

Advances in HPAI vaccination in France

*feedback from a poultry
veterinary practitioner*

Derzsy's Days 06.13.24

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ANIBIO Veterinary Group

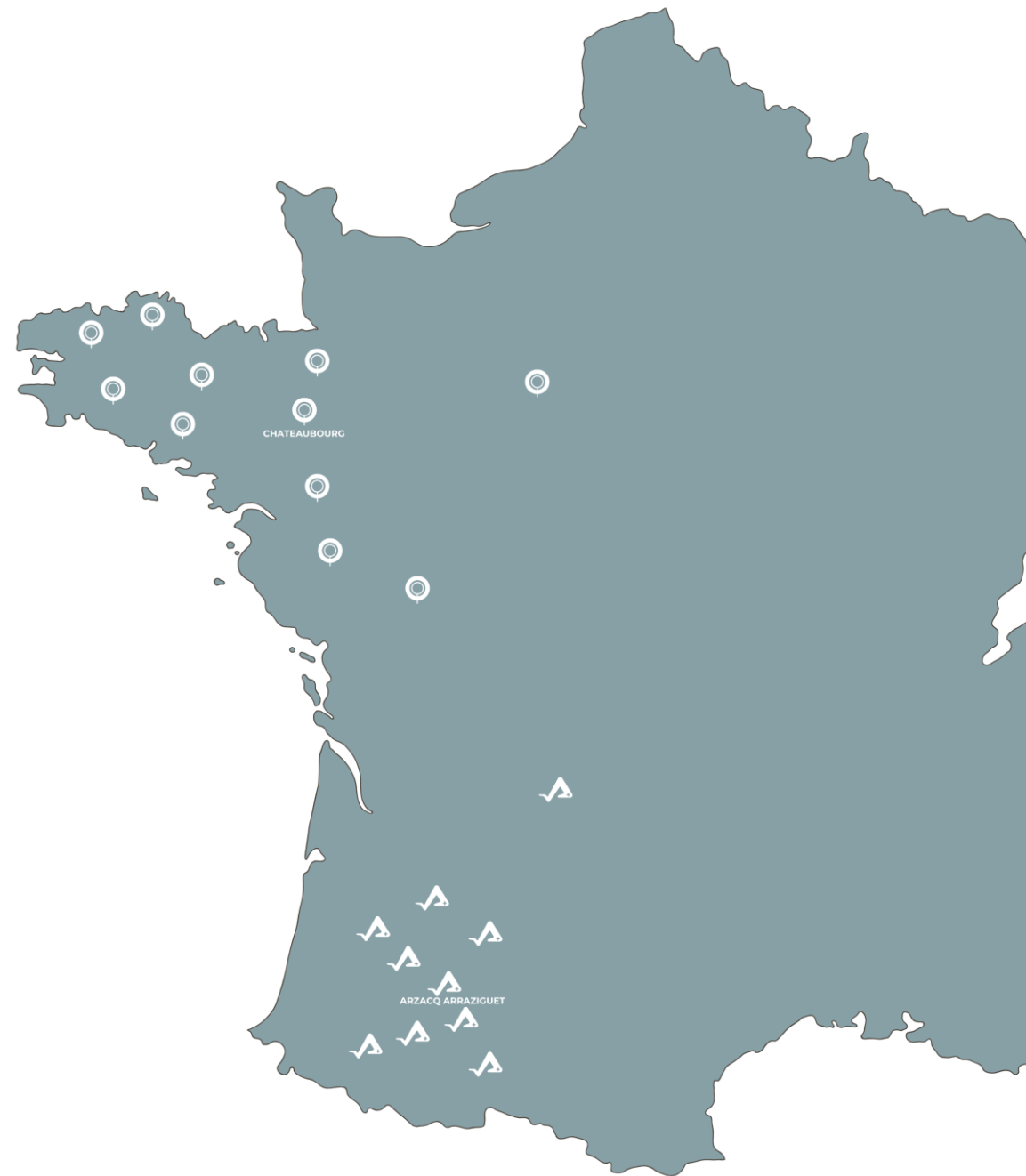
- ✓ Over 50 farm & small animals veterinarians
- ✓ 9 poultry-dedicated veterinarians

Strong Free-Range Poultry Tradition = ducks / broilers / layers

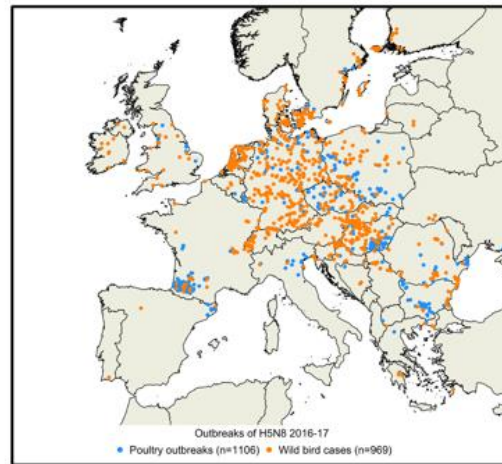
- + breeders & hatcheries, feed mills
- + meat inspection consultancy

In-house accredited laboratory Bio Chêne Vert
(necropsy, sero, bacterio, PCR, hygiene, salmo)

Close links with Chêne Vert vet practices (50 cumulative poultry vets)



AIV outbreaks put Europe (and France) on alert

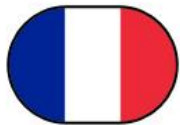


 **H5N8 clade 2.3.4.4.b**

1,218 poultry outbreaks
1,563 wild bird cases
29 EU countries

13 million birds culled

2016-17



~ 500 outbreaks

 **H5N8 clade 2.3.4.4.b**

1,385 poultry outbreaks
2,407 wild bird cases
31 EU countries

22 million birds culled

2020-21



~ 500 outbreaks

 **H5N1 clade 2.3.4.4.b**

2,398 poultry outbreaks
2,733 wild bird cases
36 EU countries

46 million birds culled

2021-22



~ 1,300 outbreaks

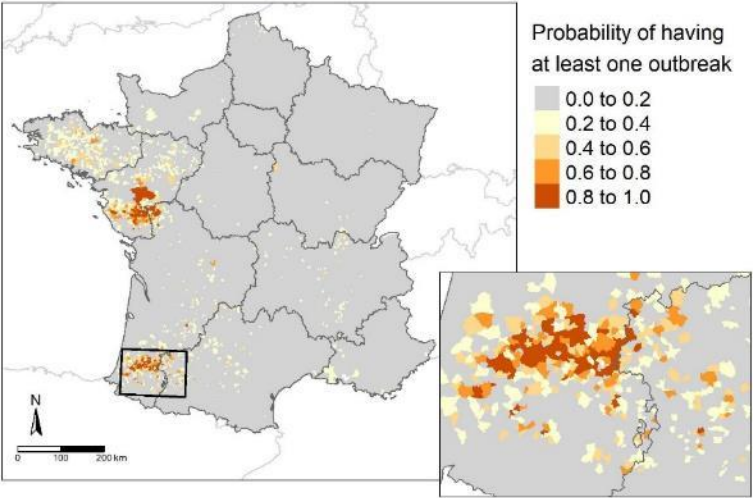
Time

Courtesy Claire Guinat,
University of Toulouse

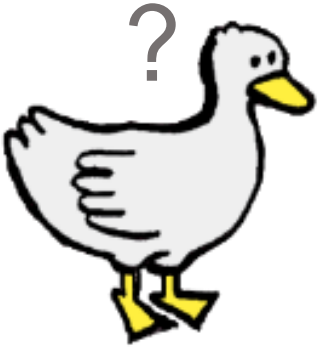
What's wrong with French ducks?

	Ducks	Geese	Broilers	Layers	Turkeys	Guineas
M. birds	60	0.7	830	46	35	25

Husbandry
(duration, FR, handlings, movements, multi sheds, thinning)



Farm number & density
(socio-economic reasons)



Biosecurity limits
(mentality, culture)



High viral sensitivity and shedding
(loads, duration)



The (not so) magic management pillars

**Early
detection**



**Reactive
culling**



**Preventive
culling**



Biosecurity



Vaccination as an extra tool

January 2022

Julien Denormandie - Minister of agriculture

“There will be no other option than to integrate vaccination in our strategy against HPAI”

POULTRY WORLD

Poultry ▾

Markets ▾

Health/Nutrition ▾

France considering vaccination against bird flu

16-08-2021 | Health | Health/Nutrition | Article



These turkeys in Denmark and millions of other birds in Europe were killed to stop an avian influenza virus.

culling will stop its current outbreak. The U.S. poultry industry is taking a wait-and-see approach. But in Europe the devastation wrought by the virus, and the cost and logistics of culling millions of birds, may be changing the calculus.

In places where the extremely infectious new strain of avian influenza has taken hold, vaccination “really has the capacity to make a huge difference,” says Richard Webby, a virologist at St. Jude Children’s Research Hospital who studies influenza in birds and other animals. In the long term, researchers say, living with H5N1 may require not just vaccines, but a restructuring of dense European poultry operations.

For 3 decades, ever more strains of avian influenza have been emerging in Asia. The current H5N1 strain arrived in Europe in 2021. It was first detected in the United States in January and continues to spread (*Science*, 29 April, pp. 441 and 459).

Some researchers are concerned that vaccinating, if not done carefully, will allow H5N1 to persist and continue to mix with strains in wild birds, with the risk that it might evolve to spread among people. The risk for the European Union and United States, although low, is probably the highest since H5N1 emerged 25 years ago, Webby says. “We really don’t want this virus lurk-

INFECTIOUS DISEASE

Wrestling with bird flu, Europe considers once-taboo vaccines

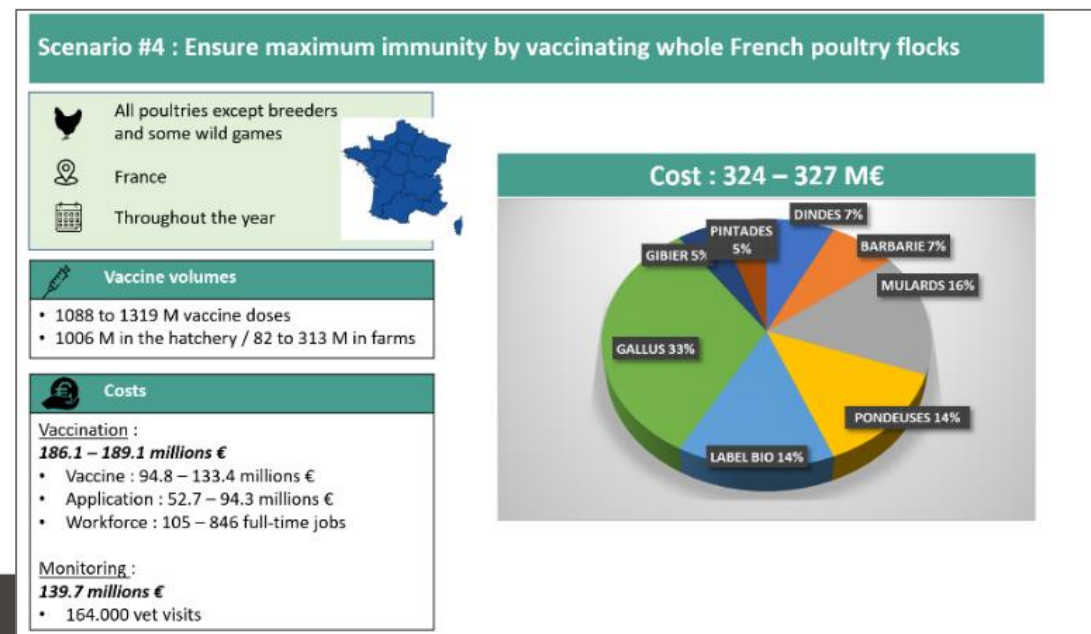
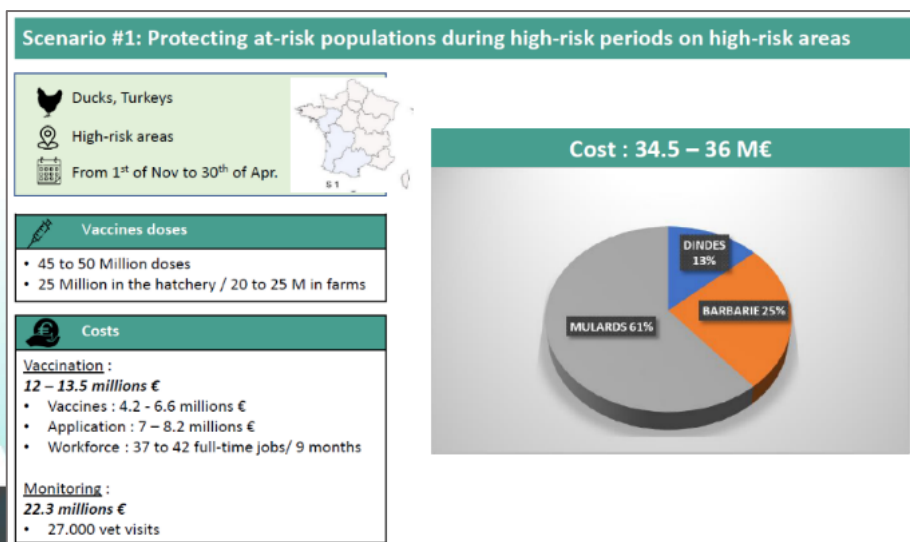
To lessen the toll of culling, some countries launch vaccine trials despite trade implications and public health risks

Poultry industry involvement

Working Autumn 22 – Spring 23 : « Poultry Industry Vaccination Group »

Field actors strongly committed to poultry sector (prod. companies, main vet practices, pharma companies)

- Ongoing reflection on the issues, interests and feasibility of HPAI vaccination
- Consider practical implementation of vaccination and surveillance (based on Europ. Deleg. Act)
- Evaluate cost of different scenarios (> 4 scenario considered)
- Share the analysis with public decision makers



Minister's decision (may 2023)

Steering Committee (> January 23)

Strategy? Preventive vaccination (Europ. Deleg. Act)

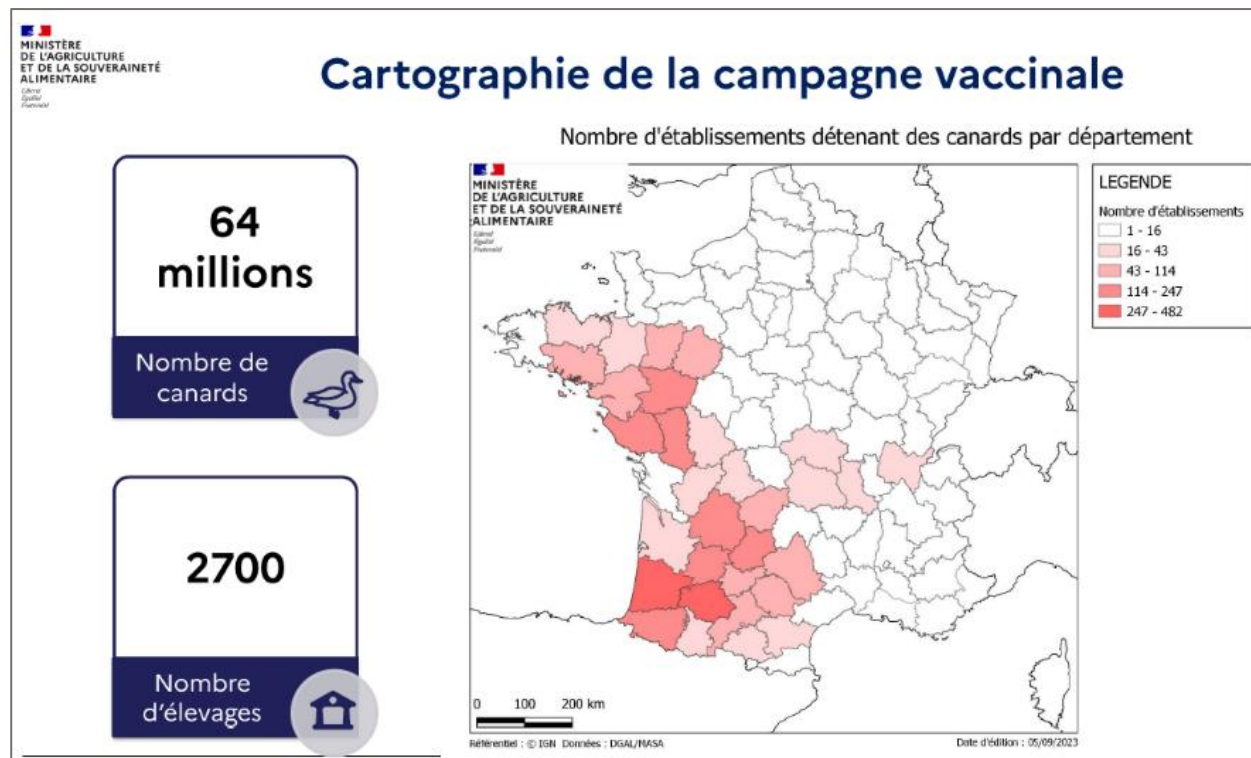
What species?

- Ducks only ; mandatory for > 250 birds
- Ban for all other species (geese!)
- Breeders on a voluntary basis (i.e non exported)

Where? All metropolitan France (Corsica excluded)

When? All year long (from Oct 2023)

Who can vaccinate? Vet or farmer or professional gangs (delegation / training / supervision)



Minister's decision (may 2023)

What vaccine?

- Conditions: efficacy clade 2.3.4.4.b ; DIVA by serology NP ; authorized by French Vet Medicine Agency
- 2 candidates =
 - BI VOLVAC B.E.S.T AI+ND. Subunit inactivated H5 + LaSota. D10 & D28 by SQ injection
 - CEVA Respons AI H5. mNRA. D1 injection at the hatchery + D28 by IM injection
- Tender June 2023 for 80M doses → **VOLVAC B.E.S.T only**

PHASE
1



Vaccin/fabricant	Espèce(s) de destination	Voie d'administration	Nombre d'injections en primovaccination	Conservation du vaccin	Durée de conservation	DIVA Sérologie ELISA NP
Volvac BEST AI+ND BOEHRINGER INGELHEIM	Poule Canard Pékin Canard de Barbarie Canard mulard	SC	Poule : 1 Canard Barbarie, mulard : 2 (à partir de 10j) Canard Pékin : 2 (à partir de 1j)	+5°C	24 mois	OUI

Minister's decision (may 2024)

What vaccine?

- Conditions: efficacy clade 2.3.4.4.b ; DIVA by serology NP ; authorized by French Vet Medicine Agency
- 2 candidates =
 - BI VOLVAC B.E.S.T AI+ND. Subunit inactivated H5 + LaSota. D10 & D28 by injection
 - CEVA Respons AI H5. mNRA. D1 injection at the hatchery + D28 by injection
- Second tender for 60M doses to be used between June and November 24
 - BI VOLVAC B.E.S.T. : 33 M doses
 - CEVA Respons : 27 M doses
- Pilot stage June – September 24 :
 - BI VOLVAC B.E.S.T. allowed for pekin + mule d.o. ducklings
 - CEVA Respons allowed for all d.o. ducklings
 - regardless the vaccine status of the breeders : assess the level of interference with MDA during the “low-risk” period



Minister's decision (may 2023)

Who pays for it?

- Co-funded by State and duck industries alone
- State will pay 85% the first year
- Same for all kinds of ducks

Practically:

- State: vaccine + part of injection labor + veterinary logistics & supervision + « active monthly surveillance » (visits & lab tests)
- Industry: « passive weekly surveillance » lab PCR + part of injection labor

How much?

- Estimated cost: 105M€ (meat + breeders)

For 60M ducks

- (21-22 HPAI crisis estimated 1.4B€)

Poste de dépense	Estimation du montant TTC (12 mois)	Circuit de paiement
Achat du vaccin	23,8 M€	Marché public
Acheminement du vaccin	3,6 M€	Marché public
Application du vaccin dont :	31,94 M€	Paiement par l'Etat
- Supervision de la vaccination par les vétérinaires	8,9 M€	
- Interventions des équipes d'attrapeurs et vaccinateurs	23,04 M€ (0,36 €/caneton)	
Surveillance passive : analyses par laboratoire reconnu	4,08 M€	Paiement par l'éleveur
Surveillance active : visite par le vétérinaire	11,6 M€	Paiement par l'Etat
Surveillance active : analyses par laboratoires agréés	29,8 M€	Paiement par l'Etat
TOTAL	104,82 M€	La participation de l'Etat s'élève à 89,1 M€ (85%) et celle des professionnels à 15,7 M€ (15%).

Oct 1st 2023: an historic day in France!

France kicks off bird flu vaccination despite trade backlash risk

By Sybille De La Hamaide

October 2, 2023 4:26 PM GMT+2 · Updated a month ago



[1/2] A person holds a test tube labelled "Bird Flu", in this picture illustration, January 14, 2023. REUTERS/Dado Ruvic/Illustration/File Photo Acquire Licensing Rights

SCIENCE | FRANCE

France to vaccinate millions of ducks against bird flu

10/02/2023

A nationwide vaccination campaign against bird flu in ducks kicked off in France on Monday, with the country hoping to put an end to costly mass culls. But the poultry industry is risking a trade backlash.



Trade restrictions

Only (?!) 5 countries are officially blocking French poultry imports. Japan, Thailand, USA, Canada, UK

A lot of misinformation or discrepancies circulating

Ongoing discussions with US. Important meeting in September. Canada +/- UK may align.

Worrying for exporters (primary breeders/meat) with little economic leverage

Fewer damages than with +1300 outbreaks



The screenshot shows a news article from Euronews. The header includes the Euronews logo and navigation links for HOME, EU, EUC, EC, EP, ECJ, and INTERNATIONAL. The main headline reads: "The United States puts the brakes on imports of vaccinated French ducks". Below the headline, it says "October 1, 2023". There are social media sharing icons for Facebook, Twitter, and Email. The article text states: "The US Department of Agriculture's inspection service has imposed new import restrictions on poultry from France because the French have started vaccinating ducks against bird flu. These restrictions also apply to live ducks, duck eggs and unprocessed duck products." To the right, there is a "POPULAR" section with two items: "The Netherlands stops aid to Turkey; also asks for EU ban" dated October 12, 2019, and "The Netherlands: Shell".

HPAI vaccination of meat ducks



2 injections VOLVAC B.E.S.T SC @0.5ml

- V1 = Mini d10 ; Max d21
- V2 = 18d-23d after V1
- Possible V1 injection @day-old (hatch) in Pekin ducks only



Changes / adaptations
to classical vaccination schemes

Workforce needed!







HPAI vaccination at hatch?

Pekin ducklings / VOLVAC BEST only

- Technical challenge: manual or machine?
- Pace, workforce
- 50g duckling receives 0,5 ml dose



Vaccin/fabricant	Espèce(s) de destination	Voie d'administration	Nombre d'injections en primovaccination
Volvac BEST AI+ND BOEHRINGER INGELHEIM	Poule Canard Pékin Canard de Barbarie Canard mulard	SC	Poule : 1 Canard Barbarie, mulard : 2 (à partir de 10j) Canard Pékin : 2 (à partir de 1j)



HPAI vaccination at hatch?

Pekin ducklings / VOLVAC BEST only

- Technical challenge: manual or machine?
- Pace, workforce
- 50g duckling receives 0,5 ml dose



HPAI vaccination on farm



BI VOLVAC B.E.S.T.

- No specific adaptation required regarding application compared to existing vacc. Programs
- Combined vaccination (pasteurellosis and/or autologous vaccines E. coli / riem.) demands skills and attention (2x .5cc = higher risk of misapplication)





HPAI vaccination at hatch?

Pekin + mule ducklings / VOLVAC BEST

- Technical challenge: manual or machine?
- Derzsy vaccine compatibility? (Deparvax / Palmivax : oil / aqueous - .2 / .5cc)
- Bill +/- claws treatment = additional mortality due to combined interventions?



HPAI vaccination at hatch?

CEVA Respons H5

- Technical challenge: 0.2cc IM shot
- Logistical challenge :
 - 80°C storage
 - Dry ice freight
 - 4 week conservation @-20°C
 - Thawing process
 - Poor automation ability
- better harmlessness (ducklings and operator)





HPAI vaccination on farm

CEVA Respons H5

- Technical challenge: 0.2cc IM shot
- Logistical challenge :
 - 80°C storage
 - 2 days conservation @+4°C
 - Appliuication within 2 hours post reconstitution
- Combination with existing SQ inac. vaccination program (pasteurellosis and/or autologous vaccines E. coli / riem.)



HPAI vaccination of breeding ducks: voluntary

Which breeding flocks must/can be vaccinated?

1. Trade of offspring (= only if no export)
2. Risk factor / likelihood of infection (study by Toulouse Vet School)
3. Proximity to strategic sites (GP, pedigree, hatcheries...)

Cost of vaccination in breeders?

85% by State / 15% by industry
Likely increase of offspring's price

La mesure de l'efficacité

- R_0 (« R-zéro ») = nombre de reproduction de base
= nombre moyen de sites qu'un site infectieux va infecter au cours de sa période infectieuse

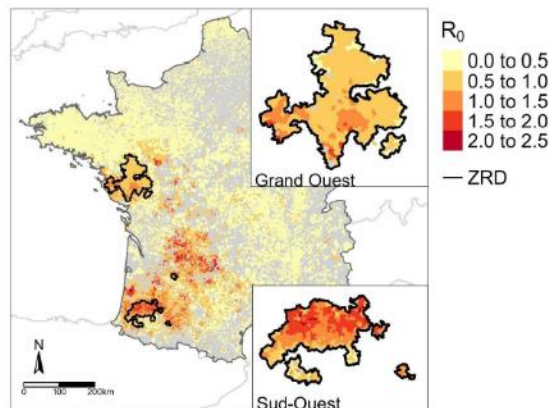


Figure : Distribution spatiale du nombre de reproduction de base R_0 moyen par commune et en particulier dans les zones à risque de diffusion (ZRD).

Résultats – ZRD ouest

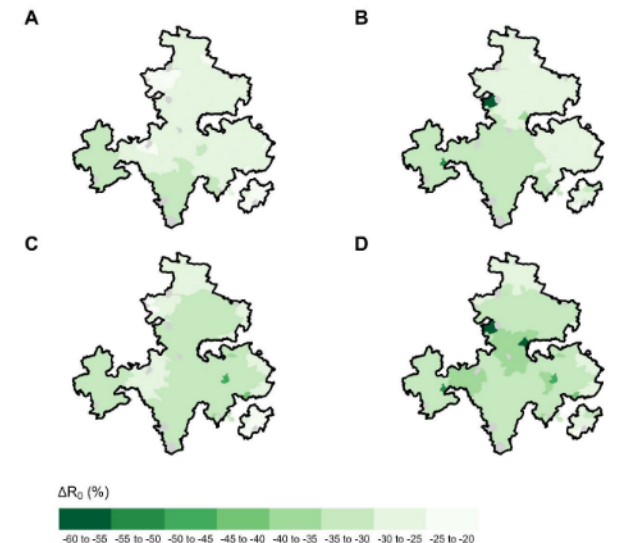
Figure 2 : Diminution relative du nombre de reproduction de base R_0 moyen par commune dans la ZRD de l'ouest pour les différents scénarios de vaccination

A : absence de vaccination des reproducteurs

B : vaccination des reproducteurs de canards de chair dans la ZRD

C : vaccination des reproducteurs de canards gras (canes Pékin) dans la ZRD

D : vaccination de tous les reproducteurs dans la ZRD.



HPAI vaccination of breeding ducks: voluntary

Evolutionary vaccination scheme

- 4 to 6 injections in rear
- Specie dependent protocol (poorer antibodies persistence for Muscovy)
- Frequency in lay ? Drop in egg prod reported (less with CEVA Respons)
- Regular serology for antibodies persistence
- “Best protection as possible, less injections as possible”

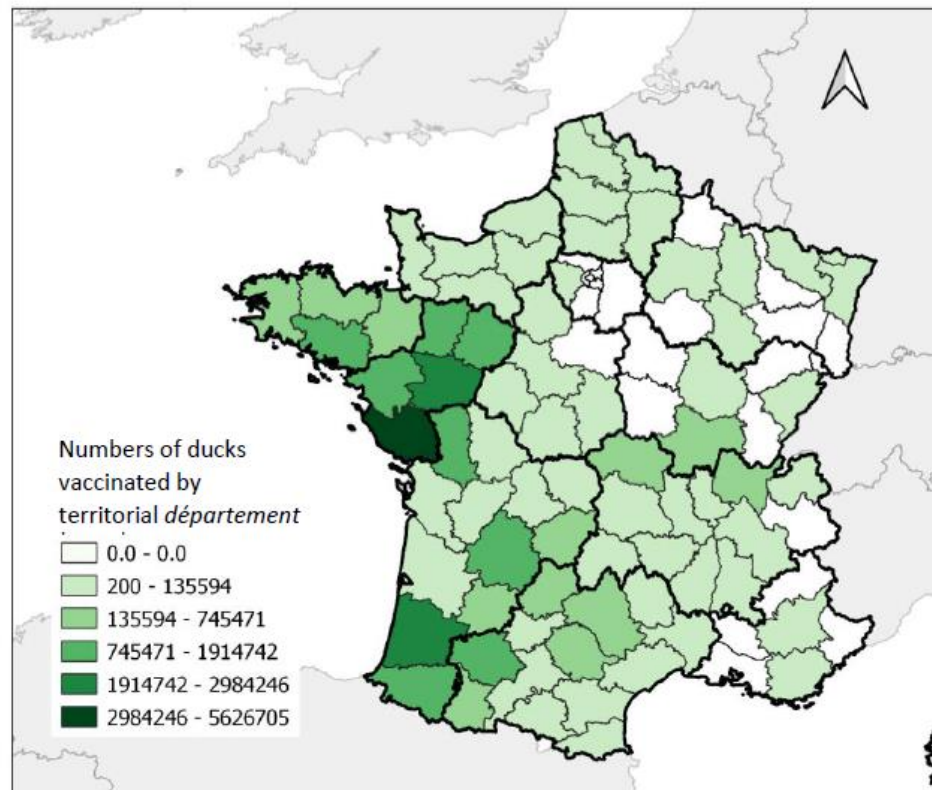
No vaccination of GPs because of trade restrictions



HPAI vaccination: volumes

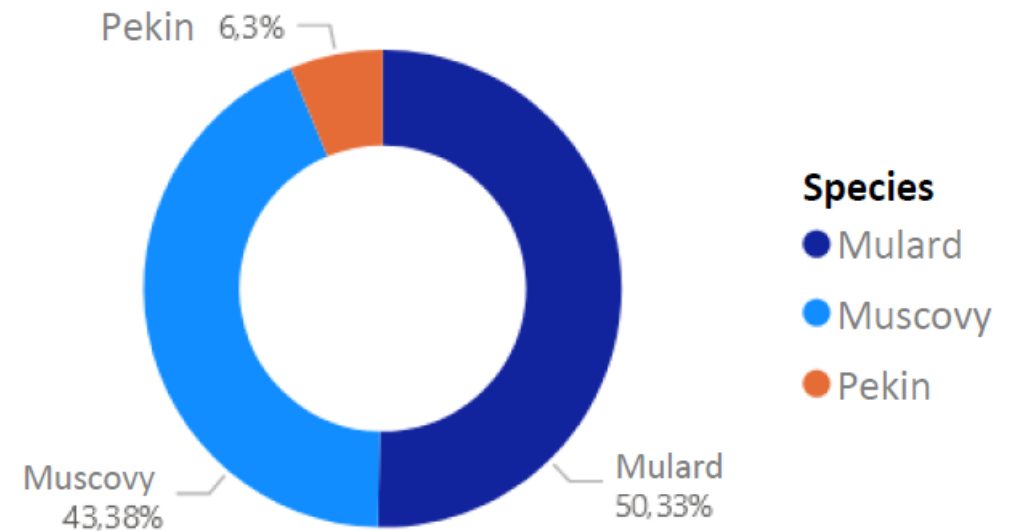
The number of birds vaccinated over the period October 2023 to March 2024 stands at **29,252,582**.

Figure 1- Number of ducks vaccinated by French territorial département



1.2. Numbers of birds vaccinated by species

Figure 2- Percentages of ducks vaccinated by species



A key point: surveillance

Following European delegated act

- Active surveillance (part of the 85% state charge):
 - Monthly PCR x60 birds (vets) → 2 or 3 visits/flock
 - Accredited labs only (= public)
- Passive surveillance (part of 15% industry charge):
 - Weekly PCR x5 dead birds (farmer)
 - Recognized labs possible (= private)
- Serology:
 - NP serology (field challenge) : accredited labs only (state charge)
 - +/- H5/PMV1 (vaccine uptake): recognized labs possible (industry charge)

MINISTÈRE DE L'AGRICULTURE ET DE LA SOUVERAINETÉ ALIMENTAIRE

Surveillance renforcée post-vaccination

Modalités	Surveillance passive renforcée	Surveillance active
Ou ?	Unité épidémiologique	
Qui ?	Eleveur ou Technicien	Vétérinaire officiel
Fréquence ?	Hebdomadaire	Tous les 30 jours : analyse virologique En fin de lot : analyse sérologique
Comment ?	Ecouvillons (ET/EOP) sur 5 cadavres	Tous les 30 jours : écouvillons (ET/EOP) sur 60 animaux et En fin de lot : prise de sang sur 20 animaux
Analyse ?	Virologie par RT-PCR temps réel gène M. Si résultat positif, screening H5/H7	Virologie par RT-PCR temps réel gène M (Si résultat positif, screening H5/H7) et Sérologie par ELISA NP
Type de laboratoire ?	Laboratoire reconnu	Laboratoire agréé

Direction Générale de l'Alimentation

A key point: surveillance

Figure 6 – Numbers of clinical visits for active surveillance month by month⁴

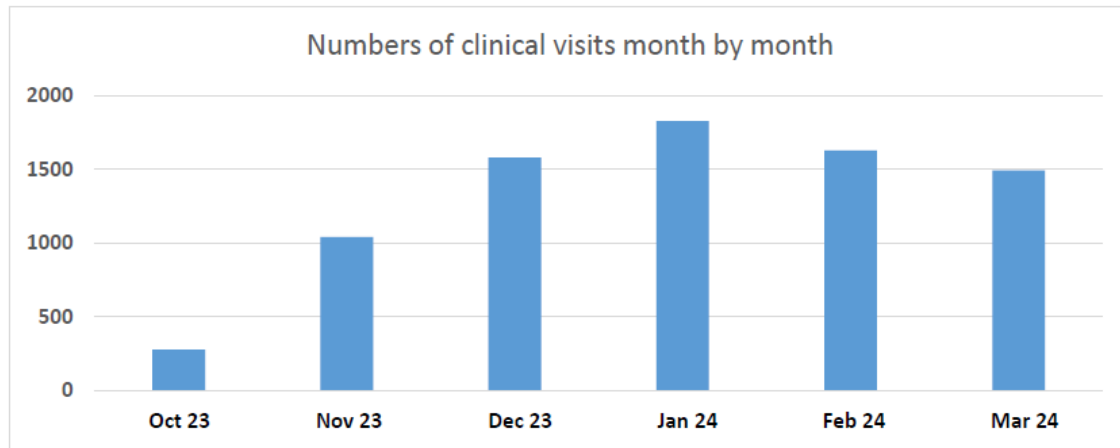
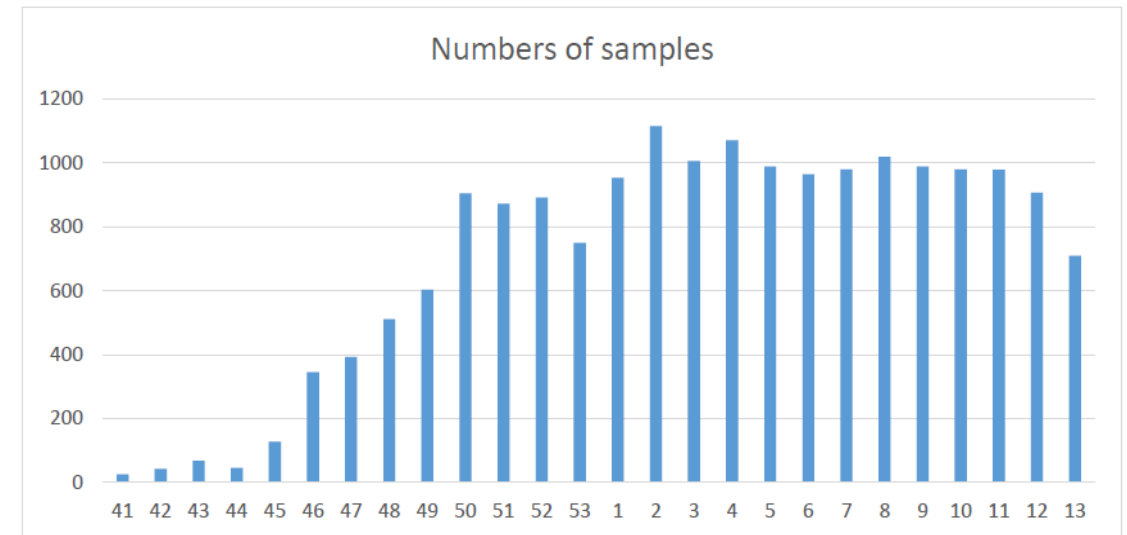


Figure 5 – Numbers of passive surveillance samples taken week by week³



Oct 23 – March 24 : 457,000+ samples (active surveillance) / 18,000+ samples (passive surveillance)

Traceability



CALYPSO

Collecting vaccine-related data from field vets: orders, prescriptions, volumes, field audits, monthly surveillance, payments



SIGAL

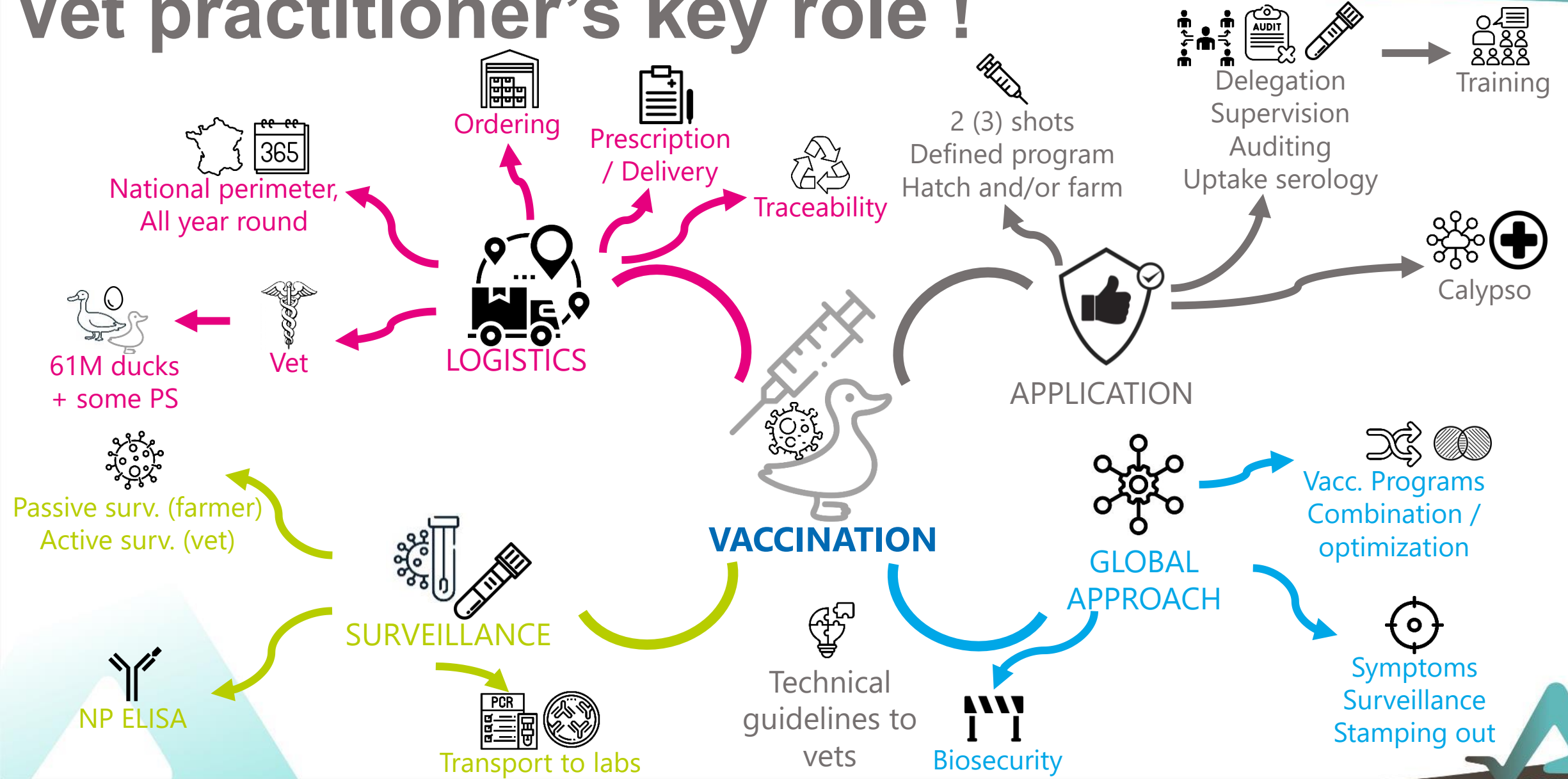
Collecting surveillance data from laboratories: active and passive surveillance



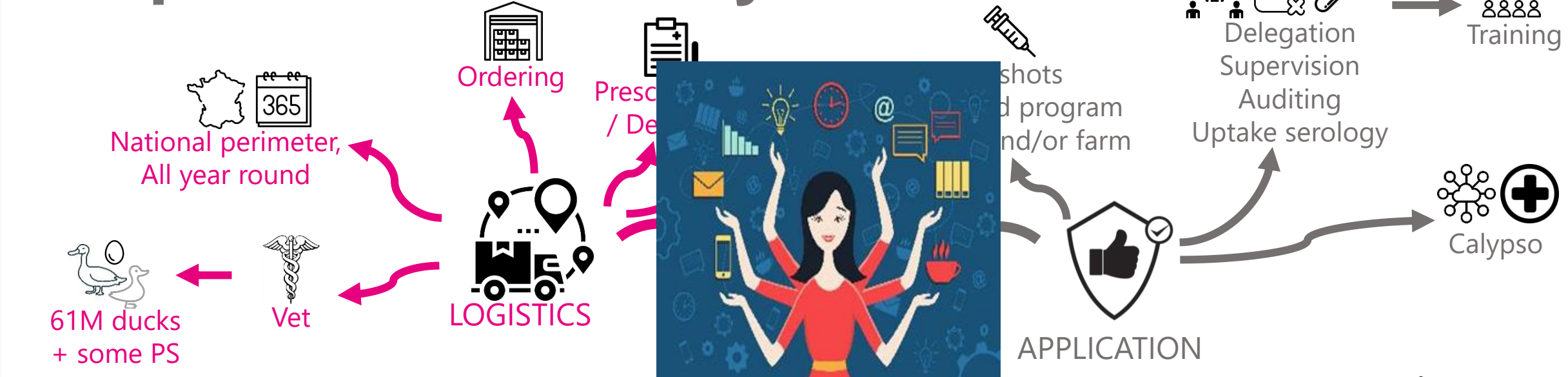
CARTOGIP

Recording farm-related data from duck industry: placement, number, age, location, vaccine status → traceability

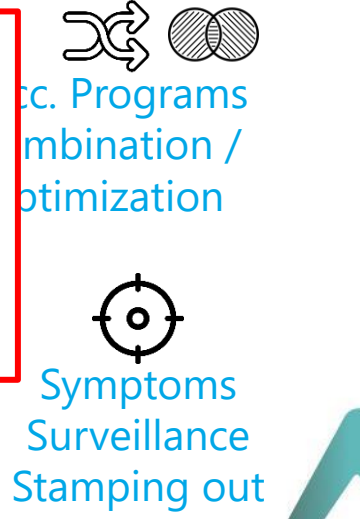
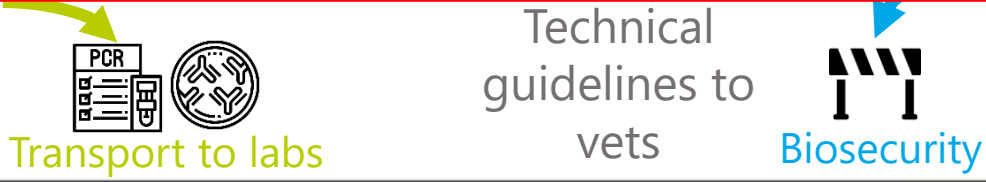
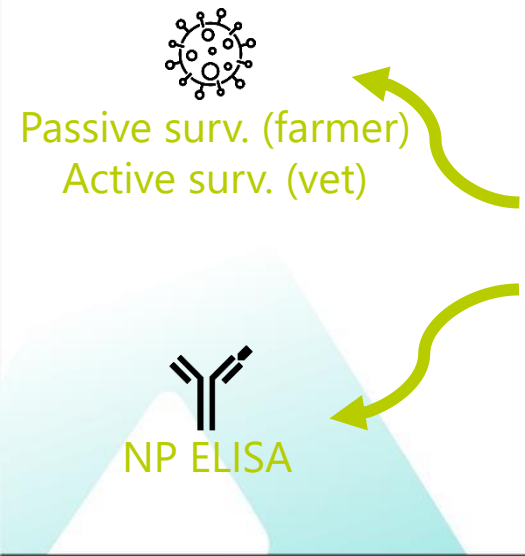
Vet practitioner's key role !



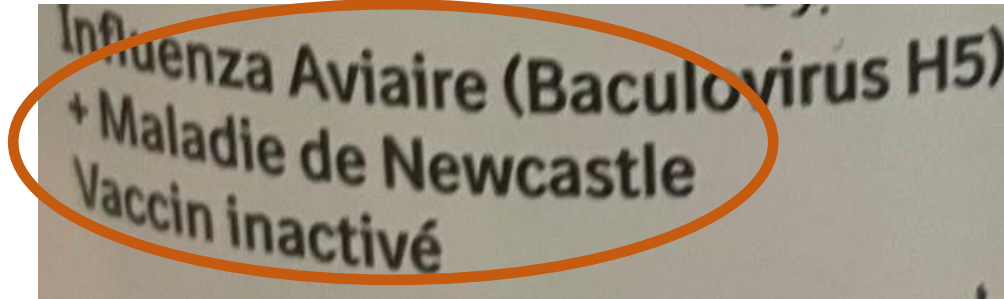
Vet practitioner's key role !



Workforce needed!
Vets and secretaries
Field / Office / Logistics



Monitoring vaccine uptake

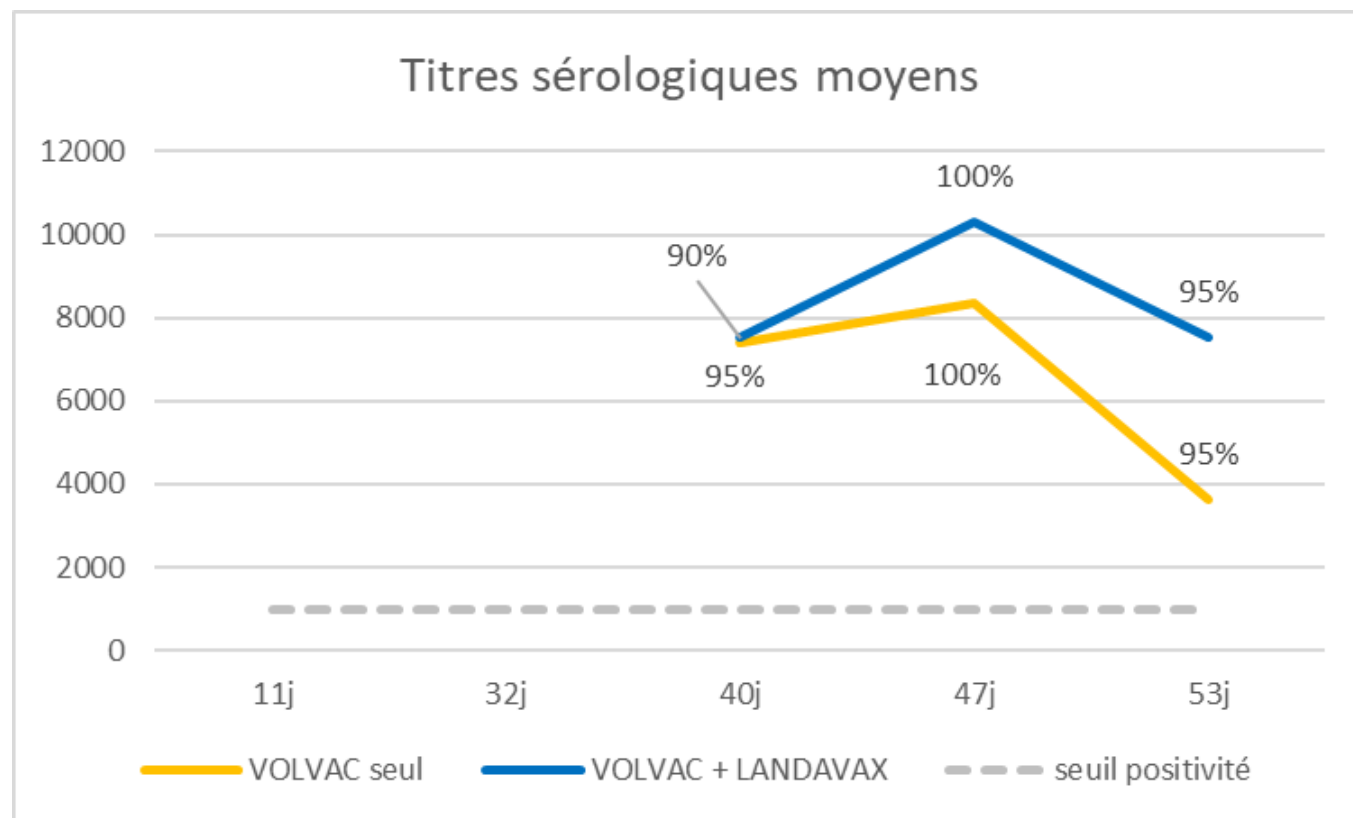


Date Prélev	AGE (j)	NEG	POS	Total général	%POS	Moyenne	âge v1	âge v2	intervalle
20231212	64	5	15	20	75,00%	2884	10	28	18
20231121	65	4	16	20	80%	3647	17	36	19
20231201	80		20	20	100,00%	8011	24	50	19
20231124	68		20	20	100%	9981	17	37	20
20231204	78		18	18	100,00%	6832	17	37	20
20231120	64	1	18	19	95%	8905	15	36	21
20231204	78	4	14	18	77,80%	4371	15	36	21
20231115	66		20	20	100%	7253	29	47	18
20231128	79		20	20	100%	6018	29	47	18



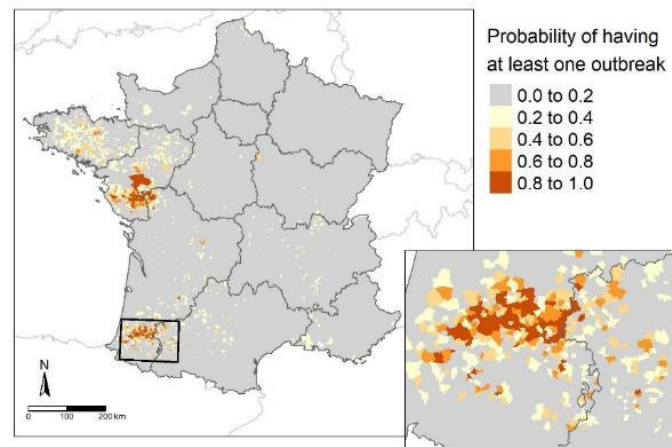
INTERPRETATION	A	%POS entre 95 et 100
(positif si titre >1000)	B	%POS entre 90 et 94.9
	C	%POS entre 80 et 89.9
	D	%POS dessous 80

Monitoring vaccine uptake



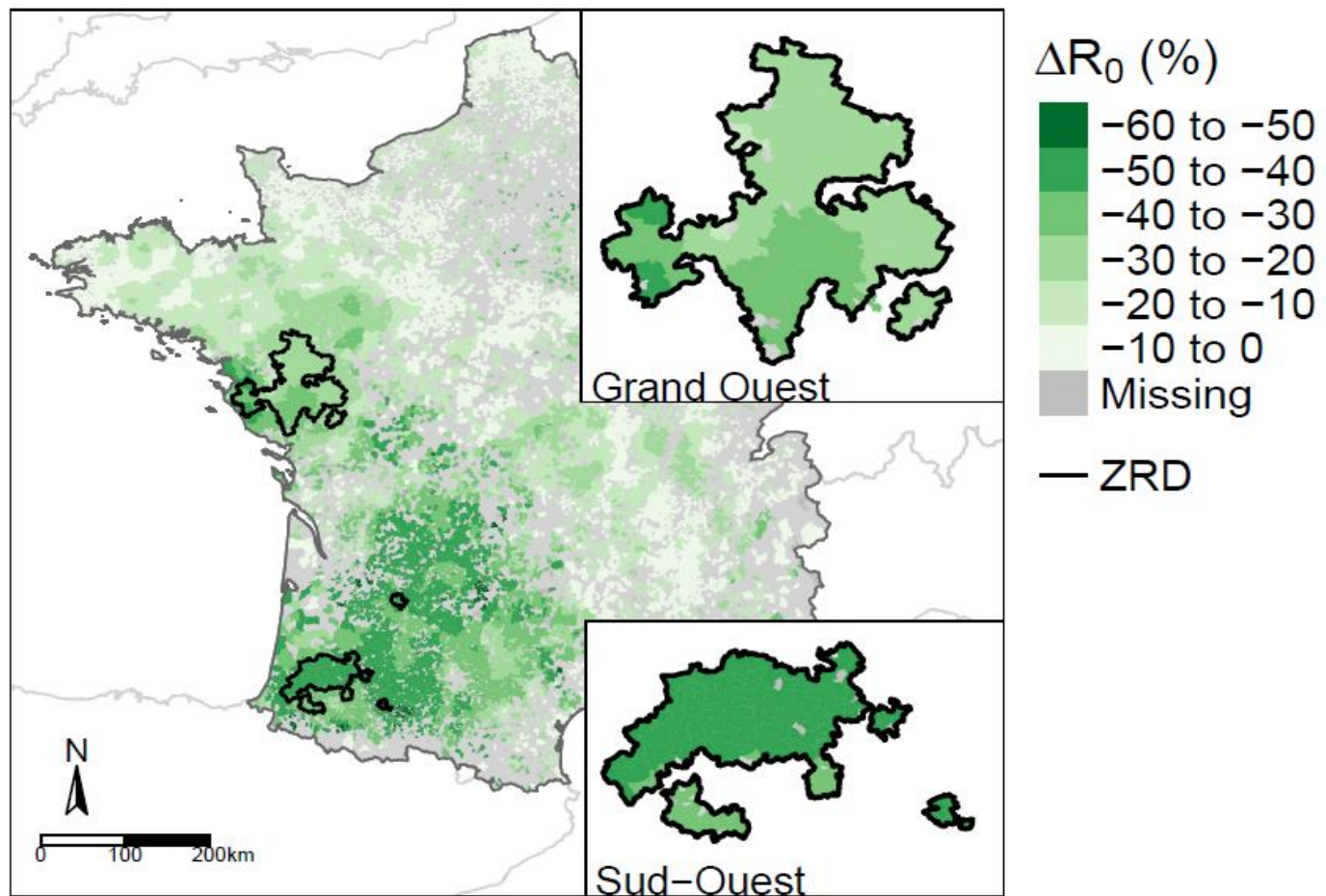
An evolving strategy

- Remains a **preventive strategy**, under European Delegated Act
- **Adjusting vaccination protocol**
 - Concerns = Duration of immunity after 10/11 wks?
 - Concerns = uneven immune response within flock
 - Adding a 3rd dose @56d on Risk Zones only
 - Adjusting breeders program



Does it work?

- Predictive models



Relative reduction of R_0 if only production sites are vaccinated

Does it work?

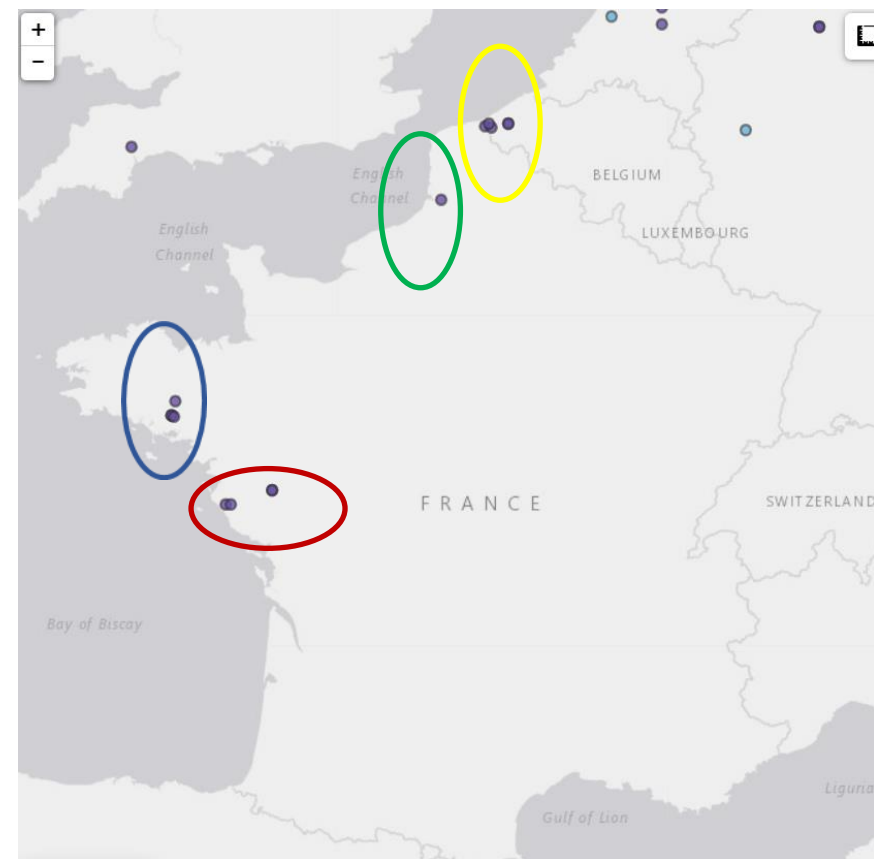
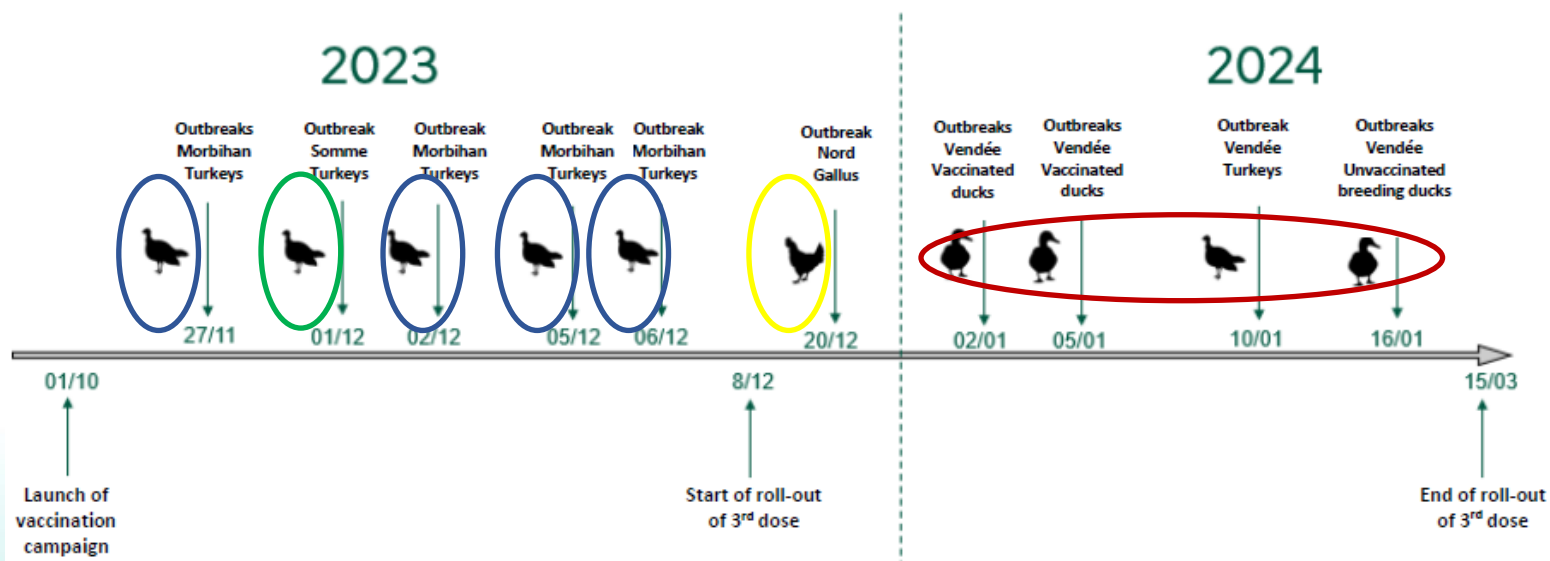
- Predictive models
- (not so high) environmental pressure



Figure 1. Localisation des cas ou foyers en avifaune sauvage, chez les oiseaux captifs et chez les volailles d'IAHP H5 en Europe ayant débuté dans le mois et la semaine précédant le 07/01/2024 inclus (source : Commission européenne ADIS le 08/01/2024, WAHIS-OMSA le 15/12/2023).

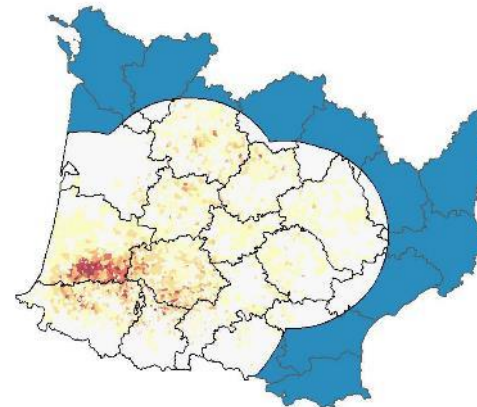
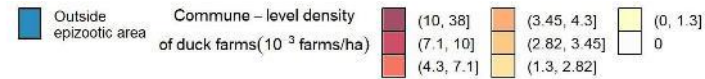
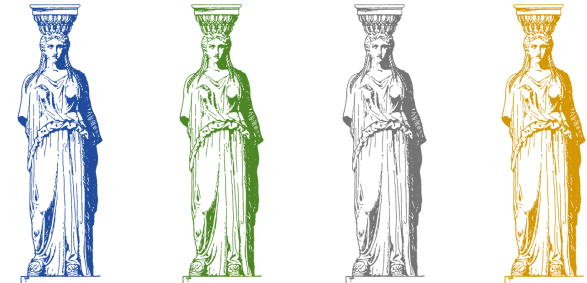
Does it work?

- Predictive models
- (not so high) environmental pressure
- 10 Outbreaks in domestic flocks



Thinking beyond

- Vaccination strategy **needs constant updates**
- **Don't break any of essential pillars !**
- **Europe (among others) is watching...**
- **Ongoing work on trade restrictions**
- **Restructuring the territory?**
 - Reduction of duck farm density
 - De-specialisation of territories



Epidemiology
Economics
Sociology

Thanks for you attention

