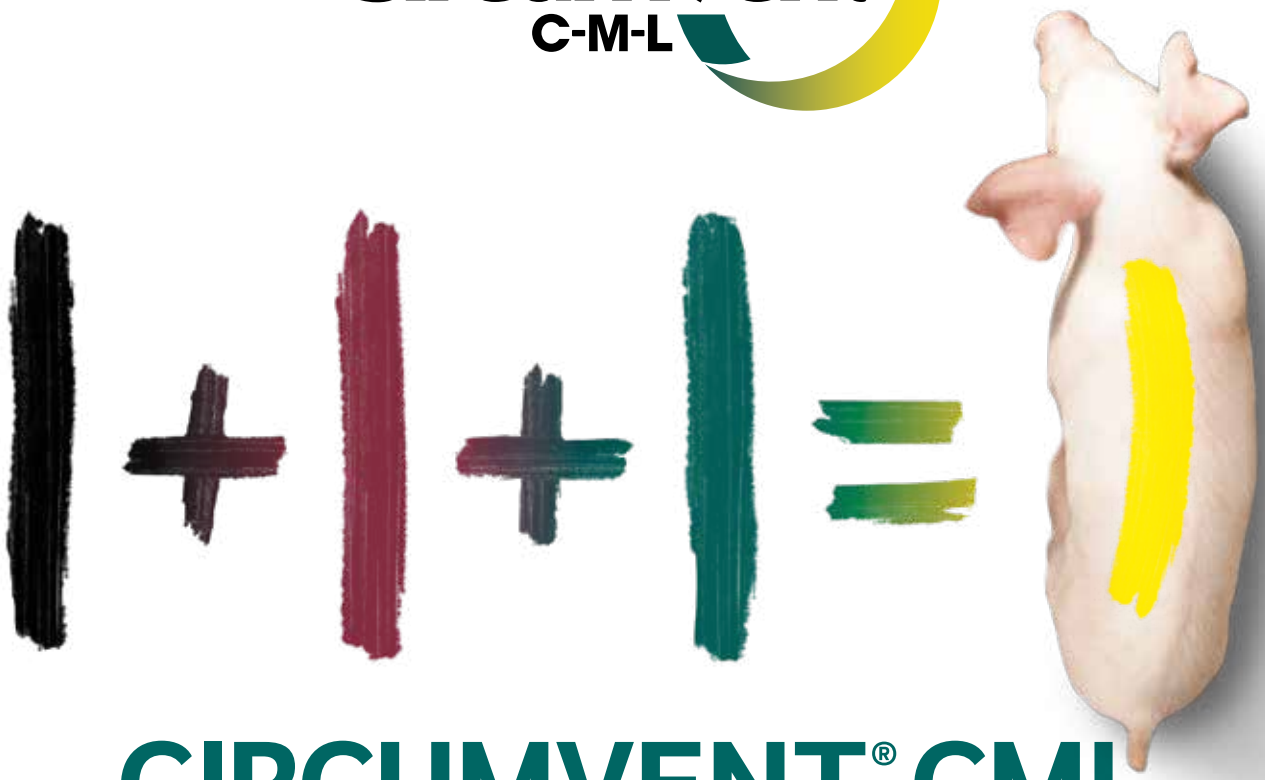
Circumvent® C-M-L



CIRCUMVENT® CML

One Revolutionary 3-in-1 Vaccine

Porcine circovirus types 2a and 2d + *Mycoplasma hyopneumoniae* + *Lawsonia intracellularis*

DRIVEN BY PREVENTION®

MERCK Animal Health

Circumvent® C-M-L

FIRST OF ITS KIND.

CIRCUMVENT® CML is the first and only vaccine that covers three major causes of disease with just one bottle.

+ FEWER INJECTIONS

- One shot covers:
  - Porcine circovirus types 2a and 2d
  - *Mycoplasma hyopneumoniae*
  - *Lawsonia intracellularis*
- Single, 2 mL IM dose for pigs 3 weeks of age or older

+ FEWER BOTTLES TO MANAGE

- Reduces inventory
- Reduces waste

+ MORE COMFORT

- Less stress for pigs
- Less labor for staff

+ MORE CONVENIENCE

- Reduces bottle handling

+ SAME CONFIDENCE

- Same antigens and Microsol Diluvac Forte® adjuvant trusted in CIRCUMVENT® PCV-M G2 and PORCILIS® ILEITIS products
- Backed by data – 10 licensing studies proving efficacy and safety

For a singularly better experience for your staff and your animals.

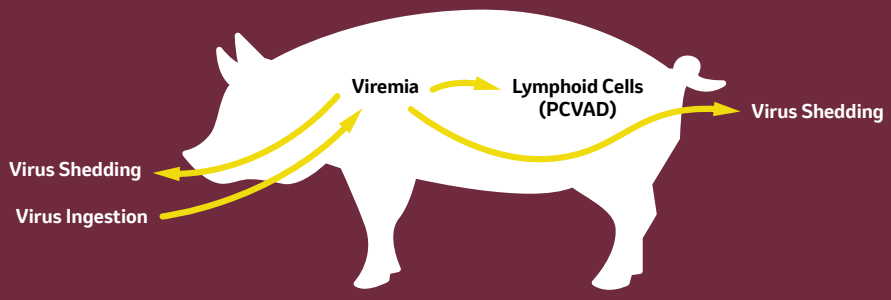
C Porcine circovirus type 2

CIRCUMVENT CML has been shown effective for the reduction of viremia and lymphoid depletion due to PCV2 infection.

Following exposure to the virus, porcine circovirus type 2 (PCV2) virus starts circulating in the blood. It's the initial step in the development of porcine circovirus associated disease (PCVAD) within the pig, but it can last up to four or five months post-infection.[1]

PCVAD can:

- Increase mortality, culls and treatments[2]
- Negatively impact average daily gain and feed conversion[2]
- Increase the severity of co-infection from porcine reproductive and respiratory syndrome (PRRSV), *Mycoplasma hyopneumoniae (M. hyo)* and influenza A virus in swine (IAV-S)[3-5]



PCVAD DISEASE PROGRESSION FROM TIME OF EXPOSURE

DAY 0 INITIAL EXPOSURE	DAYS 0-12 AFTER EXPOSURE	DAYS 12-20 AFTER EXPOSURE	DAYS 20-120+ AFTER EXPOSURE
Initial Exposure to PCV2	**Initial Infection** Undetectable viremia	**Breakout Infection** Detectable viremia, shedding, lymphoid depletion	**Completion** Pigs either resolve, are left with chronic lymphoid inflammation or the disease proves fatal.

Preventing viremia early helps to limit or eliminate infection.
Reducing virus shedding, lymphoid depletion and infection also decreases the impact of disease in later stages.

PCVAD diagnosis is determined based on:

- The presence of virus (blood and target lymphoid tissues)
- Histological or microscopic changes with the tissues (lymphoid depletion and inflammation)

C Porcine circovirus type 2

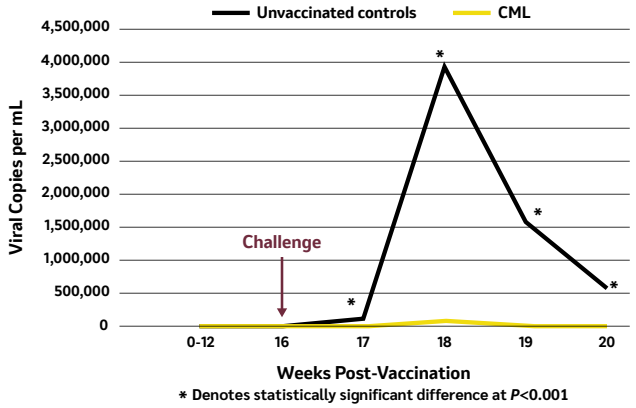
PCV2 Study Results

Vaccinating pigs with CIRCUMVENT CML significantly reduces PCVAD versus controls after a PCV2 challenge[6]

- Lymphoid depletion (LD) scores were much lower in vaccinates[6]
- The amount of virus in the blood (viremia levels) was 99% lower in vaccinated pigs[6]
- Vaccinated pigs had significantly higher antibody levels than controls[6]

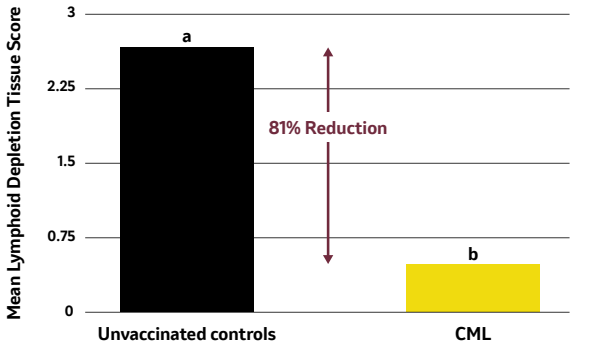
Mean PCV2d VIREMIA Scores[6]

>99% Reduction in Viremia in Vaccinates Compared to Controls



* Denotes statistically significant difference at *P*<0.001

PCV2d Duration of Immunity (DOI) Mean Lymphoid Depletion Tissue Score[6]



Different superscripts denote statistically significant difference at *P*<0.001

TESTED AND DEVELOPED UNDER TOUGH, REAL-WORLD CONDITIONS.

In the "real world," pigs face multiple co-infections. For the PCV2d fraction, a post-licensing study was done using a PRRSV and PCV2d co-challenge model. In this study, in addition to lower lymphoid depletion and lymphoid inflammation scores at necropsy and lower levels of viremia, a derived benefit of 9 lbs. heavier body weights was observed in the CIRCUMVENT CML pigs versus the controls.[7]

You can be confident that CIRCUMVENT CML will perform against the everyday disease pressure found in real barns.

PCV2d/PRRSV co-challenge study: Mean Body Weights

Body Weight (lbs.)	Controls	CIRCUMVENT CML	Lbs. difference vs controls	*P* values
Vaccination (3 weeks of age)	15.5	15.6	+0.1	0.93
Challenge (9 weeks of age)	73.8	76.2	+2.4	0.69
Necropsy (13 weeks of age)	118.4	127.4	**+9.0**	0.06

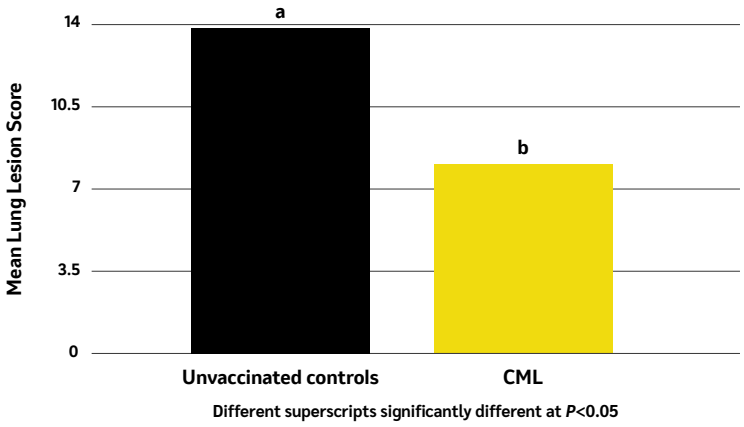
M *Mycoplasma hyopneumoniae*

CIRCUMVENT CML is effective against disease caused by *Mycoplasma hyopneumoniae*

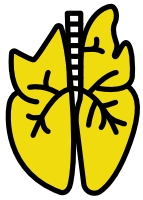
Mycoplasma hyopneumoniae is a common cause of pneumonia in pigs worldwide. It frequently leads to chronic lung infections which causes reduced average daily gain and decreased feed efficiency.[8]

M. hyopneumoniae Study Results

Mycoplasma hyopneumoniae DOI – Lung Lesions



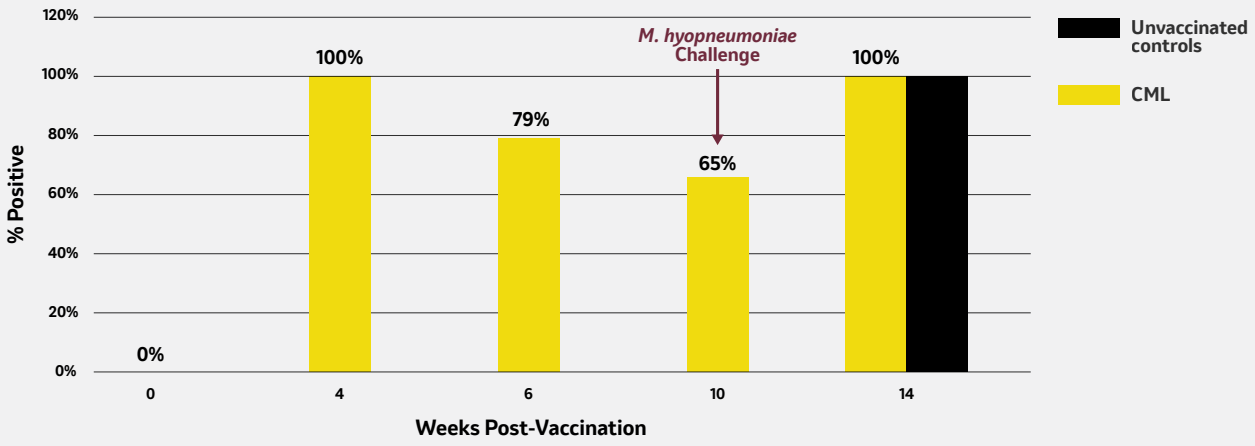
Different superscripts significantly different at $P<0.05$



Vaccinating pigs with CIRCUMVENT CML significantly reduced lung lesions versus controls after a *M. hyopneumoniae* challenge.

Lung lesions at necropsy in the vaccinated group were nearly half that of controls after challenge at 10 weeks of age.[6]

M. hyopneumoniae DOI – Seroconversion



Seroconversion to *M. hyopneumoniae* allows for vaccination compliance monitoring

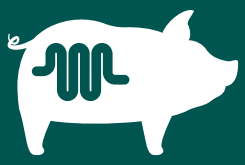
Seroconversion after vaccination with one 2 mL dose was seen in 100% of vaccinated pigs at 4 wpv.[6]

L *Lawsonia intracellularis*

CIRCUMVENT CML is effective against disease caused by *Lawsonia intracellularis*

Lawsonia intracellularis is a common pathogen that causes ileitis, an enteric disease that decreases the average daily gain of growing swine and increases the amount of feed required to reach market weight.

- Nearly 42% of grow-finish operations report clinical ileitis, and nearly 94% of herds with no clinical signs are found to have subclinical ileitis.[9,10]
- *Lawsonia intracellularis* infects immature epithelial cells of intestinal crypts, mostly in the ileum, causing thickening of the lining of the intestine. This results in decreased absorption of nutrients, which means that more feed is needed for each pound of growth.
- The disease can be subclinical with no visible signs, or can clinically present in an acute (hemorrhagic) form, which can result in mortality.
- Pigs can shed *Lawsonia* for up to 12 weeks after clinical signs have abated – and even subclinically affected pigs can shed the organism.[11]



GUT HEALTH IS CRITICAL IN YOUNG PIGS.

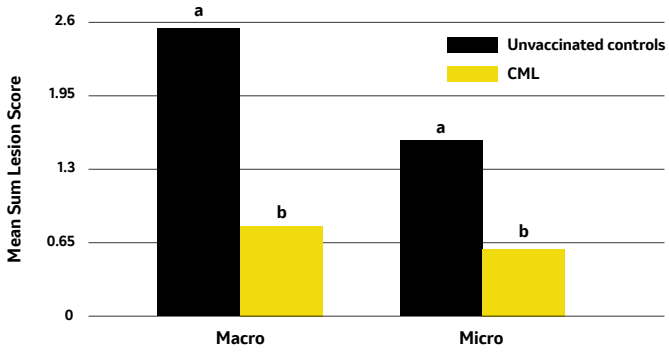
The gastrointestinal system undergoes the most rapid development in the first three months of life, establishing pig's health and level of performance.

Lawsonia intracellularis Study Results

Pigs vaccinated with CIRCUMVENT CML had reduced lesions associated with ileitis versus unvaccinated controls after a challenge of live, virulent *Lawsonia intracellularis* bacteria.

- The mean ileum lesion scores (length and severity) in the vaccinated groups were nearly half that of unvaccinated pigs.[6]
- The level bacteria in the ileum tissues at necropsy were on average 90% lower in vaccinated pigs.[6]
- The level of antibodies for *Lawsonia intracellularis* was significantly higher in vaccinates following vaccination.[6]

Lawsonia intracellularis Onset of Immunity Study Macroscopic and Microscopic Lesions[6]



Different superscripts significantly different at *P*<0.05

Lawsonia intracellularis DOI – Ileum Tissue Mean Bacterial Loads

Treatment Group	Cycle Threshold
Unvaccinated controls	16.7[a]
CIRCUMVENT CML	22.6[b]

Different superscripts within columns denote statistical significance at *P*<0.001

Circumvent® C-M-L

CIRCUMVENT CML Safety Study Results[6]

Field safety studies were performed in herds from three distinct geographical locations.

- Three total herds
- 681 healthy, 3-week-old weaned pigs
- Vaccinated with two separate vaccine serials
- Observed at vaccination, one hour after vaccination and then daily for 14 days
  - Health abnormalities
  - Systemic or local reactions (followed until resolution)

KEY TAKEAWAY

CIRCUMVENT CML is safe and effective

- Moderate local reactions that completely resolved on average within 2 weeks
- Incidence of fainting pigs was low at 0.6%*

*Immediate systemic reactions have been observed in animals administered this product. Minimize pig handling and ensure proper ventilation prior to starting vaccination.

An adjuvant designed for pigs to help stimulate a robust immune response.

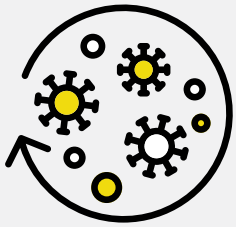
The primary burst, or immuno-inflammatory cascade, is the immune system's critical response to a new challenge. It's the first chance to create a strong, long-lasting resistance to a disease. All CIRCUMVENT G2 vaccines contain Microsol Diluvac Forte® – an adjuvant formulated specifically for pigs to help stimulate a robust primary burst and optimum immune response to keep pigs protected longer.

Same Microsol Diluvac Forte® adjuvant found in the CIRCUMVENT® PCV-M G2 and PORCILIS® ILEITIS products.

Protecting against PCV2, *M. hyopnemoniae* and *Lawsonia intracellularis* in one bottle can help protect the bottom line further by:

Cutting down on labor and waste

Increasing feed savings[2]



Providing a long DOI[6]

Reducing late-finishing mortality[2]

CONVENIENCE. VALUE. RESULTS.

Circumvent® C-M-L

One Revolutionary 3-in-1 Vaccine

Get solid protection against three of the most economically important disease-causing pathogens in swine. All with less stress, less labor and less waste.

For more information, visit
DRIVENBYPREVENTION.COM.

Scan the QR code to visit the CIRCUMVENT CML product page.

[1]Gillespie, J., Opriessnig, T., Meng, X.J., Pelzer, K. and Buechner-Maxwell, V. (2009), Porcine Circovirus Type 2 and Porcine Circovirus-Associated Disease. Journal of Veterinary Internal Medicine, 23: 1151-1163. https://doi.org/10.1111/j.1939-1676.2009.0389.x

[2]Jacela JY, Dritz SS, DeRouchey JM, et al. Field evaluation of the effects of a porcine circovirus type 2 vaccine on finishing pig growth performance, carcass characteristics, and mortality rate in a herd with a history of porcine circovirus-associated disease. J Swine Health Prod. 2011;19(1):10–18.

[3]Saade, G., Deblanc, C., Bougon, J. et al. Coinfections and their molecular consequences in the porcine respiratory tract. Vet Res 51, 80 (2020). https://doi.org/10.1186/s13567-020-00807-8

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[6]Data on File, Merck Animal Health

[7]Data on File, Merck Animal Health

[8]Thacker EL and Thacker BJ. *Mycoplasma hyopneumoniae* and PRRS in the finisher. 1999 American Association of Swine Practitioners, 483-485.

[9]USDA. 2007. Swine 2006, Part II: Reference of swine health and health management practices in the United States. 2006. USDA:APHIS:VS, CEAH. Fort Collins, CO. #N479.1207.

[10]Armbruster GA, et al. Review of *Lawsonia intracellularis* seroprevalence screening in the United States. June 2003 to July 2006. Proceedings of the 38th Annual Meeting of the American Association of Swine Veterinarians. 2007.

[11]Guedes R. Update on epidemiology and diagnosis of porcine proliferative enteropathy. *J Swine Health Prod.* 2004;12(3):134-138.

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