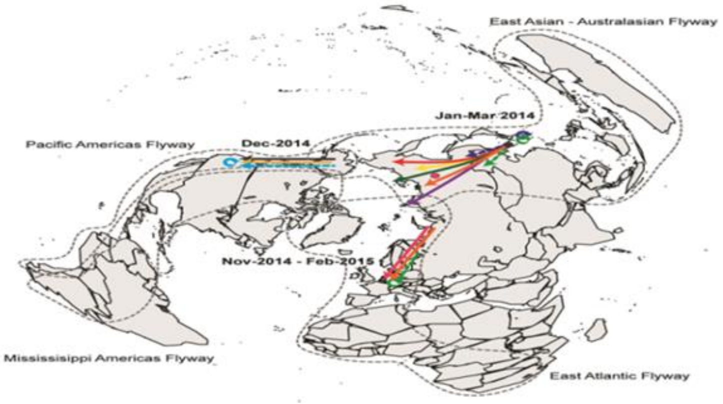
- Aquatic bird reservoir to poultry
  - – Maintenance host: domestic ducks?
- Spill over to humans via poultry interface
  - ie live bird markets



- These viruses can cause clinical outcomes/death
  - Replication in lower respiratory tract only in severe cases
- Viruses lack transmissibility in mammalian species including humans
  - Due to lack of replication in upper airway of these hosts
- Current global H5N8 HPAI epizootic (3 continents)
  - Risk to humans low (no recorded cases to date)
  - Still essentially avian virus without humanising mutations

Current global threat viruses :H5 HPAI

- H5 HPAI circulate widely and some strains maintain in wild aquatic birds
- These H5 viruses are continually evolving
  - Reassortment H5N5
- 2017 H5N8 spreads south of equator for first time
  - DRC, Uganda, Zimbabwe, South Africa
  - Prospects for eradication poor
- Autumn/winter 2017/8- further global waves with H5N8??
- c2015- present: H5N6 East Asian flyway
  - Established in wild birds mediating spread



COULD THIS VIRUS WHICH CARRIES GREATER ZOONOTIC THREAT BE THE NEXT STRAIN THAT SPREADS TRANS-CONTINENTALLY???

Future perspectives

- Understanding pathways for introduction
- Virus variability; correlates for infection risk
- Seasonality: predict future incursions
  - Rapid data sharing in real time
- Maintenance reservoirs
  - Long term dynamic/surveillance design
- Globally at risk of further outbreaks?
- Societal behaviours - education
- Spread to Central and South America?
- Trade impacts and risks
- Solutions at global scale for better interventions
  - Better veterinary vaccines

Key conclusions

- H5 HPAI has become truly panzootic affecting poultry and wild birds
  - Significant evolutionary trends and epidemiology
  - New threats to poultry production and wildlife
  - Dispersal for primary introductions through migratory waterfowl
  - Endemnicity in some areas; reincursions in others- prospects for immediate control poor!
- **We can expect further outbreaks with H5 HPAI in the next months/years**
- In developed countries strong surveillance detects many LPAI incursions and HPAI early
  - Future requirements: OIE engagement
- Continued and future threat to global food security/human health

10th International Symposium on Avian Influenza

Animal & Plant Health Agency

Avian Influenza in Poultry and Wild Birds

15 - 18 April 2018, The Grand Hotel, Brighton, UK

Poultry sessions will include:

- Global reports on AI
- Surveillance for AI
- LPAI outbreaks
- Diagnostics
- Vaccines & vaccination
- Pathobiology
- Field epidemiology
- Field control
- Education & risk communication
- Zoonoses

Wild bird sessions will include:

- Surveillance
- Ecology
- Pathobiology
- H5N1 HPAI

Important dates

Registration opens: 11 September 2017

Abstract deadline: 13 November 2017

Co-chairs: Ian Brown (UK) ; David Swayne (USA) ; Thijs Kuiken (NL)

For further information visit: www.flu-lab-net.eu

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- WHO H5 evolution working group

Llywodraeth Cymru
Welsh Government

The Scottish Government

- APHA-Weybridge laboratory work
- Flu team (c32) lead by Sharon Brookes
- Epidemiology- Pablo Alarcon, Adam Brouwer, Daisy Duncan

defra
Department for Environment Food and Rural Affairs

Animal & Plant Health Agency

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Thank you for your attention

http://flu-lab-net.eu/

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