COGLAPEST®

PUBLISHED IN "VACCINES"

Published in the special issue of the prestigious scientific journal VACCINES: «Development and Application of New Vaccine against Classical Swine Fever Virus»

The ideal vaccine to use in:

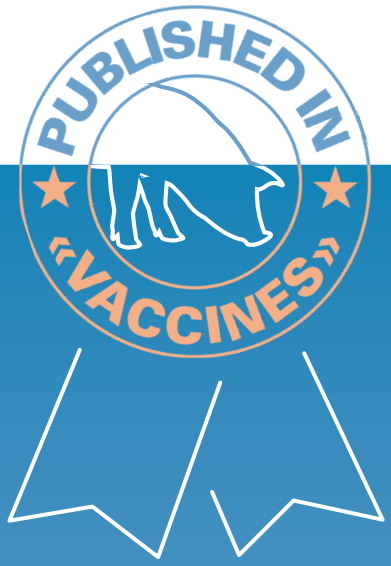
endemic regions

critical emergency situations

1st CHOICE AGAINST CLASSICAL SWINE FEVER

COGLAPEST®

ceva



PUBLISHED IN THE SPECIAL ISSUE OF THE PRESTIGIOUS SCIENTIFIC JOURNAL VACCINES :

«Development and Application of New Vaccine against Classical Swine Fever Virus»

COGLAPEST®, an OIE-recommended vaccine, **conferred solid clinical and virological protection, even against possible reinfection**.

Considering its efficacy and rapid protection capacity, this vaccine may be useful for endemic situations with continuous circulation of virus, as well as for vaccination in emergency situations.

Thus, **COGLAPEST**® is an attractive vaccine for CSFV control worldwide, particularly in current endemic situations where new viral escape mutants may be circulating.

COGLAPEST® continues to show novel applications, such as its safety and **capacity to protect as early as 5 dpv**, that suggest it as an alternative for vaccination in emergency situations.[1]

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BACKGROUND

Classical swine fever virus (CSFV) remains a challenge for the porcine industry. It is a re-emerging disease in swine, despite several years of intensive eradication programs. Inefficient vaccination programs in some endemic regions may have contributed to the emergence of new low and moderate virulence CSFV variants, which threaten the epidemiological surveillance policies.[1]

The manifestations of Classical Swine Fever (CSF) can be: peracute, acute, chronic, or prenatal. However, the clinical signs are non-specific. Especially with strains of moderate or low virulence, the virus may remain undetected in a herd for 4–8 weeks, which increases the risk of further dissemination. CSFV is able to cross the placenta and infect foetuses at any stage of pregnancy.[4]

Pigs infected with highly virulent strains shed significantly more virus in all their secretions and excretions, as the chronic forms of any CSFV strains during the entire infectious period. The chronically infected may survive for 2–3 months before dying.[4]

COGLAPEST® - a nearly 20 years history of delivering superior CSF protection in the field.

To expand and update the information about the safety in terms of vaccine virus transmission, efficacy, and immune response of COGLAPEST®, the OIE Reference Laboratory for Classical Swine Fever (Institut de Recerca i Tecnologia Agroalimentàries, Centre de Recerca en Sanitat Animal IRTA-CReSA, 08193 Barcelona, Spain) investigated the vaccine.

In addition, its clinical and virological protection capacity after CSFV challenge with a highly virulent strain was evaluated at 5 and 21 days after single vaccination.

All this is published in a CSF dedicated special issue of the high-ranking peer-reviewed magazine, Vaccines.

COGLAPEST®, a consistent tool for CSFV

THE HIGHEST SAFETY AMONGST CSF LIVE VACCINES

COGLAPEST® Vaccine Virus has absolute absence of transmission among pigs

The vaccine virus is unable to generate viremia and is not transmitted from vaccinated to contact animals, even after 21 days of close contact in the same pen.[1]

GROUP OF PIGS		Day of vaccination			4 dpv			7 dpv			14 dpv			21 dpv						
		Sera	Nasal swabs	Rectal swabs	Sera	Nasal swabs	Rectal swabs	Sera	Nasal swabs	Rectal swabs	Sera	Nasal swabs	Rectal swabs	Sera	Nasal swabs	Rectal swabs	Tonsil	Spleen	Mesenteric lymph nodes	Thymus
GROUP A (vaccinated during 21 days)	1	-	-	-	-	-	-	-	36.43	-	-	-	-	-	-	-	29.07	-	33.46	36.71
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	3	-	-	-	35.55	-	-	-	-	-	-	-	-	-	-	-				
	4	-	-	-	-	33.15	-	-	35.79	-	-	-	-	-	-	-				
	5	-	-	-	-	-	-	-	35.19	34.52	-	-	-	-	-	-				
	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
GROUP B (contact of group A)	8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
	12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Figure 1. Detection of CSFV RNA load in samples and tissues during 21 days after vaccination. CSFV RNA load was detected by RT-qPCR and is expressed as Ct values. (-) symbol indicates samples in which fluorescence was not detected. Grey area indicates that the tissues were not collected at that time, in accordance with the experimental design described in the Materials end Methods section.

COGLAPEST® strain RNA could **not** be detected **in the majority of the samples** during the 21 dpv (*Figure 1*). The vaccine virus was **unable to generate viremia**, as shown by the general lack of viral RNA detection in sera: only one animal showed low RNA load (Ct > 35) at 4 dpv. Likewise, **low RNA load in nasal and rectal swabs was sporadically** detected in one pig at 4 dpv and three at 7 dpv, with **Ct values above 33**. In addition, **low or even absence of vaccine virus RNA load** was also detected in the tissue samples from the euthanized vaccinated pigs at 21 dpv (Ct > 29), (*Figure 1*). **During the 21 dpv, no vaccine virus RNA was detected in the contact group (group B) and all the animals from both groups were clinically healthy after vaccination.**

control Worldwide

A single **COGLAPEST®** dose conferred early and solid protection against CSFV challenge at 5 and 21 days post vaccination (dpv)

THE HIGHEST EFFICACY DEMONSTRATED AFTER SEVERE CHALLENGE

Margarita strain which generates a lethal CSF form was employed for the challenge.

Both vaccinated groups showed a total absence of clinical signs after challenge with a highly virulent CSFV strain with no statistic differences among them ($p > 0.05$). Thus, complete protection against CSFV challenge was afforded as early as 5 dpv with a single dose of the Coglapest® strain.[1]

PIG ID		DAY POST CHALLENCE												
		1	2	3	4	5	6	7	8	9	10	11	12	13
GROUP A (vaccinated during 21 days)	2	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0	0	0	0	0	0
	Mean	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a
GROUP B (contact of group A)	8	0	1	1	2	3	3	3	3	3	5			
	9	0	0	0	2	3	3	5						
	10	0	1	1	2	3	3	5						
	11	0	0	0	2	2	2	2	2	2	5			
	Mean	0^a	0.5^{ab}	1^{ab}	2^{ab}	2.75^b	2.75^b	3.75^b	2.5^b	2.5^b	5^b			
GROUP C (vaccinated during 5 days)	14	0	0	0	0	0	0	0	0	0	0	0	0	0
	15	0	0	0	0	0	0	0	0	0	0	0	0	0
	16	0	0	0	0	0	0	0	0	0	0	0	0	0
	17	0	0	0	0	0	0	0	0	0	0	0	0	0
	18	0	0	0	0	0	0	0	0	0	0	0	0	0
	Mean	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a	0^a
GROUP D (control group)	19	0	1	1	2	3	4	5						
	20	0	1	1	2	3	4	5						
	21	0	1	1	1	3	4	5						
	22	0	1	0	1	3	4	5						
	23	0	1	2	2	4	4	5						
	Mean	0^a	1^b	1^b	1.6^b	3.2^b	4^b	5^b						

Figure 2. Clinical signs monitored after challenge. The individual clinical signs were recorded after CSFV Margarita strain infection. Animals 2 to 7 (group A) and 14 to 18 (group C) were challenged after 21 and 5 dpv, respectively. Animals 8 to 11 (group B), contacts for group A and 19 to 23 (group D), infection control group, were not vaccinated but challenged. Pigs were monitored daily for clinical signs during the 13 dpc or until euthanasia. Different shades of colour and the numerical clinical score represent the severity of the clinical signs as shown in the legend. Super-indexed letters in the mean clinical score value from each group are employed to represent statistically significant differences between the groups on that day; similar letters indicate no statistical difference, and different letters show statistical difference ($p < 0.05$).

- Score 0: absence of clinical signs
- Score 1: Mild fever
- Score 2: Moderate diarrhea and/or mild apathy and/or moderate fever
- Score 3: Moderate apathy and/or mild tremors and/or mild conjunctivitis and/or high fever
- Score 4: Mild dyspnoea and/or moderate conjunctivitis and/or weakness of the hindquarters
- Score 5: Severe apathy, dyspnoea, cyanosis, conjunctivitis and nervous disorder. Euthanasia
- Score 6: Death

COGLAPEST®, a suitable vaccine for critical urgent situations

Complete protection as early as 5 days post vaccination (dpv) against CSFV following a single dose

*A single dose of COGLAPEST® can activate the immune response, as shown by the **complete protection** from clinical signs afforded in animals that were challenged at 5 and 21 dpv, using a severe viral challenge, in accordance with OIE standards.*[1]

- Earlier than other MLV and E2-subunit CSF vaccines.[1, 2, 3, 4]
- The DIVA vaccine, a recombinant protein E2 subunit, demonstrates to be a particularly weak alternative: a single dose does not induce any clinical protection nor reduction of viral excretion in the 14 dpv, and this is only after at least 21 dpv, that it offers full clinical protection. 14 days after a second vaccination, transplacental infection of the foetuses and horizontal transmission to contact animals still occurred in most vaccinated animals, **critical to emergency vaccination**. Also, the "carrier sow syndrome" and, subsequently, the late-onset form of CSF is not prevented.[4]

Control animals developed the severe form of CSF after challenge, evidenced by the progressively worsening clinical signs leading euthanasia at 7-10 dpc due to animal welfare, the rapid onset of the IFN-α response, and their inability to generate a CSFV specific antibody response.[1]

Rapid CSFV protection at 5 days post vaccination (dpv) without humoral response

From 10 days post challenge (dpc), all COGLAPEST® vaccinated pigs demonstrated neutralising antibody in the standard Alfort/187 VN test, two of them also showing low titres against the Margarita challenge strain. At 13 dpc, all COGLAPEST® pigs had neutralising antibodies against both viral strains analysed.[1]

- CSFV is immunosuppressive and neutralizing antibodies may not appear until 2–3 weeks after infection.[4]

Protection against viral replication with a single dose after CSFV challenge

COGLAPEST® avoided shedding by the vaccinated pigs of CSFV after severe challenge.[1]

- Even though some animals were positive to CSFV RNA detection in swabs at 10 dpc, in all cases the RNA load was low and no virus was isolated in cell culture.[1]
- Furthermore, no viral replication was detected in spleen samples from vaccinated pigs, while in the case of tonsil and mesenteric lymph nodes, the Margarita strain RNA load detected was mostly low. Probably, the CSFV RNA load in these animals was a result of the prolonged exposure to a severe CSFV challenge, due to the close interaction between the vaccinated and contact animals that were secreting high amounts of virus.[1]

COGLAPEST®, solid and robust immunity against CSFV

COGLAPEST® strongly activates the innate and the cell mediated immunity in pigs

Remarkably, protection was achieved by COGLAPEST® as early as 5 dpv, even in the absence of antibody response. This suggests the strong activation of cellular immunity induced by the vaccine strain. Likewise, the rapid and transient activation of innate immunity, in terms of IFN-α response against CSFV, may explain the solid protection capacity afforded by COGLAPEST®, as well as its efficacy to control viral replication shortly after vaccination.[1]

- The antiviral and immunomodulatory effects of type I IFNs, such as IFN-α, have proven to be very important for impairing viral replication.[1,5] These results shed light into the mechanisms that underlie the vaccine protection against CSFV in the absence of specific humoral response. On the other hand, previous reports have shown that elevated levels of IFN-α are related to CSF disease severity.[1, 6]

COGLAPEST® induces neutralizing antibodies and CSFV E2 and Erns ELISA antibodies 14 days after vaccination

The high levels of E2 and Erns antibodies proved to have neutralising activity via the standard CSFV Alfort/187 strain virus neutralisation (VN) test, that correlated with robust virological protection.[1]

The clinical protection, all of the animals challenged at 21 dpv were protected from viremia, supporting the solid neutralising antibody protection conferred after vaccination.[1]

- The VN test is considered the reference assay for the detection of CSFV-specific antibodies.[4]
- ELISAs for the detection of anti-CSFV antibodies are useful for conducting epidemiological surveys and for monitoring CSFV-free areas.[4]
- Neutralizing antibodies are induced by the surface glycoprotein E2, while the surface protein Erns induce non-neutralizing antibodies.[4]
- E2 protein is often used as the antigen in the system. ELISA-detectable antibodies appear 10–15 days post infection, similar to the period described for the appearance of neutralizing antibodies.[4]

CONCLUSION

Two groups of pigs were vaccinated, and contact and control groups were also included. Animals were challenged with a highly virulent CSFV strain at 21- or 5-days post vaccination (dpv).

- No vaccine virus transmission was detected.
- Fast and complete clinical protection as early as 5 dpv; earlier than other CSF vaccines.
- Fully controlled viral replication after severe CSFV challenge, showing efficient virological protection despite being housed with animals excreting high CSFV titres.
- Rapid, strong and protective responses from the innate and cell mediated systems.
- Strong and fast humoral response with virus-neutralising activity, demonstrated in VN test, CSFV E2 ELISA and Erns ELISA.

These results demonstrate the high safety and efficacy of COGLAPEST® against CSFV replication.

The early, strong and safe protection capacity of COGLAPEST® makes it useful for emergency vaccination as well as in endemic situations, and **a consistent tool for CSFV control worldwide.**

COGLAPEST® EASY TO USE VACCINE

The unique vaccine with a visual control of quality inside

COGLAPEST® contains PHENOL RED as **dye to monitor the quality of the diluent used**. After the cake dissolution with a good quality diluent, the colour of the vaccine solution turns pink, which indicates the vaccine is fully potent.

VACCINATION PROGRAMME

Administration of 2 ml COGLAPEST® by deep intramuscular injection behind the ear, regardless of the age or weight of animals.

PIGLETS

From 1 single shot (from 35 days of age) in low-risk conditions (non-endemic situation, isolated farms) **to a 2 shots programme** (1st shot from 3 to 4 weeks of age, completed with a 2nd shot 3 weeks later) in high-risk conditions (CSF endemic situation, poor biosecurity).

BREEDERS

FUTURE BREEDERS:	**1st shot** at 3/5 weeks of age
BOARS:	**Twice yearly**
SOWS:	At **each reproductive cycle** 3 weeks before farrowing or 2 weeks before weaning.

Classical Swine Fever vaccination should be tailor made according to your local herd situation. Ask your CEVA Santé Animale Technical Department to help you in designing the most suitable Coglapest® vaccination programme.

This vaccine is produced in Europe, following strict European Good Manufacturing Practices.

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YOUR FIRST CHOICE AGAINST CLASSICAL SWINE FEVER.

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