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4° Working Group on HPAI Vaccination

VACCINATION OF POULTRY AGAINST HPAI – PART 2 SURVEILLANCE AND RISK MITIGATION STRATEGIES

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EUROPEAN FOOD SAFETY AUTHORITY

TERM OF REFERENCES

1. Update on the available vaccines against HPAI for poultry
2. Vaccination strategies

→ available at:

https://www.efsa.europa.eu/en/efsajournal/pub/8271

3. Surveillance in the vaccinated zone and/or vaccinated establishments
4. Restrictions and risk mitigation measures to be applied in a vaccinated establishment or a vaccination zone

→ available at:

http://www.efsa.europa.eu/en/efsajournal/pub/8755

OUTLINE

3

Surveillance

Diagnostic methods

In emergency vaccination

In preventive vaccination

4

Risk mitigation strategies

In emergency vaccination

In preventive vaccination

TOR 3 – SURVEILLANCE

SURVEILLANCE ACCORDING TO DELEGATED REGULATION (EU) 2023/361

Type of vaccination	Surveillance				
	Surveillance category	**Testing procedure**	**Frequency**	**Minimum detectable prevalence/type of information collected**	**Duration**
Emergency protective	Reinforced laboratory	Virological	2 weeks	5% prevalence with 95% confidence level	According to the duration of the recovery period
	Reinforced clinical	-	-	-	-
Preventive	Enhanced passive	Virological	Weekly	Representative sample of dead birds	As long as there are vaccinated birds in the establishment
	Active	Clinical examination	30 days	Clinical examination of poultry, check of production records, check of health records of each epidemiological unit	
		Serological or virological	30 days	5% prevalence with 95% confidence level (representative sample)	

DIAGNOSTIC METHODS

DIAGNOSTIC METHODS: RECOMMENDATIONS

- The vaccination plan should already **pre-select the most appropriate diagnostic** assays
- Members States are encouraged to conduct **additional studies to collect field experience** and validation data on alternative diagnostic methods in vaccinated establishments
- The use of **diagnostic methods with high sensitivity** is recommended → **molecular methods (PCR)**
- Serological results when aiming at demonstrating **disease freedom** must be confirmed with molecular virological investigations

Seropositive results in **DIVA-vaccinated** flocks require **confirmation by molecular** assays on swab samples

EMERGENCY VACCINATION

EMERGENCY VACCINATION

Surveillance strategy	Emergency protective vaccination scenario – Surveillance within the vaccination zone			
	Strategy E1	**Strategy E2**	**Strategy E3**	**Strategy E4**
Objective of surveillance	HPAIV early detection (to be implemented also in the peri-vaccination zone)	Assessment of vaccination effectiveness	Demonstrating freedom from HPAIV in the vaccinated establishment (to authorise the movement of birds from that establishment)	Demonstrating freedom from HPAIV in the vaccinated zone

identification of HPAIV to remove the establishment before it transmits the infection to other establishments

→ **Rh** as a measure of transmission

→ **surveillance is effective** if contributes to **Rs < 1**

EMERGENCY VACCINATION: EARLY DETECTION

- The **sampling unit is the flock** and an establishment may consist of one or more flocks
- **Mathematical model** used to investigate the required **sample size** and **sampling frequency**, **sample type** for early detection by taking into account HPAI infection dynamics and the diagnostic **test sensitivity**

TABLE 3 Within-flock transmission parameters for unvaccinated and vaccinated partially protected bird flocks (i.e. 30% of the vaccinated flocks where $R > 1$).

	Chicken layers		Ducks		Turkeys	
Parameter	**Unvaccinated**[a]	**Vaccinated**[a]	**Unvaccinated**[b,c]	**Vaccinated**[c]	**Unvaccinated**[d,e]	**Vaccinated**[f]
Transmission rate (day^{-1})	1.13	0.47	4.02|10.8	1	3.2	0.64
Latent period (days)	1	1	1|1	1	1	
Infectious period$_{survive}$ (days)	3.2	6.8	7|8.1	2.7	–	4
Infectious period$_{die}$ (days)	3.2	4.5	4.9|–	–	4	4
Case fatality (range)	0.95–1	0.2–1	0–0.8	0–0.1	0.9–1	0.37–0.62
Daily mortality not attributed to HPAI (baseline mortality rate)	0.0002		0.0004		0.0007	0.0007
Mortality at day of reporting suspicion. Mean (range)	1.66 (0.25–5.27)%					
Proposing reporting thresholds	0.08 (indoor layers)–0.13 (outdoor)%					3.21%[g]

[a]Germeraad et al. (2023).

[b]Tatár-Kis et al. (2019). The value at the left of '|' come from t

[c]Grasland et al. (2023). Values for vaccinated are the upp

are for mule ducks. These values are those provided a

[d]Ssematimba et al. (2019).

[e]Reference laboratory EURL.

[f]These values are assumed since no data on transmission parameters in vaccina ed flocks could be found.

[g]No literature was found, hence we assumed a value three times higher than the 'normal' daily mortality as a potential threshold for evaluation.

Surveillance is focused on **detecting HPAIV outbreaks** in the vaccinated flocks given that the 30% of the vaccinated ones will be only partially protected

EMERGENCY VACCINATION: EARLY DETECTION

SEIRD model

to estimate number of **infectious birds, daily mortality, duration of epidemic** for vaccinated and unvaccinated flocks

Surveillance model

to quantify **reduction in infectiousness** given surveillance

to estimate **probability of escaping detection**

Rs estimation

to **compare** different **surveillance** strategies

A strategy is effective if

→ probability to **escape detection <0.01** for more than 95% of the outbreak simulations

→ **Rs < 1**

E1, LAYERS

Efficacy of surveillance options for early detection of vaccinated-infected flocks

In flocks **>3000**

Results are reported only for effective surveillance strategies

Sample type (diagnostic test)	Sample size	Sampling interval (days)	Percentage of outbreak simulations with the probabilities of escaping detection below 1%[b]	Detection time as days post introduction (median (2.5–97.5 CI))	Prevalence (%) infectious birds (median (2.5–97.5 CI))	Prevalence (%) recovered birds (median (2.5–97.5 CI))	R_h/R_s (reproduction number) (median (2.5–97.5 CI))
Passive reporting (reference)				31 (25–43)	3.93 (3.44–4.5)	2.16 (1.86–2.46)	1.4
Mortality threshold (0.13%)				28 (22–39)	2.35 (2.01–2.75)	1.26 (1.06–1.49)	1.09 (1.04–1.1)
Dead birds (qPCR)	≤5	7	99%	20 (14–31)	0.34 (0.25–0.43)	0.18 (0.11–0.24)	0.13 (0.1–0.16)
		14	90%				
		21	51%				
		30	0%				
	≤10	7	99%	18 (13–30)	0.26 (0.19–0.34)	0.14 (0.08–0.19)	0.1 (0.08–0.13)
		14	98%	21 (15–33)	0.44 (0.35–0.56)	0.23 (0.15–0.31)	0.17 (0.15–0.2)
		21	94%				
		30	84%				
	≤15	7	99%	18 (13–30)	0.26 (0.19–0.33)	0.13 (0.08–0.19)	0.1 (0.08–0.13)
		14	99%	20 (15–32)	0.41 (0.32–0.52)	0.21 (0.15–0.29)	0.16 (0.14–0.19)
		21	97%	22 (16–34)	0.56 (0.45–0.71)	0.3 (0.21–0.39)	0.22 (0.19–0.26)
		30	92%				
Live birds (qPCR)	60	14	72%				
		30	30%				
	120	14	89%				
		30	69%				
Live birds (serology)	60	14	47%				
		30	9%				

E1, DUCKS

Efficacy of different surveillance options for early detection of vaccinated-infected flocks

In flock **≥6000**

Results are reported only for effective surveillance strategies

Sample type (diagnostic test)	Sample size	Sampling interval (days)	Percentage of outbreak simulations with the probabilities of escaping detection below 1%[b]	Detection time as days post-introduction (median (2.5–97.5 CI%))	Prevalence (%) infectious birds (median (2.5–97.5 CI))	Prevalence (%) recovered birds (median (2.5–97.5 CI))	R_h/R_s (reproduction number) (median (2.5–97.5 CI))
Passive reporting (reference)				23 (19–32)	20.5 (18.9–22.3)	33.31 (29.26–37.26)	1.8
Mortality threshold (0.17%)				17 (13–26)	5.84 (4.83–7.22)	6.13 (4.9–7.28)	0.62 (0.49–0.63)
Dead birds (qPCR)	≤5	7	98%	15 (11–24)	3.09 (2.51–3.86)	3.09 (2.33–3.88)	0.21 (0.18–0.26)
		14	70%				
		21	0[b]				
		30	0%				
	≤10	7	99%	14 (11–23)	2.35 (1.87–3.02)	2.35 (1.74–3)	0.17 (0.14–0.19)
		14	97%	16 (12–25)	4.29 (3.48–5.19)	4.37 (3.34–5.38)	0.3 (0.26–0.34)
		21	89%				
		30	36%				
	≤15	7	99%	14 (10–23)	2.33 (1.86–2.96)	2.3 (1.72–2.99)	0.16 (0.14–0.19)
		14	98%	16 (12–24)	3.93 (3.18–4.8)	3.99 (2.97–4.94)	0.28 (0.24–0.32)
		21	96%	17 (13–26)	5.5 (4.54–6.68)	5.75 (4.43–6.97)	0.39 (0.35–0.44)
		30	89%				
Live birds (qPCR)	60	14	97%	17 (13–25)	4.95 (4.03–5.98)	5.05 (3.9–6.34)	0.35 (0.32–0.39)
		30	44%				
	90	14	98%	15 (12–24)	3.34 (2.64–4.11)	3.33 (2.49–4.17)	0.23 (0.21–0.26)
		30	93%				
Live birds (serology)	60	14	97%	17 (13–25)	5.16 (4.25–6.28)	5.34 (4.17–6.62)	0.36 (0.29–0.44)
		30	93%				

E1, TURKEYS

Efficacy of different surveillance options for early detection of vaccinated-infected flocks

In flock **≥6000**

Results are reported only for effective surveillance strategies

Sample type (diagnostic test)	Sample size	Sampling interval (days)	Percentage of outbreak simulations with the probabilities of escaping detection below 1%[b]	Detection time as days post introduction (median (2.5–97.5 CI))	Prevalence (%) infectious birds (median (2.5–97.5 CI))	Prevalence (%) recovered birds (median (2.5–97.5 CI))	R_h/R_s (reproduction number) (median (2.5–97.5 CI))
Passive reporting (reference)				27 (21–38)	4.1 (3.51–4.79)	3.31 (2.83–3.83)	1.6
Mortality threshold (0.21%)				24 (19–34)	2.5 (2.07–2.96)	1.97 (1.64–2.34)	1.42 (1.68–1.04)
Dead birds (qPCR)	≤ 5	7	95%	19 (14–31)	0.66 (0.53–0.81)	0.52 (0.38–0.66)	0.28 (0.23–0.34)
		14	66%				
		21	5%				
		30	0[b]				
	≤ 10	7	99%	16 (11–28)	0.33 (0.25–0.44)	0.25 (0.16–0.36)	0.14 (0.11–0.18)
		14	94%				
		21	77%				
		30	59%				
	≤ 15	7	99%	15 (10–27)	0.26 (0.18–0.35)	0.2 (0.12–0.29)	0.11 (0.09–0.14)
		14	98%	18 (12–29)	0.46 (0.35–0.6)	0.35 (0.25–0.48)	0.2 (0.17–0.24)
		21	94%				
		30	87%				
	≤ 20	7	99%	15 (10–27)	0.25 (0.17–0.33)	0.18 (0.12–0.27)	0.1 (0.08–0.13)
		14	98%	17 (12–29)	0.42 (0.31–0.53)	0.31 (0.22–0.43)	0.18 (0.15–0.21)
		21	96%	19 (13–30)	0.59 (0.48–0.75)	0.45 (0.33–0.6)	0.26 (0.22–0.3)
		30	93%				
Live birds (qPCR)	60	14	70%				
		30	21%				
	90	14	82%				
		30	55%				
Live birds (serology)	60	14	61%				
		30	22%				

EMERGENCY SURVEILLANCE IN PERI-VACCINATION ZONE

Radius

- to contain the spread of the disease avoiding any jump outside the area with 95% confidence → a **10 km zone radius** would be needed (worst case probability of jump spread 0.004 with probability of containment equal to 96%)

Type of surveillance

- **vaccinated** establishments → the options are those for E1
- **unvaccinated** establishment → passive surveillance in gallinaceous species and weekly bucket sampling of all dead birds (up to 15) in Anseriformes

EMERGENCY VACCINATION: RECOMMENDATIONS

- **Molecular testing of dead** birds is recommended for early detection surveillance
- The effectiveness of surveillance is increased by the **repeated sampling** in time
- **Chicken layers** (≥ 3000), **ducks** (≥ 6000) and **turkeys** (≥ 6000): a number of effective options testing **dead birds** have been identified
- **Ducks** (≥ 6000): alternatives can be carried out testing **live** ducks or based on **mortality threshold but not recommended**
- Effective options should be selected according to country's specific circumstances and resources

PREVENTIVE VACCINATION

PREVENTIVE VACCINATION

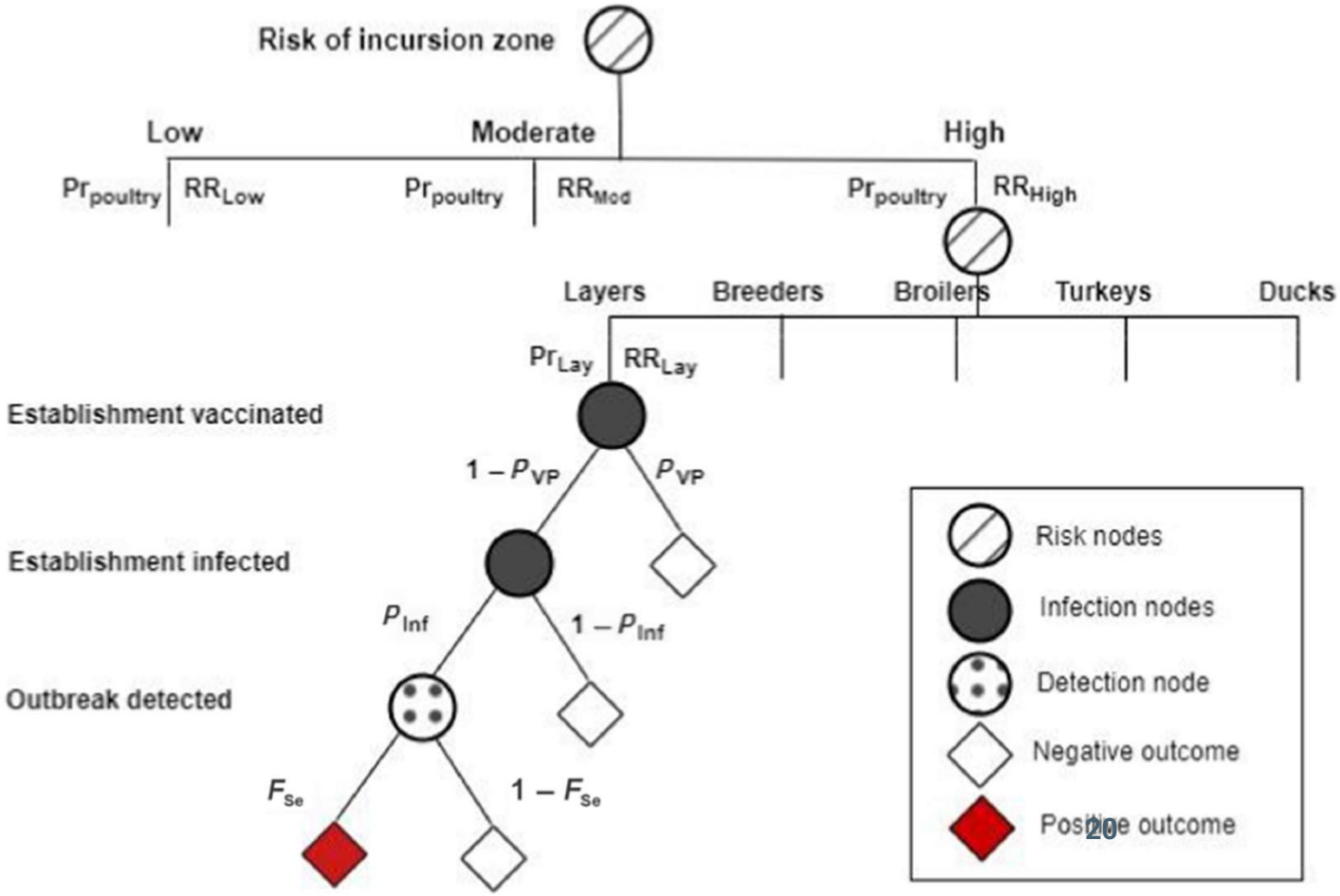
Surveillance strategy	Preventive vaccination scenario – Surveillance within vaccination zone			
	Strategy P1	**Strategy P2**	**Strategy P3**	**Strategy P4**
Objective of surveillance	Early detection in case of HPAIV introduction	Assessment of level of immune response induced by vaccination	Demonstrating freedom from HPAIV in the vaccinated establishment (to authorise the movement of birds from that establishment)	Demonstrating freedom from HPAIV in the vaccinated area (considering that also non-vaccinated establishments might be present)

the probability that at least one infected establishment is detected by the surveillance

probability that the population is free from HPAI, given that surveillance did not detect any infected establishment and assuming perfect specificity

PREVENTIVE VACCINATION: APPROACH

- **Scenario tree models** to estimate the sensitivity of the surveillance system to **demonstrate freedom** and to **early detect** HPAI
- Multiple **risk nodes and probability nodes**
- **All vaccinated** establishments under surveillance vs random sampling of a **representative number** of establishments



PREVENTIVE VACCINATION: APPROACH

- Results based on simulated scenarios in high-risk zones for HPAI in NL (chicken layers), IT (turkeys) and FR (ducks) as per Opinion part 1
- Active surveillance is assumed in all vaccinated flocks by collecting **every 30 days** in a 48-h period all **dead birds** up to a number of **15** to be tested **by qPCR**, while passive surveillance is applied in unvaccinated flocks
- Scenarios with variations in sampling intervals (30, 15 and 7 days) and **proportions of vaccinated flocks** (100%, **50%** and **25%**) were explored

PREVENTIVE VACCINATION: ASSESSMENT

Chicken layers

Farm type	Number of establishments in the high-risk zone	Time frame (days)[a]	Sensitivity of surveillance component (CSe)[b]	Early detection sensitivity (EDSe)[c]	Surveillance system sensitivity (TotalSe)[d]	Probability of freedom (Pfree)[e]
Unvaccinated breeder flocks	1	16 (14–23)	0.02 (0.01–0.03)	0.02 (0.01–0.03)	0.95 (0.70–0.99)	0.997 (0.985–0.999)
Unvaccinated broiler flocks	33	16 (14–23)	0.20 (0.08–0.34)	0.19 (0.07–0.32)		
Unvaccinated duck flocks	2	6 (5–8)	0.16 (0.07–0.28)	0.15 (0.07–0.25)		
Vaccinated Layer flocks	**242**	31 (25–43)	0.93 (0.56–0.99)	0.92 (0.56–0.99)		
Unvaccinated turkey flocks	1	7 (6–9)	0.07 (0.03–0.13)	0.06 (0.03–0.12)		

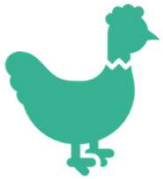
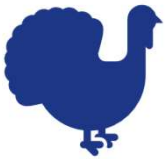
Ducks

Farm type	Number of establishments in the high-risk zone	Time frame (days)[a]
Unvaccinated breeder flocks	625	16 (14–23)
Unvaccinated broiler flocks	3194	16 (14–23)
Vaccinated duck flocks	**1907**	21 (17–30)
Unvaccinated layer flocks	1000	16 (14–23)
Unvaccinated turkey flocks	154	7 (6–9)

Turkeys

Farm type	Number of establishments in the high-risk zone	Time frame[a] (days)	Sensitivity of surveillance component (CSe)[b]	Early detection sensitivity (EDSe)[c]	Surveillance system sensitivity (TotalSe)[d]	Posterior probability free (Pfree)[e]
Unvaccinated breeder flocks	120	16 (14–23)	0.89 (0.68–0.99)	0.71 (0.58–0.71)	0.99 (0.99–1.00)	0.999 (0.999–1.00)
Unvaccinated broiler flocks	501	16 (14–23)	0.93 (0.36–0.99)	0.72 (0.34–0.80)		
Unvaccinated duck flocks	10	6 (5–8)	0.35 (0.13–0.79)	0.30 (0.12–0.58)		
Unvaccinated layer flocks	300	16 (14–23)	0.99 (0.98–1)	0.77 (0.74–0.81)		
Vaccinated turkey flocks	**385**	27 (21–38)	0.99 (0.97–1)	0.93 (0.83–1)		

PREVENTIVE VACCINATION: ASSESSMENT

	Proportion of vaccinated establishments under surveillance				
	100%	50%	25%	EDSe	Pfree
	monthly	-	weekly	>92%	>99%
	monthly	every 2 weeks	-	>74%	>98%
	monthly	-	weekly	>93%	>98%

PREVENTIVE VACCINATION: RECOMMENDATIONS

- **Molecular** virological testing of up to **15 dead birds every 30** days in vaccinated flocks is recommended to effectively **demonstrate disease freedom with > 99% confidence** within high-risk zones for HPAIV infection
- If the aim is to **increase the early detection** surveillance sensitivities, then it is recommended to **reduce the sampling intervals**
- Maintaining **passive surveillance efforts in unvaccinated** establishments in vaccinated zones is recommended to enhance the overall sensitivity of the surveillance system

TOR 4 – RISK MITIGATION STRATEGIES

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To enable safe movement of vaccinated birds EFSA recommends:

Emergency vaccination

- existing rules set out in Reg 2023/361 and Reg 2020/687 are valid and **molecular testing is recommended:** all up to a number of 15 dead birds no earlier than 72 h before movement
- testing could coincide with the sampling session of the surveillance in place

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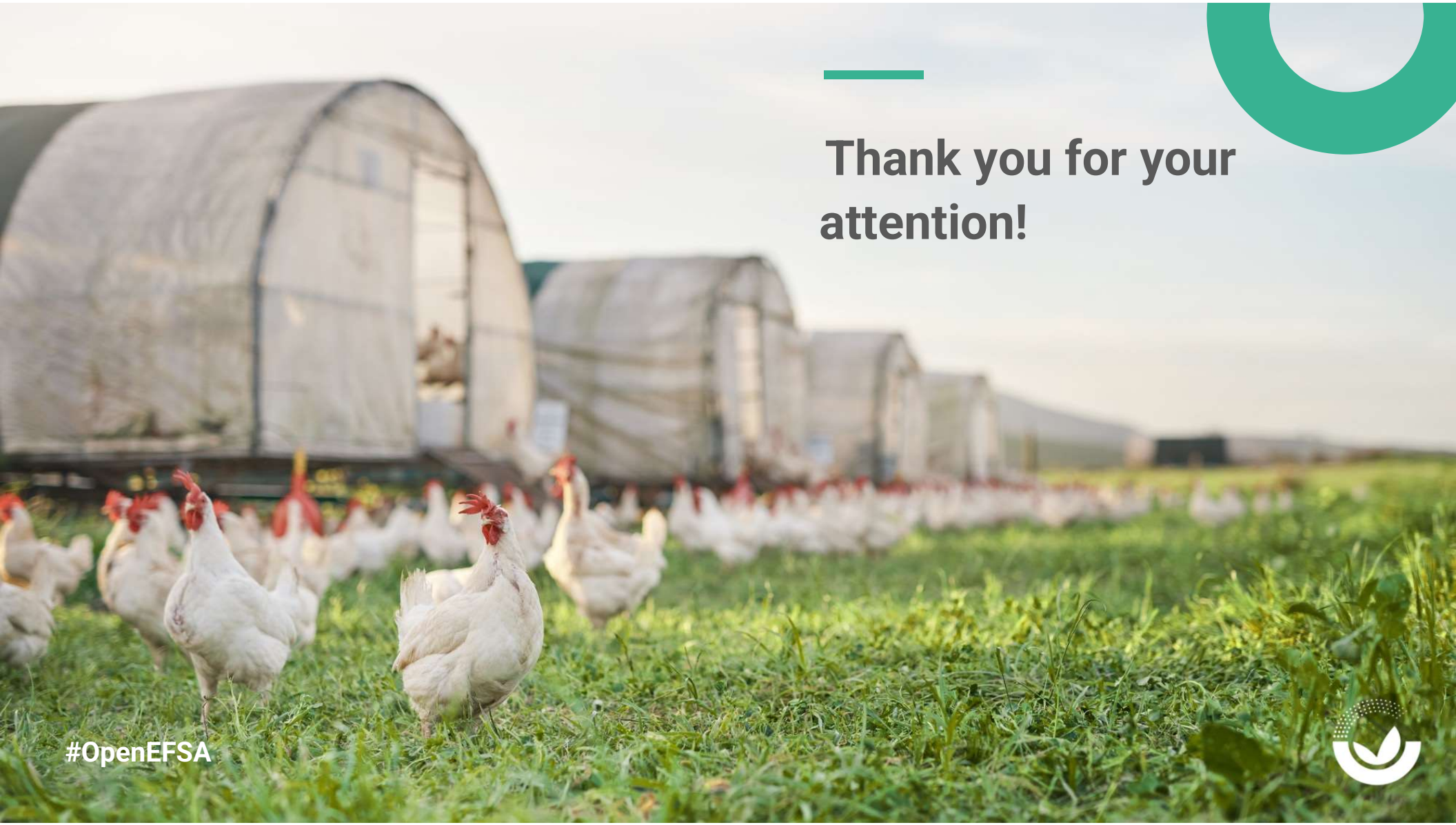
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