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Research Article

Convenience and economic benefit of early one-shot *Mycoplasma hyopneumoniae* vaccination at 3 days of age in a commercial sow farm

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Abstract

Mycoplasma hyopneumoniae (*M. hyopneumoniae*) is the primary pathogen of enzootic pneumonia, a chronic respiratory disease in pigs. Vaccination of piglets to protect against *M. hyopneumoniae* can be performed at several ages, depending on product label specifications. Early intervention in the first week of life may have advantages, since piglets can already become infected with *M. hyopneumoniae* during the suckling period, resulting in a significant percentage of *M. hyopneumoniae*-positive piglets around weaning. The current study compared convenience and economic benefits of *M. hyopneumoniae* vaccination in piglets of 3, 7 and 14 days of age. Duration of piglet vaccination at 3 days of age was significantly ($P < 0.05$) shorter (2.64 ± 0.08 seconds) as compared to 7 days of age (4.90 ± 0.18 seconds) and 14 days of age (6.04 ± 0.22 seconds). Economic calculation in a 1000-sow unit, using a vaccination convenience calculator, demonstrated that although the total number of piglets vaccinated is lower (- 443 and - 838 at 7 and 14 days of age, respectively) at a later vaccination age, the related increase in vaccine cost in the early vaccination group (Group 1) was largely compensated by the decrease in cost of overall vaccination time (€ 1,115.61 and € 1,461.00 lower at 3 days of age as compared to 7 and 14 days of age, respectively). In conclusion, *M. hyopneumoniae* vaccination at 3 days of age has several advantages over later vaccination at 7 or 14 days of age. Besides the benefits in convenience of piglet handling at that age, we could also demonstrate economic benefits of early *M. hyopneumoniae* vaccination.

Abbreviations

AE: Adverse Events; ANOVA: Analysis of Variance; DNT: Dermonecrotic Toxin; IAV-S: Influenza A Virus–Swine; *M. hyopneumoniae: Mycoplasma hyopneumoniae;* OOI: Onset of Immunity; PCV-2: Porcine Circo Virus type 2; *P. multocida: Pasteurella multocida;* PRDC: Porcine Respiratory Disease Complex; PRRSV: Porcine Reproductive and Respiratory Syndrome Virus; SEM: Standard Error of the Mean

Introduction

Mycoplasma hyopneumoniae (*M. hyopneumoniae*) is the primary pathogen of enzootic pneumonia, a chronic respiratory disease in pigs. The disease causes major economic losses to the pig industry worldwide due to the reduced performance of the pigs (growth rate, feed conversion) and the increased use of antimicrobials [1,2]. Moreover, *M. hyopneumoniae* plays a major role within the Porcine Respiratory Disease Complex (PRDC) as the principal agent of enzootic pneumonia, a chronic respiratory disease that mainly affects finishing pigs [3].

Control of *M. hyopneumoniae* can be accomplished by improvement of management practices and housing conditions, by antimicrobial medication and vaccination. Vaccination with commercial bacterins has become an important tool to control *M. hyopneumoniae* infections. These vaccines, consisting of adjuvanted whole-cell preparations, are administered intramuscularly [1,4]. They have been shown to induce partial protection resulting in reduction of clinical signs and lung lesions, and improvement of performance [2,5]. Major advantages of vaccination include improvement of

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daily weight gain (2-8%), feed conversion ratio (2-5%) and sometimes mortality rate. Additionally, shorter time to reach slaughter weight, reduced clinical signs, lung lesions and lower treatments costs are observed [1]. Commercial vaccines also reduce the number of organisms in the respiratory tract [6-8] and decrease the infection level in a vaccinated herd [9]. However, vaccination only resulted in a limited reduction of the transmission ratio of *M. hyopneumoniae* under both experimental [7] and field conditions [10]. Comparing different vaccination strategies against *M. hyopneumoniae* indicates varying levels of protection [11]. Indeed, an effective disease control program for *M. hyopneumoniae* does not only include vaccination at the right time, but also involves optimization of management conditions for the most appropriate response to the vaccination [12].

Piglets are born free of *M. hyopneumoniae*, as *in utero* transmission has not been documented, and first exposure events occur during the lactation period, where piglets are in contact with dams shedding the microorganism [13]. Early infection with an increasing prevalence rising from 1.5% of *M. hyopneumoniae*-positive piglets at 1 week of age to 3.8% at 3 weeks of age has been demonstrated [14]. Several studies have confirmed the presence of *M. hyopneumoniae* infection around weaning (3-4 weeks of age) [14-19] and during the post-weaning period [14,15,17,20]. Vaccination of suckling piglets against *M. hyopneumoniae* has the advantage that immunity can be induced before pigs become infected, and that less pathogens are present that can interfere with the immune response [1].

In Europe, one-shot and two-shot vaccines against *M. hyopneumoniae* are available [2]. One-shot vaccines require less labor and can be implemented more easily in routine management practices in the farm. Moreover, single vaccination at either 7 or 21 days of age was demonstrated to be efficacious in a pig herd with clinical respiratory disease during the second half of the fattening period [21]. Vaccinating piglets 3 days prior to weaning conferred slightly better results under both experimental [22] and field conditions [23] as compared to vaccination at weaning, which may be explained by the fact that weaning is a stressful event that may decrease general immunity [24]. Therefore, early vaccination is advised in occasions where early infection can be detected [17-19]. However, sow vaccination against *M. hyopneumoniae*, which is applied in an increasing number of farms to reduce excretion of *M. hyopneumoniae* by gilts and sow to their offspring during the lactation period [25,26], might interfere with early piglet vaccination in some cases. Nevertheless, others have shown that piglets vaccinated early in life in the presence of maternally derived antibodies due to sow vaccination against *M. hyopneumoniae* are able to mount an effective immune response, resulting in adequate protection against natural [27] or experimental [28] *M. hyopneumoniae* infection in the second half of the fattening period. Moreover, piglets with *M. hyopneumoniae*-specific maternally derived immunity had both primary (antigen-specific lymphoproliferation) and secondary (delayed type hypersensitivity) *M. hyopneumoniae*-specific cell-mediated immunity responses following *M. hyopneumoniae* vaccination [29].

As multiple pathogens are involved in PRDC on many farms, vaccination against several pathogens within PRDC should be considered. Combined vaccines, especially *M. hyopneumoniae* and PCV-2 [6,30-31] or PRRSV [32], have recently been developed. However, these combined dual vaccines can only be administered from 21 days of age [2]. In contrast, single *M. hyopneumoniae* vaccines are registered for intramuscular administration from 3 days onwards (Stellamune® One; Elanco AH). Other one-shot *M. hyopneumoniae* vaccines can be administered from 7 days of age (Suvaxyn® MH-ONE; Zoetis), whereas most other *M. hyopneumoniae* vaccines can only be administered at 14 days of age (Porcilis® MHYO ID Once; MSD) or 21 days of age (Ingelvac® Mycoflex; Boehringer Ingelheim; Hyogen®; Ceva). Whereas Stellamune® One (onset of immunity (OOI) 18 days) and Suvaxyn® MHYO-ONE (OOI 14 days) can induce immunity in the piglets before or at weaning (21 days of age), the other vaccines only develop protective immunity from 35 days of age onwards (OOI 14-21 days, depending on the specific vaccine).

The aim of the present study was to evaluate the convenience of administering a one-shot *M. hyopneumoniae* vaccine (Stellamune® One; Elanco AH) at 3 days of age compared to a later vaccination of suckling piglets during the lactation period at 7 and 14 days of age. Convenience was measured as time required for vaccination of an individual piglet. Besides convenience, a calculation of potential economic benefit of the different vaccination schedules was performed.

Material and methods

Selection of the breeding herd

Inclusion criteria used to select the breeding herd are depicted in a flowchart (Figure 1). These criteria included at least a batch farrowing management and willingness of the pig owner and stockman to collaborate in the study. In addition, batches should contain at least 3 * 20 sows. These inclusion criteria were key for the study to be representative for modern pig production management and the guarantee to have enough litters and piglets available for sufficiently effective data generation in only one batch of manipulation and data collection. The study design aimed at dividing the production batch into 3 groups of at least 20 litters to perform the different vaccination timepoints in one of each groups.

A brief description of the herd, including health status, general management, ventilation, bedding, feeding system, current vaccination and treatment protocol of sows and suckling piglets, and management practices at processing time will be provided in the results section. Typically, processing of piglets included tail docking and teeth grinding. No antimicrobial treatment was administered at the same time as processing.

Vaccination groups and vaccine administration

Three experimental groups were included in the study, according to the time of vaccination of the piglets in each group:

Group 1: Piglets vaccinated at 3 days of age during processing

Group 2: Piglets vaccinated at 7 days of age on a special vaccination moment

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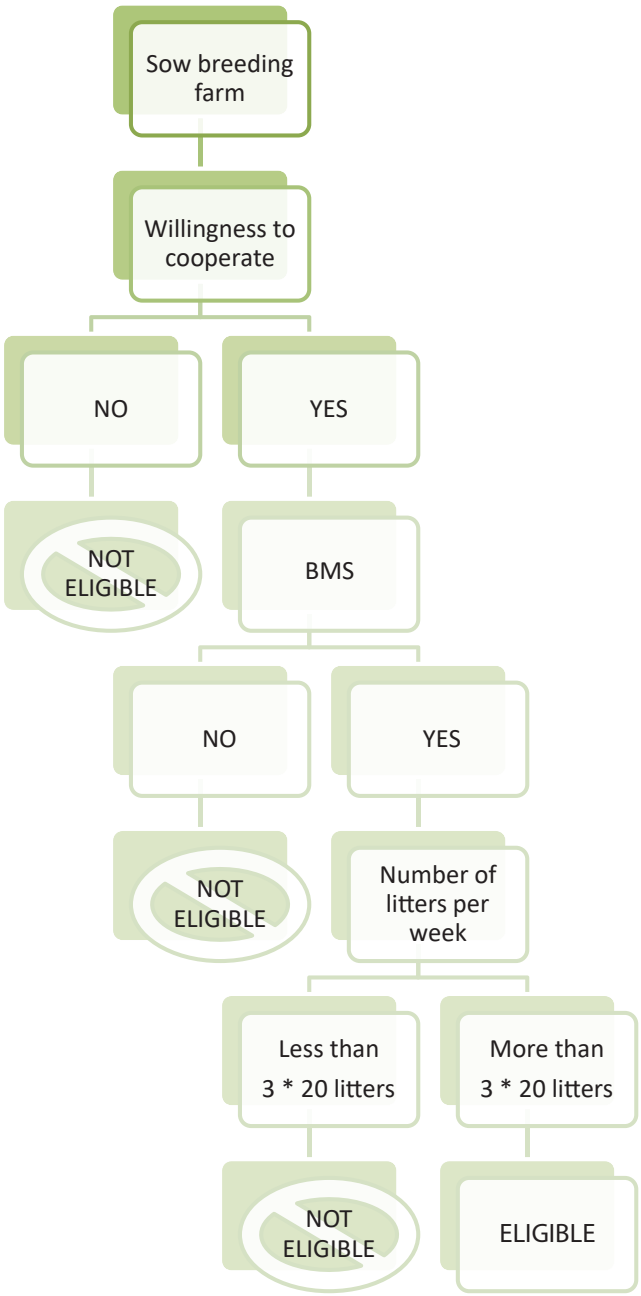

Figure 1: Flowchart for selection of the breeding herd to perform the vaccination study. BMS: batch-management system.

Group 3: Piglets vaccinated at 14 days of age on a special vaccination moment

A minimum of 20 litters of piglets was included in each group for a final number of at least 200 piglets per group. The experimental unit in this study was the piglet.

Piglets in each group received a single 2-ml dose of a one-shot *M. hyopneumoniae* vaccine (Stellamune® One; Elanco AH), administered by deep intramuscular route in the lateral neck muscle, following manufacturer's recommendations.

The same operator vaccinated the piglets in the 3 study groups. The vaccination technique was similar across groups, using a similar syringe, and picking up and restraining the piglets for the administration of the vaccine.

Duration of vaccination

The time used to administer the vaccine was measured by stopwatch and recorded as following by the investigator:

In Group 1 (piglets vaccinated at processing, day 3 of age) two parameters were measured:

Total duration of intervention per litter: The start time was the moment of entering the farrowing pen to pick up the first piglet for the intervention. The finishing time was when the last piglet in the litter had been processed (including vaccination with Stellamune® One). Total duration of the intervention per litter and number of piglets processed in the litter were recorded.

Duration of vaccination per litter: Additionally, vaccination time was recorded by piglet. Vaccination start time was marked by the end of the previous intervention during routine processing (when the piglet was transferred to the operator for vaccination or when the operator holds the syringe for vaccination if same operator performed both interventions). Finishing time was determined by restraining release immediately after vaccination. Duration of vaccination per litter and number of piglets processed in the litter were recorded. In each litter, average duration of vaccination per piglet was calculated by dividing the total duration of intervention per litter by the total number of piglets in the litter.

In Group 2 (piglets vaccinated at 7 days) and Group 3 (piglets vaccinated at 14 days) one parameter was measured:

Total duration of intervention per litter: The start time was at the moment of entering the farrowing pen to collect the first piglet for the intervention. The finishing time was determined by the release of the last piglet in the litter after vaccination with Stellamune® One. Total duration of the intervention per litter and number of piglets processed in the litter were recorded. In each litter, average duration of vaccination per piglet was calculated by dividing the total duration of intervention per litter by the total number of piglets in the litter. No other inventions (ear tagging, injections) than routine processing of *M. hyopneumoniae* vaccination were performed at the time of measuring the duration of the interventions.

Adverse events

In this study, an Adverse Event (AE) was defined as any observation in animals or humans that was unfavourable and unintended and occurred after the use of Stellamune® One, whether or not considered to be product related. A serious adverse event was any adverse event which resulted in death, was life-threatening, resulted in persistent or significant disability/incapacity or that required professional treatment/intervention above and beyond routine preventive measures or common first aid. A non-serious AE was defined as any abnormal health observation occurring during the treatment phase that was not defined as a serious AE.

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Economic calculation of vaccination cost at specific timepoint

In order to evaluate the economic impact of vaccination at 3, 7 or 14 days of age, a calculator was built taking into account multiple performance and economic parameters related to specific vaccination age such as percentage of pre-weaning mortality, proportion of pre-weaning mortality between day 1-3, 4-7, 8-14 and beyond day 14, vaccine cost per dose, hourly rate for hired labor, number of daily working hours, number of workers needed for vaccination, actual number of sows present on-farm, duration of vaccination per pig at 3, 7 and 14 days of age.

Data processing and statistical analysis

Duration of vaccination was considered as a primary parameter for the evaluation of the convenience of vaccination with a one-shot *M. hyopneumoniae* vaccine. Data generated in this study were analysed for differences in duration of vaccination between Group 1, and Group 2 and 3, using JMP version 14.0. A one way ANOVA (Tukey–Kramer HSD) was used to compare mean vaccination time across experimental groups with a significance level of 0.05.

Results

Description of farm management practices

The vaccination trial was carried out on a farrow-to-wean sow farm with 2,000 sows on-site. The farm was managed in a 1-week batch-management system with weaning at 25 days of age. Sow were housed in a group housing system with groups of 20 sows according to local regulations. Every week, approximately 100 sows were transferred to the farrowing house 7 days prior to farrowing. Compartment climatization was performed through mechanical ventilation using ventilation fans and room temperature was kept at 20°C throughout the entire production phase. Newborn piglets had a local heat source through an infrared heating lamp and a heated floor pad. Sows were fed twice daily during gestation and three times daily during lactation.

The sow herd had a conventional health status and were positive for *M. hyopneumoniae*, PRRSV, PCV-2, *Sarcoptes scabiei* var. *suis*, and atrophic rhinitis (dermonecrotic toxine (DNT) positive *P. multocida*). Sows were vaccinated during gestation to protect against PRRSV, *E. coli*, IAV-S and atrophic rhinitis. Sows were treated with parasiticides 14 days prior to farrowing for prevention of mange (*S. scabiei* var. *suis*). Piglets were vaccinated against *M. hyopneumoniae* at 3 days of age and PCV-2 at 3 weeks of age.

Duration of piglet vaccination

All results related to vaccination of the piglets at day 3, 7 and 14 for the three different treatment groups are given in Table 1.

In Group 1 (pigs vaccinated at processing, day 3 of age), the total duration of processing per litter was 128.7 ± 8.04 (mean ± SEM) seconds. Per piglet, the processing lasted 10.2 ± 0.37 (mean ± SEM) seconds. The start time was the moment of entering the farrowing pen to pick up the first piglet for the intervention. The finishing time was when the last piglet in the litter had been processed (including vaccination with Stellamune® One). The average total duration of vaccination at the end of processing was 34.2 ± 1.95 (mean ± SEM) seconds, with an average of 2.64 ± 0.08 (mean ± SEM) seconds per piglet.

In Group 2 (pigs vaccinated at 7 days), the average total duration of vaccination was 59.3 ± 2.38 (mean ± SEM) seconds, with an average of 4.90 ± 0.18 (mean ± SEM) seconds per piglet. In Group 3 (pigs vaccinated at 14 days), the average total duration of vaccination was 71.8 ± 3.58 (mean ± SEM) seconds, with an average of 6.04 ± 0.22 (mean ± SEM) seconds per piglet.

Statistical differences ($P < 0.05$) in total duration of vaccination were detected among the different experimental groups.

Economical cost calculation of piglet vaccination at different piglet ages

The input variables for the vaccination convenience calculator related to piglet age of vaccination are given in Table 2.

In Table 3, the vaccination convenience calculator output generated with specific input variables (Table 2: 1,000 sows, 33.5 piglets weaned per sow per year and 13.1% pre-weaning mortality) is given.

Although the total number of piglets vaccinated is lower (- 443 and - 838 in Group 2 and 3, respectively) at a later vaccination age, the related increase in vaccine cost in the early vaccination group (Group 1) is largely compensated by the lower cost for overall vaccination time (number of hours for 3 workers to perform the vaccination task). Overall, the total cost of vaccination (cost of vaccine + working hours) in Group 1 is € 1,115.61 lower as compared to Group 2 and € 1,461.00 lower as compared to Group 3. The increased total cost of vaccination in Group 2 and 3 was mainly due to the higher amount of time (+ 2.77 and + 4.11 days per worker in Group 2 and 3, respectively) to be invested in the vaccination activity.

Discussion

The present study results clearly demonstrated that early piglet vaccination against *M. hyopneumoniae* at 3 days of age

Table 1: Data related to the vaccination of piglets at day 3, 7 and 14, including number of litters vaccinated, total number of piglets vaccinated, number of piglets vaccinated per litter, total duration of vaccination per litter and duration of vaccination per piglet. Data are means ± SEM. Statistical differences ($P < 0.05$) are indicated by different letters in superscript.

Age at vaccination	Day 3	Day 7	Day 14
Parameter			
Number of litters included	20	20	20
Total number of piglets vaccinated	257	245	238
Number of piglets per litter	12.85 ± 0.62	12.25 ± 0.48	11.9 ± 0.43
Duration of vaccination per litter (s)	34.2 ± 1.95	59.3 ± 2.38	71.8 ± 3.58
Duration of vaccination per piglet (s)	2.64 ± 0.08^{a}	4.90 ± 0.18^{b}	6.04 ± 0.22^{c}

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has an economic advantage over other strategies with an older age of piglet vaccination. This is mainly due to the fact that at 3 days of age, *M. hyopneumoniae* vaccination can be included in other processing tasks such as teeth grinding and tail docking, whereas vaccination at 7 or 14 days of age is a stand-alone activity with no other standard processing tasks to be performed at this timepoint. Although the time saving for an early *M. hyopneumoniae* vaccination seems to be negligible (- 2.26 and - 3.40 seconds as compared to Group 2 and 3, respectively), the vaccination convenience calculator clearly showed the impact of total number of piglets to be processed on the outcome. Even when taking into account the number of additionally vaccinated piglets that die later during the suckling period, the economic benefit of early vaccination still remains better as compared to the other piglet vaccination ages.

Besides the convenience and economic aspects of vaccination, efficacy of vaccination against *M. hyopneumoniae* is also important to consider. Several epidemiological field studies have demonstrated that piglets might already be infected with *M. hyopneumoniae* at weaning [10,17,18] and piglet immunity seems to be compromised immediately post-weaning [24]. Others have shown that piglets vaccinated early in life, even in the presence of maternally derived

Table 2: Input variables for the vaccination convenience calculator related to piglet age of vaccination.

Performance parameter	Input value
Mortality during suckling period	
Pre-weaning mortality (%)	13.1
Proportion of pre-weaning mortality from day 1 to day 3 (%)	76.3
Proportion of pre-weaning mortality from day 4 to day 7 (%)	10.1
Proportion of pre-weaning mortality from day 8 to day 14 (%)	9.0
Proportion pre-weaning mortality from day 15 to weaning (%)	4.6
Vaccine related parameters	
Vaccine price/ dose (€)	1.05
Hourly rate of working force (€ / h)	23
Hours per working day (h)	7.6
Number of workers for vaccination activity	3.0
Sow production parameters	
Actual number of sows on farm	1,000
Actual weaned piglets per sow per year	33.5
Duration of piglet vaccination depending on vaccination age	
Duration (s) vaccination/pig at d3	2.64
Duration (s) vaccination/pig at d7	4.90
Duration (s) vaccination/pig at d14	6.04

Table 3: Vaccination convenience calculator output generated with the following performance input variables: 1,000 sows, 33.5 piglets weaned per sow per year, 13.1% pre-weaning mortality. All detailed input parameters are given in Table 2.

	Group 1	Group 2	Group 3	*Δ d7 – d3*	*Δ d14 – d3*
Vaccination age of piglets	Day 3	Day 7	Day 14		
Sow production parameters	cc				
Number of sows	1,000	1,000	1,000		
Weaned pig/sow / year	33.5	33.5	33.5		
Total pigs weaned / year	33,500	33,500	c33,500		
Total pigs born / year	37,889	37,889	37,889		
Piglet mortality					
Dead pigs (d 0-weaning)	4,389	4,389	4,389		
Dead pigs (d 1-3)	3,348	3,348	3,348		
Dead pigs (d 4-7)	443	443	443c		
Dead pigs (d 8-14)	395	395	395		
Dead pigs (d 15-weaning)	202	202	202		
Dead pigs vaccinated	1,040	597	202	*-443*	*-838*
Piglet vaccination parameters					
Total pigs vaccinated	34,540	34,097	33,702	*-443*	*-838*
Duration (s) vaccination / pig	2.64	4.90	6.04	*+2.26*	*+3.40*
Total duration (h)	25.33	46.41	56.54	*+21.08*	*+31.21*
Total working days (1 person)	3.33	6.11	7.44	*+2.77*	*+4.11*
Cost vaccination time (€) / worker	633.23	1160,24	1413.61	*+527.00*	*+780.37*
Total cost vaccination time (€ for total workforce)	1,899.70	3,480.72	4,240.82	*+1,581.01*	*+2,341.11*
Total cost vaccination time / weaned piglet (€) for total workforce	0.570	0.104	0.127	*+0.047*	*+0.070*
Total cost of vaccination (incl. vaccine & labor)					
Total vaccine cost (€ / year)	36,267.08	35,801.68	35,386.96	*-465.40*	*-880.11*
Cost vaccination dose / weaned piglet (€)	1.083	1.069	1.056	*-0.014*	*-0.026*
Total vaccination cost (time + vaccine dose) / weaned piglet (€)	1.139	1.173	1.183	*+0.034*	*+0.044*
Total vaccination cost / year (€)	38,166.78	39,282.40	39,627.78	*+1,115.61*	*+1,461.00*

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antibodies due to sow vaccination against *M. hyopneumoniae* are able to mount an effective immune response, resulting in adequate protection against natural [27] or experimental [28] *M. hyopneumoniae* infection in the second half of the fattening period. Indeed, efficacy of an early *M. hyopneumoniae* vaccination has been documented in case active immunity can be established before the exposure to the pathogen. When compared with post-weaned piglets, suckling piglets are less infected with pathogens, such as PRRSV, IAV-S and PCV-2, which may cause problems after weaning and interfere with the establishment of a protective immune response to *M. hyopneumoniae* vaccination [1]. Early vaccination also has the advantage that immunity is induced at a young age. This may be important, as the onset of infection may vary between herds and within a herd among successive batches [14,33-35]. Apart from inducing early protection, it is also important that early vaccinated pigs remain protected until the end of the fattening period, as in most pig herds, the highest infection levels of *M. hyopneumoniae* occur during the grow-finishing period [36]. Several studies have assessed the efficacy of vaccination at seven days of age against *M. hyopneumoniae* challenge infection under experimental conditions. This early vaccination at seven days of age has been demonstrated effective in reducing lung lesions and/or clinical signs in several challenge infections either at two [37], four [28], six [7], eight [10] or nineteen [6] weeks post-infection.

Conclusions

In conclusion, *M. hyopneumoniae* vaccination at 3 days of age has several advantages over later vaccination at 7 or 14 days of age. Besides the benefits in convenience of piglet handling at that age, we could also demonstrate economic benefits of an early *M. hyopneumoniae* vaccination.

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Declarations

Ethics approval and consent to participate – Field trial with Veterinary Medicinal Product approved for use in swine. No additional ethical approval needed. Consent to participate was obtained following full information of the farm owner on the protocol to be carried out.

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Author's contributions

FV coordinated the entire study from study design to data collection and analysis to the manuscript.

Author's information

FV is currently a Principal Technical Consultant Swine for Benelux / UK&ROI within Elanco Animal Health. He holds a DVM, a Master in Veterinary Public Health and Food Safety, a PhD in Veterinary Sciences and a PhD in Applied Biological Sciences, has a specific interest in swine respiratory health and the specific approach to improve respiratory health through non-antibiotic solutions and preventive vaccination. He is also EBVS™ European Veterinary Specialist in Porcine Health Management.

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