Animal & Plant Health Agency

Vaccination against HPAI

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Technical Item II: 5th October 2022

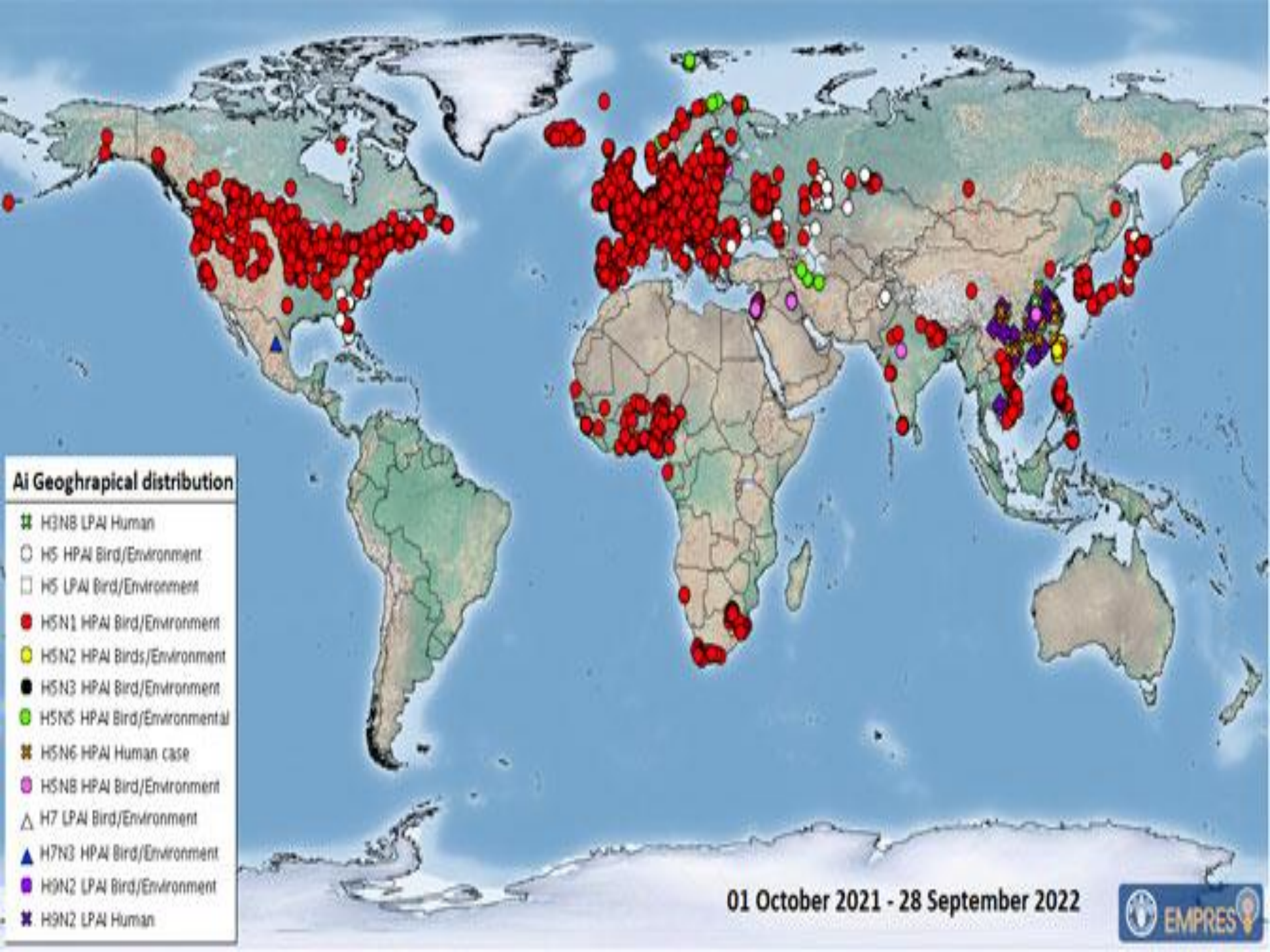
Technical item II objectives

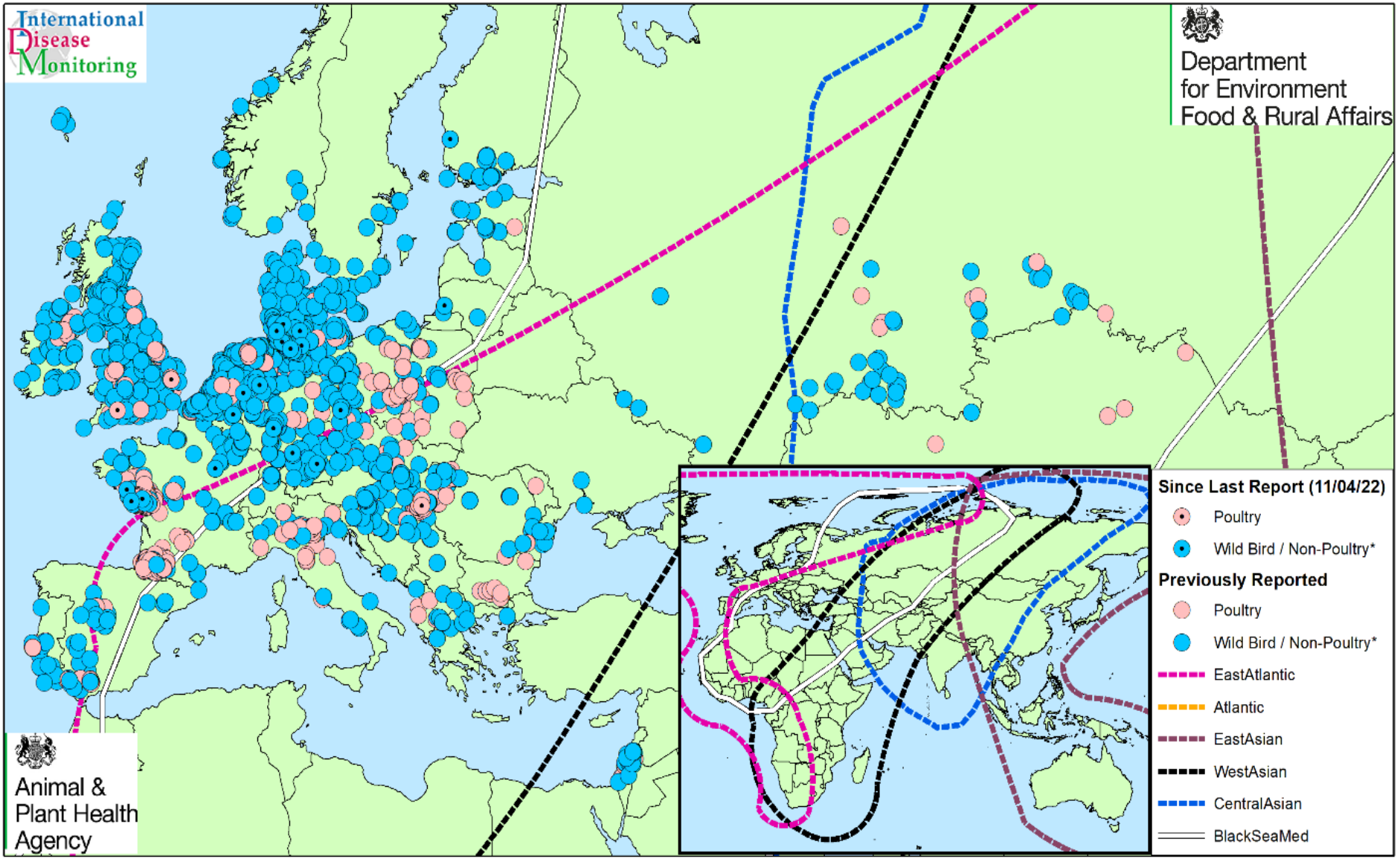
1. Set a framework of questions to make science – based decisions regarding vaccination policy against infection with HPAI viruses is Europe

2. To organise the mechanism which would support WOAH and Members in addressing these questions

To vaccinate or not??

- What has changed?
- Are current control approaches sustainable?
- Future risk and possible need for vaccination
  - Benefits/cons
  - Dispelling myths
- First principles of vaccination; focus AI
- Barriers
- Practical considerations
- Activity in the region to prepare/develop contingency


Ai Geoghrapical distribution
H3N8 LPAI Human
H5 HPAI Bird/Environment
H5 LPAI Bird/Environment
H5N1 HPAI Bird/Environment
H5N2 HPAI Birds/Environment
H5N3 HPAI Bird/Environment
H5N5 HPAI Bird/Environmental
H5N6 HPAI Human case
H5N8 HPAI Bird/Environment
H7 LPAI Bird/Environment
H7N3 HPAI Bird/Environment
H9N2 LPAI Bird/Environment
H9N2 LPAI Human
01 October 2021 - 28 September 2022
EMPRES



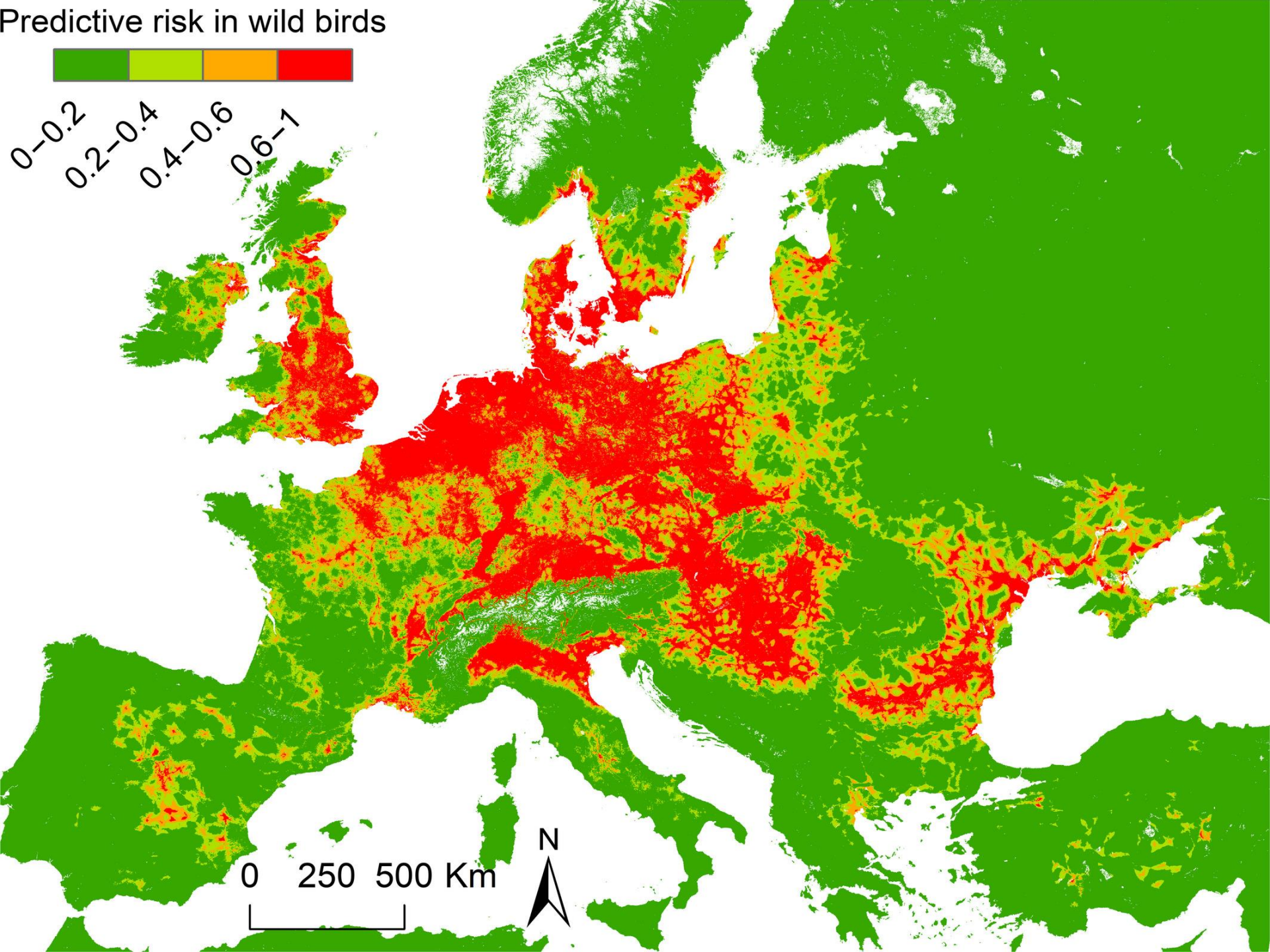
Date: 19/04/2022

Map prepared by IDM

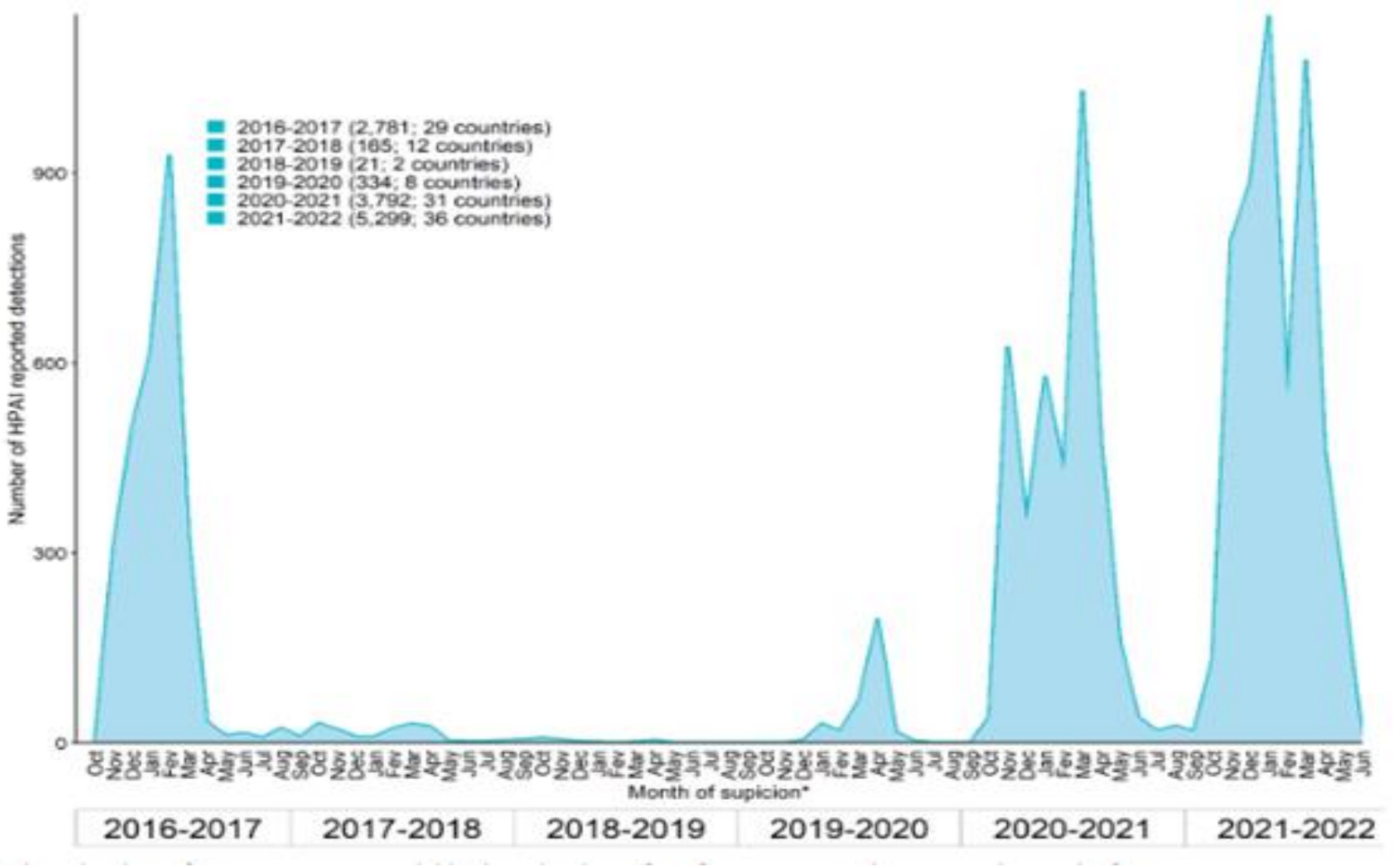
Highly Pathogenic Avian Influenza in Poultry and Non-Poultry*
September 2021 - April 2022
Overlay: Migratory Bird Flyways

OIE Data Only

*OIE Defined


Predictive risk in wild birds
0–0.2
0.2–0.4
0.4–0.6
0.6–1
0 250 500 Km
N

European HPAI epidemic waves 2016-2022



EFSA Avian Influenza overview march –June 2022; https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7415

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Epidemiology of H5 HPAI epizootics with ‘clade 2.3.4.4b’ viruses

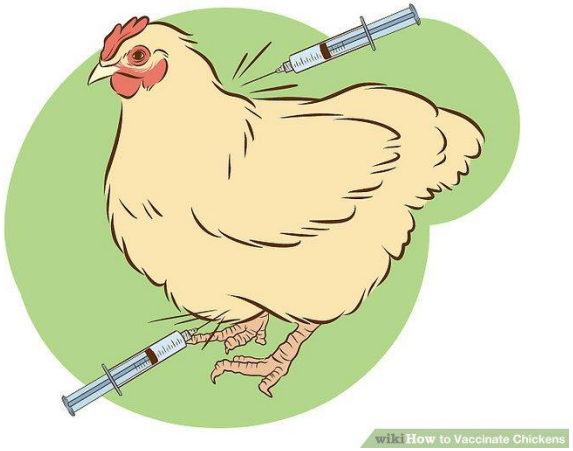
- Primary incursions wild bird mediated
  - Large epizootics
- Secondary spread between poultry premises

- Lethal outcomes high mortality
  - Some attenuation in disease in adult domestic ducks/geese
- Large virus diversity both at serotype and genetic level
  - *H5N1 dominant late 2021; New incursions from east*

- Range of measures to control in WOAH Europe region
  - Stamping out, control zones, housing orders, vaccination prohibited in many countries

Desired results of vaccination against AI

- freedom from disease
- no effect on production or other serious expense
- no trade embargoes
- Eradication if enzootic infection



Criteria for vaccine suitability

Swayne and Sims (2020) proposed 8 criteria

- Inexpensive
- usable in multiple avian species
- provide protection after a single dose
- can be applied by low-cost mass application methods
- allow easy identification of infected birds within the vaccinated population
- produce a protective humoral response in the presence of maternal antibodies
- be applied at one day of age in hatchery or *in ovo*;
- antigenically close to field virus.

No current vaccine or vaccine technology meets all eight criteria so the user must select the licensed vaccine that best meets their needs.

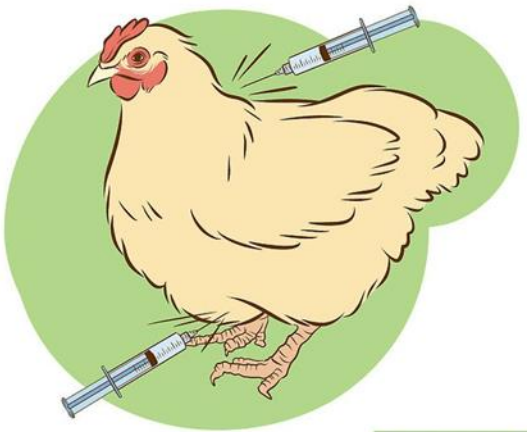
Swayne D.E. & Sims L. (2020). Avian influenza. In: Veterinary Vaccines: Principles and Applications, Metwally S, El Idrissi M., Viljoen G., eds. Wiley, Chichester, United Kingdom, 229–251

Avian influenza vaccination

Current vaccines can result in:

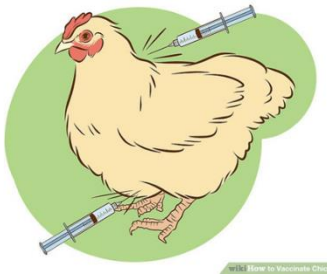
- Protection against clinical signs
- Decrease bird susceptibility to infection
- Reduction in virus excretion
- Reduction in transmission (birds and humans)

BUT……



AI vaccination - caution

- AI virus may infect and replicate in vaccinated birds without clinical signs
- As a corollary HPAI as defined by OIE may still be confirmed in such birds
- Coverage rates in key at risk populations need to be >60% (ideally 80%)
- Infection with HPAI virus without clinical signs may lead to spread and an endemic situation



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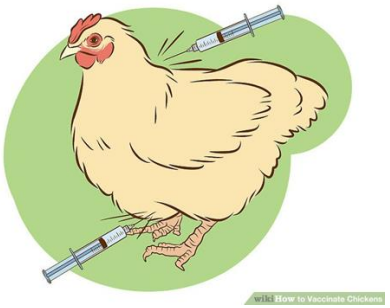
Vaccination will only work when applied in combination with other measures

Vaccination is not a substitute for weak farm biosecurity

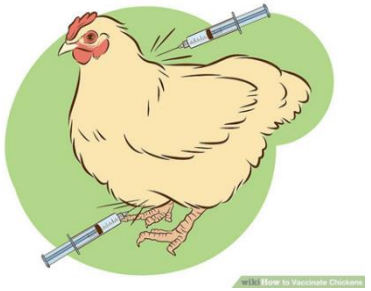
Challenges associated with use of vaccination



- Clearly defined objectives/Exit strategy
- Supplementary tool for control of outbreaks
  - Biosecurity
  - Stamping out of infected flocks
  - Buffer zones
- Proactive surveillance necessary in vaccinated populations
  - DIVA
  - Serological monitoring
  - Use of sentinels
- Antigenic variability in field strains
- Target populations?
- Ease of delivery
- System for control of statutory disease needs to be subject to supervision by competent veterinary authority
- Trade impacts
- Management of public health implications/assurance
- Experiences of last scale vaccination for control of HPAI limited

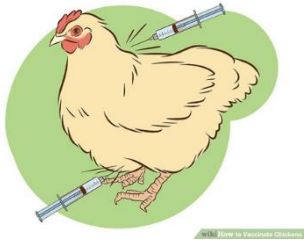
Veterinary inactivated vaccines for AI (advantages and disadvantages)

- Inactivated whole AI virus – with adjuvant; produced versus field strain (ie rg viruses in China versus evolving H5)
  - Relatively cheap, multiple hosts, easy to standardise, can be adapted to field virus, licensure
  - Generally 2 doses for protection; NO mass application, lack DIVA, poor in overcoming maternal antibody, or hatchery application



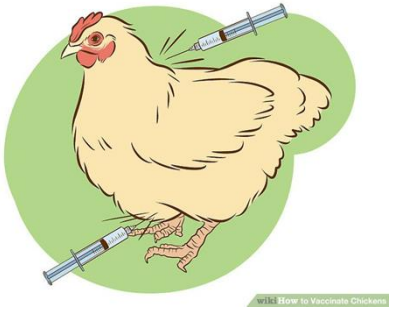
Veterinary vectored vaccines for AI (advantages and disadvantages)

- Live vector – avian virus carrying an AI gene insert ie H5 HA
  - Number of delivery vectors (Avian Paramyxovirus type 1, DVE, Fowlpox, Herpesvirus Turkey
  - Relatively cheap, easy to standardise, can be adapted to field virus, mass application including at hatchery, DIVA applicable
  - Host specificity (define target population), licensure for field, natural immunity in population to vector



Veterinary sub-unit or nucleic acid vaccines for AI (advantages and disadvantages)

- In vitro produced HA
  - Adaptable to changing virus, DIVA, multiple hosts
  - Poor knowledge for field application, expensive to produce, delivery?
- Nucleic acid
  - Adaptable to changing virus, DIVA, multiple hosts
  - Poor knowledge for field application, expensive to produce, delivery?, 2 doses minimum

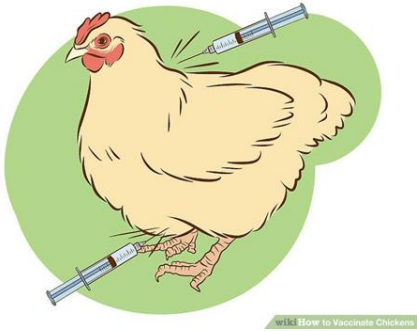


Vaccination as a tool for prevention/control

- 420 billion doses (since 2002)
  - >99% in 4 countries; China (91%), Egypt (4.65%), Indonesia (2.3%) & Vietnam (1.43%)
  - Ten countries or regions 0.7% of total (high risk targeting or management tool during eradication)
  - Newly vaccinating Iran, Kazakhstan and Bangladesh
- Inactivated (90%) and live recombinant vectored vaccines (<10%)
- Challenges to induce sufficient flock immunity in susceptible key species
- Variable outcomes

China: best experience of H5 HPAI vaccination?

- Vaccinating since approximately 2000
- Reduced disease/infection burden
- Applied to all commercial poultry but live bird markets?
- Formal system for review of vaccine strain v circulating field strains
- H5 HPAI goose/Guangdong lineage viruses have evolved continuously
- 14 updates to vaccine to match against the changing virus
- Complicated by co-circulation of multiple sub families
  - Cross protection not assured
  - More than one strain included in vaccine
- Emergence of ‘fit’ virus variants
  - Public health risk
  - Clade 2.3.4.4b H5N6 increased human cases 2021/22

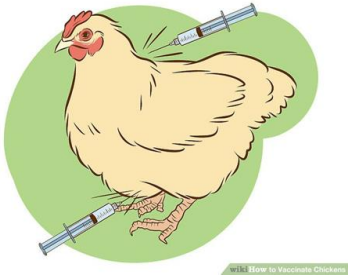


WOAH Animal Health Code: 2022 adopted updated AI chapter

''*Vaccination* will not affect the high pathogenicity avian influenza status of a free country or *zone* if *surveillance* supports the absence of *infection*, in accordance with Article 10.4.28.,... ''

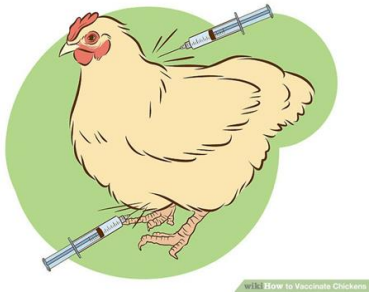
''*Vaccination* can be used as an effective complementary control tool when a *stamping-out policy* alone is not sufficient. Whether to vaccinate or not should be decided by the *Veterinary Authority* on the basis of the avian influenza situation as well as the ability of the *Veterinary Services* to implement the *vaccination* strategy,...''

Requirements to do surveillance in vaccinated populations, zones or compartments to provide evidence of absence of infection



Surveillance in vaccinated birds- WOAH guidance

- In all vaccinated *flocks* tests should be performed to ensure the absence of virus circulation. The tests should be repeated at a frequency that is proportionate to the *risk* in the country, *zone* or *compartment*. The use of sentinel *poultry* may provide further confidence in the absence of virus circulation.
- Member Countries seeking the demonstration of freedom from high pathogenicity avian influenza in vaccinated population should refer to the chapter on avian influenza (*infection* with avian influenza viruses) in the *Terrestrial Manual*.
- Evidence to show the effectiveness of the *vaccination* programme should also be provided.



Framework considerations for harmonised use of vaccination against HPAI in the Europe region

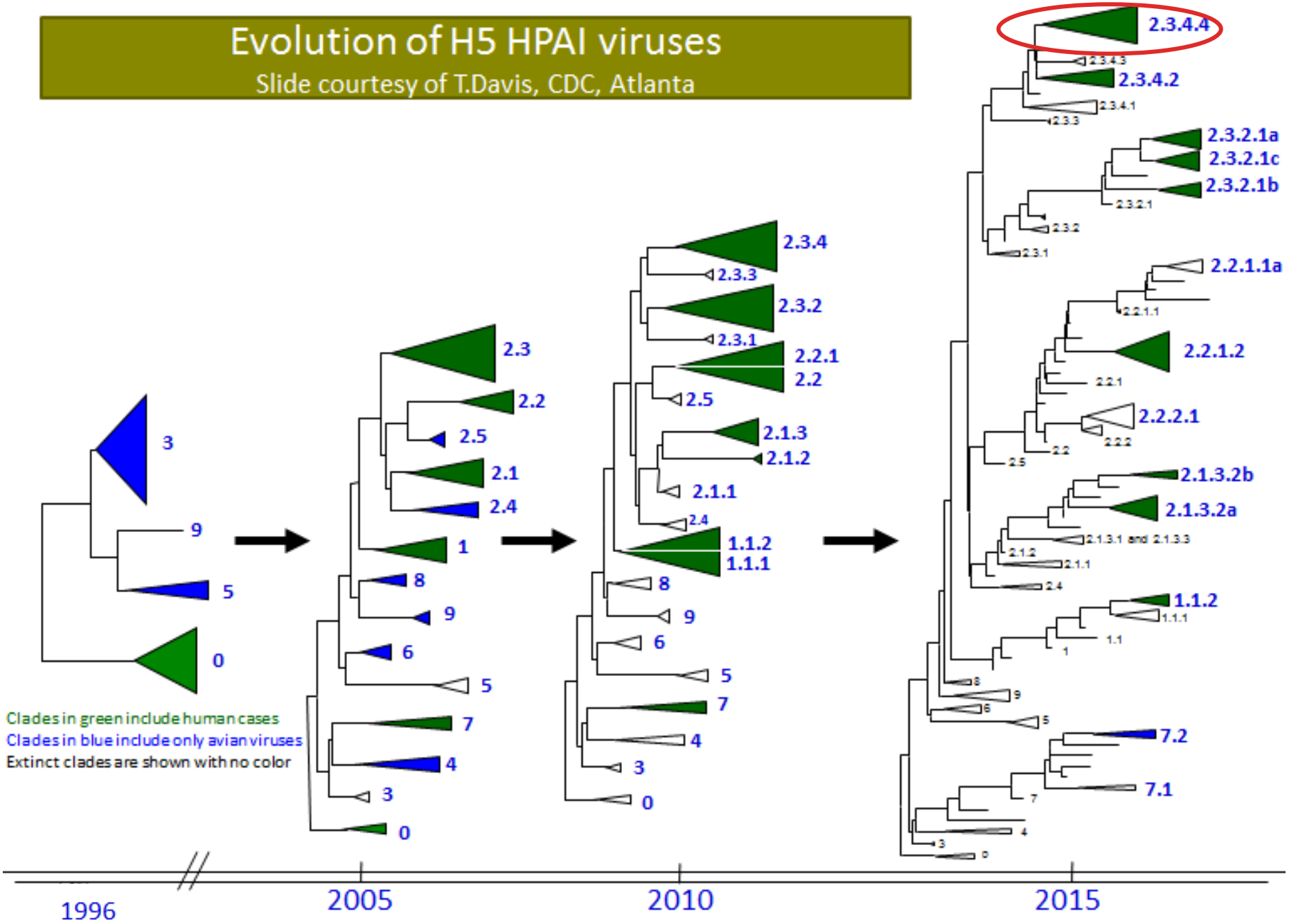
- Continual risk with epizootic waves
- Programme scope and integration in overarching disease control and threat mitigation
  - Targeted/non targeted; preventative or emergency; species; geography inc DPPA
- Programme duration
- Vaccine type
- Surveillance requirements including DIVA approach
- Safeguards for movements of birds and products
- Trade impacts (as applicable)

Framework considerations for harmonised use of vaccination against HPAI in the Europe region

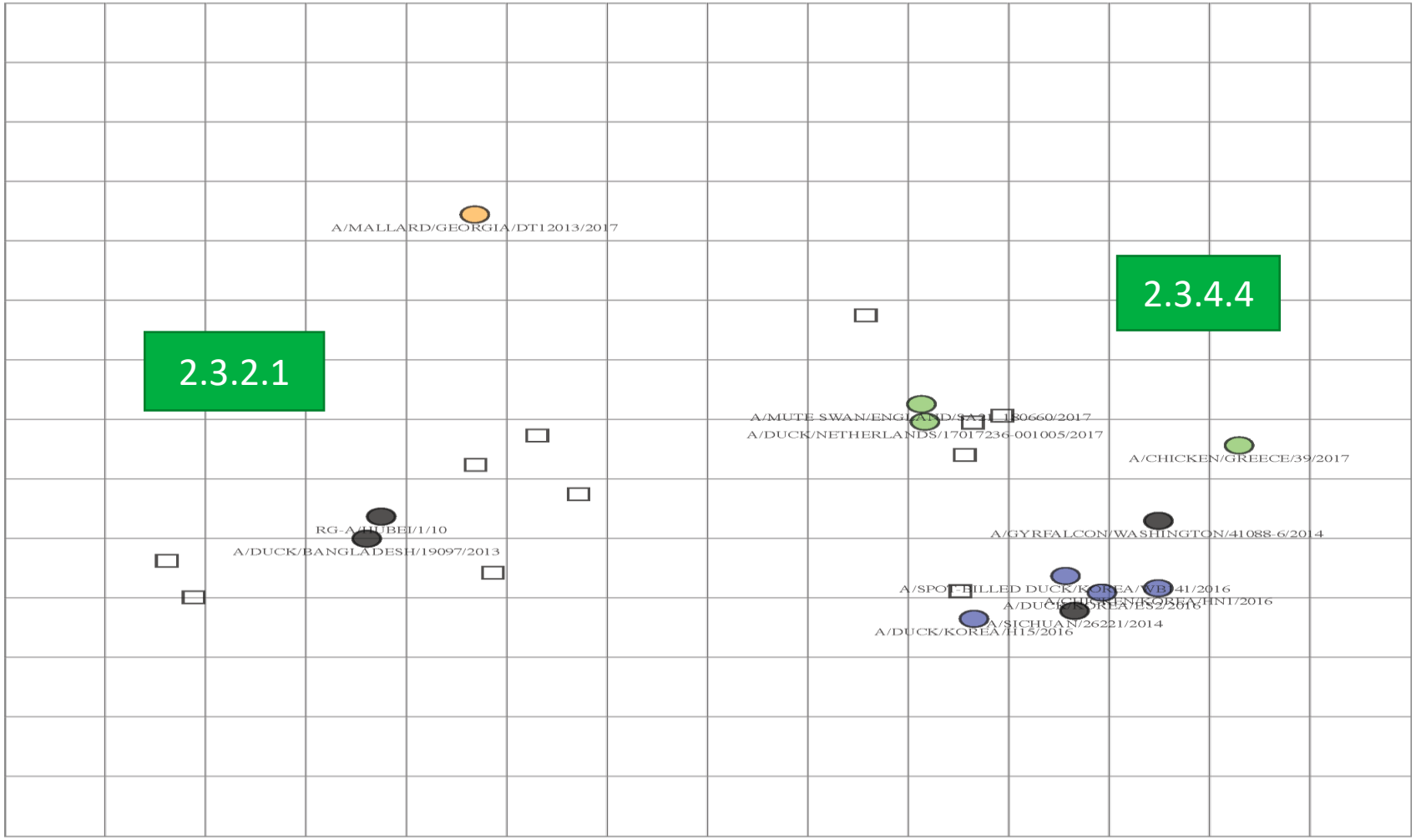
- System for continuous review of programme implementation and effectiveness including cost benefit analysis
- System for continuous assessment of vaccine effectiveness and need for updates
- Programme financing and legal framework (from vaccine market authorization to proper training in vaccination)
- Management of possible impacts for public health and social perception.
- Vaccination should be part of contingency planning even if not adopted

Evolution of H5 HPAI viruses

Slide courtesy of T.Davis, CDC, Atlanta



Mapping antigenic changes in H5 HPAI viruses



Antigenic map of H5 LPAI and HPAI viruses from HI assay data generated by APHA-UK
Viruses are shown as colored circles, polyclonal ferret sera as grey squares
Reference viruses: grey
LPAI H5N2: orange
HPAI 2.3.4.4 H5N6 viruses in green (Europe) and blue (Republic of Korea)

One grid square represents 1 antigenic unit or a 2-fold difference in HI assay titer.

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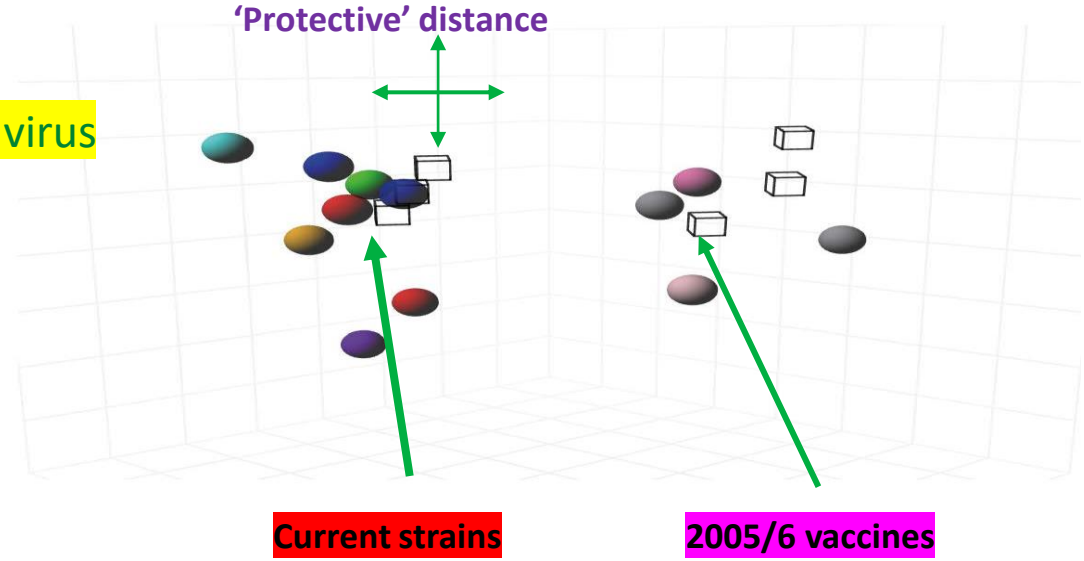
Vaccines must be antigenically matched to circulating strains for efficacy

- Antigenically matched vaccines to field strains
  - can prevent disease, reduce shedding of virus, but may not completely prevent transmission to naïve birds

- Poorly matched vaccines to field strains
  - Reduce disease signs, may partially reduce virus shedding but will not stop transmission between birds/flocks
  - Without active monitoring of vaccinated flocks may at worst enable silent spread

Map of vaccine antibody match to field virus



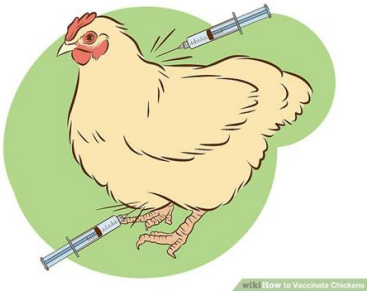
Lewis et al 2021 Vaccine

Vaccine strain matching

- International scanning for new threats/changes in virus: ref labs
- Viruses from vaccinated birds rapidly characterised
  - Including any change in zoonotic risk profile
- Information fed into ongoing assessment of vaccine effectiveness
- OFFLU new system for defining match amongst vaccine strains to field virus
- Discontinued us of non protective vaccines
- New vaccine designs offer promise for broader protective effect

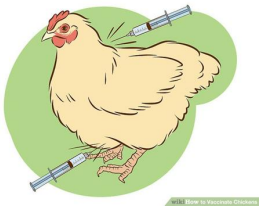
Potential application in a Europe setting?

- Challenges
  - Vaccine bank provision?
  - Ensure appropriate high quality vaccines
  - Efficacy versus changing virus
  - DIVA can be applied??
  - Licensure issues
  - Cost benefit?
- Consideration of wider impacts
  - Trade
  - Surveillance intensity/cost to prove freedom
  - Vaccine escape
  - Public health perception/threat



What is happening in EU/Europe

- Increased pressure to consider vaccination
- Amendments to EU AHL proposed to allow preventative and emergency vaccination
- EU Delegated Act 2020/7144 governance of veterinary medicinal products for prevention and control of certain listed diseases, should be published in 2022; European regulatory framework that allows the use of vaccine solutions for prevention or control purposes.
- Consistency with WOAH Animal Health Code
- Assessment of the feasibility and cost-benefit aspects in MS
- EMA to review evaluation of vaccines for licensure



- OFFLU applying a concept for global poultry vaccine matching

Key conclusions

- Continual and increased risk: panzootic with continual virus evolution
- Although many vaccines are used few have proven utility to prevent H5 HPAI infection at population level
- Lack ease of delivery and efficacy versus a diverse family of viruses
  - Prime/boost (vector followed by inactivated)
- Innovations in vaccine design have largely not been invested in for AI for different field applications
  - Universal vaccines?
- Target hosts: anseriformes present greatest challenge
- Differentiating Infected from Vaccinated Animals
  - Relevant for some areas/regions likely important for trade
- Produced in accord with international standards (WOAH)
- Surveillance needs to provide assurances including for trade
- System for timely tracking vaccine match to field virus
- Vaccine bank utility?
- Multiple stakeholder support under control of the Veterinary Authority

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Thank you for your attention

https://science.vla.gov.uk/fluglobalnet/

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