

An interview with  
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Zoetis Global Biologicals Swine

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## MetaStim® : The best balance of humoral, cellular immunity

**Q:** What’s the purpose of an adjuvant?

**DF:** Adjuvants are the instruction manual for the immune system. They play an important role in determining the type of immunity activated. When properly paired with vaccines, adjuvants can steer the animal’s response toward the best, most effective type of immunity for a given pathogen.

**Q:** MetaStim® is the adjuvant in Foster Gold® PCV MH, which is for healthy pigs 3 days of age or older against porcine circovirus type 2 (PCV2) as well as respiratory disease due to *Mycoplasma hyopneumoniae* (*M. hyo*). Why MetaStim?

**DF:** We evaluated several adjuvants. MetaStim provided the best combination of humoral and cellular immunity against PCV2.<sup>1</sup> There are other advantages. MetaStim is an oil-in-water emulsion with an oil content of less than 1% by volume. It provides a strong immune response, but there’s minimal reactivity.<sup>2</sup> Injection site reactions are rare and negligible, which was demonstrated in a large three-state field trial with Foster Gold PCV MH.<sup>3</sup>

MetaStim is also responsible for the vaccine’s long duration of immunity (DOI), which is 23 weeks for PCV2. That’s longer than the DOI for any other PCV2 vaccine in the US, which contain different adjuvants. The DOI is 23 weeks for *M. hyo* as well.

**Q:** How do humoral and cellular immunity differ?

**DF:** Humoral means body fluids. Humoral immunity involves the release of pathogen-fighting antibodies into serum or fluid. Cellular immunity happens by direct action of a cell — T lymphocytes destroy cells that are infected. Both types of immunity are important.

*continued*



“Antibodies...can't get to a virus once it's in a cell — and that's where cell-mediated immunity comes in.”

**Q: Tell us more about why both types of immunity are important.**

**DF:** Humoral immunity can be very effective at preventing the initial entry of a virus at the mucosal surface. It can neutralize virus in blood. Antibodies, however, can't get to a virus once it's in a cell — and that's where cell-mediated immunity comes in.

I'll use PCV2 again as an example. It's a persistent virus that can hide out in some cells, such as macrophages, and then spread, usually to lymph nodes. Ultimately, the virus replicates in lymphocytes and kills them, causing immune suppression. The pig is left susceptible to other infectious diseases.

Activating both humoral and cellular immunity provides a double whammy against PCV2. There is evidence that *M. hyo* can also persist in cells,<sup>4</sup> which is one more reason why we chose MetaStim for the adjuvant in Foster Gold PCV MH.

**Q: Don't other adjuvants stimulate both types of immunity?**

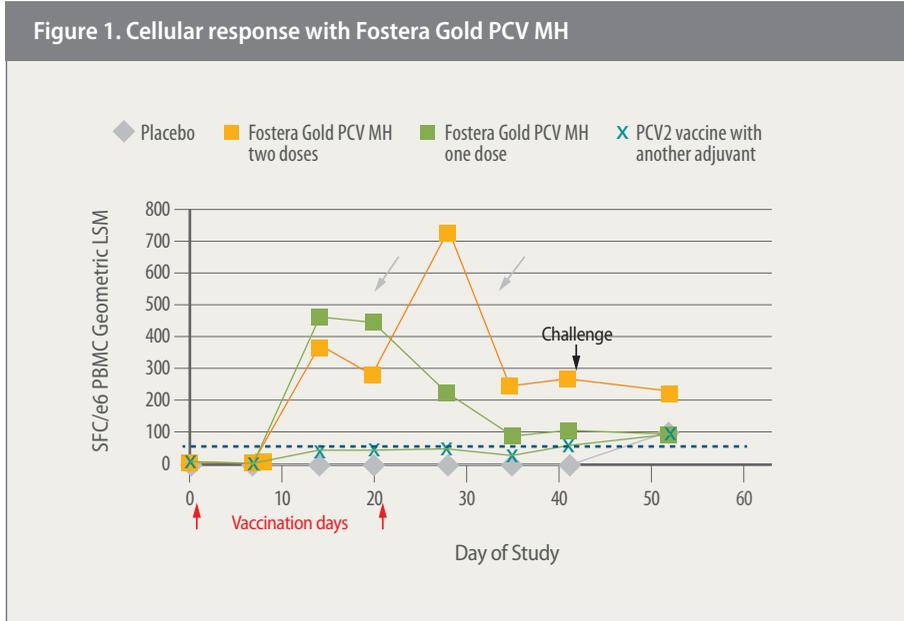
**DF:** Most do but the relative amounts of each type of immune response vary. Vaccines with a high mineral oil content may induce a higher immediate antibody response but less cellular immunity. The goal of adjuvant selection is to induce the best balance of humoral and cellular immunity for a given pathogen. We found MetaStim to be the best choice for use in Foster Gold PCV MH.

**Q: What evidence is there MetaStim induces both humoral and cellular immunity in pigs?**

**DF:** This is something we've studied extensively. When MetaStim was used as the adjuvant for the PCV2a/PCV2b/*M. hyo* combination in Foster Gold PCV MH, there were high antibody titers following two doses of vaccine. Even in pigs that received only one dose of vaccine, there was a rapid PCV2 antibody response in challenged pigs. This indicates a robust priming of the humoral immune response with a single dose of vaccine. In addition, the cellular response was significantly higher compared to the response after two doses of a PCV2 vaccine with a different adjuvant (Figure 1).<sup>5</sup>

**Q: But do your experimental studies with MetaStim translate into success in the field?**

**DF:** They do. One of several studies involved more than 880 pigs on a Midwest farm.<sup>6</sup> Pigs were vaccinated with Foster Gold PCV MH or with other commercial PCV2 plus



\* Vaccination induced a biologically relevant CMI response if specific IFN $\gamma$  (interferon gamma) secretion was above 50 SFC/10e6 PBMC. Post-challenge, PCV2-specific T cells move into the tissues and out of the blood to protect against PCV2 infection.

*M. hyo* vaccines. Then we challenged pigs with PCV2d, the most prevalent PCV2 genotype in US herds, as well as *M. hyo*. Pigs that received Foster Gold PCV MH had significantly less ( $p < 0.05$ ) PCV2 viremia than unvaccinated controls, and they had fewer lung lesions and higher final weights than pigs that received the other PCV2/*M. hyo* vaccines.<sup>7</sup>

**Q: What do you most want pork producers and veterinarians to know about MetaStim?**

**DF:** That in the course of our PCV2 research program, we have extensively tested a wide variety of adjuvants, including current and experimental formulations. We have yet to find an adjuvant that outperforms MetaStim’s safety and efficacy in PCV2 challenge studies.

For more information, contact Dennis Foss (dennis.foss@zoetis.com) or your Zoetis representative.

“ Activating both humoral and cellular immunity provides a double whammy against PCV2. ”

<sup>1</sup> Data on file, Study Report No. B820R-US-17-747, Zoetis LLC.

<sup>2</sup> Data on file, Study Report No. B921R-US-16-609, Zoetis LLC.

<sup>3</sup> Ibid.

<sup>4</sup> Raymond BBA, et al. *Mycoplasma hyopneumoniae* resides intracellularly within porcine epithelial cells. *Sci Rep.* 2018;8:17697.

<sup>5</sup> Data on file, Study Report No. B820R-US-17-747, Zoetis LLC.

<sup>6</sup> Data on file, Study Report No. 16 PRGBIO-01-01, Zoetis LLC.

<sup>7</sup> Ibid.

**toolbox**

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