DUO™

READY TO MIX

Circovac
+ Hyogen

Making a difference together

Ceva

DUO™

CIRCOVAC® & HYOGEN®

***Porcine Circovirus type 2 (PCV2) and Mycoplasma hyopneumoniae (M.hyo)* belong to the most important infectious agents in swine affecting health of commercial pigs and causing diseases and production losses worldwide.**

PCV2 alone is a major cause of PCVD (Porcine Circovirus Diseases) including various clinical syndroms and subclinical condition, the latter being even most economically important. M.hyo is the major cause of Enzootic pneumonia in growing-finishing pigs. PCV2 and M.hyo (Tico et al 2013, Maes et al 2017) together with porcine reproductive and respiratory syndrome virus (PRRSV) are considered to be the most important pathogens that cause Porcine Respiratory Disease Complex (PRDC).

Prevention of PCVD and Enzootic pneumonia is performed in most of swine farms worldwide by vaccination of piglets. The level of maternal immunity which might interfere with the post-vaccination response decreases usually for PCV2 and *M.hyopneumoniae* rather fast.

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

DUO™

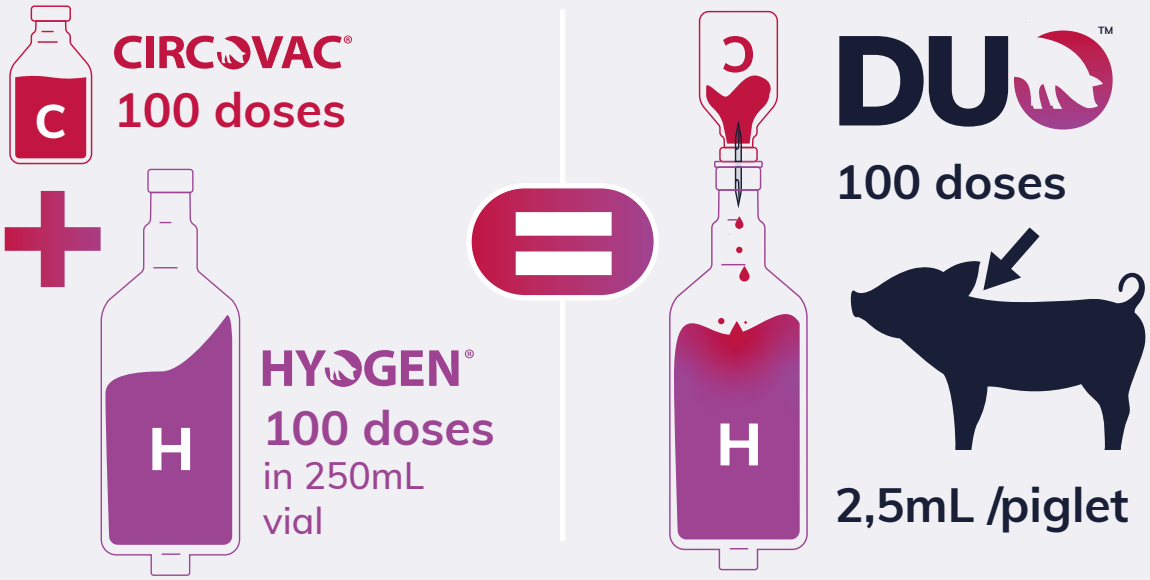
CIRCOVAC®

NEW
- **Longer protection:** until **26 weeks of age**
- **Inactivated whole PCV2 virus**
- **First licenced PCV2 vaccine** for both piglets and sows
- **Provides a whole life piglet protection** meaning from early age (through the passive immunity transmitted from vaccinated mother) to the end of finishing period.
- **Efficacy described in multiple field and experimental studies** using various PCV2 genotypes **including PCV2d** (Palya et al 2018).

HYOGEN®

- **Inactivated vaccine** composed of *Mycoplasma hyopneumoniae* bacterin adjuvanted with highly efficient immunostimulant Imuvant™.
- **Unique Ceva's M.hyo strain BA2940-99** originated as a field isolate that caused both clinical and pathological disease in growing pigs.
- **Assessed as the most efficient M.hyo vaccine** in reducing the lung lesion score in slaughter pigs in different surveys (Lasierra et al 2021, Cvjetkovic et al 2021).

NEW
- **Hyogen® is now available in 100 doses (200 mL)** that matches perfectly with Circovac® 100 piglet doses presentation.



DUO™: an excellent mixability

Mixing Circovac® with Hyogen® prior to the administration facilitates one shot injection of both antigens. The mixture provides a homogenous, smooth and stable suspension.

The colored vaccines

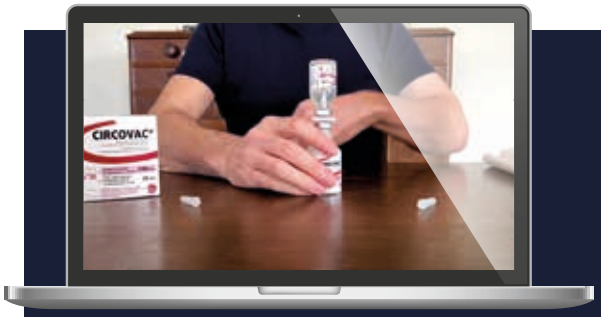
Mixing the colored vaccines

The mixture

New lab data about viscosity and syringeability

	Viscosity (Centipoise)	Syringeability (Seconds)
Circovac®	5.2	6.2±0.1
Hyogen®	2.0	4.8±0.1
DUO™	**2.1**	**4.9±0.1**

Very easy to inject!



Tutorial how to mix it properly

The efficacy scientifically demonstrated

PCV2 or M.hyo challenge

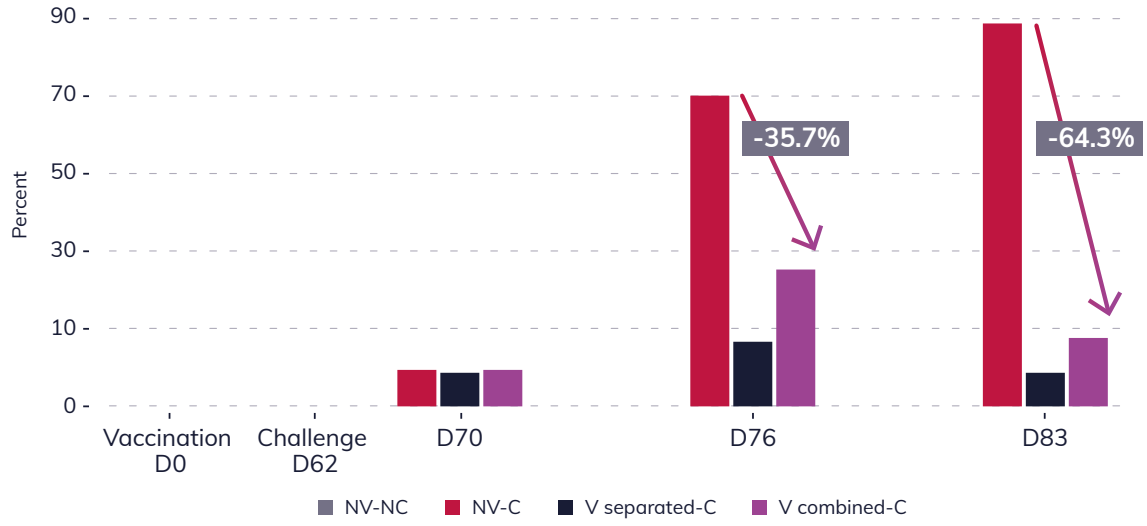
The aim of the trials described below (Sibila et al, 2020) was to compare the efficacy of Circovac® and Hyogen® when injected separately or combined by means of M.hyo or PCV-2 experimental challenges.

Groups	Vaccination (3 weeks of age)	Challenge (12 weeks of age)
Non Vaccinated Non challenged (NV-NC)	Phosphate Buffer Saline (PBS) 2,5mL	Placebo
Non Vaccinated Challenged (NV-C)	Phosphate Buffer Saline (PBS) 2,5mL	PCV2b or M.hyo
Separated Vaccination (VS)	Circovac 0,5mL and Hyogen 2mL	PCV2b or M.hyo
Combined vaccination (VC)	DUO (Circovac +Hyogen 2,5mL)	PCV2b or M.hyo

The efficacy scientifically demonstrated

PCV2 efficacy trial

Fig 1. Percentage of PCV2 qPCR positive pigs



Circovac® alone or used with Hyogen® (DUO™) reduced significantly the percentage of PCV2 positive pigs compared to control 2 and 3 weeks post challenge. There was no significant difference between Circovac® alone and DUO™ at any time points.

Tab 1. PCV2 immunohistochemistry (IHC) results

Treatment	Number of animals with all lymphoid tissues scored 0 by IHC per treatment group
	0
NV-NC	3 (100%)
NV-C	5 (35.7%)
V Separated-C	15 (100%)
DUO V Combined-C	12 (85.7%)

No significant differences on the number of lymphoid tissues scoring ≥1 between both vaccinated groups were detected.

This experiment confirmed equal efficacy of Circovac® administered separately or mixed with Hyogen® against PCV2.

M.hyo efficacy trial

At 12 WOA, animals from challenged groups were endotracheally challenged with a M.hyo isolate on two consecutive days

Tab 2. **M.hyo macroscopic and microscopic compatible lung lesions assessment**

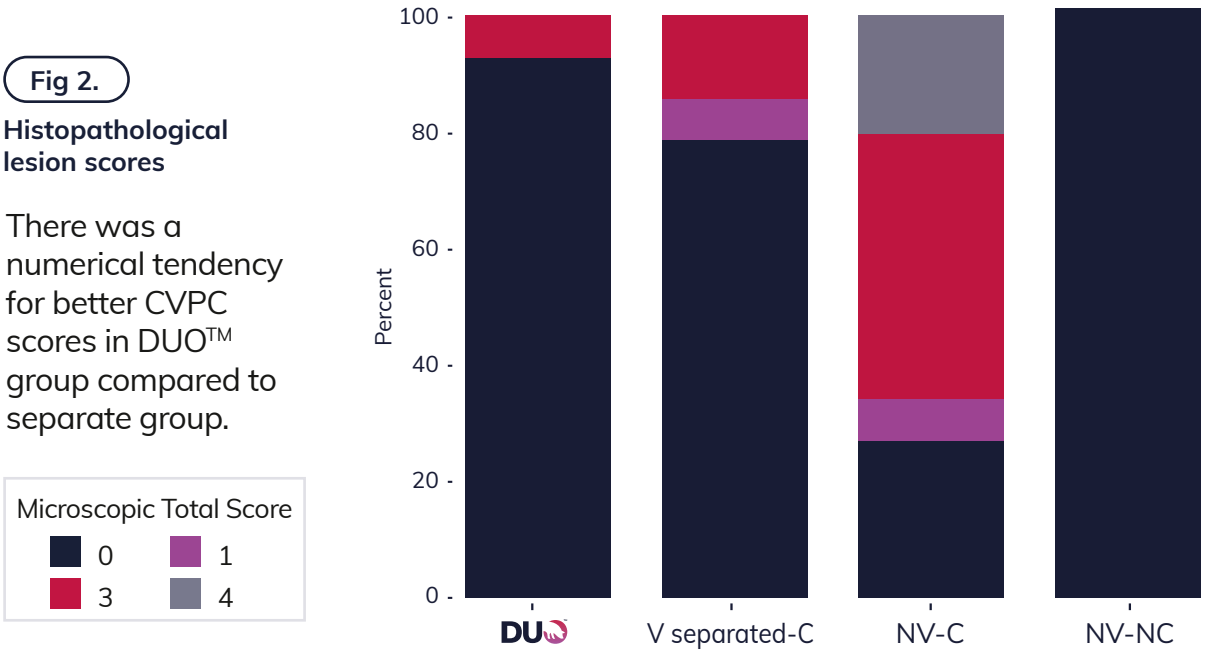
Treatment	Percentage of animals showing CVPC (%)	Mean CVPC Score (Max-Min)
NV-NC	0	0
NV-C	66.6	4.84[b] (38.63-0)
V Separated-C	14.3	0.11 [a] (1.20-0)
DUO™ V Combined-C	7.15	0.04 [a] (0.53-0)

Vaccinated groups differed significantly from the control, but not between themselves. Numerical lower prevalence of CVPC (Cranioventral pulmonary consolidation) in DUO™ group.

Fig 2.

Histopathological lesion scores

There was a numerical tendency for better CVPC scores in DUO™ group compared to separate group.



DUO offered equivalent virological, bacteriological and pathological outcomes as compared to these vaccines administered separately.

The protection against the development of lung lesions was even numerically improved in DUO™ group.

DUO™ offers long lasting protection

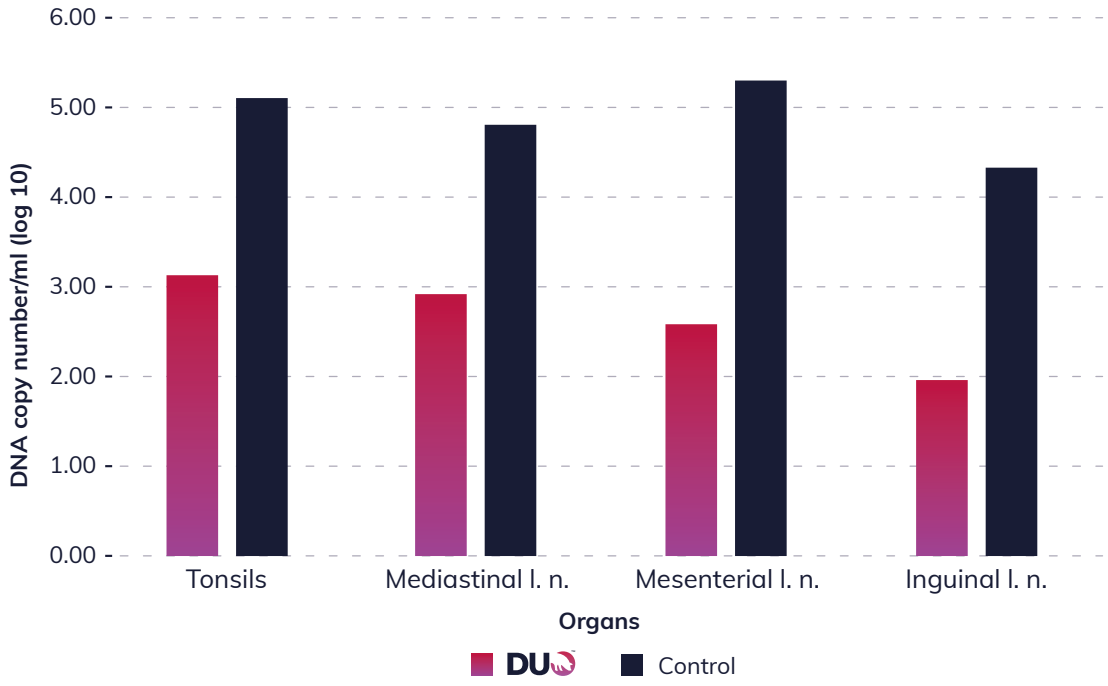
DUO™ protects piglets against PCV2 at 26 weeks of age. Ref. Ceva Dossier: A-R-A2/S/2114/19

Piglets were vaccinated at 3 WOA with Circovac® and Hyogen® (DUO™) or not vaccinated as controls.

They were then challenged at 26 WOA (23 weeks post vaccination) with a PCV2a strain.

Fig 3. PCV2 loads in lymphoid tissues 4 weeks post challenge

Mean PCV2 DNA copy numbers in organ samples (log10 DNA copies/ml)



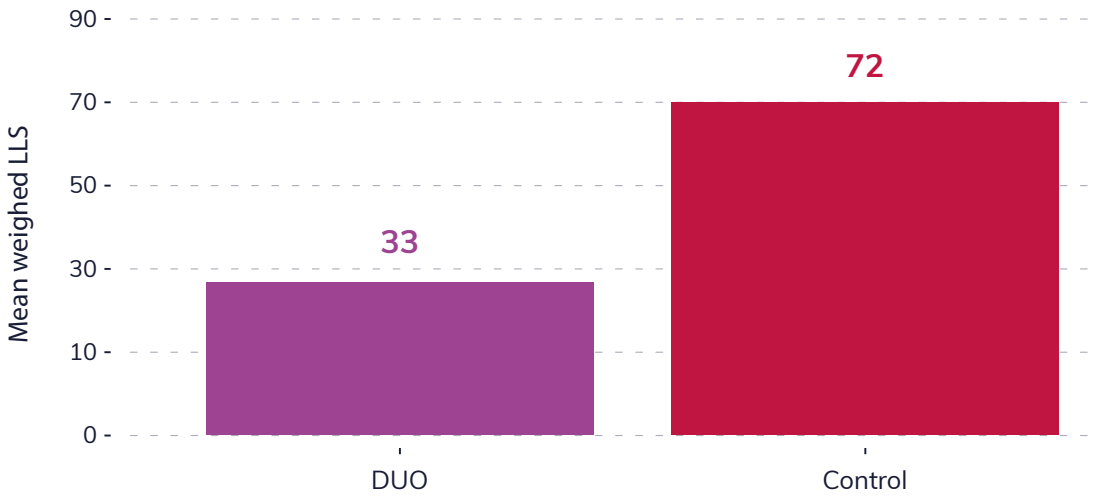
- Significantly lower PCV2 copy numbers in the vaccinated group compared to the control group.
- Significant protection until 23 weeks after vaccination.

DUO™ protects piglets against M.hyo at 26 weeks of age Ref. Ceva Dossier: DB-024-2019

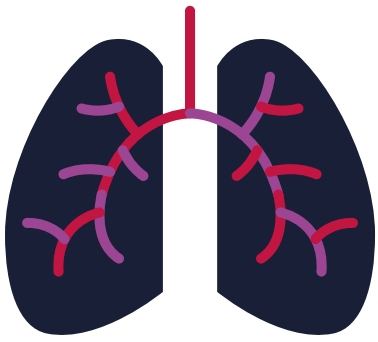
26 weeks of age

Piglets were vaccinated at 3 WOA with DUO™ or not vaccinated as controls. They were then challenged at 26 WOA (23 weeks post vaccination) with a M.hyo strain.

Fig 4. **Lung lesions Score (LLS) after *Mycoplasma hyopneumoniae* challenge**



- Significantly lower lung lesion scores in DUO™ group compared to the control group



This experiment highlighted the long lasting duration of immunity, covering the whole finishing period.

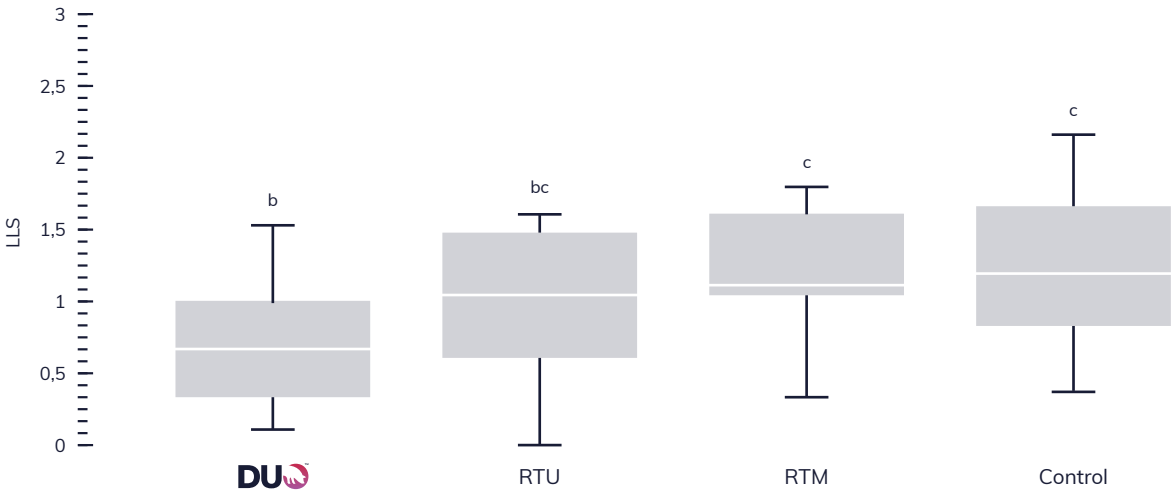
DUO™ provides an outstanding Mycoplasma protection

In this experiment (Kiss et al 2021), three-weeks old piglets were vaccinated either with DUO™ or with various PCV2+M.hyo RTU or RTM vaccines.

Piglets were vaccinated at 3 weeks of age.

Groups	Challenge
DUO™	12 weeks of age
RTU	12 weeks of age
RTM	12 weeks of age

Fig 5. **Lung lesion score after *M. hyopneumoniae* challenge.**



This study demonstrated that DUO™ outperformed the already combined PCV2+M.hyo RTU and also the RTM vaccines concerning the protection against the development of lung lesions due to M.hyo.

Conclusion

- Swine producers require reduction of shots administered to each pig
- DUO™ provides this convenience for the control of PCV2 and M.hyo infections
- DUO™ offers protection against PCV2 and M.hyo until 26 weeks of age

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.

Circovac: emulsion and suspension for emulsion for injection for pigs. Each ml of reconstituted vaccine contains: Inactivated porcine circovirus type 2 (PCV2)[3] 1.8 log10 ELISA Units. Excipient: Thiomersal:0.10 mg. Adjuvant: Light paraffin oil 247 to 250.5 mg. Indications: Piglets: Active immunisation of piglets to reduce faecal excretion of PCV2 and virus load in blood, and as an aid to reduce PCV2-linked clinical signs, including wasting, weight loss and mortality as well as to reduce virus load and lesions in lymphoid tissues associated with PCV2 infection. Safety and efficacy data are available which demonstrate that this vaccine can be mixed with Hyogen and administered to piglets at one injection site. When mixed with Hyogen, vaccinate only piglets from 3 weeks of age. Onset of immunity: 3 weeks after vaccination when mixed with Hyogen. Duration of immunity: 23 weeks when mixed with Hyogen.

Hyogen: emulsion for injection for pigs. Per dose. Active substance: Inactivated *Mycoplasma hyopneumoniae* 2940 strain: min. 5.5 EU. Adjuvants: Light liquid paraffin187 µl. *Escherichia coli* J5 LPS is max 38000 Endotoxin unit. Excipient: Thiomersal 50 µg. Indications: For the active immunization of fattening pigs from 3 weeks of age to reduce the occurrence and severity of lung lesions caused by *Mycoplasma hyopneumoniae* infection.Store and transport refrigerated (2 °C - 8 °C). Do not freeze. Withdrawal period: Zero days.

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