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Safety of Single-Dose Vaccination with Fostera™ PCV MH in Young Pigs

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Vaccinations against porcine circovirus-associated disease (PCVAD) caused by PCV Type 2, and enzootic pneumonia caused by *Mycoplasma hyopneumoniae (M. hyo)*, have become critical and fundamental components of most swine health programs. Herd protection has historically required separate vaccinations for each pathogen, but the recent advent of combination vaccines containing both antigens offers to greatly reduce the labor and animal stress involved in vaccination protocols.

Development of a porcine circovirus (PCV)/ *M. hyo* combination vaccine involves multiple technical factors that can impact safety, efficacy, and ease-of-use (e.g., field mixing, multiple doses, etc.). Regardless of the efficacy or convenience benefits a combination vaccine may offer, no veterinarian or producer is willing to use a product that compromises animal safety (e.g., clinical abnormalities, serious injection site reactions, etc.). Therefore, Zoetis has devoted significant research and development to enable an innovative manufacturing process that yields a highly effective and user-friendly combination PCV/*M. hyo* vaccine with an excellent safety profile that minimizes the risk of clinical abnormalities and injection site reactions.

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Fostera™ PCV MH

Fostera™ PCV MH, from Zoetis, is the first and only combination, **one-bottle** vaccine that helps to protect swine from ***both*** PCVAD and enzootic mycoplasma pneumonia after administration of a ***single dose*** (other combination vaccines require mixing in the field or multiple doses). Fostera PCV MH was uniquely developed to ensure proper antigen/adjuvant balance, helping deliver safe and effective protection against both PCVAD and enzootic mycoplasma pneumonia.

A single 2-mL intramuscular (IM) dose of Fostera PCV MH is licensed for the vaccination of healthy pigs at 3 weeks of age or older as an aid in preventing viremia, lymphoid depletion, and colonization of lymphoid tissue caused by PCV2; and as an aid in reducing PCV2 virus shedding and enzootic pneumonia caused by *M. hyo*. Thus, Fostera PCV MH helps provide disease protection afforded by other monovalent Zoetis products: protection from *M. hyo* similar to RespiSure-ONE,® and protection against PCVAD similar to Fostera PCV, all in a convenient one-bottle, one-dose formulation.

Control pigs and Fostera PCV MH vaccinates had similar low rates of abnormal health events.

As part of the body of research conducted for licensure of Fostera PCV MH, a multi-site field-safety study evaluated local injection site reactions and systemic events after administration of a single dose of Fostera PCV MH to young pigs at approximately 3 weeks of age.[1]

Experiment Design

The study involved 790 weaned pigs, 17 to 27 days of age, that were enrolled at 3 separate commercial production sites in North Carolina (n=250), Kentucky (n=253), and Illinois (n=287). Healthy pigs at each site were randomly assigned to 2 treatment groups (approximately 3:1 ratio). On study day 0, each pig received a single-dose, 2-mL IM injection in the right neck with either:

- Fostera PCV MH (n=632);
- Saline (non-vaccinated control, n=158).

All animals were observed for adverse reactions within 1 and 6 hours post-vaccination, and clinical observations were conducted at approximately weekly intervals starting on day 1 until study conclusion on day 21. All injection sites were observed and palpated on days 1 and 7 for adverse reactions, with any reactions rechecked daily until resolution. Animals were also observed daily for any clinical disease or adverse events requiring treatment. All cases were determined whether to be related to vaccine or saline administration, and any pigs that died were necropsied and a diagnosis determined when possible. Personnel performing clinical observations, injection site reaction measurements, post-mortem examinations, or laboratory measurements were masked as to treatment group assignments.

The non-vaccinated control group provided baseline information regarding the current herd health conditions at each site. Thus, the incidence and severity of health events in the Fostera PCV MH group were compared to those occurring in the control group. Data were analyzed by appropriate statistical methods using the pig as the experimental unit. The protocol was reviewed and approved by the Zoetis Kalamazoo Ethical Review Board. A Zoetis Animal Welfare Risk Assessment was completed for each site prior to initiation of the study.

Results

No confounding disease factors were detected during the study which affected evaluation of vaccine safety. No clinical signs of PCV2 or *M. hyo* pneumonia were observed, but other clinical signs of disease were occasionally present in some animals (e.g., diarrhea, pneumonia, lethargy, cough, jowl abscess, lame, thin, gaunt, rough hair coat). Three pigs died at the NC site (pneumonia, trauma), and 17 mortalities were recorded at the KY site due to chronic bronchopneumonia.

At approximately 1 hour after vaccination, 3.2% of control pigs and 2.7% of Fostera PCV MH vaccinates demonstrated abnormal post-vaccination clinical symptoms (depression, dyspnea, and/or cough, lameness, mild gauntness, etc.). By 6 hours post-vaccination, the rate had fallen to 1.3% for controls and 1.1% for vaccinates. Thus, the rate of abnormal post-vaccination observations was approximately the same or less in Fostera PCV MH vaccinates than in controls, suggesting no acute abnormalities attributable to use of the single-dose combination vaccine.

The incidence of injection site reactions are summarized in Table 1. With the exception of 7 pigs (1.1%) in the Fostera PCV MH group (all at IL site), all other animals in the study demonstrated 'normal' post-vaccination injection sites on day 1 (not more than a visible injection site with < 0.5 cm diameter zone of swelling only associated with the injection site, and no evidence of irritation). Injection site reactions in the 7 pigs were characterized as 'mild' (0.5-1.5 cm diameter swelling, possible evidence of irritation such as occasional rubbing), and these mild reactions resolved by study day 3.

Table 1 – Incidence of injection site reactions and anaphylactic reactions (summary of 3 sites).

Treatment	No. pigs	Injection site reactions		Anaphylactic reactions
		Day 1	Day 7	
Control	158	0%	0%	0%
Fostera PCV MH	632	1.1%	0%	0%

Also noted in Table 1 is the complete absence of anaphylactic reactions in study animals. Rates of all other abnormal health events in Fostera PCV MH vaccinates were similar to rates that occurred in control pigs. These events, along with necropsy diagnoses and diagnostic laboratory results, were consistent with herd health observations and not related to administration of Fostera PCV MH.

Conclusions

Results of this multi-site clinical field study confirm the safety of single-dose Fostera PCV MH in 3-week-old pigs. The incidence of abnormal health events was similar between animals vaccinated with Fostera PCV MH and controls, and only a very low incidence (1.1%) of mild, quick-resolving injection site reactions was observed.

Study results suggest that the extensive research effort by Zoetis scientists to develop a safe PCV/M. *hyo* one-bottle vaccine has been successful. The excellent safety profile of Fostera PCV MH allows pork producers and veterinarians to deploy the novel single-dose combination vaccine in their herds with the confidence that safety will not be compromised.

References

1. Data on file, Study Report No. B921R-US-12-009, Zoetis Inc.

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