EU PiG

EU PiG Innovation Group

Technical Report

Health Management

Authored by:

Consortium members of work package 2 lead by Andrea Ladinig, University of Veterinary Medicine, Vienna, Austria

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 727933.

Challenge: Optimal vaccination strategies

1. Introduction

Commercial vaccines are widely available for general diseases caused by bacteria or viruses and for diseases of the respiratory tract; there are less for diseases of the gastrointestinal tract. Autogenous vaccines (AV) are used in case of regional or unique strains of a pathogen, no response to available vaccines (e.g. strain not available in commercial vaccine) or resistance of antimicrobials (1–3). Common use for AVs is vaccination of sows to prevent piglets from disease e.g. *E. coli*, Clostridia and Rotavirus (4, 5) or weaner pigs from e.g. Glasser´s disease, Salmonella, *Actinobacillus pleuropneumonia* (APP) and *Streptococcus suis* (6, 7).

There are three main categories of vaccines: live, killed and genetically engineered (e.g. recombinant, subunit vaccine). In general, live vaccines (LV) show a wider range of immunologic response than inactivated vaccines, since natural infection is imitated with a "weakened" microorganism, which lost most of its disease-causing potential. However, there is a risk of reversion to virulence by back mutations and causing symptomatic affections. Killed vaccines are often combined with adjuvants, substances that trigger the immune response but with potentially irritating effects (8). Recombinant vaccines show a better stability compared to traditional vaccines but production costs are high and there is a risk of mutation in host DNA using DNA vaccines. Subunit vaccines are generally safe to use, they cannot cause disease and have less side effects because of purified antigenic components but might be less immunogenic than LVs (9).

Routes of application

Four routes are used in routine vaccination: intramuscular, subcutaneous, intradermal and oral. Traditionally, vaccines are administered intramuscularly with a needle and syringe. This method is inexpensive and easily adaptable. However, needle injections introduce stress, pain and increase the risk to transmit diseases, needles are not generally changed between animals or litters. Needles also have a negative impact on carcass quality because of the deep tissue damage and increased chance for abscess formation. Concerning intradermal vaccination with a needle free injector (e. g. IDAL® or Hipradermic), where a high-pressure stream of fluid is forced through the skin via mechanical pressure, benefits are dose-sparing, cost savings, prevention of abscess formation, no risk of pathogen transmission, no damage of muscle, no risk of breakage of the needle and in the pig less pain perception (10–12). Kauffold et Sigmarsson showed that piglets vaccinated intradermally were more active, were suckling more and had more social contacts than piglets injected with a needle in the postvaccination observation period ($P<0.01$) (13). Temple et al. showed that sows vaccinated with a needle were less active than sows vaccinated intradermally ($P=0.031$) (11).

2. Research Questions

The aim of the project is to point out a number of vaccination strategies and the different routes of application. It should be shown how these practices use different strategies to improve health on farms and their innovative reaction to various problems related to pig production. Furthermore, potential gaps in knowledge should be detected which may eventually lead to better understanding what is needed in the future to improve health management in the swine industry.

3. Methodology

In order to identify the top five best practices across all the EU PiG regions a series of criteria have been used, which are able to measure the effectiveness of the collected practices to match the specific challenge.

The following set of criteria have been scored for each practice.

- **Excellence/Technical Quality**
  - Clarity of the practice being proposed
  - Soundness of the concept
  - Knowledge exchange potential from the proposed practice
  - Scientific and/or technical evidence supporting the proposed practice

- **Impact**
  - The extent to which the practice addresses the challenges pointed out by the Regional Pig Innovation Groups (RPIGs)
  - Clear/obvious benefits/relevance to the industry
  - Impact on cost of production on farm and/or provide added value to the farming business or economy
  - The extent to which the proposed practice would result in enhanced technical expertise within the industry e.g. commercial exploitation, generation of new skills and/or attracting new entrants in to the industry

- **Exploitation/Probability of Success**
  - The relevance of the practice to each Member State (MS) or pig producing region/system
  - Timeframes for uptake and realisation of benefits from implementation of the proposed practice are reasonable

- The extent to which there are clear opportunities for the industry to implement the practice/innovation
- Degree of development/adaptation of the practice to production systems of more than one MS

- **Innovation**
  - Evaluation of innovation (novelty) with the good practice
  - Level of innovation according to the Technology Readiness Level (TRL)

Scores had to be in the range of 0-5 (to the nearest full number). When an evaluator identified significant shortcomings, this was reflected by a lower score for the criterion concerned. The guidelines for scoring is shown below (no half scores could be used).

0	The practice cannot be assessed due to missing or incomplete information.
1 – Poor	The practice is inadequately described, or there are serious inherent weaknesses.
2 – Fair	The practice broadly addresses the criterion, but there are significant weaknesses.
3 – Good	The practice addresses the criterion well, but a number of shortcomings are present.
4 – Very Good	The practice addresses the criterion very well, but a small number of shortcomings are present.
5 – Excellent	The practice successfully addresses all relevant aspects of the criterion. Any shortcomings are minor.

The selection of the top five best practices followed the procedure described below:

1. Members of the Thematic Group (TG) were asked to score all submitted best practices according to the defined guidelines and sent their scoring sheets to the TG leader
2. In addition to the scores, TG members provided brief comments indicating weak points or particular strengths of submitted best practices
3. A conference call was used to discuss the scoring results and select the top five best practices. During this call, the top 10 best practices were discussed based on the ranking submitted by thematic group members. The discussion of the top ranked best practices was started from the lowest rank, i.e. best practice with the highest average score, to rank number 10. A selection of the top five best practices was made during the call.
4. A summary of all discussions was sent out after the call to review the decision of the selected five best practices by thematic group memebers.

4. Results and Discussion

4.1. Validation of top five practices

The following top five best practices within the challenge of optimising the use of different vaccination strageties have been selected by the thematic group:

Title of best practice	Country
Cross-company PRRS approach, 13 participating farmers supported by researchers	Belgium
Long-term use of vaccination schemes based on clinical observation and controlled by a continuous monitoring system	Germany
Improvement of production efficiency in a sow herd by the use of autogenous vaccine against piglet diarrhoea	Austria
Intradermal vaccination	Denmark
Intense monitoring in four steps of health status as basis of knowledge for determination of a vaccination strategy	Belgium

Cross-company PRRS approach, 13 participating farmers supported by researchers

There was an unstable PRRS situation at various nearby pig farms in Belgium. In 2015, 13 farms (piglet rearing, sow farms and finishing farms) in the same region decided to go together towards a stable and healthy farm. The idea was based on sharing information and working out a common strategy in the context of PRRS and the health status of the farms. This is intended to improve the production results, both technically and financially. Business leaders want to learn from each other through intensive and open communication.
After consultation with the internal and external partners, a joint vaccination strategy was implemented in combination with an improved biosecurity status at the individual farms and information exchange about diseases and other relevant problems. PRRS strains are typified so that biosafety leaks can be detected. Based on the individual results of the audits an individual plan or approach for each farm was set up.

Learning outcomes so far:

- Increase in awareness of the importance of biosafety and continuous monitoring by the farmers
- Awareness that solving health problems in general and in PRRS specifically, requires a total approach
- All farms have the same veterinarian by now
- All farms use the same vaccines and the same vaccination scheme

- 30% less problems than in 2015

Future plans:

- Common source for the sperm

Porcine reproductive and respiratory syndrome virus (PRRSV) is one of the most economically significant pathogens in swine industries of many countries. It is reported that annual economical losses due to PRRSV are $664 million in USA (14). It has been shown that PRRSV can be controlled and possibly eliminated in individual farms via multiple strategies, such as gilt acclimation (15), depopulation/repopulation (15), mass vaccination (16), test & removal (17), herd closure with/without intentional exposure (18) and so on. However, re-infection with new strains of PRRSV is still frequent, and area spread of the virus is the biggest challenge we have been facing in regards to PRRSV control today. Transmission routes of PRRSV have been scientifically proven already, and biosecurity interventions should be practiced based on published criteria. Due to the fact that area spread of the virus is the biggest challenge of PRRS control, area regional approach on control/elimination has been initiated in more than 25 regions in North America (19, 20) or in the Netherlands (21) and Japan (22). So far, all those activities/programs are totally swine producer-driven at voluntary basis, along with collaborations of universities or industrial partners. Area regional approaches require a great deal of communication and information sharing among the participating producers, vets, and all other supporters within that region. It indicates that area regional approach is one of the most important keys for PRRSV control/elimination in the future. The idea for this project therefore is not new, but very relevant and challenging, since no PRRS control is alike; in this case one single veterinarian is doing the work and implementing one single vaccination scheme.
This best practice has been selected by the TG members since they agreed that it describes an innovative approach in Europe; area regional control programs for PRRSV are used in the US but are not widely distributed in Europe.

Cons:

- The only future approach is to manage the sperm situation.
- 30% less problems: does it mean, clinical problems or viremia or seropositivity; depending on these variants, it could be successful or unsuccessful.
- No information on vaccination schemes is given.
- No information on the monitoring system is provided.
- No information on biosecurity checks is given.

Long-term use of vaccination schemes based on clinical observation and controlled by a continuous monitoring system

On a German multiplier farm (2,100 sows) the attempt for *Mycoplasma hyopneumoniae* (M. hyo) eradication failed in the beginning. The monitoring program for the major pathogens i.e. PRRSV, APP, PMT started immediately (2-6 times/year). Clinical sneezing and coughing first occurred after six months in piglets at the end of nursery and in gilts and led to additional blood/bronchoalveolar lavage sampling. M. hyo antigen and antibodies were detected while other major respiratory pathogens were negative. M. hyo vaccination was introduced and a quick reduction of clinical problems could be observed. Slaughterhouse checks of M. hyo affected pigs showed typical lesions while M. hyo vaccinated gilts were without/little signs of M. hyo infection. In contrast to affected groups with frequent antibiotic treatment, no treatments were necessary after introduction of the vaccination.
The implemented vaccination and monitoring are still performed. The situation is stable and will be continued as this led to high satisfaction of the farmer and his customers buying the gilts and fattener piglets.
Thematic group members have selected this best practice as they liked the idea of a targeted approach for on farm vaccination programs and monitoring of diseases. This best practice has been chosen over other best practices describing monitoring of diseases since it appeared more complete including not only serological profiling but also slaughterhouse checks.

Output:

- HACCP concept is simple and easy to perform in combination with long term vaccination prophylaxis
- Sustainable production and reduced workload as no treatments, especially antibiotics, are necessary
- High satisfaction of farmer and customers due to reliable respiratory healthy fatteners and gilts
- Due to efforts in antibiotic reduction the knowledge of the responsible pathogens is crucial for the choice of the adequate vaccination scheme
- A continuous broad and frequent monitoring can bring deep insights in the major pathogens involved in clinical problems. When the conditions are stable and biosecurity protocols are in place, vaccination schemes can last over long years with very good results bringing health stability, low workload, limited antibiotic use and trust to the products of these farms

Mycoplasma hyopneumoniae, the primary pathogen of enzootic pneumonia, occurs worldwide and causes major economic losses to the pig industry. The organism adheres to and damages the ciliated epithelium of the respiratory tract. Affected pigs show chronic coughing, are more susceptible to other respiratory infections and have a reduced performance (23). Control of M. hyo infections can be accomplished in a number of different

ways, namely by optimization of management practices and housing conditions, the use of antimicrobials and vaccination (24).
In the present farm, biosecurity and management conditions were improved and a (not described) vaccination regime was implemented, antimicrobial treatment was not necessary.

Pros:

- Good diagnostic approach/monitoring system
- Combination of vaccination and management improvement

Cons:

- No new approach, the majority of European farms vaccinate against M. hyo

Improvement of production efficiency in a sow herd by the use of autogenous vaccine against piglet diarrhea

The farm, located in Austria, had to deal with diarrhea in suckling piglets on a regular basis. After implementation of proper diagnostic investigations, an autogenous vaccine including different strains of *E. coli* and *Clostridium perfringens* type A was produced. Sows are vaccinated prior to farrowing in order to protect piglets via passive immunity. The vaccine had to be optimized a few times, i.e. in case of re-occurrence of diarrhea, samples were submitted for diagnostics and if new strains were detected those were included in the vaccine. Since the autogenous vaccine has been introduced, treatment of suckling piglets due to diarrhea could be reduced to individual treatments. The number of piglets weaned per sow, per year increased from 27 to 30. The weaning weight of piglets could be increased, which is an important economic factor for this farm since piglets are sold directly after weaning.

In swine there is no materno-fetal transfer of immunoglobulins via the placenta and newborn piglets receive their passive immunity postnatally through colostrum intake. Therefore – in case of very early diseases like suckling piglet diarrhea – piglets can only be protected if they take up enough maternal antibodies against the causative agent via the colostrum. To reach the antibody levels required by newborn piglets, sows are vaccinated in late pregnancy (25). There are numerous commercial vaccines against diverse *E.coli* strains and also *Clostridium perfringens* type A on the market, but not in all possible combinations (25). For best results, problem causing agents must be diagnosted prior to vaccination in order to get the right vaccine. In some countries, the production of autogenous farm-specific vaccines is allowed, which has the advantage that it can be adapted at any time and more than only the standardized strains can be included.
Currently, no commercial vaccines are available in case of double infection of *E.coli* and *Clostridium perfringe*ns type A. Therefore, the only possible way to avoid the use of two different commercial vaccines is the production of autogenous vaccines. Successful use of autogenous vaccines against *Clostridium perfringens* type A in combination with *E.coli* have been reported from Ireland (5).
The present farm shows that the use of autogenous vaccines can be successful in case the right pathogens are included in the vaccine: not only were the clinical signs reduced, but also the weaning weight increased.
Thematic group members selected this best practice since it was found to be innovative in some countries. However, the members were well aware that the legal situation varies among different European countries and therefore, this best practice cannot be easily implemented all across Europe.
Pros:

- Good diagnostic approach, confirmed by optimal effect of vaccine.

Cons:

- No new approach

Intradermal vaccination

The piglet producing Danish farm is vaccinating the piglets against PCV-2 and *M.hyopneumoniae* with intradermal vaccines using the IDAL® device. These vaccines are used in swine productions all over the EU, though to a much lesser extent than the intramuscular vaccines. From the immunological point of view, intradermal and intramuscular vaccination both induce a comparable cellular and humoral immune response against different pathogens (26–29).

According to the farmer, there are some advantages using the intradermal vaccination:

1. "The procedure reduces the spread of infectious pathogens between pigs." In fact, needles can serve as mechanical vectors for the spread of hematogenously transferable pathogens like porcine reproductive and respiratory syndrome virus (PRRSV) (30, 31) and *Mycoplasma suis* (32), though it was shown under experimental conditions there was still a risk of a needle free injection of acting as a vector.
2. "It is easier to use, since 1,000 doses can be applied per battery charge." Therefore, the changing of needles is no longer necessary.
3. "Less time is used on vaccination since it is easier to administer the vaccine".
4. "Pigs are less affected by the vaccine, when intradermal vaccination is used". It was seen that needle-free intradermal vaccination in gestating sows reduced fear and pain reaction (11). Göller et al. (2016) reported a greater activity in suckling piglets the day after intradermal vaccination compared with the intramuscular route (33). Intradermally vaccinated piglets also presented an increased suckling behaviour which was associated with a reduced level of stress. It is described for intramuscular injections that there are local reactions, but also after intradermal application painful swellings might be observed in rare cases (MSD Manual).

But there are even more advantages:

- Intradermal vaccination reduces the risk of self-injection of the people vaccinating.
- There are more points of application when using the intradermal vaccination, compared to intramuscular vaccination. Besides the neck, also the back muscles and the hind legs can be used.

Thematic group members selected this best practice based on all the benefits mentioned before. This best practice has been favoured over other best practices describing the use of intradermal vaccine application since a direct comparison to the intramuscular route of vaccination can be drawn in the described farm.

The only disadvantage according to the farmer is the lack of combination vaccines. At the moment, PCV-2 and *M.hyopneumoniae* can not be mixed, two different intradermal shots must be applied. This is time-consuming. However, a device to administer two vaccines intradermally at the same time, side by side into the skin is being launched at the moment by MSD animal health. Cost: 2-3 devices for intradermal vaccines and service of the device.

Benefits: less time required, smaller doses of vaccines, fewer animals with infections. Intradermal vaccines can improve animal welfare and reduce infections independently of country.

Intense monitoring in four steps of health status as basis of knowledge for determine a vaccination strategy

This best practice involves:

- Vaccination regime: Parvovirus vaccination in sows 10 days after farrowing, basic vaccination at 26 and 30 weeks of age; one shot *M.hyopneumoniae* vaccine applicated with the IDAL® (MSD); since three months a Glaesser´s vaccination is in place as a reaction of deaths of piglets caused by *Haemophilus parasuis* one week after birth.
- Two times a year they make a full analysis (four steps):
    - There's a slaughter line study for mycoplasma using the BOLLO-score (Spanish method, scale from 1 to 5 measuring the lung damages)
    - A saliva test at 4 and 8 weeks for the presence of PRRSV
    - A blood test at 8, 12 and 20 weeks for circovirus
    - A biosecurity audit

Followed by a discussion of the results. This monitoring determines if there's need for vaccination.

The sows give birth to 29.5 piglets a year. The piglets are stronger, get off to a better start and are easier to wean. Piglets are 7.5 kg at weaning on day 28. The piglets grow 70 to a 100 grams more per day than two years ago. Only 1% of the pigs have lungs with pleurisy injury (score 3 and 4). The APP index is 0.01, whereas the mean was 0.63, mycoplasma takes place in 0.48% of the cases (average = 25%) and *M.hyopneumoniae* index was 0.01 instead of 0.49.

Similar to the German best practice, thematic group members have selected this best practice as they liked the idea of a targeted approach for on-farm vaccination programs and monitoring of diseases.
Essentially, disease monitoring is always a very good tool to expand knowledge about prevalences of certain pathogens in a farm. In this farm, the screening was focused on three main pathogens: Porcine reproductive and respiratory syndrome virus, *Mycoplasma hyopneumoniae* and Porcine Circovirus 2, immune-depressing and respiratory agents, all playing a role in the porcine respiratory disease complex. *Mycoplasma hyopneumoniae* is one of the most important primary bacterial respiratory pathogens associated with

pneumonia (34). M.hyo in combination with other cause swine enzootic pneumonia (EP). Gross lung lesions in pigs affected by enzootic pneumonia consist of cranioventral pulmonary consolidation (CVPC) are usually distributed bilaterally in the apical, intermediate, accessory and cranial parts of the diaphragmatic lobes (24). Several lung scoring methods are currently in place for evaluating CVPC at the abattoir, where the evaluation of lung lesions is commonly used to estimate the prevalence and severity of respiratory diseases and their impact on carcass market price, risk factor assessment and vaccine efficacy (35, 36). Still, not every CVPC necessarily is M. hyo associated and from time to time also direct detection of the causative agent is necessary.

Oral fluid collected by means of ropes has the potential to replace serum for monitoring and surveillance of important swine pathogens. Surveillance of PRRSV infection in swine populations via testing of oral fluid specimens is well-documented (37–40). Based on the information of this application, it is assumed that direct detection using PCR methods were performed.

PCV-2 has been one of the most present viruses within the domestic pig population, reaching seroprevalence levels near to 100% (41). This virus has an ubiquitous nature in the pig population and is the causative agent of a number of clinical and subclinical conditions named Porcine Circovirus Diseases (PCVDs) (42). Serum is the most commonly used sample to assess PCV2 antibody and genome detection (42). In this farm it is assumed that they take serum samples for direct detection. Oliver-Ferrando et al. suggested serological testing of piglets at the age of 3, 6, 9 and 12 weeks (43). Here, piglets are screened at 8, 12 and 20 weeks, but it is not known if antibody or antigen detection is performed.

Pros:

- Screenings performed on a regular basis.

Cons:

- There are no analysis methods described, therefore no conclusion can be made of the efficiency of the outcome.
- Lung scoring at the abbatoir is a good method to get an overview of the respiratory health, but cranioventral consolidations of the lungs do not necessarily implicate *M.hyopneumoniae* infection. Pleuritis is not necessarily associated with APP infection. From the veterinarian perspective, further diagnostic approaches are necessary.
- Only respiratory signs are screened, no information about enteric signs are given.
- No information about PRRS status is given; “PRRS-vaccination not needed” does not necessarily mean the farm is free of PRRS.
- It is not mentioned how biosecurity is checked on farm. There is no audit protocol / checklist available to get an overview about biosecurity controls.

4.2. Cost-benefit analysis of the EU PiG Ambassador

The costs and benefits of this good practice applied on 13 Belgian pig farmers, who collaborate together to optimise vaccination against PRRS, have been calculated for an average pig farm in Belgium represented in the Interpig database of 2017. A specific data collection has been carried out focused on the changes in the key performance indicators and on the eventual extra costs related to this strategy.
From 2015 and onwards the pig farms are screened twice a year on the presence of PRRS, circo-virus and influenza by means of blood samples. When all data of the farms have been analysed, the pig farmers gather together to discuss the results with an expert. From the comparison it turned out that some pig farmers have to dedicate more attention to quarantine, other need to disinfect better, other again changed their veterinarian. The costs related to this biannual screening amounts €1,400 per farm, which corresponds to €0.89 per slaughter pig. The screening activity has shown that the pig farms on average are vaccinating too much against circo and by reducing this type of vaccinations 32% of veterinary and medicines costs can be saved.

After three years of applying this cross-company strategy, the pig farmers agreed upon the following effects that have been reached on average on the participating farms:

- 2.5 more piglets weaned per sow
- a more than 5% increase of the piglet weight at weaning
- a higher daily liveweight gain of weaners (+5%)
- a 5% better feed conversion rate of the finishing pigs

In general, the piglets and weaners have become more robust and resilient. The costs and benefits of this good practice are reported in the table below.

Table – Costs and benefits of the cross-company PRRS approach

	Interpig BE	With cross-company PRRS approach	% var.
Veterinarian and medicine (euro/sow/year)	97	65	-32.7
Extra fixed costs (screening twice a year) (€/finishing pig)	0	0.89	
Transfer weight from breeding to rearing unit (kg)	6.6	6.9	5.3
Pigs weaned per sow/year	29.8	32.3	8.4
Rearing Daily Liveweight Gain (g/day)	362	380.1	5.0
Finishing Feed Conversion Rate	2.76	2.62	-5.0
Results			
Gross Margin II ratio (over feed costs and other var. costs)	28.36	31.94	12.6
Total production costs (euro/kg cold weight)	1.43	1.36	-4.9

From the analysis it turns out that the costs of screening, which is carried out twice a year, are amply paid back by lower veterinarian and medicine costs because of “over-vaccination”, better performing sows, piglets and weaners, and an improved feed conversion rate of the finishing pigs. The final result of this strategy is an increase of the gross margin by 12.6% and a reduction of the production costs of pig meat by 4.9%. This good practice of optimising the vaccinations on pig farms has demonstrated to be highly valid and economically viable.

4.3. Experts input into the Cost Benefit analysis

In general, experts agreed on the cost benefit analysis. They also stated that the benefit could vary greatly between farms and of course, between different regions in Europe, since a lot of factors will have an influence on both costs and benefits.

However, some concerns were raised on the description of over vaccinating aginst PCV2 in the winning best practice. Some experts believe that it is not possible to over vaccinate against PCV2 since it had been shown in the past that as soon as vaccination against PCV2 is stopped or reduced, clinical problems will return leading to reduced growth performance (more or less obvious), increased mortality, increased use of antibiotics, etc..

Also, some experts mentioned that the extra time needed for vaccination might not have been accounted for during the cost benefit analysis. It was not quite clear to some experts if the reduced costs of veterinary services are related to a reduction of diseases in participating farms or a better price for pharmaceuticals provided by the veterinarian who is now in charge of all participating farms.

4.4. Conclusions and advice to the industry

The idea of regional control programs of diseases and sharing of information among farmers within a specific region was highly appreciated by experts. Although this idea is not new, it has not been widely adopted within Europe. In the case of the selected winning best practice, PRRS was the driver to start cooperating beyond the limits of the individual farm. However, the cooperation and knowledge exchange of farmers will not only help to combat PRRS but also other disease and should therefore lead to better health and performance across participating farms.

5. The Future

Control and monitoring of diseases is and will always be challenging on swine farms. The prophylactic use of vaccines provides an important tool to prevent clinical disease and losses in pig production, reduce losses due to lower performance of pigs but also provides an opportunity to reduce the need of treatment of sick pigs. This is particularly important in times when the use of antimicrobials in farm animals is considered a public health risk. The development of new and innovative vaccines by pharmaceutical companies should therefore be highly encouraged.

In general it can be concluded that it is important to collaborate with counsellors and colleagues to find specific vaccination strategies for each farm depending on the diasease status of the particular farm and also farms located close-by. Proper diagnostic investigations will be key in order to know which diseases are of relevance for a particular farm and set-up proper vaccination protocols.

References

1. National hogfarmer. The Pros and Cons of Using Autogenous Hog Vaccines. http://www.nationalhogfarmer.com/mag/farming_pros_cons_using,

2. Phibro. Taylor made swine vaccine. http://www.mvplabs.com/products/autogenous-swine-vaccines

3. Noe T. Tot-Lebend-Markiert_Mono_kombi-Stallspezifisch? http://www.pigpool.de/infopool-schwein/impfungen/tot--lebend--markiert--mono--kombi--stallspezifisch-/did_2052025.html

4. Hur J, Lee JH. Comparative evaluation of a vaccine candidate expressing enterotoxigenic Escherichia coli (ETEC) adhesins for colibacillosis with a commercial vaccine using a pig model. Vaccine 2012; 30(26):3829–33.

5. Borobia J. Evaluation of an Autogenous Rotavirus Type A, Clostridium perfringens Toxovar A & E. coli Vaccine in a Commercial Pig Irish Unit. In: 10th European Symposium of Porcine Health Management 2018. p. 341.

6. McOrist S, Bowles R, Blackall P. Autogenous sow vaccination for Glasser's disease in weaner pigs in two large swine farm systems. Journal of Swine Health and Production 2009; 17(2):90–6.

7. Borobia J, Üffing B. Evaluation of an autogenous Salmonella Typhimurium vaccine in pigs in Northern Ireland. In: International Pig Veterinary Society 2016. p. 285.

8. Keystone JS. Travel medicine. 3rd ed. Oxford: Saunders; 2013. Available from: URL: http://search.ebscohost.com/login.aspx?direct=true&scope=site&db=nlebk&db=nlabk&AN=520832.

9. Vartak A, Sucheck SJ. Recent Advances in Subunit Vaccine Carriers. Vaccines (Basel) 2016; 4(2).

10. agriland team. Needle-free injection gun revolutionises pig vaccinations. http://www.agriland.ie/farming-news/needle-free-injection-gun-revolutionises-pig-vaccinations/

11. Temple D, Escribano D, Jiménez M, Mainau E, Cerón JJ, Manteca X. Effect of the needle-free "intra dermal application of liquids" vaccination on the welfare of pregnant sows. Porcine Health Manag 2017; 3:9.

12. Hickling JK, Jones KR, Friede M, Zehrung D, Chen D, Kristensen D. Intradermal delivery of vaccines: potential benefits and current challenges. Bulletin of the World Health Organization 2011; 89:221–6.

13. MSD. The IDAL way. http://fs1.5mpublishing.com/msd/ThePigSite/idal/The%20IDAL%20Way%20Brochure-3FED.pdf

14. Holtkamp DJ, Kliebenstein JB, Neumann E, Zimmerman JJ, Rotto H, Yoder TK et al. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on United States pork producers. Journal of Swine Health and Production 2013; 21:72.

15. Dee S, Joo HS, Pijoan C. Control of porcine reproductive and respiratory syndrome virus transmission: handling infected seedstock. The Compendium on continuing education for the practicing veterinarian (USA) 1994.

16. Dee SA, Joo HS, Henry S, Tokach L, Park BK, Molitor T et al. Detecting subpopulations after PRRS virus infection in large breeding herds using multiple serologic tests. Swine Health and Production 1996; 4(4):181.

17. Dee SA, Bierk MD, Deen J, Molitor TW. An evaluation of test and removal for the elimination of porcine reproductive and respiratory syndrome virus from 5 swine farms. Canadian Journal of Veterinary Research 2001; 65(1):22.

18. Torremorell M, Baker R. Eradication of PRRS virus by changing the pig flow and the introduction of negative replacements into positive sow farms 2000.

19. Morrison RB, Goede D, Tousignant S, Perez A. Current incidence, prevalence and state of control of PRRS virus in North America. In: International PRRS Congress, Ghent, 2015. p. 21.

20. Mondaca E, Batista L, Cano J-P, Díaz E, Philips R, Polson D. General guidelines for porcine reproductive and respiratory syndrome regional control and elimination projects. Journal of Swine Health and Production 2014; 22(2):84–8.

21. De Jong, B., Wertenbroek, N. Results of area regional control project in pig dense area The Netherland. In: International Pig Veterinary Society 2018.

22. Otake, S., Arai, S., Furuichi, T., Furukama, M., Hayakawa, Y., Ikedam K., Ishizeki, S., Iseki, H., Koike, F., Mizukami, Y., Miyashita, M., Nakatake, S., Notsute, M., Kano, R., Shibuya, T., Ishikawa, H., Tsunemitsu, H. he initiative of PRRS area regional control/elimination in Japan (P-JET: PRRS-Japan Elimination Team). In: ISERPD.

23. Thacker EL, Minion FC. Mycoplasmosis. Diseases of Swine 2012:779–97.

24. Maes D, Segales J, Meyns T, Sibila M, Pieters M, Haesebrouck F. Control of Mycoplasma hyopneumoniae infections in pigs. Veterinary microbiology 2008; 126(4):297–309.

25. Matías J, Berzosa M, Pastor Y, Irache JM, Gamazo C. Maternal Vaccination. Immunization of Sows during Pregnancy against ETEC Infections. Vaccines (Basel) 2017; 5(4):48.

26. Beffort L, Weiß C, Fiebig K, Jolie R, Ritzmann M, Eddicks M. Field study on the safety and efficacy of intradermal versus intramuscular vaccination against Mycoplasma hyopneumoniae. Veterinary Record 2017:vetrec-2017.

27. Martelli P, Saleri R, Cavalli V, Angelis E de, Ferrari L, Benetti M et al. Systemic and local immune response in pigs intradermally and intramuscularly injected with inactivated Mycoplasma hyopneumoniae vaccines. Veterinary microbiology 2014; 168(2-4):357–64.

28. Tassis PD, Papatsiros VG, Nell T, Maes D, Alexopoulos C, Kyriakis SC et al. Clinical evaluation of intradermal vaccination against porcine enzootic pneumonia (Mycoplasma hyopneumoniae). Veterinary Record 2012; 170(10):261.

29. Jones GF, Rapp-Gabrielson V, Wilke R, Thacker EL, Thacker BJ, Gergen L et al. Intradermal vaccination for Mycoplasma hyopneumoniae. Journal of Swine Health and Production 2005; 13(1):19–27.

30. Baker, SR, Mondaca E, Polson D, Dee SA. Evaluation of a needle-free injection device to prevent hematogenous transmission of porcine reproductive and respiratory syndrome virus. Journal of Swine Health and Production 2012; 20(3):123–8.

31. Otake S, Dee SA, Rossow KD, Moon RD, Pijoan C. Mechanical transmission of porcine reproductive and respiratory syndrome virus by mosquitoes, Aedes vexans (Meigen). Can J Vet Res 2002; 66(3):191–5.

32. Busser EV de, Mateusen B, Vicca J, Le Hoelzle, Haesebrouck F, Maes D. Mycoplasma suis infection in suckling pigs on a Belgian farm. Vlaams Diergeneeskundig Tijdschrift 2008; 77(3):182–6.

33. Göller M, Knöppel HP, Fiebig K, Kemper N. ntradermal vaccine application: effects on suckling behaviour. In: International Pig Veterinary Society 2016. p. 625.

34. Fraile L, Alegre A, López-Jiménez R, Nofrarías M, Segalés J. Risk factors associated with pleuritis and cranio-ventral pulmonary consolidation in slaughter-aged pigs. The Veterinary Journal 2010; 184(3):326–33.

35. Sibila M, Pieters M, Molitor T, Maes D, Haesebrouck F, Segalés J. Current perspectives on the diagnosis and epidemiology of Mycoplasma hyopneumoniae infection. The Veterinary Journal 2009; 181(3):221–31.

36. Merialdi G, Dottori M, Bonilauri P, Luppi A, Gozio S, Pozzi P et al. Survey of pleuritis and pulmonary lesions in pigs at abattoir with a focus on the extent of the condition and herd risk factors. The Veterinary Journal 2012; 193(1):234–9.

37. Prickett JR, Zimmerman JJ. The development of oral fluid-based diagnostics and applications in veterinary medicine. Animal Health Research Reviews 2010; 11(2):207–16.

38. Kittawornrat A, Prickett J, Chittick W, Wang C, Engle M, Johnson J et al. Porcine reproductive and respiratory syndrome virus (PRRSV) in serum and oral fluid samples from individual boars: will oral fluid replace serum for PRRSV surveillance? Virus research 2010; 154(1-2):170–6.

39. Kittawornrat A, Engle M, Panyasing Y, Olsen C, Schwartz K, Rice A et al. Kinetics of the porcine reproductive and respiratory syndrome virus (PRRSV) humoral immune response in swine serum and oral fluids collected from individual boars. BMC veterinary research 2013; 9(1):61.

40. Ramirez A, Wang C, Prickett JR, Pogranichniy R, Yoon K-J, Main R et al. Efficient surveillance of pig populations using oral fluids. Preventive veterinary medicine 2012; 104(3-4):292–300.

41. Segalés J, Kekarainen T, Cortey M. The natural history of porcine circovirus type 2: from an inoffensive virus to a devastating swine disease? Veterinary microbiology 2013; 165(1-2):13–20.

42. Segalés J. Porcine circovirus type 2 (PCV2) infections: clinical signs, pathology and laboratory diagnosis. Virus research 2012; 164(1-2):10–9.

43. Oliver-Ferrando S, Segalés J, López-Soria S, Callén A, Merdy O, Joisel F et al. Evaluation of natural porcine circovirus type 2 (PCV2) subclinical infection and seroconversion dynamics in piglets vaccinated at different ages. Veterinary research 2016; 47(1):121.

Challenge: Alternatives to the use of zinc oxide

1. Introduction

Zinc oxide is used in many countries throughout Europe for the prevention of post-weaning diarrhea and edema disease in weaned piglets. High doses of Zinc oxide in the diet of weaned piglets prevents diarrhea by inhibiting the attachment of pathogenic *E. coli* to the intestinal mucosa and reduces the secretion of ions into the intestinal lumen thus enhancing water resportion (1). Some authors described immuno-modulatory activities, e.g. reduction of pro inflammatory histamine and inhibiting the proliferation and activation of intestinal mast cells (2). However, the application of high doses of Zinc oxide also effects the microbial composition and leads to lasting effects during the development of the intestinal microbiota (3). Furthermore, Zinc oxide accumulates in soil and the application of Zinc-rich manure in the fields is considered as an environmental pollutant and therefore poses a health hazard. Some European countries have already banned the therapeutic use of Zinc oxide whereas in other countries it's still used as a common disease preventing strategy. Due to the intention of the European Commission in phasing out the therapeutic use of Zinc oxide, it is necessary to think of alternatives (1).

Studies with organic acids like benzoic acid and medium chain fatty acids (MCFA) have shown the first promising approaches. Organic acids reduce pH-values in the gastrointestinal tract and their antimicrobial properties can prevent the overgrowth of bacteria like *Salmonella* and *E.coli* and increase the secretion of pancreatic enzymes (4). MCFA have also considerable antimicrobial properties with a similar mode of action to organic acids (5). Combining organic acids and MCFA in the piglet's diet, showed a significantly increased feed intake, growth rate and feed/weight gain ration compared to a combination of Zinc oxide and antibiotics (6).

Furthermore, research demonstrated that essential oils might be great alternatives to antibiotics and Zinc oxide in feed. Their positive effects on inflammation, oxidative stress, the intestinal microbiome, gut chemo-sensing and bacterial quorum sensing led to better production performance in animals in different studies (7).

Antimicrobial peptides are produced by several species including bacteria, insects, plants and vertebrates and they can be protective against bacteria, fungi, parasites, viruses and cancer cells. Their characteristics make them desirable alternatives to antibiotics or the use of Zinc oxide. Bacteriocins are ribosomally synthesized antimicrobial peptides produced by bacteria that inhibit the growth of similar or closely related bacterial strains. To date, they are used in the preservation of foods and only a few studies focused on their use in swine production. Colicins are a class of bacteriocin produced by and effective against *E.coli* and closely related strains. They have been shown to be effective against many pathogenic *E. coli* strains including those responsible for post-weaning diarrhea and edema disease in pigs (8, 9).

The use of bacteriophages, which are viral entities that multiply inside bacteria, for phage therapy was popular during the 1940s. Presently phage therapy is out of fashion, although their inherent antimicrobial properties make them perfect candidates for controlling bacterial diseases. The supplementation of bacteriophages to the diet of weaning pigs resulted in a better growth performance, digestibility and gut development and therefore, the effects are comparable to Zinc oxide and organic acids (10).

Moreover, probiotics, prebiotics and synbiotics are used as feed additives. The dietary supplementation of probiotics enhances gut health, nutrient digestibility and growth performance (11).

2. Research Questions

The purpose of this project is to show different alternatives to the use of zinc oxide as already used successfully on farms across Europe. Different strategies and innovative ideas were used to improve gut health and to reduce the use of zinc oxide or antibiotics. Furthermore, gaps of knowledge should be detected which lead to new research questions to improve the overall understanding what is needed in the future to enhance gut health in pig production.

3. Methodology

In order to identify the top five best practices across all the EU PiG regions a series of criteria has been used, which are able to measure the effectiveness of the collected practices to match the specific challenge.

The following set of criteria have been scored for each practice.

- **Excellence/Technical Quality**
  - Clarity of the practice being proposed
  - Soundness of the concept
  - Knowledge exchange potential from the proposed practice
  - Scientific and/or technical evidence supporting the proposed practice
- **Impact**
  - The extent to which the practice addresses the challenges pointed out by the Regional Pig Innovation Groups (RPIGs)
  - Clear/obvious benefits/relevance to the industry

  - Impact on cost of production on farm and/or provide added value to the farming business or economy
  - The extent to which the proposed practice would result in enhanced technical expertise within the industry e.g. commercial exploitation, generation of new skills and/or attracting new entrants in to the industry

- **Exploitation/Probability of Success**
  - The relevance of the practice to each Member State (MS) or pig producing region/system
  - Timeframes for uptake and realisation of benefits from implementation of the proposed practice are reasonable
  - The extent to which there are clear opportunities for the industry to implement the practice/innovation
  - Degree of development/adaptation of the practice to production systems of more than one MS

- **Innovation**
  - Evaluation of innovation (novelty) with the good practice
  - Level of innovation according to the Technology Readiness Level (TRL)

Scores had to be in the range of 0-5 (to the nearest full number). When an evaluator identified significant shortcomings, this was reflected by a lower score for the criterion concerned. The guidelines for scoring is shown below (no half scores could be used).

0	The practice cannot be assessed due to missing or incomplete information.
1 – Poor	The practice is inadequately described, or there are serious inherent weaknesses.
2 – Fair	The practice broadly addresses the criterion, but there are significant weaknesses.
3 – Good	The practice addresses the criterion well, but a number of shortcomings are present.
4 – Very Good	The practice addresses the criterion very well, but a small number of shortcomings are present.
5 - Excellent	The practice successfully addresses all relevant aspects of the criterion. Any shortcomings are minor.

The selection of the top five best practices followed the procedure described below:

1. Members of the Thematic Group (TG) were asked to score all submitted best practices according to the defined guidelines and sent their scoring sheets to the TG leader

2. In addition to the scores, TG members provided brief comments indicating weak points or particular strengths of submitted best practices
3. A conference call was used to discuss the scoring results and select the top 5 best practices. During this call, the top 10 best practices were discussed based on the ranking submitted by TG members. The discussion of the top ranked best practices was started from the lowest rank, i.e. best practice with the highest average score, to rank number 10. A selection of the top 5 best practices was made during the call.
4. A summary of all discussions was sent out after the call to review the decision of the selected five best practices by TG members.

4. Results and Discussion

4.1. Validation of top five practices

The following top 5 best practices within the challenge of finding alternatives to the use of zinc oxide have been selected by the thematic group:

Title of best practice	Country
Fermenting liquid feed, an alternative to Zinc Oxide	Netherlands
Comparing and closely measuring effects from different kinds of feeds as alternative for zinc oxide in own stable	Belgium
Zinc Oxide free: SPF, gut health, pre and probiotics, ABF and vaccinations	Finland
Vaccination and improving feeding in post-weaning phase	France
Reducing protein levels to counter withdrawal of zinc oxide	Ireland

Fermenting liquid feed, an alternative to Zinc Oxide

The company **Van Asten Group** (Sterksel, Netherlands) started fermentation of feed in 2008. Learning from experience and looking at cheesemakers, they started a 3 year trial to make a failure free system. The main innovation is cleaning with 70 degree hot water and also add raw material in hot water to kill all present bacteria. Afterwards, cold water and the liquid active bacteria are added to reduce temperature and secure a fast growth. The temperature and cleanliness is important to have good lactic acid values and low acetic acid. The feed stays homogeneous and there is no segregation while feeding which prevents diarrhea. The lactic acid metabolizes ANF and difficult to digest starch, therefore, it works as a probiotic and lowers the pH to reduce the risk of bacterial growth. Fermented liquid feed stabilizes the intestines and improves the growth of the pigs. For maximum effect, it is fed together with a wheat barley mixture and plant based proteins. Initially, they had a reduction of 50% of antibiotics use and now they are working up to antibiotic free.
To get the maximum result in weaned piglets, the sows should also be fed fermented feed as well as the piglets at the sow. This should positively influence intestine quality and bacterial life in the intestines. The 3 years test to develop a failure-free system was started together with ForFarmers and Weda Holland. At the moment van Asten is doing research with the support of the EU for fermenting Local Proteins. The laboratory tests show a strong reduction of ANF in peas and beans meaning they can be fed to piglets without gastric distortion.
Van Asten tries to market pigs without antibiotics, they expect to realize this quickly. Besides they are working on Non GMO and Regional feeding of pigs. The fermentation of peas and beans will be a key element in the success of this process and the access to the market.

The system is successfully implemented at 3 of the locations in the Netherlands and Germany of the van Asten group and several other farms in Europe. In addition, it is in the start-up phase at another location of van Asten in Germany and is it planned for a new location in the Netherlands (2019). The use of liquid feeding systems is wide spread in the EU. This system can be easily implemented and handled by a person who is able to run a liquid feeding system. Enough capacity is needed to prepare the fermented product and the fermented feed can be stored in tanks for at least 24 hours. Liquid feed is often stated as an ideal feed for weaned piglets. However, there are also plenty of opportunities for sows and growing-finishing pigs. The use of fermented liquid feed appears to be a cost effective alternative to the use of antibiotic growth promoters.

The use of fermented feed or lactic acid seems to have many health promoting effects and therefore can improve the performance of suckling piglets, weaner pigs and growing-finishing pigs. Lactic bacteria and yeast which occurred naturally in feed ingredients, start to produce lactic acid, acetic acid and ethanol when mixing the feed with water (12). The produced acids reduce firstly the pH in the feed and inhibit the growth of pathogenic bacteria in the feed and secondly they reduce the pH in the stomach of the pigs and impede an overgrowth of pathogens like coliforms and *Salmonella* in the gastrointestinal tract (13). Many publications highlighted the potential of fermented liquid feed as an alternative to the use of antibiotics (14, 15), it can enhance the quality of the feed and improve the overall health of the animals (16).

This best practice has been selected by thematic group members since it was well described and included a proper cost benefit analysis in the description. Also, thematic group members agreed that fermented liquid feed could be a good idea as an alternative to the use of zinc oxide, although there was some doubt about the quality and standardization of the fermentation process on farm.

Comparing and closely measuring effects from different kinds of feeds as alternative for zinc oxide in own stable

Kris Gios´s farm (Oosterhoven, Belgium) is free of AB since 2012. Before Sep ’17, he used a feed containing 2000 ppm of zinc oxide to prevent weaning diarrhea and to improve the intestinal health. He asked his feeding company to come up with an alternative without zinc oxide. They came up with a feed containing herbs like oregano and other natural products. This feed is given to the piglets 7 days before weaning (3 mg herbs/kg feed) until 7 days after weaning. From 7 to 28 days after weaning the dose is 1.5 mg herbs/kg feed. He has now used this feed for 3 months and he is very positive about it. His farm is still free of AB, which was his biggest concern. So he has eliminated high doses of zinc oxide, without sacrificing the health status of his farm. He also tried a different feed using another principle. They add inert fibers to the classic feed. These fibers are low on energy and they help to calm the intestine.
He compares both feeds within his barn and keeps close tracks of the key performance indicators (KPI) like growth and feed conversion. He makes 3 exact groups of the same size (one with normal feed, one with the herbs added, and the last one with the inert fibers added). Every day he puts the piglets on a scale, keeps track of amount of feed given so he can closely monitor what the effects are for each feed formulation. In this way he can determine what the best feed will be for him in the future. Both feed formulations seem to work properly.
This best practice has been selected by thematic group members since they agreed that fibre contents in feed can heavily influence the gut microbiome and therefore support gut health in pigs. Some group members were however missing some more detailed information on some of the feed ingredients described in the best practice.

Herbs can be used as feed additives and they may influence animal welfare and performance of pigs in a positive way. Pigs which were fed with herbs presented less skin lesions and less negative social behaviour (17). Chinese herbs modulate the nutritional metabolism, immune response and intestinal health and therefore, are a good alternative to replace antibiotics or zinc oxide (18).
Furthermore, inert fibre is a good opportunity to improve gastrointestinal health and growth performance. Inert fibre in post-weaning diets decreased the digesta retention time and modified the gut microbiota in a way which resulted in a decreased proliferation of pathogens in the small intestine (19).

Zinc Oxide free: SPF, gut health, pre and probiotics, ABF and vaccinations

Yhteisporsas Oy´s farm (Laihia, Finland) is mainly produces zinc oxide and AB free (ABF). Atria Family Farm has 900 sows and is producing piglets with intact tails which are 80-95% ABF from birth to 38kg. This is possible due to an excellent production environment, optimal feeding, health and vaccination strategies. The specific pathogen free (SPF) status declares them free of enzootic pneumonia, swine dysentery, salmonellosis, mange and atrophic rhinitis. Oral vaccination against *Lawsonia intracellularis* and intradermal vaccination against PCV2 is applied to piglets. There is no need for zinc oxide as the gut health is good and nursery diarrhoea is rare.

<u>Important factors:</u>

- Tailored feeding solutions
- Health status: SPF in combination with vaccinations
- Excellent nursery conditions and stocking density: two-climate boxes, efficient heating and ventilation, all in-all out production
- Excellent feeding capacity and quality (pneumatic/liquid)
- Piglets get high quality (pre-)starter feed to learn eating behaviour and "acclimatize" gut villi to feed
- High quality/balanced nursery feed fed five to eight times daily: energy, fibers, pre&probiotics, addition of acid, feed hygiene and water quality, optimal ground feed to avoid gut damage
- Focus on digestability and gut health.

Thematic group members liked this best practice since it described a holistic approach with several measures taken in order to avoid the use of zinc oxide. Also, they agreed that the SPF status and absence of several pathogens can be crucial for piglets around weaning.

A lot of factors influence overall health in pigs. Management and biosecurity are essential for the growth of healthy pigs (23). A lot of bacterial diseases require antibiotic treatments and secondary bacterial infections following virual infections make an antibiotic use necessary. Many strategies are known to improve animal health (24). A high health status, so called SPF pigs (Specific Pathogen Free), reduces the need for antibiotics and increases the production yield (25). The quality of the water is very important for overall health (26) and the correct feed with high quality ingredients help the pigs to perform better (27). It is especially important for young piglets to use a combination of good-quality feed combined with special feed additives to improve the maturation of the intestine (27).
It is also necessary to think about housing conditions and stocking density when talking about animal health. Hygiene measures like cleaning and disinfection are important as well as climate conditions (28).

Vaccination and improving feeding in post-weaning phase

The company **"The clever farmers"** (Vannes, France): Before the onset of edema disease in 2013, treatments with Colistin were made punctually during diarrhea attacks. In 2013 edema disease appeared on the breeding farm. Zinc sulphate was then added to reduce the losses associated with edema disease (from 5% to 20% mortality depending on the batch). Colistin and Marbofloxacin treatment was often necessary in addition to zinc to reduce the losses. Breeders have chosen to vaccinate piglets against post-weaning diarrhea and edema disease. Several assays were performed to ensure a good vaccine response in piglets. Moreover, the farmers are acidifying the starter feed and pre-fattening feed (mixture of different acids: formic acid, propionic acid, benzoic acid and phosphoric acid). Finally, the farmers have equipped the pens with troughs to deliver high-moisture corn once a day (3.5 kg of high-moisture corn for 35 piglets) during the first 15 days. High-moisture corn enhances the acidity of the ingestion and provides probiotic bacteria. The benefits of this good practice are directly transferable to farms using zinc oxide or colistin.
Thematic group members liked this best practice as it also described a holistic approach including different measures like the use of vaccines or the use of acids as well as high moisture corn.

It is generally known that vaccines can protect animals against bacterial and viral diseases and thereby, reduce the need for antimicrobials (20). Vaccinations are important in disease prevention and are the fundamental basis of a healthy pig herd. Vaccines stimulate the immune system in a way that it is able to recognise specific pathogens and destroy them. Stimulating the immune system is a "long-lasting" protection against diseases and a primed immune system improves health (21). Vaccinating the piglets against postweaning diarrhea and edema disease protects them but this protection may not be complete because hygienic precautions should be considered as well (22).
Organic acids reduce the pH value in the gastrointestinal tract and prohibit an overgrowth of pathogenic bacteria in the intestine. Furthermore, they enhance gut health by providing nutrients for probiotic bacteria (4).

Reducing protein levels to counter withdrawal of zinc oxide

McAuliffes Farm (Ireland): In order to remove Zinc Oxide from the pig diet McAuliffes reduced protein levels in feed from 21% to 18%. There has been no evidence of postweaning scours and production costs have been reduced as a result.

Although this best practice was not very well described, all nutritionists within the TG agreed that the reduction of the protein levels in the diet could reduce weaning diarrhea and therefore replace the use of zinc oxide. Some more detailed information was provided during the conference call of the TG describing other measures taken on farm in addition to the reduction of the protein levels in the diet, like lowering the stocking density and providing more and better enrichment material.

Feeding the right quality and quantity of protein are important factors regarding nutrition and the incidence of diarrhoea (29). Many authors described the connection between high protein levels in feed and the development of dysbiosis in the gut and diarrhoea (30). In the absence of in-feed antibiotics, pigs fed with lower protein levels (17%) had a decreased incidence of diarrhoea compared to higher levels (19-23.7%) and better growth rates (31).

Reducing the levels of protein in pig diets limited the availability of non-digested protein to potential enteric pathogens which leads to decreased risk of post-weaning diarrhoea. However, low protein diets may lead to reduction in postweaning growth. It is therefore important to improve protein quality and to use more digestible protein sources to avoid a decline in growth (32). By improving the protein quality, pigs which were fed with animal protein sources (dried skimmed milk powder) performed better than pigs offered soy based diets (33). Some authors suggest to supplement the low protein diets with limiting amino acids (lysine, methionine, threonine and tryptophan) to improve the digestibility of low protein diets (34).

4.2. Cost and benefit analysis of the EU PiG Ambassador

The good practice related to the substitution of zinc oxide, frequently used in the feed of piglets, consists of adding herbs like oregano and other natural products to the feed ration or using inert fibres. The pig farmer in Belgium has registered the KPI's of groups of pigs to which the alternative feed was administered compared to a control group of pigs, that were fed with feed containing zinc oxide. Data collected concerned the extra costs of the alternative feed, change in the Average Daily Gain (ADG), Feed Conversion Rate (FCR) and losses and mortality rate of the weaners. The C/B analysis has concentrated its attention on the impact of the change in KPIs and price of the alternative feeds on the production cost of a piglet of 25 kg and the total production costs of pig meat in a setting of a farrow-to-finish pig farm. The economic impact of the practice has been simulated on the average Belgian pig farm represented in the Interpig database of 2017.

In the following table the impact of the use of oregano and other herbs on the production costs has been demonstrated.

Table – Costs and benefits of the use of oregano and other herbs on the production costs of weaners

	Interpig BE	With herbs	% var.
Average price of purchase weaner/rearer feed, euro/tonne	370.0	378.7	2.3
Rearing Daily Liveweight Gain (g/day)	362	416	15.1
Rearing Feed Conversion Ratio	1.75	1.58	-9.7
Rearing mortality rate	4%	2%	-50.0
Results			
Piglet cost at 25 kg, euro/pig	53.86	52.20	-3.1
Total costs, (euro/slaughter pig)	1.431	1.429	-0.1

The use of oregano and herbs allows the full substitution of zinc oxide in the feed ration of weaners. The price of this feed is only 2.3% higher, generates a higher and better ADG and FCR and reduces the weaners mortality rate by 50%. The total impact is a reduction of the production costs of weaners by 3.1% and a 0.1% reduction of production costs per kg of pig meat.

The use of inert fibres as a substitute of zinc oxide has been analysed subsequently. In the table below the outcome of the C/B analysis is shown.

Compared to oregano and herbs the use of addition of inert fibres is more costly. The average price of weaner feed increases by 8.1%. ADG and FCR improve with 5.5 and 11.4% respectively. Also the mortality rate of weaners with the use of inert fibres declines from 4 down to 2%. The overall effect of these technical improvements generates a reduction of the production costs of weaners of 2.4% and the production costs of pig meat of 0.7%.

Both alternatives to the use of zinc oxide do not create very significant economic impacts, but these are sufficiently attractive to be taken into consideration by pig farmers in Europe, who are doing efforts to find valid alternatives for the use of zinc oxide.

Table – Costs and benefits of the use of inert fibres on the production costs of weaners

	Interpig BE	With inert fibres	% var.
Average price of purchase weaner/rearer feed, euro/tonne	370.0	400.0	8.1
Rearing Daily Liveweight Gain (g/day)	362	382	5.5
Rearing Feed Conversion Ratio	1.75	1.55	-11.4
Rearing mortality rate	4%	2%	-50.0
Results			
Piglet cost at 25 kg, euro/pig	53.86	52.57	-2.4
Total costs, (euro/slaughter pig)	1.43	1.42	-0.7

4.3. Experts input into the Cost Benefit analysis

In general, experts were sceptical of the cost benefit analysis of the EU pig ambassador within the challenge of finding alternatives to the use of zinc oxide. Some experts provided the feedback that they think that the benefits of using herbs and inert fibres are overrated in this report. Even if correct for the particular farm, the feedback of experts was that in general it is not realistic that herbs and inert fibres would be able to outperform zinc oxide.

4.4. Conclusions and advice to the industry

The use of herbs like oregano and other natural products in feed or the use of inert fibres might be suitable alternatives to the use of zinc oxide. However, the effect of those feed ingredients have to be tested for each farm individually in order to make sure they can replace the use of antimicrobials or zinc oxide without reduction in performance.

5. The Future

Several approaches might be able to overcome the use of zinc oxide in feed of weaner piglets. Experts involved in the thematic group agreed that it is not possible to find one product or solution to substituting zinc oxide which will work on each farm. Also, the approach of phasing out zinc oxide should be a more holistic one including several strategies such as different feeding trategies, feeding compounds, improvement of management, internal buiosecurity, general health status of pigs, quality of piglets around weaning, etc.. One very important aspect when searching for alternatives to zinc oxide is to make sure that the alternative solution does not lead to an increase in antimicrobial usage.

References

1. http://www.thepigsite.com/articles/5389/zinc-oxide-alternatives-for-weaned-pigs-organic-acids-and-mcfas/
2. Kim, J.C., Hansen, C.F., Mullana, B.P. & Pluske, J.R. (2012) Nutrition and pathology of weaner pigs: nutritional strategies to support barrier function in the gastrointestinal tract. Anim. Feed Sci. Technol. 173, 3–16.
3. Kim, J.C., Hansen, C.F., Mullana, B.P. & Pluske, J.R. (2012) Nutrition and pathology of weaner pigs: nutritional strategies to support barrier function in the gastrointestinal tract. Anim. Feed Sci. Technol. 173, 3–16.
4. Harada E, Niiyama M. and B. Syuto. 1986. Comparison of pancreatic exocrine secretion via endogenous secretin by intestinal infusion of hydrochloric acid and monocarboxylic acid in anesthetized piglets. Jpn. J. Physiol., 36(5): 843- 856.
5. Decuypere, J. A. and N. A. Dierick. 2003. The combined use of triacylglycerols containing medium-chain fatty acids and exogenous lipolytic enzymes as an alternative to in-feed antibiotics in piglets: concept, possibilities and limitations. An overview. Nutrition Research Reviews 16: 193–209.
6. Kuang, Y., Y. Wang, Y. Zhang, Y. Song, X. Zhang, Y. Lin, L. Che, S. Xu, D. Wu, B. And Z. Xue. 2015. Fang Effects of dietary combinations of organic acids and medium chain fatty acids as replacement of zinc oxide on growth, digestibility and immunity of weaned pigs.
7. Omonijo, F. A., Ni, L., Gong, j., Wang, q., Lahaye, L., Yang, C. 2017. Essential oils as alternatives to antibiotics in swine production, Animal Nutrition, 1-11.
8. Stahl, C. H., Callaway, T. R., Lincoln, L. M., Lonergan, S. M., Genovese, K. J. 2004. Inhibitory activities of colicins agains Escherichia coli strains responsible for postweaning diarrhea and edema disease in swine. Antimicrob Agents Chemother, 48: 3119-3121.
9. Qutler, S. A., Lonergan, S. M., Cornick, N., Johnson, A. L., Stahl, C. H. 2007. Dietary inclusion of colicin E1 is effective in preventing postweaning diarrhea caused by F18-positive Escherichia coli in pigs. Antimicrob Agents Chemother,51: 3830-3835.
10. Housseindoust, A. R., Lee, S. H., Kim, J. S., Choi, Y. H., Noh, H. S., Lee, J. H., Jha, P. K., Kwon, I. K., Chae, B. J. 2017. Dietary bacteriophages as an alternative for zinc oxide or organic acids to control diarrhoea and improve the performance of weanling piglets. Veterinarni Medicina, 62: 53-61.
11. Liao, S. F., Nyachoti, M. 2017. Using probiotics to improve swine gut health and nutrient utilization. Animal Nutrition, 3: 331-343.
12. Missotten JAM, Michiels J, Degroote J, De Smet S. 2015. Fermented liquid feed for pigs: An ancient technique for the future. Journal of Animal Science and Biotechnology 6(1):1–9.
13. Canibe N, Jensen BB: Fermented liquid feed – microbial and nutritional aspects and impact on enteric diseases in pigs. Anim Feed Sci Technol 2012, 173:17–40. 10.1016/j.anifeedsci.2011.12.021

14. Plumed-Ferrer C, Von Wright A: Fermented pig liquid feed: nutritional, safety and regulatory aspects.J Appl Microbiol 2009, 106:351–68. 10.1111/j.1365-2672.2008.03938.x
15. Kil DY, Stein HH: Invited review: management and feeding strategies to ameliorate the impact of removing antibiotic growth promotors from diets fed to weanling pigs.Can J Anim Sci 2010, 90:447–60. 10.4141/cjas10028
16. https://www.allaboutfeed.net/Home/General/2010/1/Pigs-benefit-from-fermented-liquid-diets-AAF011461W/
17. https://www.pigprogress.net/Piglets/Articles/2018/4/Herbs-and-toys-enhancing-growing-pig-welfare-266626E/
18. https://www.pigprogress.net/Finishers/Articles/2014/10/Chinese-herbs-as-alternatives-to-antibiotics-in-feed-1613894W/
19. https://www.pig333.com/articles/effect-of-fermentable-and-inert-fibre-in-weaning-piglets_11494/
20. Hoelzer K, Bielke L, Blake DP, Cox E, Cutting SM, Devriendt B, Erlacher-Vindel E, Goossens E, Karaca K, Lemiere S, et al. 2018. Vaccines as alternatives to antibiotics for food producing animals. Part 1: Challenges and needs. Veterinary Research 49(1):1–10.
21. https://www.pigprogress.net/Special-Focus/Alternative-Growth-Promotion/Boehringer/
22. https://www.pigprogress.net/Health/Health-Tool/diseases/Diarrhoea-postweaning/
23. https://www.pigprogress.net/Health/Articles/2018/1/Healthy-pigs-Is-all-in-all-out-the-right-concept-241203E/
24. https://www.wattagnet.com/articles/27536-how-to-naturally-improve-pig-poultry-health-status
25. https://www.pigprogress.net/Health/Articles/2018/5/Yielding-better-returns-with-SPF-pigs-281658E/?dossier=35213&widgetid=1
26. https://www.pigprogress.net/Health/Articles/2018/5/Water-A-basic-need-281657E/?dossier=35213&widgetid=1
27. https://www.pigprogress.net/Nutrition/Articles/2018/9/A-balanced-approach-in-sow-and-piglet-diets-327524E/
28. https://www.pigprogress.net/Health/Articles/2018/5/HEALTH-Eight-Danish-tips-to-help-reduce-antibiotics-278315E/
29. https://www.pigprogress.net/Piglets/Articles/2017/11/Smart-protein-use-needed-for-piglet-health-214322E/
30. J.R. Pluske, D.W. Pethick, D.E. Hopwood, D.J. Hampson. Nutritional influences on some major enteric bacterial diseases of pig. Nutr Res Rev, 15 (2) (2002), pp. 333-371
31. Wu Y, Jiang Z, Zheng C, Wang L, Zhu C, Yang X, Wen X, Ma X. 2015. Effects of protein sources and levels in antibiotic-free diets on diarrhea, intestinal morphology, and expression of tight junctions in weaned piglets. Animal Nutrition 1(3):170–176.
32. I.J. Wellock, J.G.M. Houdijk, A.C. Miller, B.P. Gill, I.Kyriazakis. The effect of weaner diet protein content and diet quality on the long-term performance of pigs to slaughter. J. Anim. Sci. 2009, 87:1261-1269.
33. https://www.pig333.com/articles/dietary-protein-in-piglet-diets_2137/

34. M. Nyachoti and B. Jayaraman. Low crude protein diet and its effect on diarrhea in swine. 16th Midwest swine Nutrition Conference, 2016 (16): 17-22