HIGHLY PATHOGENIC AVIAN INFLUENZA

VACCINATION RULES IN THE EU

WOAH 90TH GENERAL SESSION

Paris, 22 May 2023

European Commission,
DG Health and Food Safety
Unit G2 – Animal Health

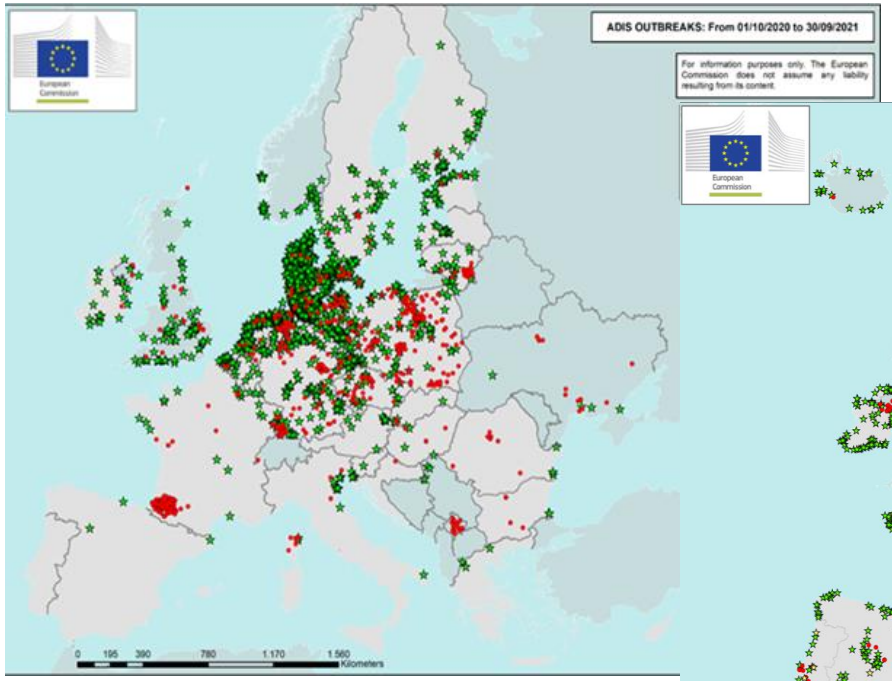
Health and Food Safety

Outline of the presentation

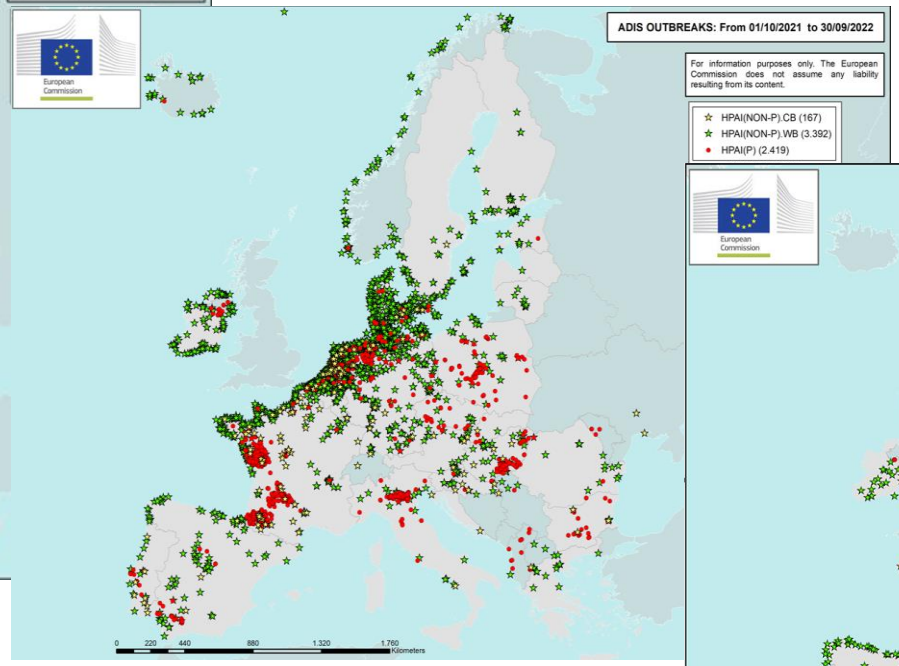
- HPAI situation in the EU
- Animal Health Law – EU legislative framework for animal health
- Rules on vaccination
- Vaccination and scientific trials in certain EU Member States

HPAI in Europe in birds in 2020 - 2023

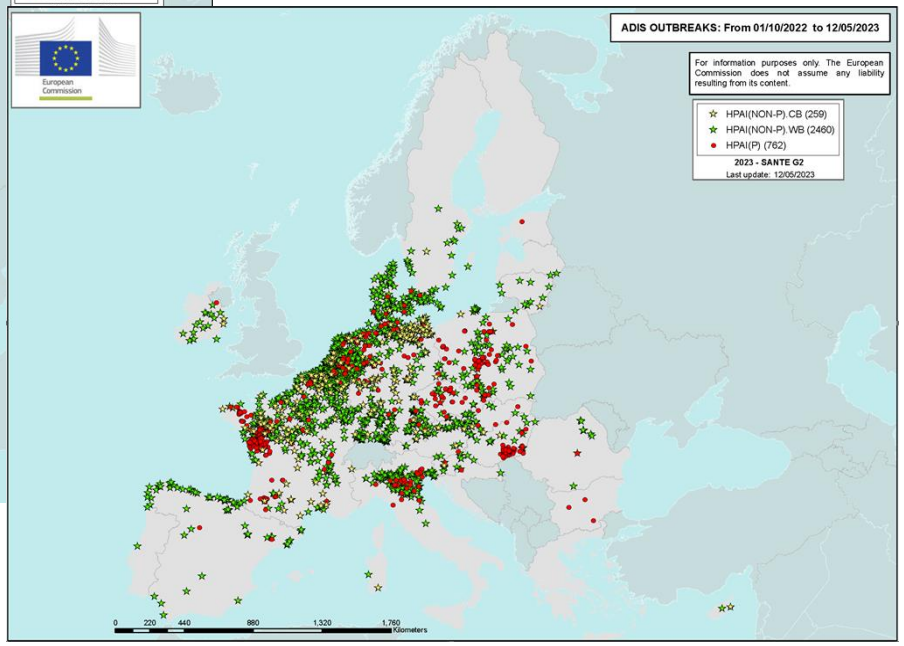
Oct 2020 – Sept 2021



Oct 2021 – Sept 2022



Oct 2022 – 12 May 2023



Virus spread with wild birds in all parts of Europe

Recurrent clusters in poultry in certain areas with high density of certain poultry production

European Commission

Number of HPAI detections 2020-2023

Distribution of total number of HPAI virus detections reported in Europe by week of suspicion and

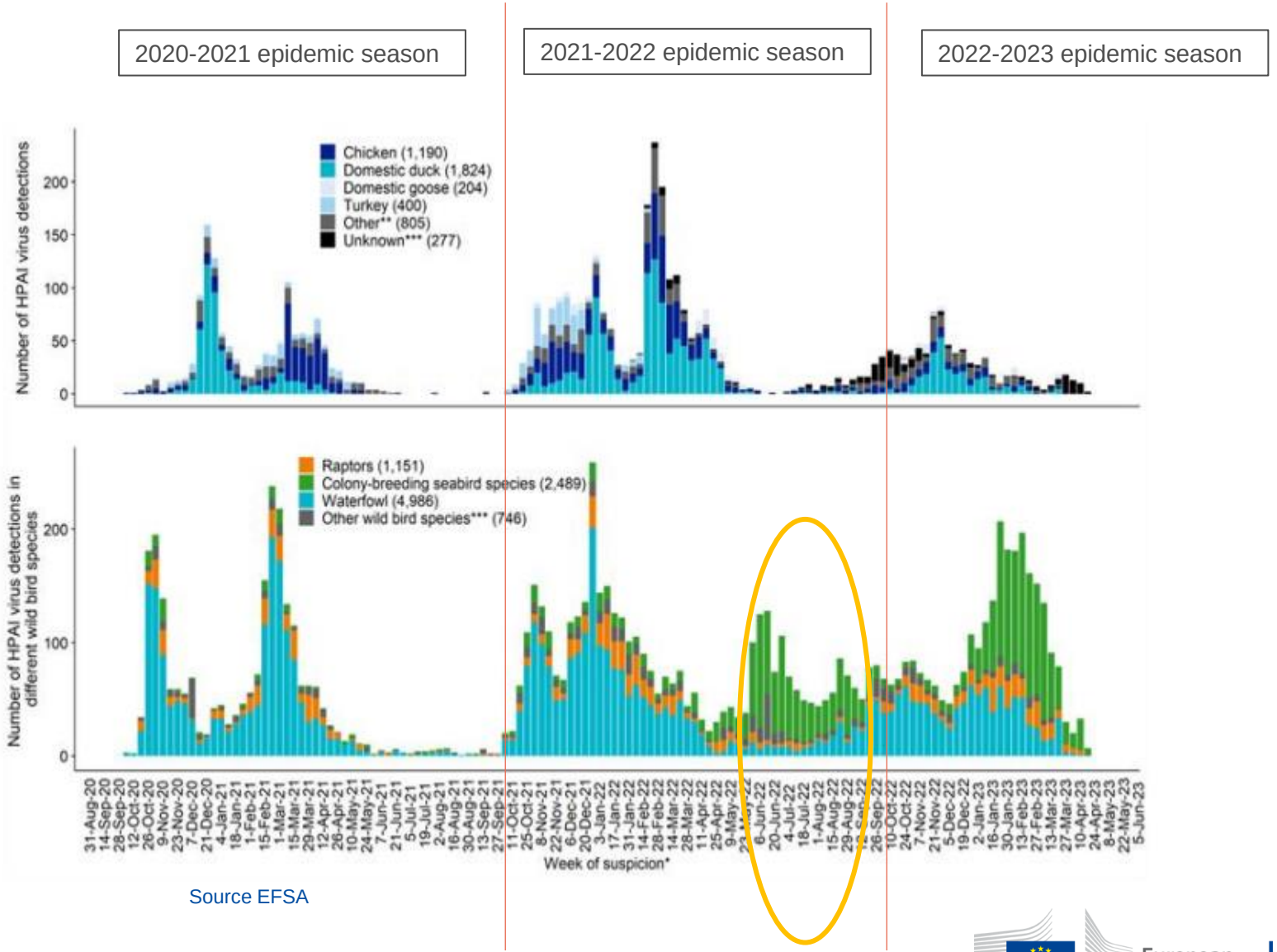
- affected poultry categories (up)
- affected wild bird categories (down)

Poultry:

- High peaks of outbreaks in the past
- Currently reduced number of outbreaks
- Main affected specie: ducks

Wild birds:

- Seasonality in the past, related with autumn and spring migration
- Main affected species: waterfowl
- Worrying trend since spring 2022:
  - Persistence of HPAI virus in wild birds during summer
  - new species highly affected playing a role in spreading, i.e. seabirds breeding in colonies



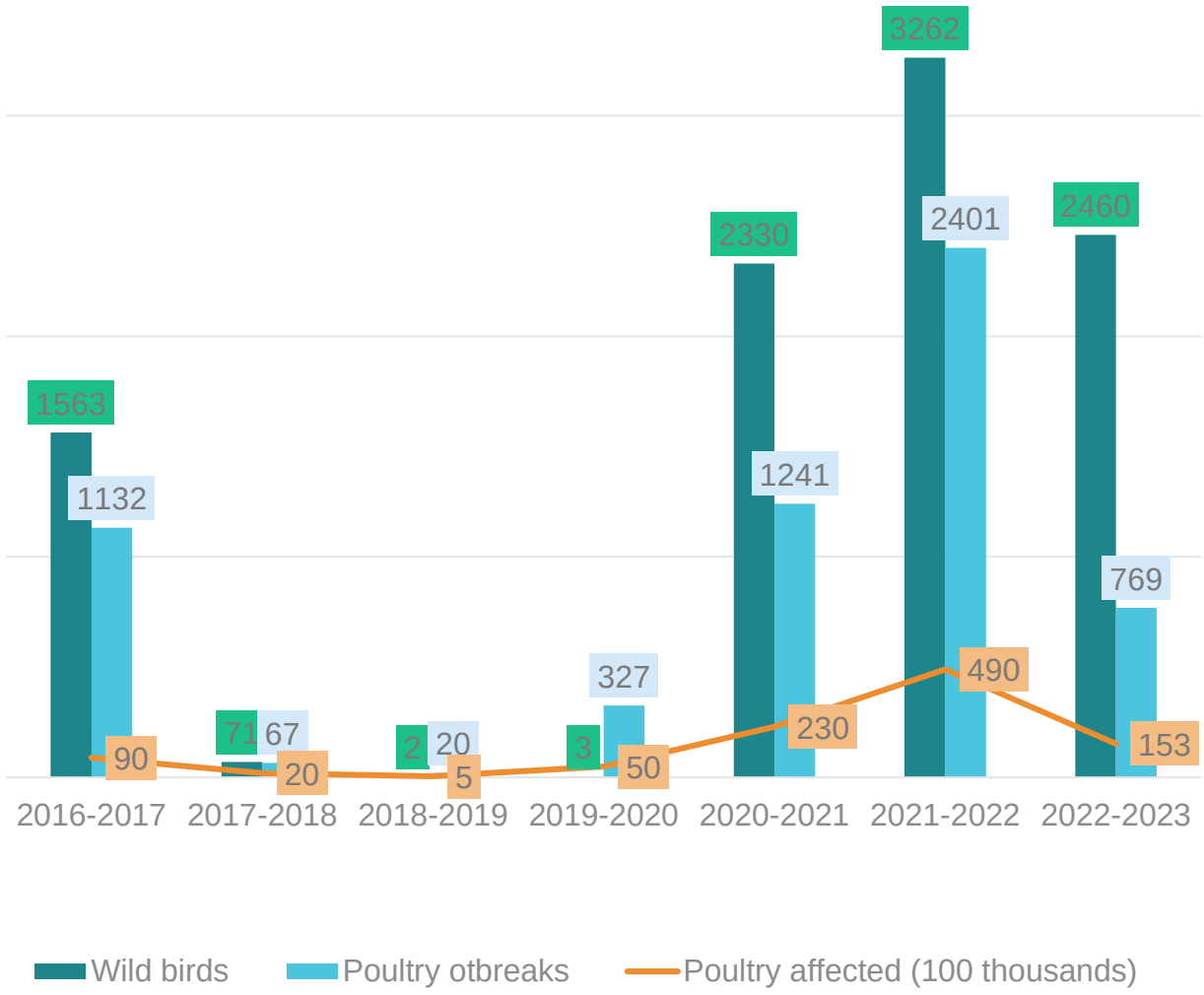
Source EFSA

Summary of HPAI epidemic seasons in figures

2022-2023 the most severe HPAI epidemic season ever experienced by EU with the highest number of outbreaks in wild birds and poultry

Current epidemic season:

- still high number of outbreaks in wild birds
- less outbreaks in poultry (improved biosecurity and preventive measures e.g. reduced density in high risk areas)



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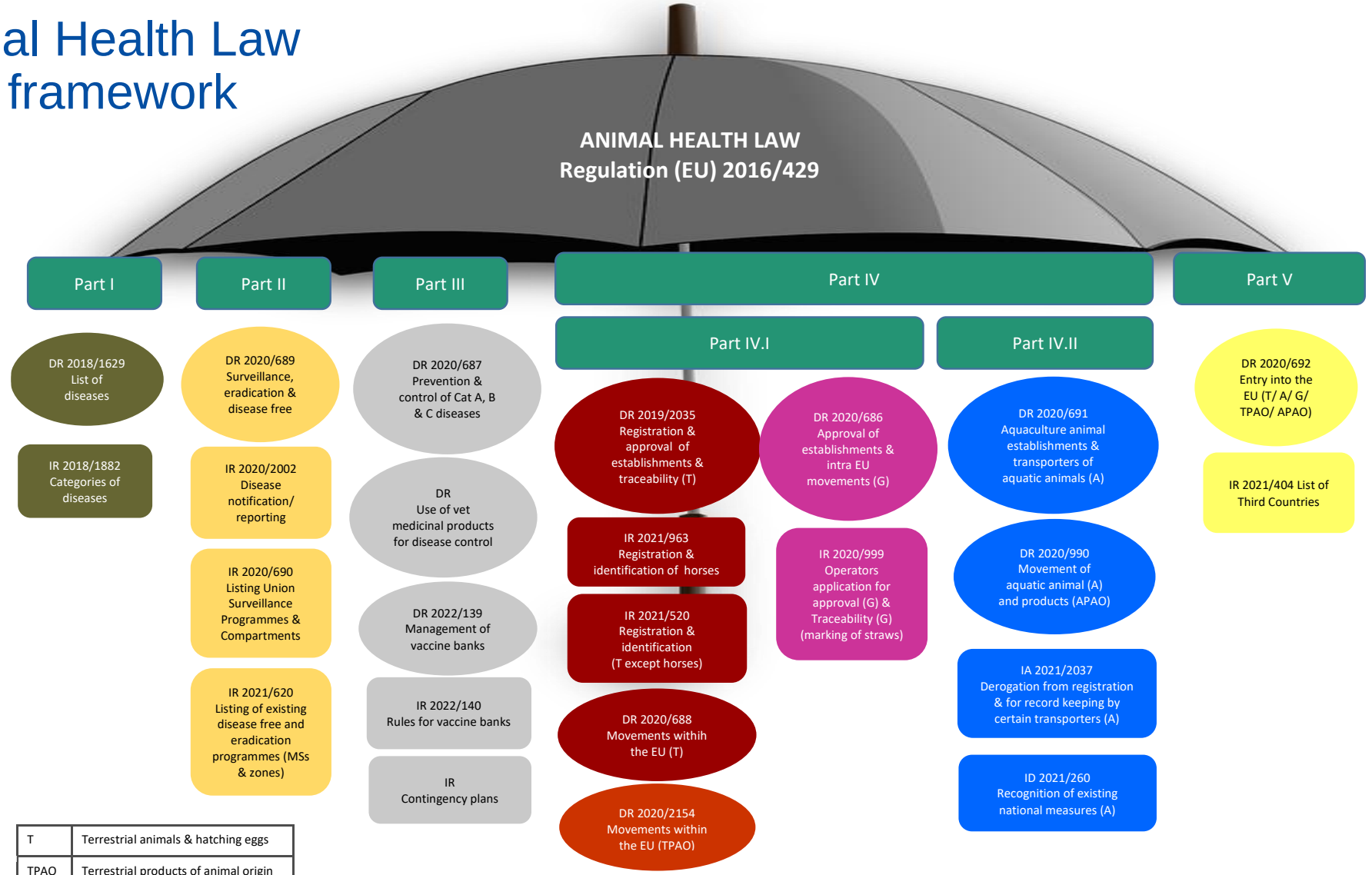
ANIMAL HEALTH LAW

Animal Health Law legal framework



T	Terrestrial animals & hatching eggs
TPAO	Terrestrial products of animal origin
A	Aquatic animals
APAO	Aquatic products of animal origin
G	Germinal products

Delegated Regulation (DR)

Implementing Regulation (IR) or Implementing Decision (ID)

European Commission

AHL: Rules for the use of VMPs for disease prevention and control

Article 46(1)

Provides for the possibility for the Member States to take measures concerning **the use of (ALL) veterinary medicinal products** to ensure the most efficient **prevention or control** of **(ALL)** listed diseases. These measures may cover prohibitions, restrictions and compulsory use of veterinary medicinal products and must be previously assessed as appropriate and necessary.

Article 47(1) (empowerment)

Empowers the Commission to adopt delegated acts concerning:

- ✓ prohibitions and restrictions on the use of veterinary medicinal products;
- ✓ specific conditions for the use of veterinary medicinal products for a specific listed disease;
- ✓ risk-mitigation measures to prevent the spread of listed diseases through animals treated with the veterinary medicinal products or products from such animals;
- ✓ surveillance for specific listed diseases following the use of vaccines and other veterinary medicinal products.

Article 69 - Emergency vaccination:

To take into account Art. 46(1) and delegated acts adopted pursuant to Art. 47

Delegated Regulation (EU) 2023/361

on the use of veterinary medicinal products for disease prevention and control

Approach

Rules on the use of **certain VMPs** for prevention and control of **certain listed diseases - Terrestrial and Aquatic animals**

Circumstances under which **vaccines for category A** diseases can be used

Which **VMPs cannot be used for category A and B** diseases *(including some vaccines, i.e. Rinderpest and Mycobacterium tuberculosis complex)*

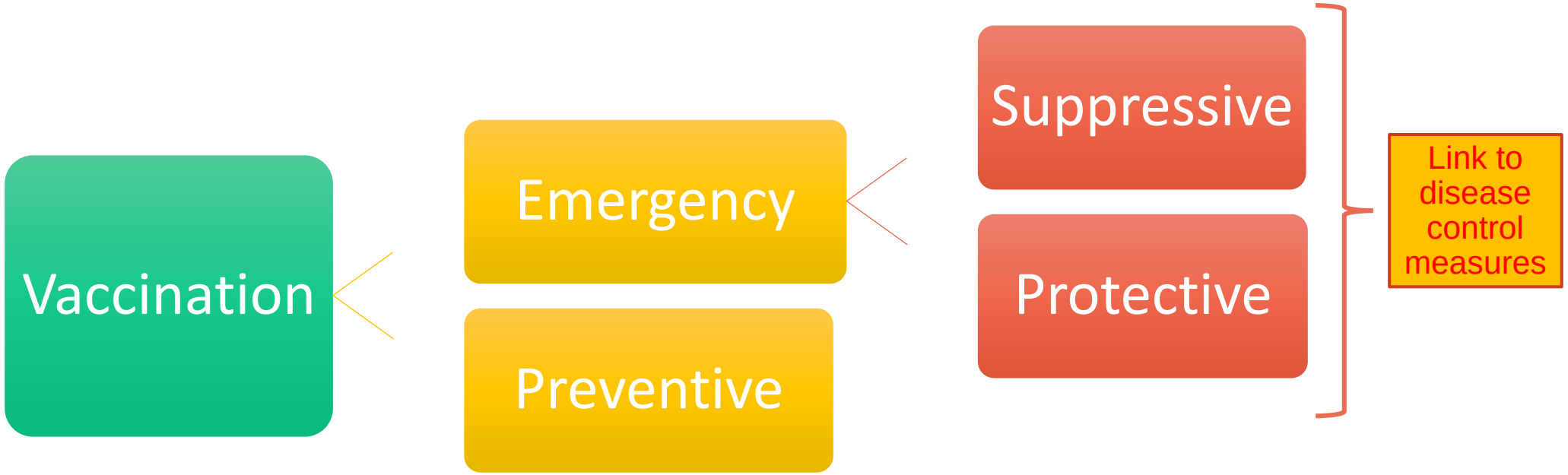
Rules on the use of **vaccines** for prevention and control of category A diseases **– Terrestrial animals (partially Aquatic)**

- Preconditions
- Strategies
- General rules
- Risk-mitigation measures (movement restrictions)

Disease-specific conditions

- Implementation + post vaccination surveillance
- Measures (movement prohibitions for animals and products) in the vaccination zone
- Recovery of the previous animal health status

Vaccination strategies for HPAI



Stamping out : compulsory measure in all establishments where HPAI is detected

Specific rules for vaccination against HPAI

Vaccines

- that **do not contain live AI virus** (attenuated or not)

Risk mitigation measures

- General **prohibition for movements** of vaccinated poultry and their products
- **Derogations** to move, **under conditions**

Reinforced surveillance

- **clinical** and **laboratory** (official activity)
- to assess **effectiveness** (emergency protective vaccination)
- to **early detect infection** with HPAI virus

Traceability/Certificates

- **Emergency vaccination:** certificates for movements from vaccination zone within MS and to other MS
- **Preventive vaccination:** certificates for poultry and hatching eggs when moved to other MS

Decision Making - Implementation process
for the use of vaccines against HPAI

Member State

- **Assessment of the situation** based on specific criteria (*Annex II of DR (EU) 2023/361)*
- **DECISION TO VACCINATE *(strategy selection etc.)***
- Preparation of official vaccination plan (*in accordance with information required in Annex III of DR (EU) 2023/361)*

Member State

- Preliminary information sent *to the other MS and the COM (at least 2 days before start of vaccination)*
- **INITIATION OF VACCINATION**
- Official vaccination plan sent *to the other MS and the COM (at the latest 2 weeks after start of vaccination)*

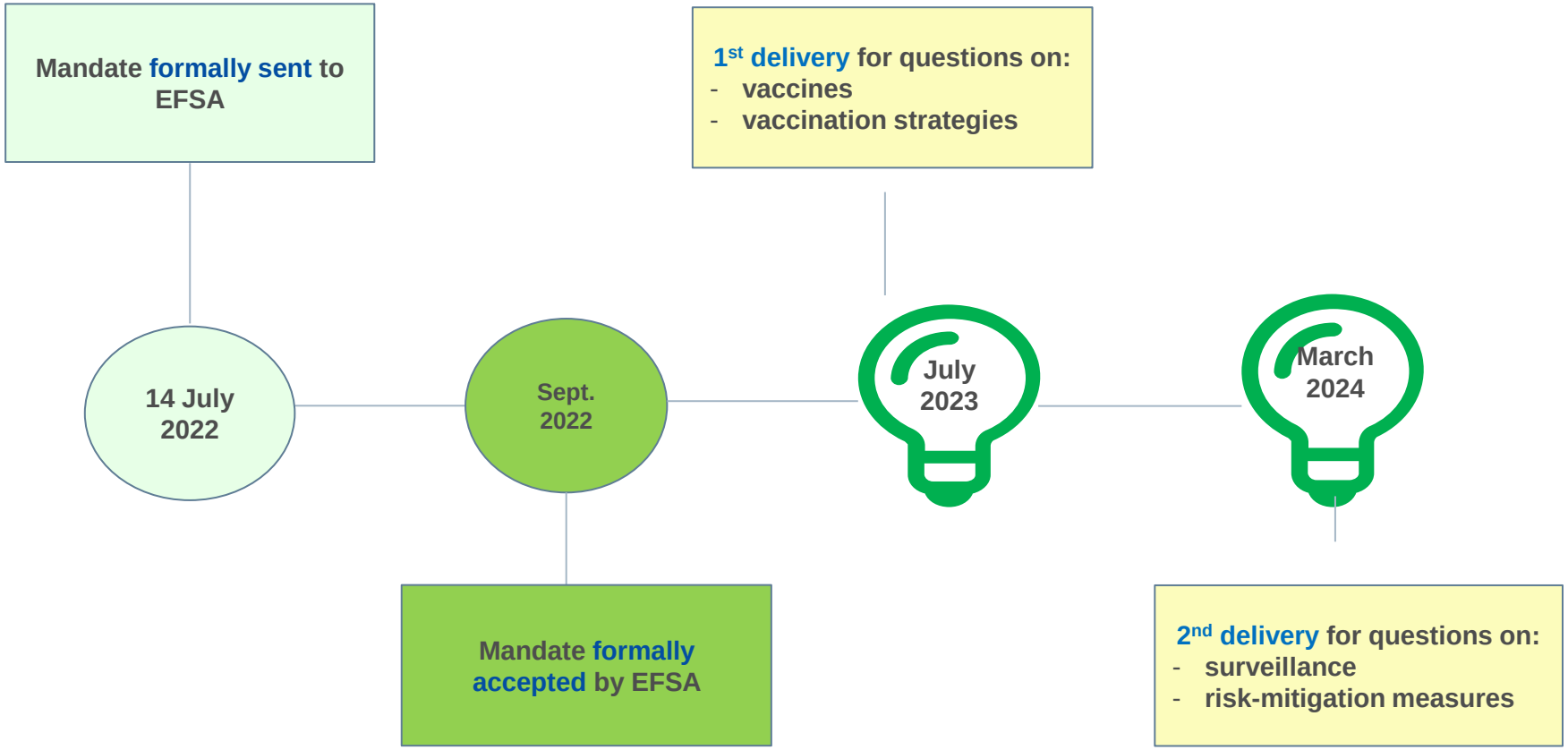
COM

Review of the national **measures in the official vaccination plan**. **May act with additional measures** in accordance with Article 71 of Regulation (EU) 2016/429

Member State

- **Disease-specific surveillance – Risk mitigation measures** *(Annex XIII of DR (EU) 2023/361)*
- **Regular reports** sent *to the other MS and the COM (content / intervals according to the vaccination strategy – Annexes V and VI of DR (EU) 2023/361)*

EFSA mandate for HPAI vaccination



VACCINATION SCIENTIFIC TRIALS

in certain EU Member States

State Veterinary Administration

Vaccination against HPAI in the Czech Republic

90th Annual General Session of the World Assembly of Delegates of the World Organisation for Animal Health (WOAH)

21.05.2023 – 25.05.2023, Paris

CZECH REPUBLIC

vaccination

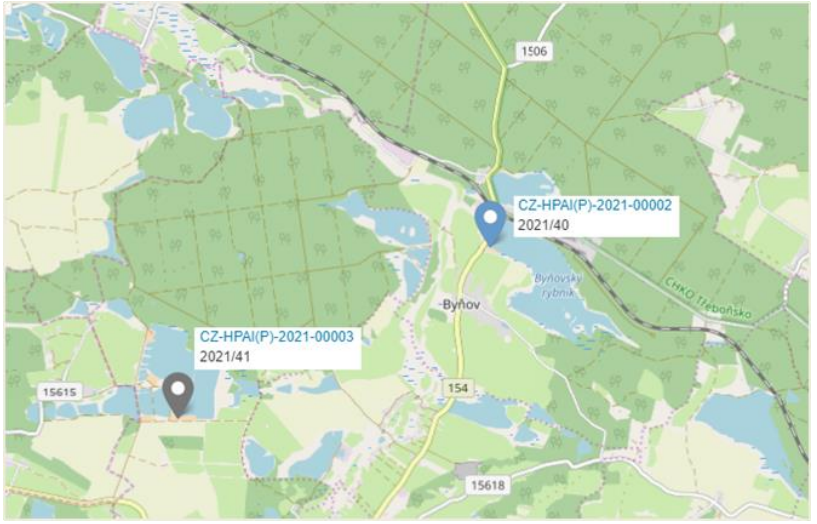
in the genetic reserve for national breed of geese

State Veterinary Administration

The occurence of HPAI in the establishment with Czech geese in 2021

- The establishment (2 farms) is registered as a **poultry genetic resource** at the Ministry of Agriculture of the Czech Republic (grandparent breeding flocks).
- **2 HPAI outbreaks** – HPAI **H5N1** confirmed on 18 November 2021 and 20 November 2021

  – a total of **4 855 breeding geese** (9 flocks)
- All geese with clinical sings were immediately culled.
- Geese without clinical sings were **repeatedly virologically tested by PCR.**
- Geese **with negative PCR test results** → **selection of geese with a high genetic value to restore the breed** → **813 geese selected for vaccination.**
- Culling of the other geese – positive PCR or not suitable for further breeding.



State Veterinary Administration

Emergency vaccination

- SVA granted the derogation from culling for geese with negative results of virological tests in accordance with Article 13(2d) of DR (EU) 2020/687.
- **The vaccination plan** approved by the Central Veterinary Administration.
- **Vaccine: Nobilis Influenza H5N2** emulsion for injection for chickens

  (inactivated viral vaccine)

  1st dose on 16 February 2022 – 813 geese

  2nd dose on 18 March 2022 – 813 geese

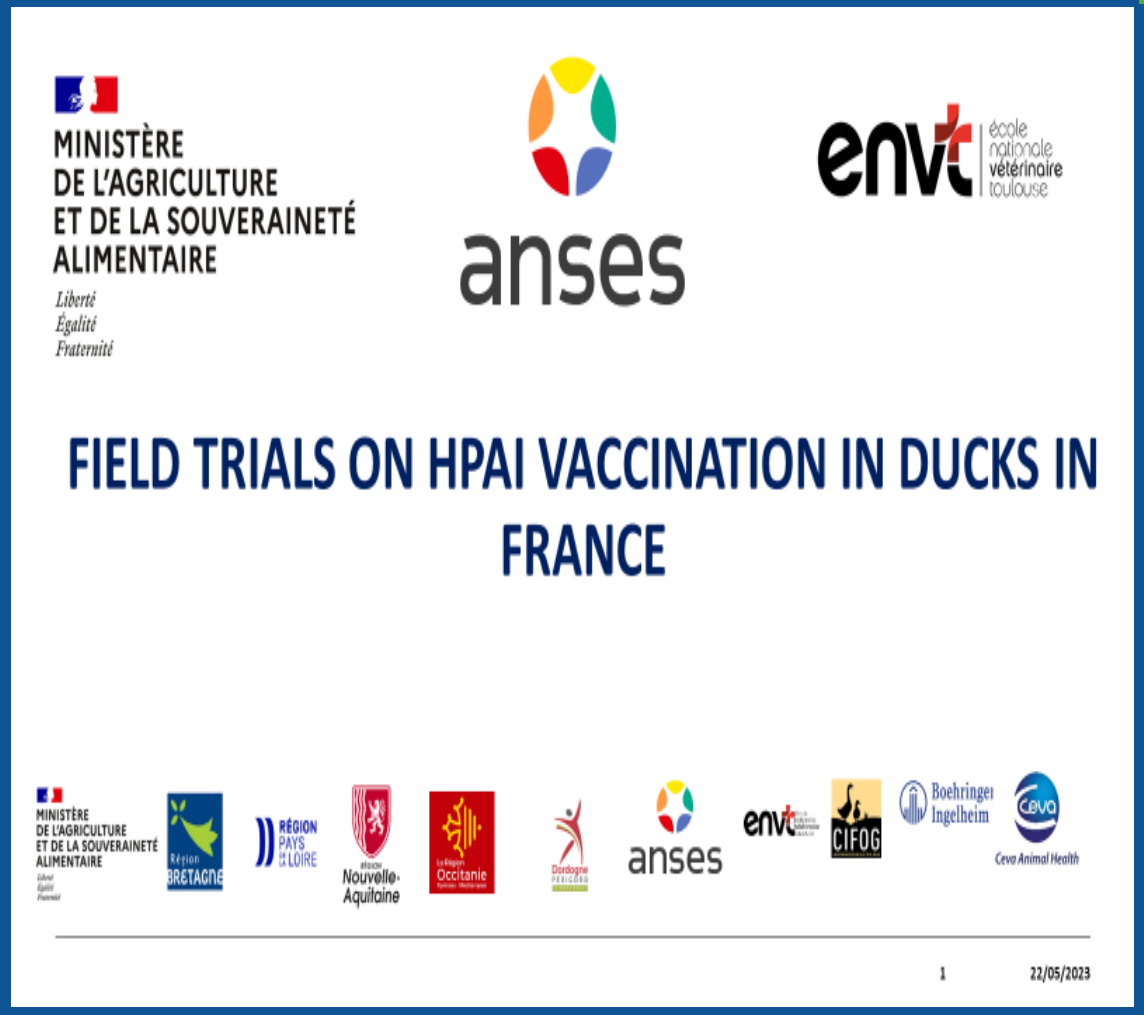
  3rd dose on 5 October 2022 – 659 geese

Laboratory testing after vaccination:

- 24 March 2022 (after 2nd dose) – cloacal swabs from 120 geese, virological testing (real-time RT-PCR) → **negative for AI** → emergency veterinary measures in the outbreaks were lifted.
- 5 October 2022 – cloacal swabs from 80 geese, virological testing (real time RT-PCR) → **negative for AI**.

Conclusion:

- Using of emergency vaccination, **it was possible to save the national breed „Czech goose“** with more than fifty years of tradition in the Czech Republic.
- Poultry breeders and the public perceive the possibility of vaccination very positively.



FRANCE

in ducks

MINISTÈRE
DE L'AGRICULTURE
ET DE LA SOUVERAINETÉ
ALIMENTAIRE
Liberté
Égalité
Fraternité

Experimental trials in mule ducks: M&M

Inventory of AI vaccines and call of interest of vaccine producers in animal health ANMV

↓

Selection of 2 vaccine candidates

↓

Experimental trials

1. Field trials

Phase 1 :

3 flocks included for each of 2 vaccines (500 to 2000 birds each):
Monitoring (PCR + serology) during the growing period to week-11

→ **Vaccination practices & innocuity**

→ **Monitoring of seroconversion / DIVA (ELISA NP and H5)**

Phase 2 :

Same plan on a small scale (100 birds / vaccine + control)

2. Infectious challenge in BSL3 Facilities

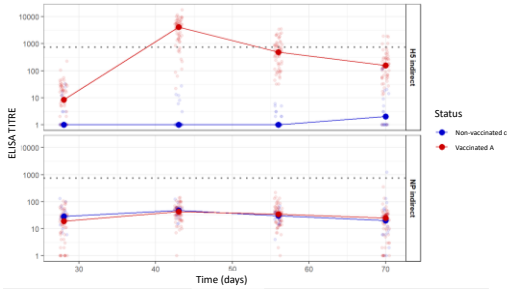
Challenge-tests at Week-7 and -11 of age

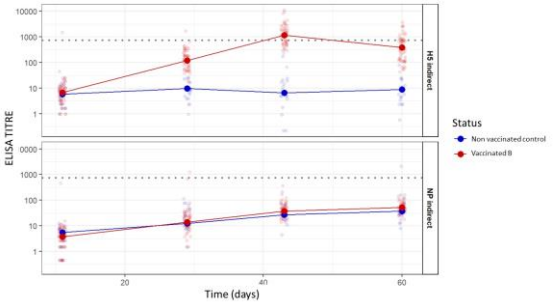
→ **Impact of vaccination on viral excretion (Phase 1)**

→ **Impact of vaccination on viral transmission (R0) (Phase 2)**

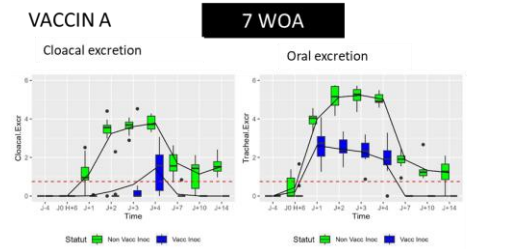
Experimental trials in mule ducks: Results

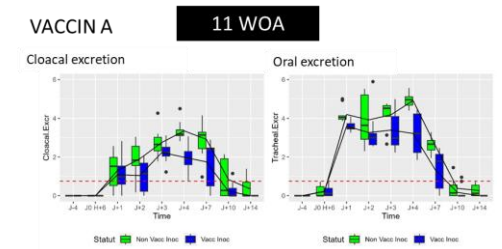
- **Field trials**:
  - Positive assessment of the feasibility of administration and **innocuity** of both vaccines
  - The combination of serology methods (NP & H5 ELISA) suitable for a DIVA strategy with serological profiles consistent for both vaccines

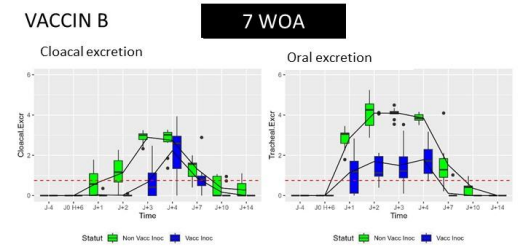


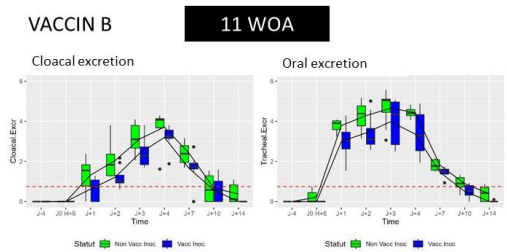


- **Infectious challenge trials in BSL3 facilities**:
  - **Excretion**: significant reduction in oral and cloacal viral shedding in vaccinated animals but less reduction after the challenge at 11 weeks of age compared at 7 weeks of age with similar results for both vaccines









	$\beta_1\ (h^{-1})$	$\beta_2\ (h^{-1})$	Infectious period (d)	R_{01}	R_{02}
Non vaccinated	0.45 (0.15,0.96)	0.15 (0.07,0.3)	8.1	88 (29.7, 186)	29.7 (13.5, 59.2)
Vaccin A	0.009 (5e-4, 0.042)	-	2.7 *	0.62 (0.03, 2.7)	-
Vaccin B	0.008 (4e-4, 0.035)	-	1.5**	0.28 (0.02, 1.26)	-

- **Transmission:** good control of the direct transmission R_{01}<1 and of the airborne transmission R_{02} by both vaccines

European Commission

CEVA SANTÉ ANIMALE
CEVA-PHYLAXIA VETERINARY BIOLOGICALS CO. LTD.
HUNGARY, BUDAPEST

MINISTRY OF AGRICULTURE

HPAI vaccine-development: Hungary

Side-event to the 90th WOAH GS, Paris

21st-25th May, 2023

HUNGARY

in geese

Vaccine development – an overview

- **Field safety and efficacy test of CEVA Response AI H5 vaccine in geese**
  - **Developer:** Ceva Santé Animale (Ceva-Phylaxia Veterinary Biologicals Co. Ltd.; Hungary, Budapest)
  - **Vaccine tested:** CEVA Response AI H5 (Synthetic RNA Vaccine against H5 Avian Influenza) is a synthetic RNA vaccine developed against Highly Pathogenic Avian Influenza virus subtype H5 (H5 HPAIV)
    - Vaccine for waterfowl
    - Market authorization is underway (not on the market)

Vaccine development – an overview

- **Field safety and efficacy test of CEVA Response AI H5 vaccine in geese**
  - **Specifics of the field trial:**
    - Conducted by the developer, under strict control and supervision of the Hungarian veterinary authorities;
    - Started on the 22 September, 2022;
    - Involving one goose parent stock (1204 animals: 602 vaccinated, 602 control group);
  - **Results:** very promising
    - **Safety:** mortality of vaccinated animals – 2.93% vs. mortality of control goup – 76.23%
    - **Efficacy:** virus shedding decrease by 2log10

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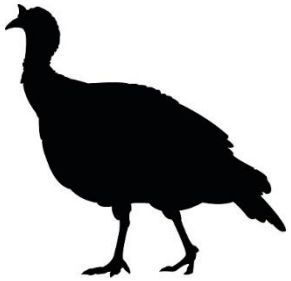
Italian data on vaccine efficacy tests against 2.3.4.4b clade HPAI H5N1 virus in turkeys (*Meleagris gallopavo*)

Vaccine efficacy trials in turkeys were funded by
Istituto Zooprofilattico Sperimentale delle Venezie
and
The Italian Ministry of Health

ITALY

in turkeys

Vaccination schemes tested



HVT live cell-associated

Subunit vaccine
(recombinant HA)

DNA vaccine

Italy carried out tests on **fattening turkey** as they are the most critical species for the introduction and the diffusion of AIVs in DPPA

The choice of vaccination schemes was based on the:

- Use of new generation vaccines effective against clade 2.3.4.4b
- Sustainable vaccination scheme in the field (max 2 interventions within the first month)
- Possibility of having a long-lasting immunity
- Compatibility with DIVA strategy

The schemes tested were:

Heterologous vaccination

- HVT-H5 vaccine alone on the first day of life (1d)
- HVT-H5 vaccine (1d) + sub-unit vaccine booster at 28 days (28d)
- HVT-H5 vaccine (1d) + DNA vaccine booster (28d)

Homologous vaccination

- Sub-unit vaccine at 8 and 28 days
- DNA vaccine at 8 and 28 days

Infection

Performed with a recent H5N1 HPAI strain at 40, 50 and 100 days of age

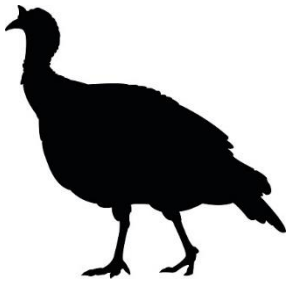
Results and next studies

Results

- HVT vaccine alone at 40 and 50 days gave suboptimal protection (therefore no tests were carried out at 100 days).
- Good clinical protection was obtained with booster (100% survival) at 50 days. The reduction in shedding was most evident with the DNA vaccine booster.
- At 100 days, vaccine protection decreased to 80% and 70% with heterologous vaccination, using respectively protein based and DNA vaccines.
- The homologous vaccination provided very unsatisfactory results (25% to 40% protection).

Tests scheduled in the forthcoming weeks

- New heterologous combinations with HVT-H5 vaccines and boosters based on new traditional (water-in-oil inactivated) and RNA vaccines.
- New challenges using an HVT-H5 vaccine expressing a hemagglutinin derived from the dominant clade H5 virus (2.3.4.4b).
- Results expected by the end of the summer.



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Vaccine trial Netherlands

NETHERLANDS

in chickens from laying type

Health and Food Safety

Vaccine trial Netherlands

Transmission experiment under High Containment conditions WBVR

- Four vaccines tested: 2 HVT-vaccines, 1 DNA vaccine, 1 H5N2 LPAI conventional vaccine
- 4 groups of 10 chickens; 1 control group
- Vaccination at day of hatch
- Challenge-infection of 5 birds per group with H5N1 virus; age 8 weeks
- Measuring antibodies, virus shedding and virus transmission to in-contact chickens
- Calculation of reproduction ratio

Results:

- HVT vaccines effective in preventing signs; R=0 [95% confidence interval 0 ; 0.7]
- DNA still some clinical signs; R=1.9 [95% confidence interval 0.6 ; 5.2]
- H5N2: some clinical signs, R=1.5 [95% confidence interval 0.3 ; 3.4]

Field trial Netherlands

- Vaccination of DOC in the hatchery with HVT vaccine
- Housing chickens on a ‘normal’ farm during production period
- Transmission experiments at WBVR with vaccinated birds at age
  - 8 weeks; 18 weeks; end of production:
  - Aim is
    - measuring efficacy of vaccination applied in the field
    - duration of immunity
- Start probably September 2023
- End 2025

Thank you

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