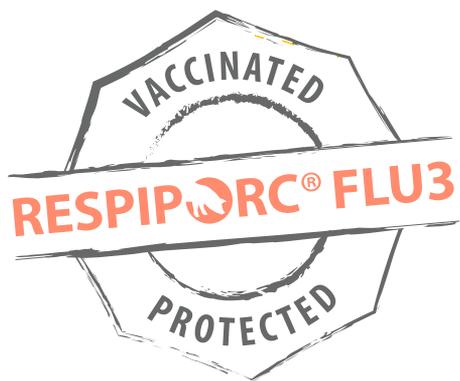




**BUNDLED POWER
FOR BROADEST INFLUENZA
PROTECTION.**



Together, beyond animal health



Protecting against influenza – protecting your farm

An increasing number of pig farms are permanently infected with influenza, often involving several strains and resulting in recurrent infections with atypical clinical symptoms.



Pathogen

Influenza A virus, Orthomyxoviridae

Subtypes are classified according to the presence of haemagglutinin (HA) and neuraminidase (NA) on the surface of the cell membranes of the virus.

Frequent viral pathogen of the respiratory tract in pigs and an important part of the PRDC.



Clinical course

The disease can affect pigs and piglets at any age.

Acute form

- Fever, coughing, dyspnea, apathy, anorexia

Endemic form

- Persistence of pathogen in the herd
- Non-specific clinical signs: reduced vitality, reproduction disorders in sows (return to oestrus, abortions), occasionally fever followed by hypothermia, sporadic coughing

Pandemic influenza can be part of both clinical manifestations.



Diagnosis

Virus detection: nasal swabs, lung tissue samples, BALF and oral fluids

Serology (preferably nonvaccinated animals): serum samples, if needed paired samples



Therapy

None since it is a viral infection which means that at best, clinical signs or secondary bacterial infections can be treated. **Prophylaxis** is the best protection.

Prophylaxis

Trust the **broadest protection** with the bundled power of the unique influenza vaccine portfolio of Ceva: the trivalent **RESPIPORC FLU3** vaccine against the classical (H1N1, H1N2, H3N2) influenza strains and the **RESPIPORC FLU PAN H1N1** against the pandemic strains.



For further information and the latest news on influenza please visit
www.swine.ceva.com/products/vaccines/swine-influenza

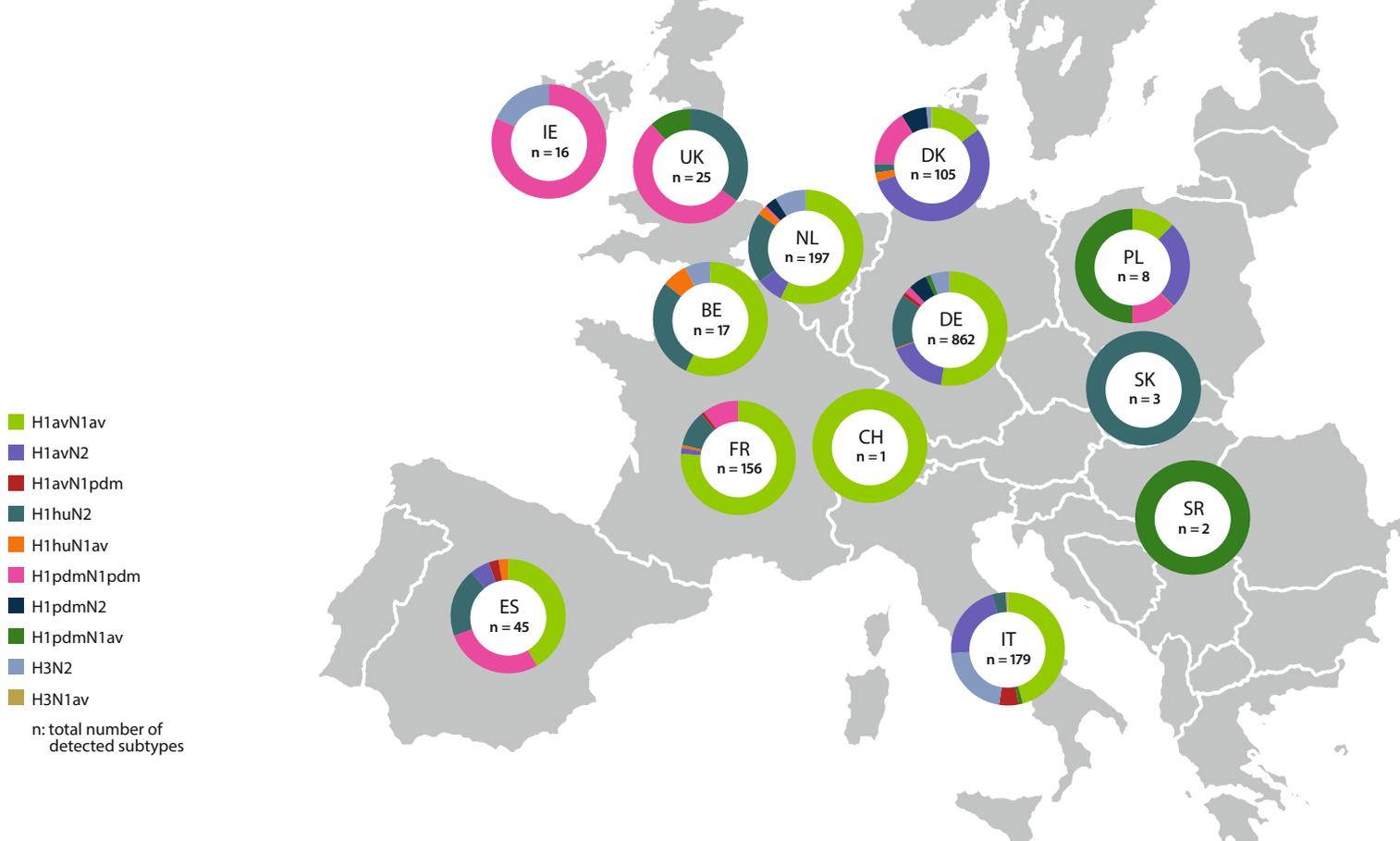
Classical influenza strains are widely established, pandemic influenza is on the rise

Ceva offers diagnostic support to determine the SIV situation in the field by providing technical support and intensive cooperation with veterinarians and leading scientists.

“The passive surveillance, which was carried out in the frame of this thesis from April 2015 to December 2017, comprised over 18,000 samples from almost 2,500 farms from 17 European countries. It targeted samples collected from pigs showing a clinically apparent respiratory disease. [...]”

A high incidence of IAV-infections in about one quarter of the pigs were detected in a season-independent manner. More than half of the participating farms were affected. Findings included all four swine influenza A virus (SIV) lineages and various reassortants between them. Increased detection of pandemic H1N1/2009, its reassortants and co-infections with different H1-subtypes were repeatedly documented.”

Diss. D. Henritzi, 2019

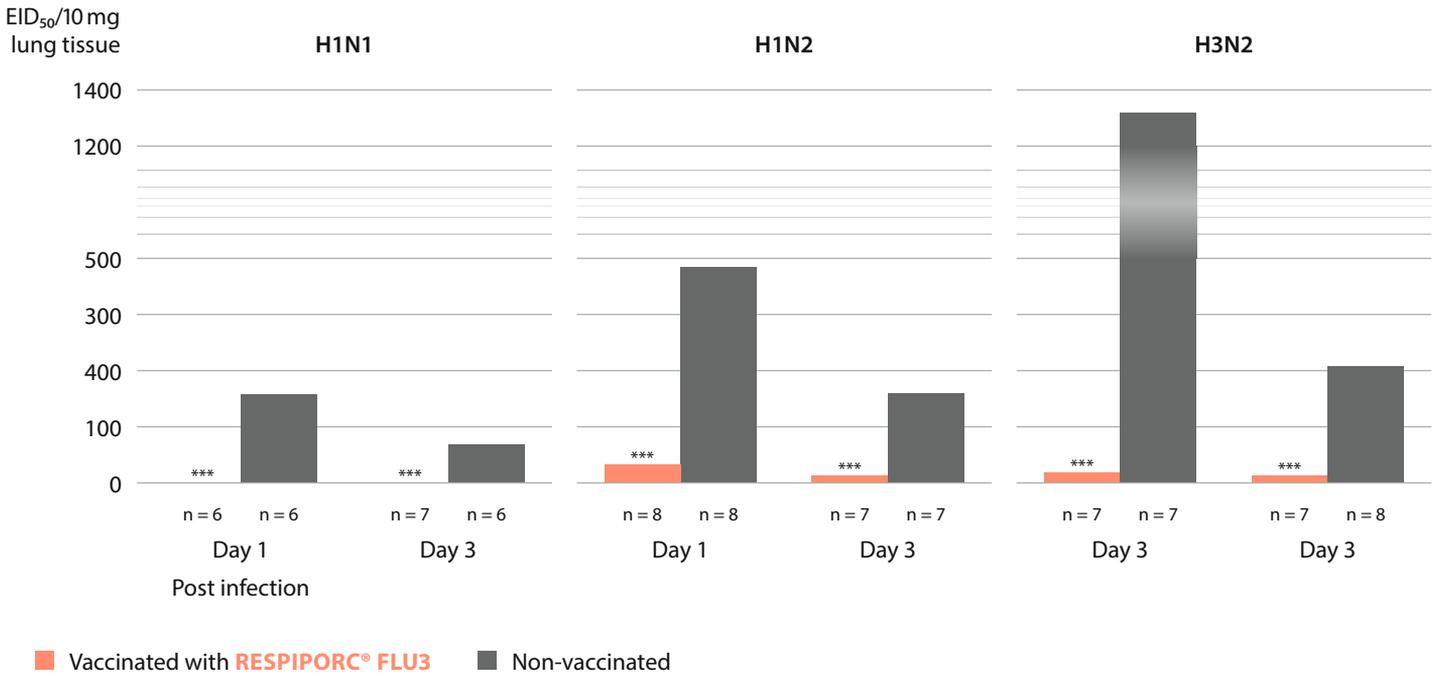


The graphic was modified after the dissertation of Dinah Henritzi, Epidemiology of swine influenza viruses in Europe: Surveillance of domestic pig populations in several European countries 2015-2017, Hannover, 2018

Source Italy: modified acc. to Simon et al. (2014) PLOS ONE | DOI:10.1371/journal.pone.0115815 December 26, 2014

RESPIPORC® FLU3 is protective against all predominant classical influenza strains in the field

RESPIPORC® FLU3 reduces the virus load in the lungs significantly¹



RESPIPORC® FLU3 reduces the dyspnoea score significantly¹



¹ Challenge trials from the registration dossier of Respiporc FLU3: Record F/S/0135/07, Challenge strain: FLUAV/sw/Bad Griesbach/IDT5604/2006 (H1N1); Record F/S/0949/07, Challenge strain: FLUAV/sw/Kitzen/IDT6142/2007 (H1N2); Record F/S/0512/07, Challenge strain: FLUAV/sw/Damme/IDT5673/2006 (H3N2);

A total of 84 56-day-old pigs were similarly divided into six groups for aerosol challenge with three different influenza strains. Pigs vaccinated twice with Respiporc FLU3 (on day 56 and day 77 of age) and non-vaccinated pigs were compared.

The pigs were assigned to each of the groups in similar numbers and challenged 7 days after the vaccinated pigs got their second dose of Respiporc FLU3.

Half of the pigs were euthanised on day 1 and the other half of the pigs on day 3. The virus lung load was determined with the egg infectious dose 50 (EID50) by infecting embryonated chicken eggs either with homogenized and titrated lung tissue from day 1 or day 3 after the challenge.

The resulting virus load was calculated for 10 mg lung tissue used for isolation. The course of body temperature and dyspnoea scores were recorded at 6 different points in time between 0 and 72 hours after the challenge.

Economic impact of an influenza outbreak

NEW DATA

In a 700-sows breeding herd, gilts in quarantine and in the mating room were infected with H1avN1 swIAV

2015 Dec	2016 Jan	2016 Feb	2016 Mar	2016 Apr	2016 May	2016 Jun	2016 Jul	2016 Aug	2016 Sep	2016 Oct	2016 Nov	2016 Dec	2017 Jan	2017 Feb	2017 Mar
							GILTS NOT EXPOSED		GILTS EXPOSED		DIFFERENCE				
Number of considered gilts							117 (6 batches)		108 (6 batches)						
Fertility rate							95.1 %		83.2 %		- 11.9				
Antipyretic treatment cost (monthly average)							37 €		512 €		+ 475 €				
Economic impact of this swIAV exposure per infected gilt									16 €/gilt						

Valérie Normand et al., Economic impact of an influenza outbreak in replacement gilts from a 700 sow herd and clinical satisfaction after Respiporc® FLU3 implementation, ESPHM 2019

RESPIPORC® FLU3 protects clinically against new H1N2 variant

NEW DATA

Challenge with H1N2 Virus
(first isolated in the 1990s)

5x 	5x 
NON-VACCINATED	VACCINATED
✗ Typical clinical symptoms	<ul style="list-style-type: none"> ✓ Effective cellular response ✓ Clinical protection fulfilled ✓ Sufficient production of neutralising antibodies ✓ No excretion of the virus

Challenge with a new H1N2
(detected 2013 in France)

5x 	5x 
NON-VACCINATED	VACCINATED
✗ Typical clinical symptoms, more severe	<ul style="list-style-type: none"> ✓ Effective cellular response ✓ Clinical protection fulfilled ✓ Few post-vaccine neutralising antibodies ✓ Excretion of the virus not completely blocked

Céline DEBLANC et al., Study of pig responses to infection with a new variant of H1N2 influenza virus and evaluation of vaccine protection, Journées Recherche Porcine, 51, 259-264, 2019

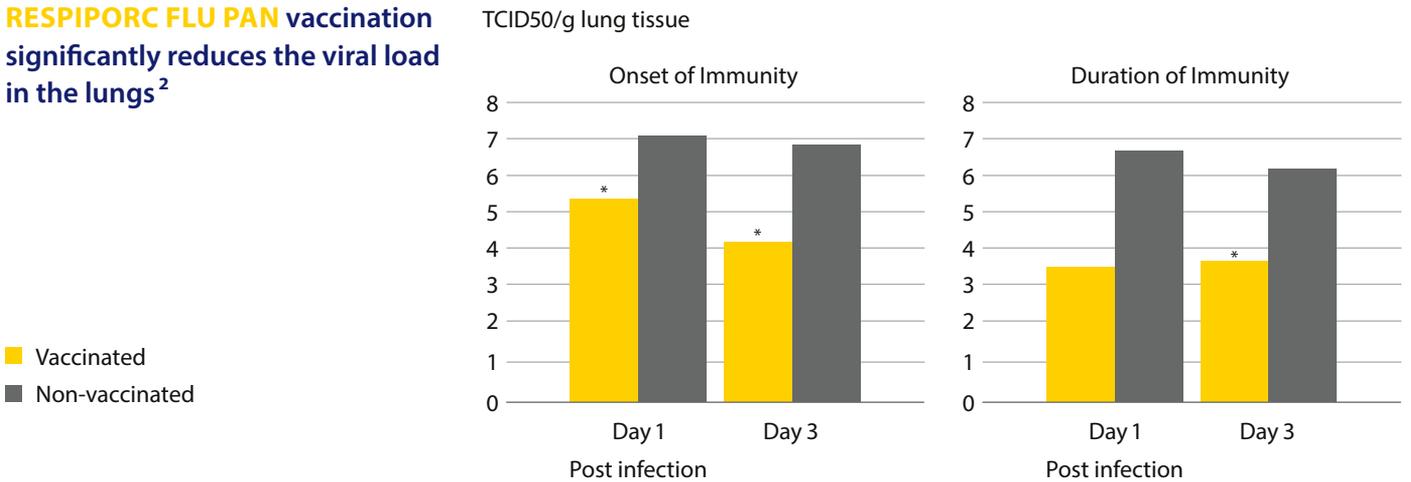
RESPIPORC® FLU3 vaccination schedule, effective for all farm types



For sows: Vaccination and booster can be conducted at any stage of gestation and also through lactation. Vaccination of the sow two weeks before farrowing will protect the piglets until 33rd day of life. **For pigs:** Vaccination from the 56th day of life.

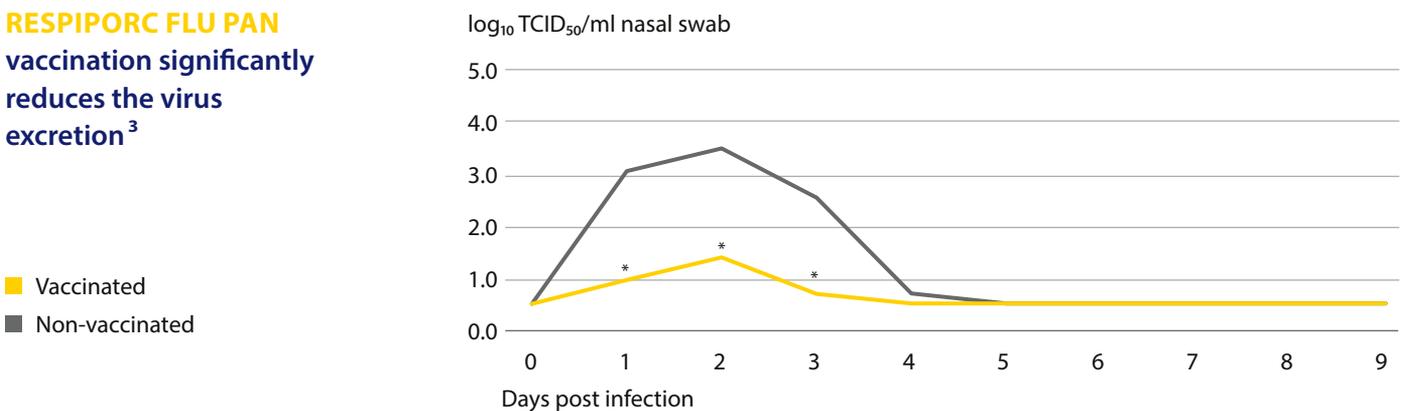
RESPIPORC® FLU PAN is protective against pandemic influenza strains in the field

RESPIPORC FLU PAN vaccination significantly reduces the viral load in the lungs²

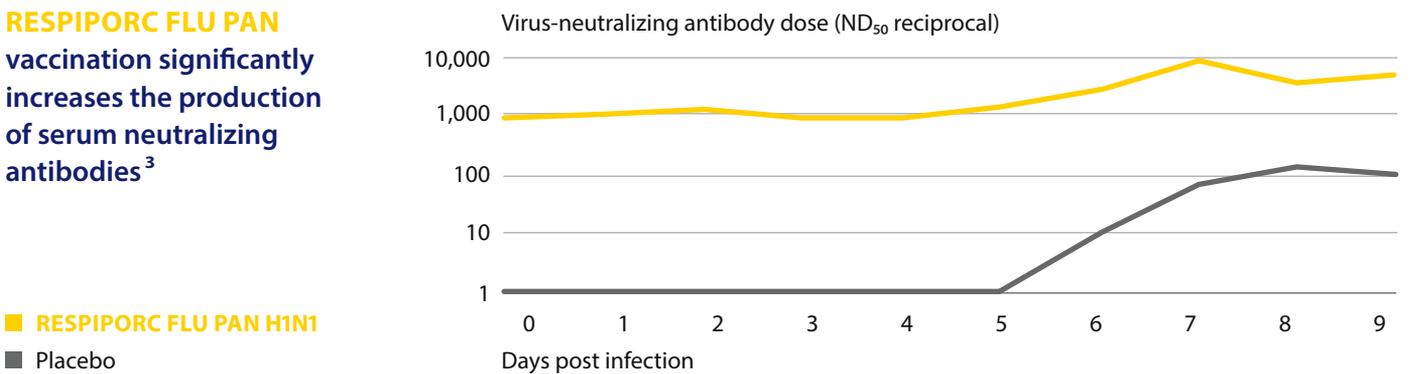


² 16 54-day-old pigs (OOI) and 19 53-day-old pigs (DOI) per group respectively were aerosol challenged with the strain FLUAV/sw/Schallern/IDT19989/2014 panH1N1. Pigs vaccinated twice with Respiporc FLUPAN H1N1 on day 54 (53) and day 85 (84), and non-vaccinated pigs were compared. The pigs were assigned to each of the groups in similar numbers and challenged either 7 days (OOI) or 3 months (DOI) after the vaccinated pigs got their second vaccination with Respiporc FLUPAN H1N1. A part of the pigs were euthanised on day 1 and another part on day 3. The virus lung load was determined with the tissue culture infectious dose 50 (TCID50) by titrating lung tissue homogenate in cell culture. The resulting virus load was calculated for 1 g lung tissue used for isolation.

RESPIPORC FLU PAN vaccination significantly reduces the virus excretion³



RESPIPORC FLU PAN vaccination significantly increases the production of serum neutralizing antibodies³



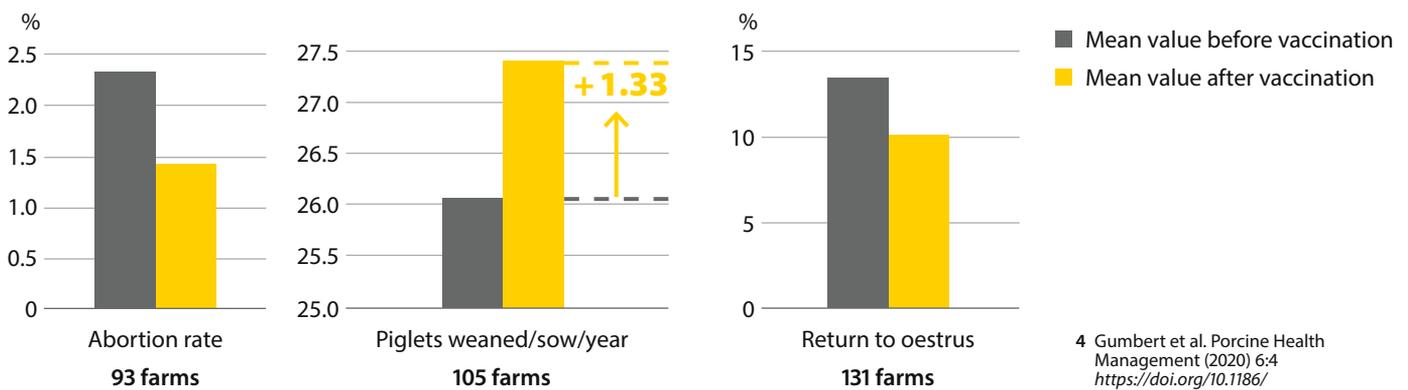
³ In total the study included 39 pigs 53–55 days old. 19 pigs received vaccination with Respiporc FLUPAN H1N1 and a second vaccination 3 weeks later. The non-vaccinated group contained 20 pigs. Seven days after the second administration of the vaccine the challenge was conducted with a heterologous pandemic H1N1 strain FLUAV/sw/Teo(Spain)/AR641/2016 panH1N1. Virus shedding followed a marked pattern. Vaccinated pigs shed significantly less virus in comparison to unvaccinated ones on study days 1–3. After infection antibodies raised to very high titres. Unvaccinated pigs were found seronegative at the time of challenge and developed less pronounced antibody titres after infection.

2, 3 Challenge trials from the registration dossier of Respiporc FLU PAN H1N1: ²TV 001/15 (OOI, 7 days) and TV 242/14 (DOI, 3 months) and ³TV 158/16 (Field/OOI2) respectively Pesch et al., Development of a monovalent pig vaccine based on a human pandemic H1N1 (2009) strain, ESPHM 2018, Barcelona

RESPIPORC® FLU PAN improves reproduction data significantly

NEW DATA

Reproductive performance in sow herds infected with pandemic influenza A virus was evaluated before and after implementation of the vaccination with RESPIPORC® FLU PAN⁴.



Sows are protected during the whole reproduction cycle, during pregnancy, suckling period and mating.

Breeding farms experience a positive return on investment (ROI).

1.33 extra piglets weaned per sow per year pays back 5.11 times the cost of the yearly vaccine treatment (considering 3 vaccinations in sows and 2 in gilts).

Considering that 1 time pays back the vaccine, the other **4.11 times are benefit**.

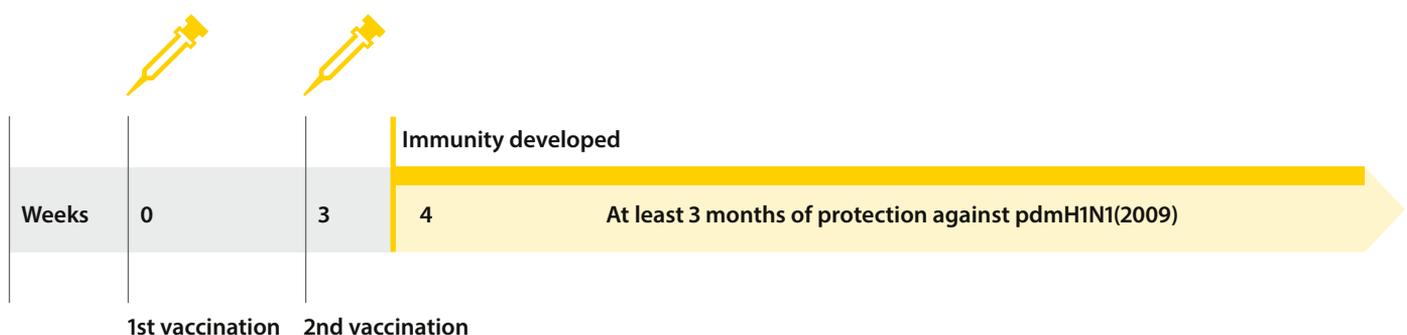
This represents **€28,000 per year in a 1000-sow farm** (based on costs of production, not market price).

Source: economical calculator of SIP Consultors, Barcelona, Spain



The video shows authentically an acute outbreak of pandemic influenza in a sow herd and the devastating impact on the piglets.

RESPIPORC® FLU PAN H1N1 vaccination schedule



Vaccination of pigs from the 56th day of life.

RESPIPORC® FLU3

RESPIPORC® FLU PAN

The innovative, differentiated and unique solution against SIV.

Broadest protection by bundled power

Positive ROI by improved reproduction parameters⁴

Unique diagnostic support



For further information on diagnostic support please visit
www.swine.ceva.com/products/vaccines/swine-influenza



RESPIPORC FLU3 Suspension for injection for pigs. **Composition:** Each dose of 2 ml contains: Active substances: Strains of inactivated influenza A virus/swine/Bakum/IDT1769/2003 (H3N2) $\geq 10.53 \log_2$ GMNU¹, Haselünne/IDT2617/2003 (H1N1) $\geq 10.22 \log_2$ GMNU¹, Bakum/1832/2000 (H1N2) $\geq 12.34 \log_2$ GMNU¹, Adjuvant: Carbomer 971 P NF 2.0 mg, Excipient: Thiomersal 0.21 mg **Indications:** Active immunisation of pigs from the age of 56 days onwards including pregnant sows against swine influenza caused by subtypes H1N1, H3N2 and H1N2 to reduce clinical signs and viral lung load after infection. Onset of immunity: 7 days after primary vaccination, Duration of immunity: 4 months in pigs vaccinated between the age of 56 and 96 days and 6 months in pigs vaccinated for the first time at 96 days and above. Active immunisation of pregnant sows after finished primary immunisation by administration of a single dose 14 days prior to farrowing to develop high colostral immunity which provides clinical protection of piglets for at least 33 days after birth. **Contraindications:** None. **Adverse reactions:** A transient slight swelling may occur on very rare occasions after vaccination at the site of injection, regressing within 2 days. On very rare occasions, a slight transient rectal temperature increase might occur after vaccination ("very rare" corresponds to a frequency of adverse reactions less than 1 animal in 10,000 animals, including isolated reports). **Withdrawal period:** Zero days. **To be supplied only on veterinary prescription!** **Marketing authorisation holder:** IDT Biologika GmbH, Am Pharmapark, 06861 Dessau-Rosslau, Germany. ¹GMNU = Geometric mean of neutralizing units induced in Guinea pigs after twice immunisation with 0.5ml of this vaccine

Respiporc FLUPAN H1N1 Suspension for injection for pigs. **Composition:** Each dose of 1 ml contains: Active substance: Inactivated influenza A virus/human Strain: A/Jena/VI5258/2009(H1N1)pdm09 16–64 HU1 Adjuvant: Carbomer 971 P NF 2 mg Excipient: Thiomersal 0.1 mg. **Indication:** Active immunisation of pigs from the age of 8 weeks onwards against pandemic H1N1 porcine influenza virus to reduce viral lung load and virus excretion. Onset of immunity: 7 days after primary vaccination. Duration of immunity: 3 months after primary vaccination. **Contraindications:** None. **Adverse reactions:** A transient increase in rectal temperature, not exceeding 2 °C, is common after vaccination and this does not persist for more than one day. A transient swelling up to 2 cm³ may occur at the site of injection, these reactions are common but resolve within 5 days. **Withdrawal period:** Zero days. **To be supplied only on veterinary prescription!** **Marketing authorisation holder:** IDT Biologika GmbH, Am Pharmapark, 06861 Dessau-Rosslau, Germany. * 1 HU = haemagglutinating units in the vaccine. * Colony Forming Units

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