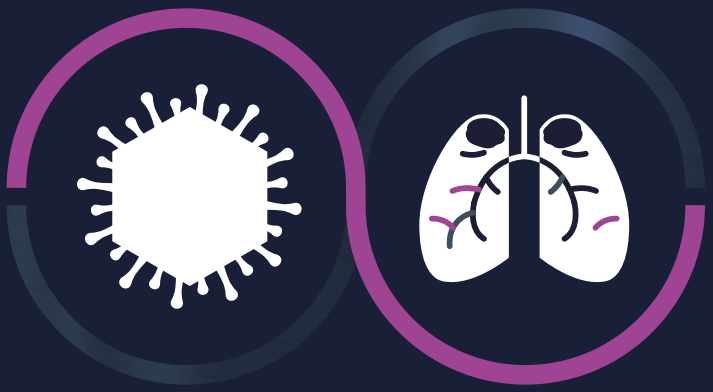
PCV2 & M Hyo prevention



When something doesn't exist you invent it.

Unique

RTU Combination

CIRBLOC® M Hyo

Significant reduction of losses due to PCV2 and ***M. hyo*** infections is achieved in most of swine farms worldwide by vaccination of piglets

Epidemiology

Evolving prevalence of PCV2 genotypes

Currently with PCV2a, PCV2b, and PCV2d being widely distributed, **PCV2d is most frequently up to exclusively found especially in clinically affected herds.**
Recently, 100% of isolates from diseased pigs were identified as PCV2d in Belgium (Wei 2019), 100% in Spain (Sibila 2021) and 60% in Austria (Weissenbacher-Lang 2020).
When **random sample** selection is performed, **PCV2a and PCV2b** are still circulating in pig herds **but PCV2d is remaining the main circulating genotype** (Saporiti 2020).

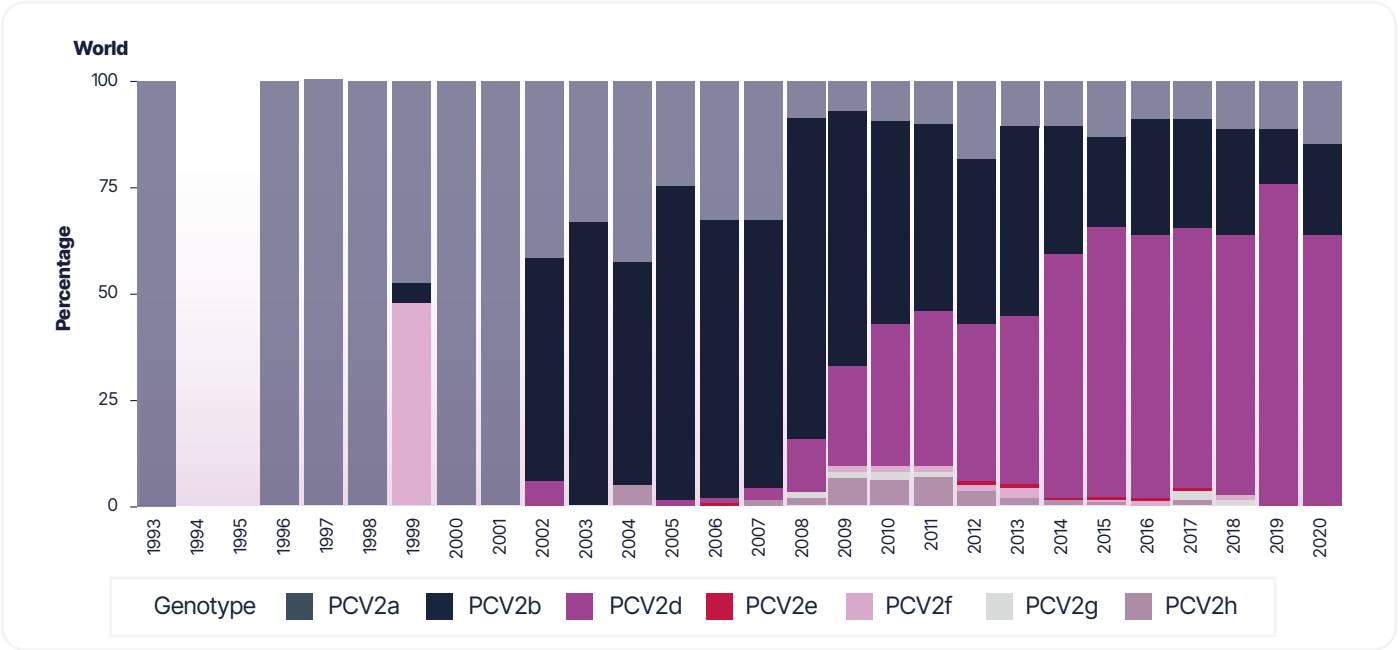


Fig 1. PCV-2 genotype frequency pattern at European and world levels. (Sibila 2021)

The **cross protection against various PCV2 genotypes, but especially against PCV2d** is crucial for the reduction of losses caused by PCV2.

The level of maternal immunity which might interfere with the post-vaccination response decreases usually for PCV2 and ***M. hyo*** rather fast.

That allows vaccinating piglets against both agents at the same time from 3 weeks of age (WOA), typically around weaning.

The prevalence of Enzootic pneumonia remains high in the pig population

> ***It is evident that the control of Enzootic pneumonia requires vaccines highly efficient against M.hyo and up to now at least some of the combined PCV2+Mhyo RTU products provide only suboptimal protection with lung lesion index not significantly different from non-vaccinated control pigs.***
>
> ***(López-Lorenzo, 2021)***

LUNG PROGRAM appeared to be a relevant method to evaluate the prevalence and the severity of Enzootic pneumonia (EP)-like lesions, the benefits of a vaccination program in specific farm cases (trials, new program) as well as for the long term monitoring on a farm and even at country level.

2023

17,900
batches of pigs checked

1,300,000
lungs scored

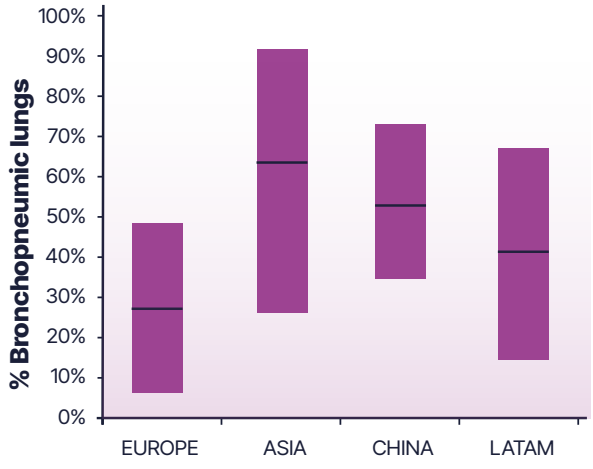
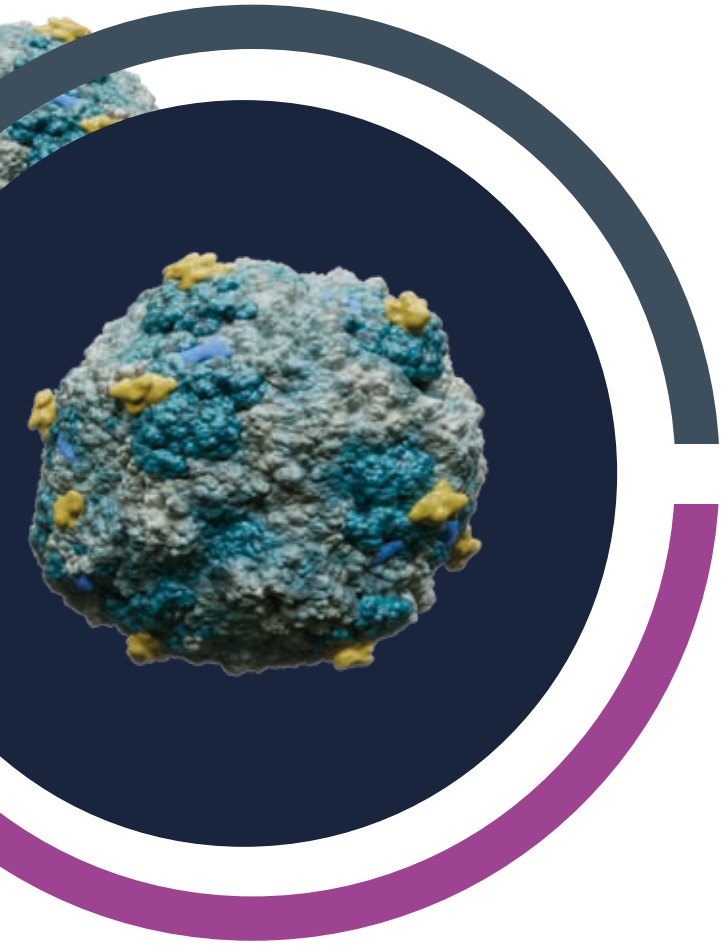


Fig 2. Consolidated data in 2023 show the persisting high prevalence of EP like lesions (Krejci 2024).

CIRBLOC® MHyo : Unique vaccine formulation



PCV2d antigen - The consensus approach

The evolution in PCV2 epidemiology inspired Ceva to develop **a vaccine based on PCV2d strain**.

Ceva research team considered also the inter- and intra-genotype genetic variation of PCV2 and modified the vaccine strain by several aminoacid changes to create a ‹‹ **consensus** ›› virus to induce more universal and specific immune responses and confer highest degree of protection against all circulating strains of PCV2.

The PCV2 capsid protein, which is the dominant immunogenic antigen is expressed and produced using a baculovirus expression system.

Besides selecting the vaccine strain, the designed manufacturing process utilizes the **combination of cell lines** to maximize antigen yield. The downstream steps applied produce a stable, potent and high purity PCV2 antigenic material that does not interfere with ***M. hyo*** component.

Adjuvant - optimized for PCV2 & *M. hyo* RTU

In order to guarantee the compatibility between PCV2 and ***M. hyo***, great stability, safety and long shelf-life, yet induce strong and efficient immune responses, Ceva developed and optimized adjuvant utilizing highly refined mineral oil (liquid paraffin) in a tested and selected concentration.

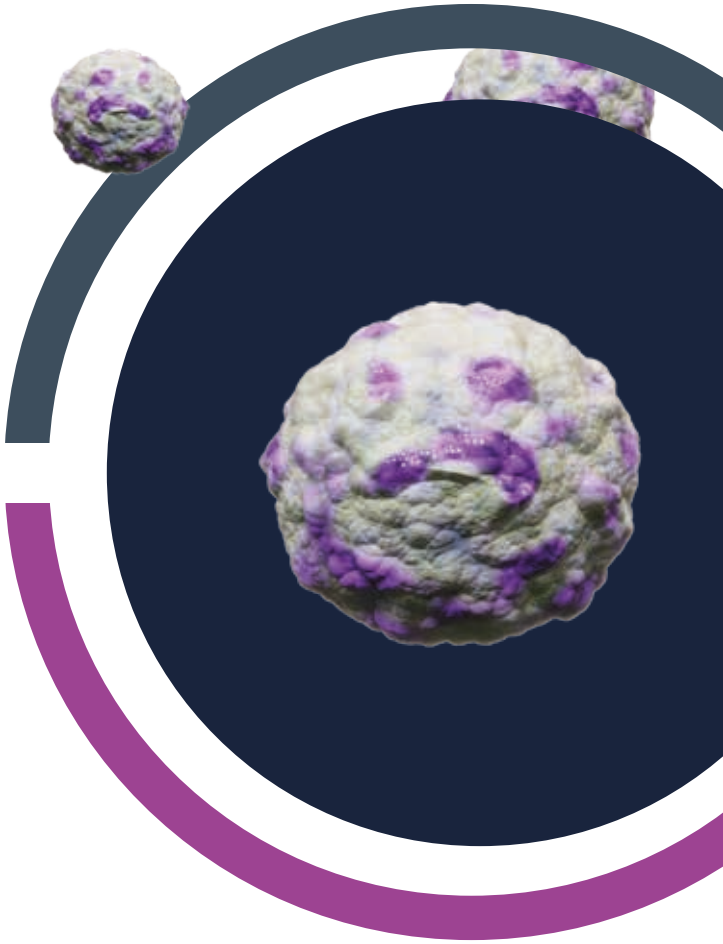
This adjuvant allows for the activation of innate immune responses, promotes PCV2 and ***M. hyo*** antigen presentation and the development of specific immunity.

M. hyo antigen - Hyogen backbone based

The **proprietary inactivated bacterin of *Mycoplasma hyopneumoniae* strain 2940** already used in Hyogen® constitutes also the ***M. hyo*** antigenic part of CIRBLOC® M Hyo.

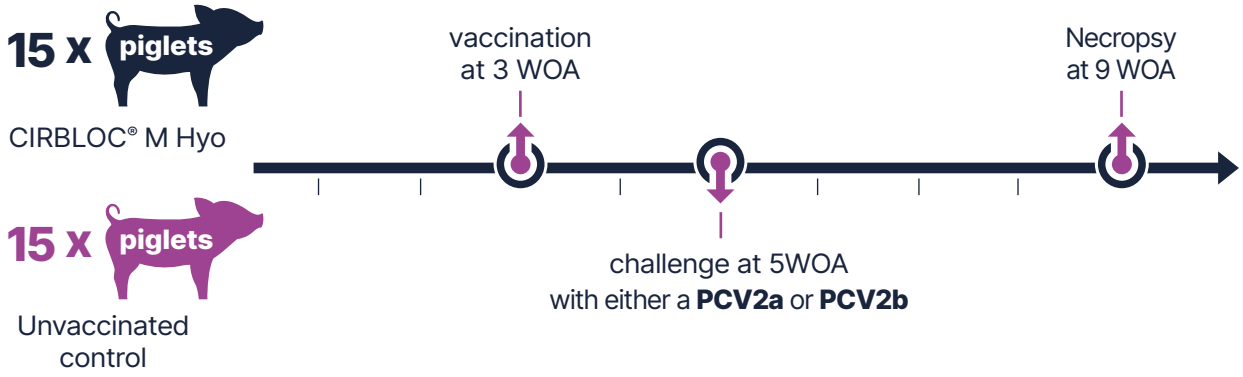
This strain was initially **isolated as a highly virulent agent** of Enzootic pneumonia clinical case, and thus it possesses major factors of virulence, important also in the induction of efficient protective immune responses.

The antigen production includes critical operations such as the inactivation that ensure the **preservation of protein and lipid structures** important to **maintain high antigenicity.**



CIRBLOC® M Hyo efficacy: supported by strong scientific data

PCV2 efficient protection demonstrated against all relevant genotypes. (Ceva registration dossier - ECG-167-2021 for PCV2a and ECG-063-2021 for PCV2b)



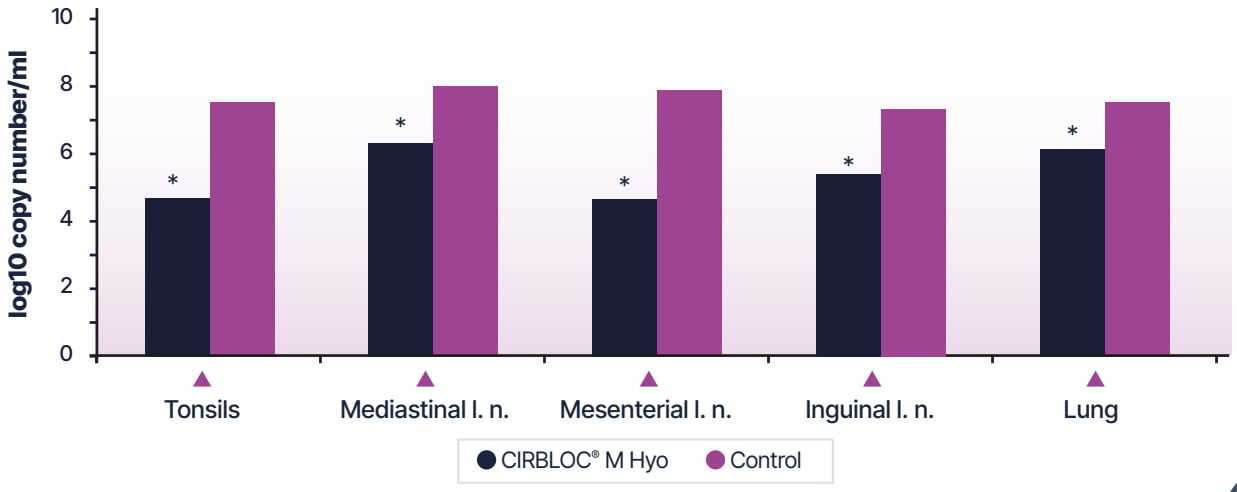
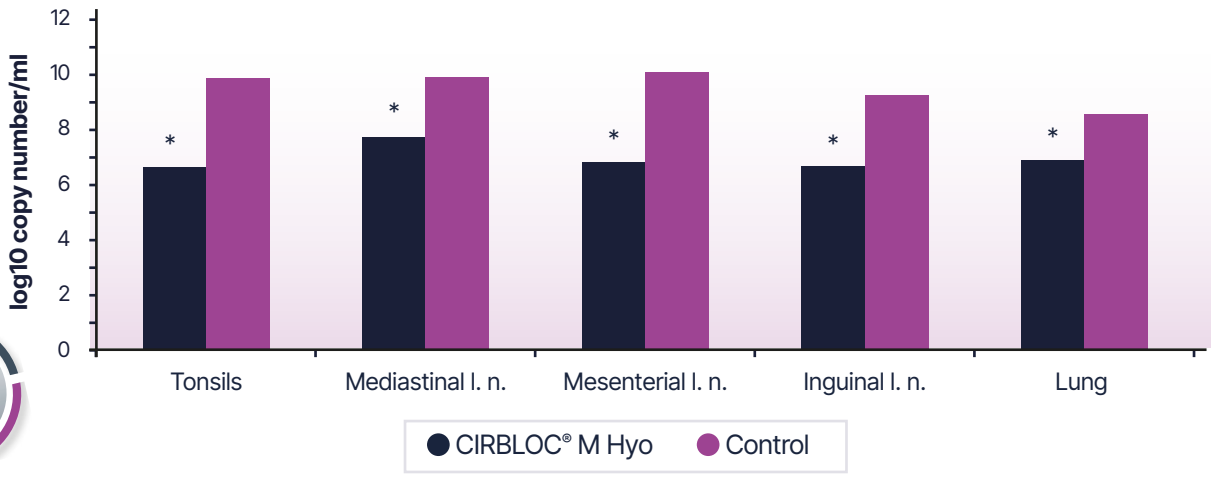


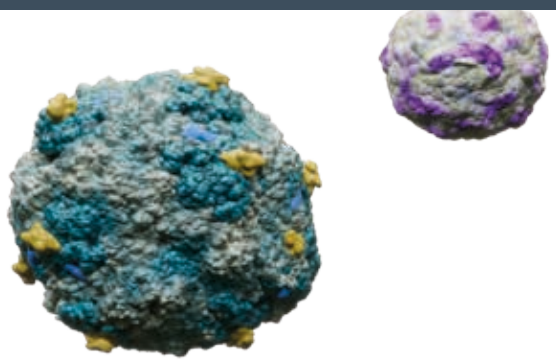
Fig 3. Geometric mean PCV2 a DNA copy numbers in the organ samples (log10 copy number/ml) * p<0,05

PCV2a PROTECTION PROVEN

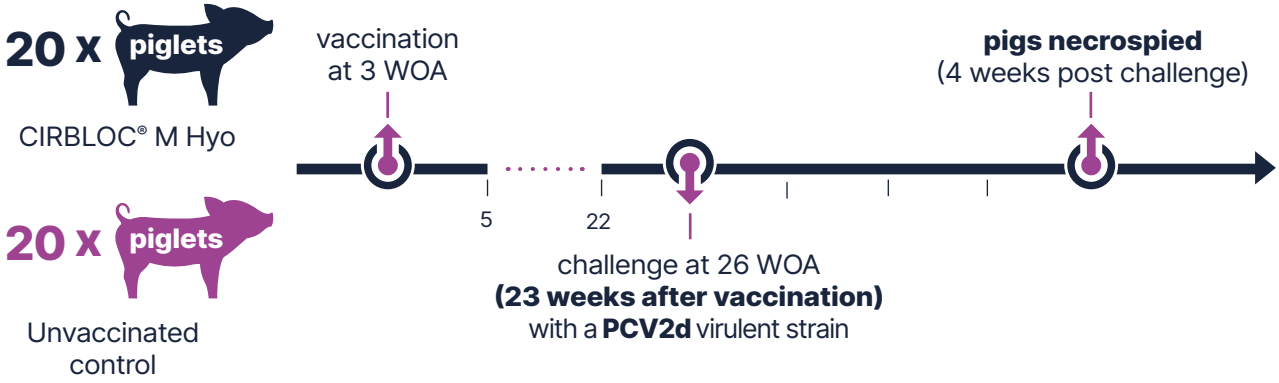


PCV2b PROTECTION PROVEN

Fig 4. Geometric mean PCV2 b DNA copy numbers in the organ samples (log10 copy number/ml) * p<0,05



(Ceva registration dossier - Ref ECG-062-2021)



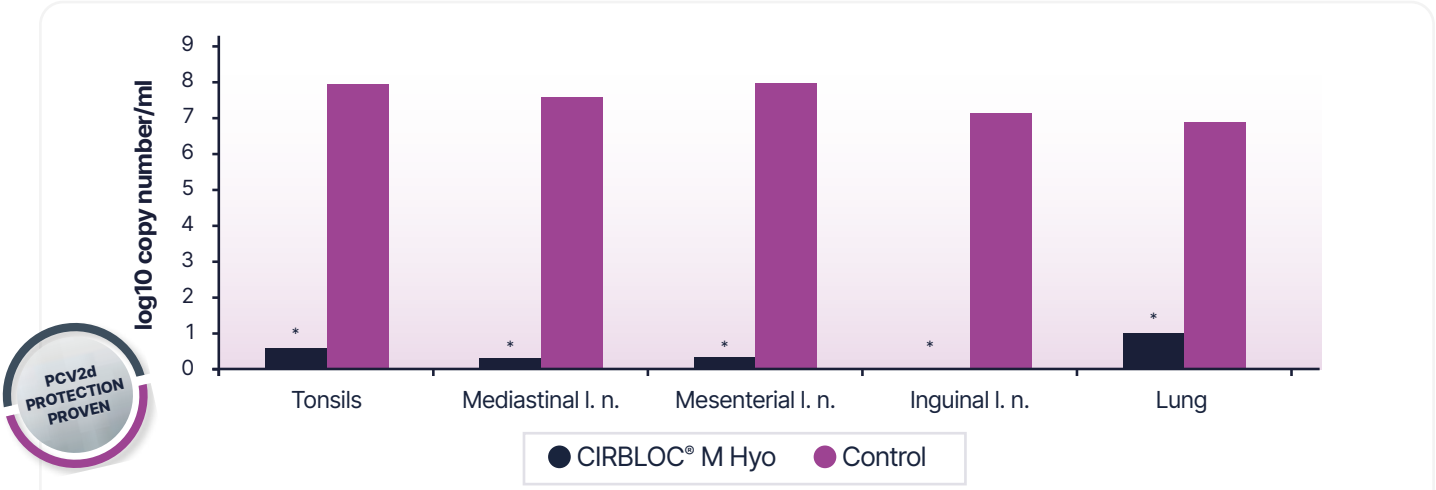
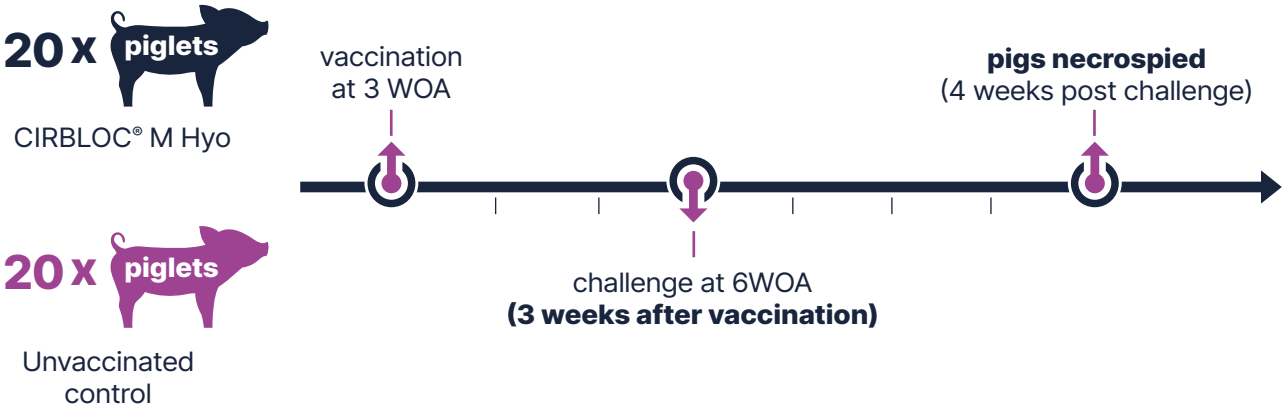


Fig 5. Geometric mean PCV2d DNA copy numbers in the organ samples (log10 copy number/ml) * p<0,05

- **2 weeks OOI and 23 weeks DOI + cross protection against PCV2a, PCV2b and PCV2d were demonstrated**
- **In all the trials, a significant reduction of viremia and virus load in tissues where PCV2 replication takes place (tonsils, lymph nodes, lung) was measured**

M. hyo significant protection (Ceva registration dossier)

3 weeks onset of immunity (Ref. ECG-183-2020)



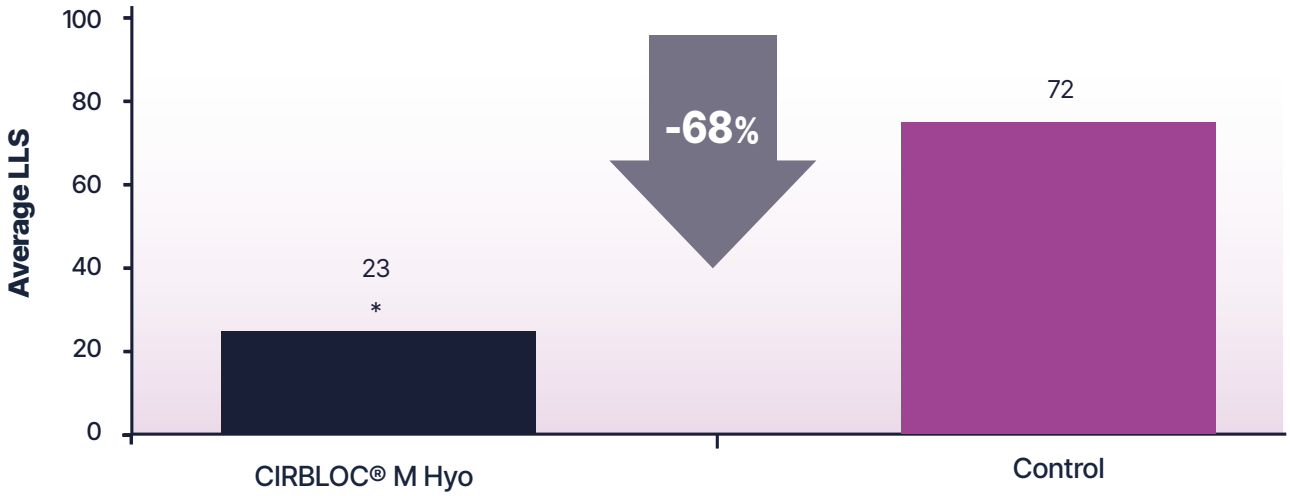
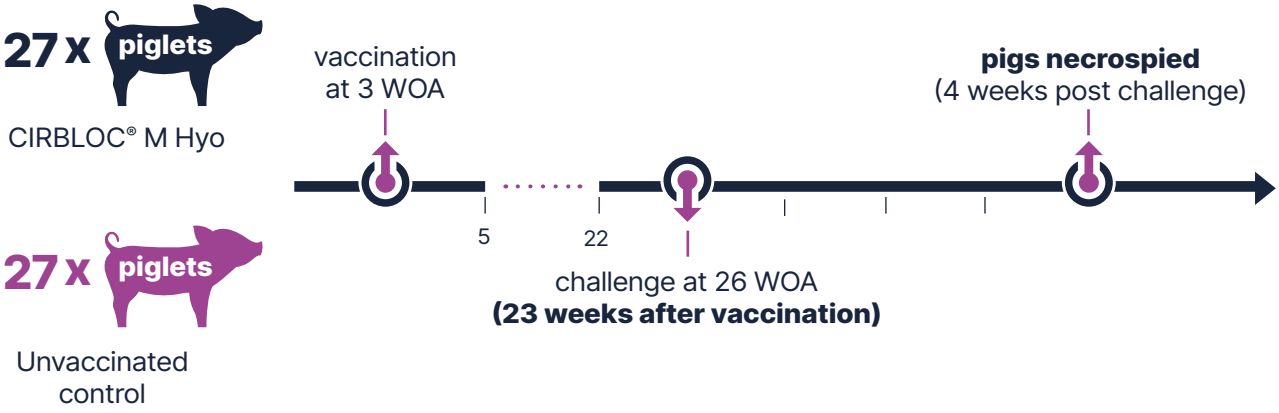


Fig 6. Lung lesion score after a challenge 3 weeks post vaccination * $p < 0.05$

23 weeks duration of immunity (Ref. ECG-081-2021)



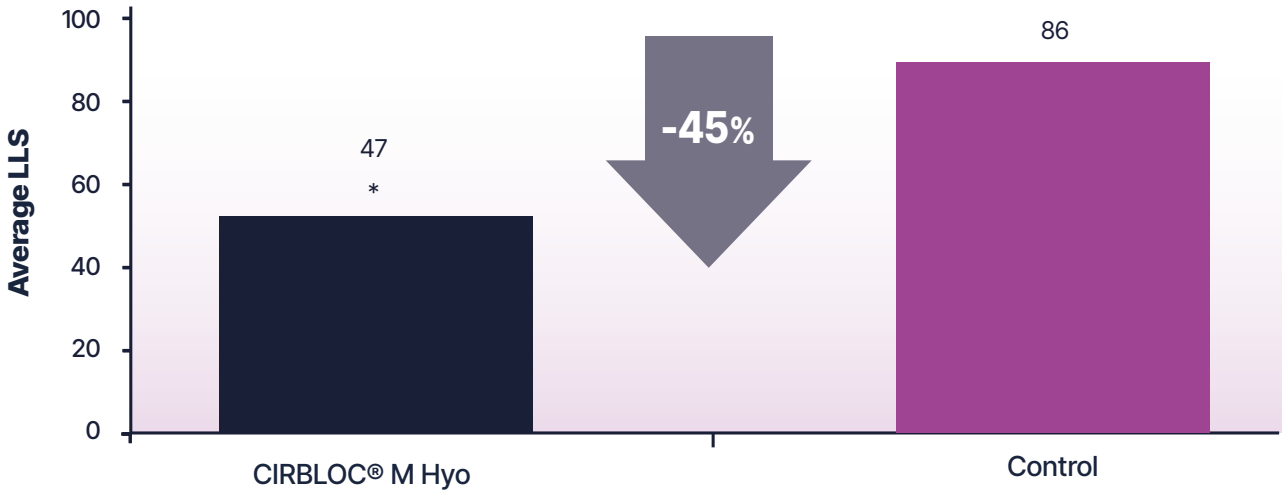
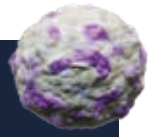


Fig 7. Lung lesion score after a challenge 23 weeks post vaccination * p < 0.05

Significant *M. hyo* protection was demonstrated in favour of CIRBLOC® M Hyo from 3 weeks until at least 23 weeks post vaccination.

Efficacy confirmed in the field (Ceva registration dossier - Ref. ECG-068-2021)



- **The PCV2b infection was confirmed on this farm with viremia from 9 till 24 WOA**

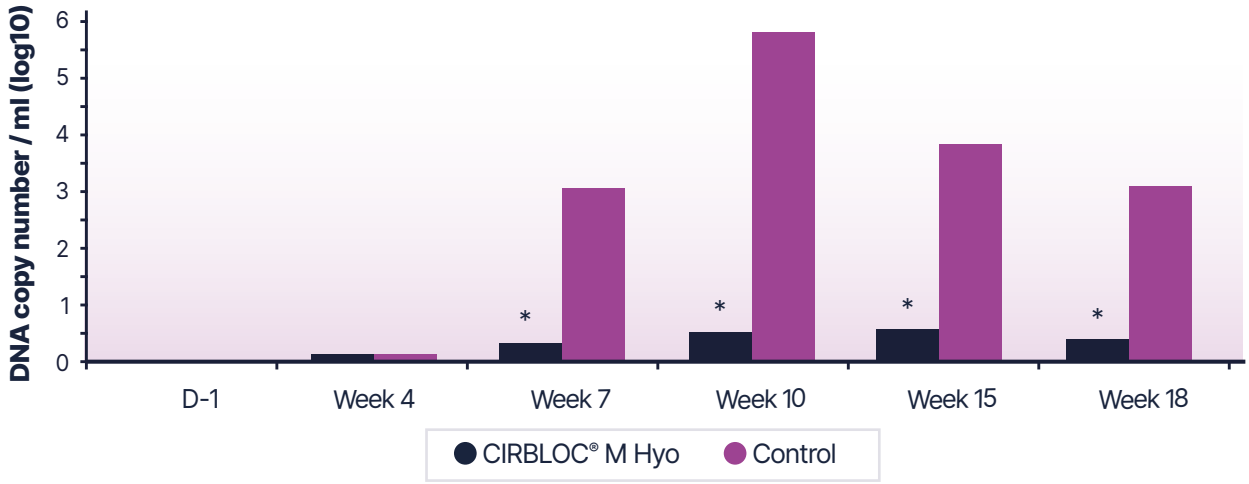


Fig 8. Significant reduction of viremia * p<0,05

- **At each time point from week 7 the reduction of the viremia was significant**
- **A significant reduction of virus loads in different organs was also measured**
- **Fecal shedding was significantly reduced at every sample point from 7 WOA as well**

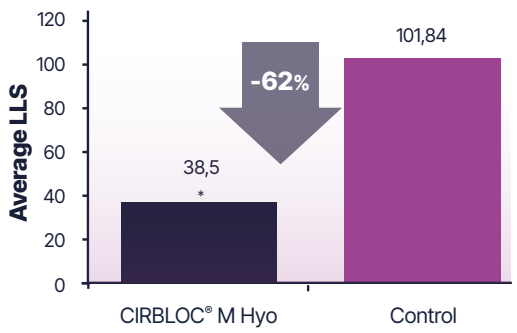


Fig 9. Mean of lung scores per group * p<0.05

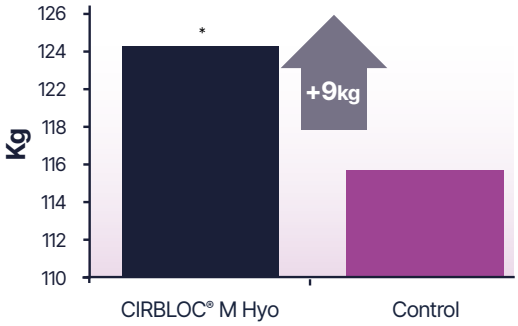


Fig 10. Final body weight (kg) * p<0.05

CIRBLOC® M Hyo provides a significant reduction of lung lesion scores. A significant reduction (p<0,05) of the *M. Hyo* load in the lungs and in tracheobronchial fluid has been measured.

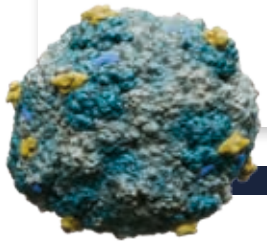
Thanks to CIRBLOC® M Hyo:

+ 47 grams ADG **+ 9 kg** FINAL WEIGHT

The overall calculated benefit using **Respinomics was**

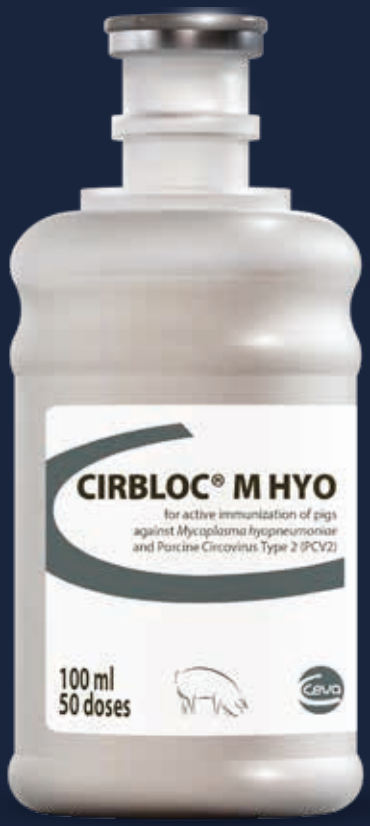
7,9€

Respinomics™



Conclusions

- **Recent changes in especially PCV2 epidemiology and needs for convenience and welfare demand updated approaches in PCVD and Enzootic pneumonia control.**
- **CIRBLOC® M Hyo meets the requirements for safe, highly efficient, ready-to-use single dose vaccination against PCV2 and *M. hyo* in weaned piglets.**



Ready to Use

PCV2 & M.hyo

The best length of protection

Protection against all relevant PCV2 genotypes

Hyogen® backbone based formulation

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For more details, see the SPC applicable in your country.

This document contains information on a veterinary biological product sold in several different countries and areas where it may be marketed under different trade names and pursuant to different regulatory approvals. Accordingly, Ceva give no guarantee that the details presented are correct with respect to all locations. In addition, the safety and efficacy data and the withholding periods may be different depending on local regulations. Please consult your veterinarian for further information.

Cirbloc® M Hyo: emulsion for injection for pigs. One dose (2 ml) contains: Active substances: Inactivated bacterin of Mycoplasma hyopneumoniae strain 2940 min. 184 AU. Recombinant baculo-PCV2 virus VLP antigen (ORF2 capsid protein) min. 19.6 µg. Adjuvant: Light liquid paraffin 277 µl. Indications for use: For the active immunisation of pigs to reduce viraemia, virus load in lungs and lymphoid tissues, virus shedding caused by porcine circovirus type 2 (PCV2) infection, and bacterial load and severity of lung lesions caused by Mycoplasma hyopneumoniae infection, and under field conditions, to reduce the loss in body weight gain. Onset of immunity: PCV2: 2 weeks after vaccination. M. hyopneumoniae: 3 weeks after vaccination. Duration of immunity: PCV2: 23 weeks after vaccination. M. hyopneumoniae: 23 weeks after vaccination. Vaccinate pigs by the intramuscular route in the neck. A single dose of 2 ml in pigs from 3 weeks of age. Allow it to reach room temperature (15 °C – 25 °C). Shake well before use. Apply usual aseptic procedures. Withdrawal period: Zero days. Store and transport refrigerated (2 °C – 8 °C).Do not freeze. Shelf life after first opening the container: 10 hours.

Ceva Santé Animale S.A.- www.ceva.com
10, av. de La Ballastière - 33500 Libourne- France- Phone: 00 33 (0)5 57 55 40 40