Veterinary Medicines Directorate

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Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ingelvac PRRSFLEX EU Lyophilisate and Solvent for Suspension for Injection for Pigs

PuAR correct as of 15/03/2018 when RMS was transferred to IE. Please contact the RMS for future updates

Date Created: 19th May 2015

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0535/001/DC
Name, strength and pharmaceutical form	Ingelvac PRRSFLEX EU Lyophilisate and Solvent for Suspension for Injection for Pigs
Applicant	Boehringer Ingelheim Ltd, Ellesfield Avenue, Bracknell, Berkshire RG12 8YS, UK
Active substance(s)	Live attenuated Porcine Respiratory and Reproductive Syndrome Virus (PRRSV), strain 94881 (genotype 1) At least: $10^{4.4}$ $TCID_{50}$-$10^{6.6}$ $TCID_{50}$* *Tissue Culture Infectious Dose 50
ATC Vetcode	QI09AD03
Target species	Pigs
Indication for use	For active immunisation of clinically healthy pigs at 17 days of age and older from farms affected with European (genotype 1) Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) to reduce virus load in blood in seropositive animals under field conditions. Under experimental challenge conditions in which only seronegative animals were included, it was demonstrated that vaccination reduces lung lesions, virus load in blood and lung tissues as well as negative effects of infection on daily weight gain. A significant reduction of the respiratory clinical signs could additionally be demonstrated at the onset of immunity.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 32 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	22nd January 2015
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain.

I. SCIENTIFIC OVERVIEW

Ingelvac PRRSFLEX EU Lyophilisate and Solvent for Suspension for Injection for Pigs is a live veterinary vaccine. It is indicated for the active immunisation of clinically healthy pigs at 17 days of age and older from farms affected with European (genotype 1) Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) to reduce virus load in blood in seropositive animals under field conditions. Under experimental challenge conditions in which only seronegative animals were included, it was demonstrated that vaccination reduces lung lesions, virus load in blood and lung tissues as well as negative effects of infection on daily weight gain. A significant reduction of the respiratory clinical signs could additionally be demonstrated at the onset of immunity. The product is a lyophilised powder formulation containing $10^{4.4}$ $TCID_{50}$ -$10^{6.6}$ $TCID_{50}$ of PRRSV strain 94881 (genotype 1) per 1 ml dose following reconstitution. The vaccine is administered by intramuscular injection.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC[1]. The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy[2] of the product was demonstrated according to the claims made in

[1] SPC – Summary of product Characteristics.

the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

II.A. Composition

The lyophilised powder fraction contains live attenuated Porcine Respiratory and Reproductive Syndrome Virus (PRRSV), strain 94881 genotype 1 ($10^{4.4}$ $TCID_{50}$ - $10^{6.6}$ $TCID_{50}$ per 1 ml dose) as the active ingredient and the excipients sucrose, gelatin, potassium hydroxide, glutamic acid, potassium dihydrogen phosphate, dipotassium phosphate and sodium chloride.

The solvent supplied for reconstitution of the lyophilised powder fraction is phosphate buffered saline (PBS) solution.

The container/closure system for the lyophilisate consists of a Type I glass vial with bromobutyl rubber stopper and aluminium seal. The container / closure for the solvent consist of high density polyethylene (HDPE) vials with a bromo- or chlorobutyl rubber stopper and aluminium seal. The lyophilisate fraction is presented in 10 ml (10 doses), 50 ml (50 doses), 100 ml (100 doses) or 250 ml (250 doses) vials and are packaged in cartons with 1, 12 or 25 vials. The particulars of the containers and control performed are provided and conform to the regulation.

The vaccine strain originates from a European PRRSv field strain. Attenuation of this strain was performed by serial passaging in cell cultures to produce the vaccine strain. The choice of the vaccine strain is satisfactorily justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The product is manufactured by inoculation of cells with the Working Seed Virus (WSV). Following inoculation and propagation steps the antigen is harvested, stabilised and frozen. For the formulation of the final blend, virus suspensions are thawed and mixed with stabiliser and diluent to adjust concentrations as required and then filled into sterilised vials before lyophilisation is performed. Stoppers are inserted and the vials are sealed with aluminium caps. Process validation data on the product have been presented in accordance with the relevant European guidelines.

[2] Efficacy – The production of a desired or intended result.

II.C. Control of Starting Materials

The active substance is Porcine Respiratory and Reproductive Syndrome Virus. Starting materials used in product comply with the relevant Ph. Eur. monographs.

Biological starting materials used are in compliance with the relevant Ph. Eur. monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the relevant Ph. Eur. monographs and guidelines.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

II.E. Control Tests on the Intermediate Product

The tests performed during production of the antigen are described and the results of a sufficient number of consecutive runs, conforming to the specifications, are provided.

II.F. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified. The final product is tested for appearance, pH, identification, potency, sterility, residual moisture, extraneous agents and mycoplasma.

The demonstration of the batch to batch consistency is based on the results of data provided for a sufficient number of lyophilised powder batches and solvent batches including production scale size batches. Other supportive data provided confirm the consistency of the production processes.

G. Stability

Stability data on batches of the lyophilised powder and solvent batches have been provided in accordance with applicable European guidelines, demonstrating the stability of the lyophilised fraction over 12 month shelf life and over 3 years for the solvent, when stored at 2-8°C.

The in-use shelf-life of the reconstituted vaccine, 8 hours, is supported by the data provided.

H. Genetically Modified Organisms

None.

J. Other Information

Shelf life of the vaccine lyophilisate as package for sale:	1 year
Shelf life of the solvent as packaged for sale:	3 years
Shelf life after reconstitution according to directions:	8 hours

Store and transport refrigerated (2°C - 8°C)
Do not freeze.
Protect from light.

III. SAFETY ASSESSMENT

All batches used in the safety studies were representative of the production process. The dose to be used was that recommended for use and contained the maximum antigen content to be included in the finished product. Studies were performed in accordance with the requirements of Directive 2001/82/EC, as amended, and the relevant guidelines.

Laboratory trials

The safety of a single dose, an overdose and the repeated administration of one dose of the product in target animals, and the special requirements for live vaccines, were investigated in five, well-conducted studies. In each safety study, a suitable number of animals were used and were in compliance with the general safety Ph. Eur. monograph.

The safety of a single dose or a single overdose was investigated in one study where two groups of piglets each were respectively administered intramuscularly either a single dose (containing 6.3 $\log_{10}$ $TCID_{50}$) or an overdose (containing 7.2 $\log_{10}$ $TCID_{50}$) of the vaccine. A control group was also included. The piglets were observed for 14 days after vaccination. Little difference was observed between piglets vaccinated with a single dose or an overdose. No systemic reactions or difference in growth rates between groups were noted. Following administration of an overdose (10x), there were no additional adverse reactions further to those observed after a single dose.

Further supportive studies were carried out to examine the safety of a repeated 10x overdose of the vaccine in two week old piglets compared to negative controls. In the studies a suitable number of piglets received two 10x overdoses of the vaccine two weeks apart via intramuscular injection. Clinical signs such as

body weights, rectal temperatures, injection site reactions and general health observations were monitored. No statistically significant differences were noted between vaccinates and controls except an increase in body temperature observed after vaccination. This reaction is indicated in the Summary of Product Characteristics (SPC).

The vaccine is intended for use in piglets from 17 days of age on farms infected with European PRRSv. The safety of the vaccine has not been established during pregnancy or lactation. The use of the vaccine is contraindicated in breeding animals, in PRRSv-naïve herds and in cases of hypersensitivity to any of the substance included in the formulation.

Spread and dissemination of the vaccine strain

A study was designed to evaluate the dissemination of the vaccine within the target tissues of piglets and to investigate the spread of the vaccine to unvaccinated naïve in-contact sentinel piglets. A sufficient number of piglets were inoculated with an overdose of the vaccine. Sentinels (non-treated) as well as control animals (placebo-treated) were also included. Dissemination of the vaccine strain in the vaccinated animal was investigated by looking for the presence of vaccine virus in samples of blood, lymphoid tissue and lung lavage during the 91 days of study and in tissue samples collected at necropsy. Shedding and duration of shedding were assessed by the presence of the vaccine virus in nasal, oral and faecal swab samples. The spread of the vaccine strain from vaccinated animals to unvaccinated animals was investigated by looking for the presence of the vaccine virus in the blood and tissues of sentinel animals.

It was concluded that vaccinated animals may excrete the vaccine strain by faecal excretion and in some cases, by oral secretion. The vaccine strain may spread up to 3 weeks after vaccination to unvaccinated cohabitant animals without any clinical consequence.

Reversion of virulence of the vaccine strain

Serial passage studies were performed with PRRS master seed virus at a titre higher than the maximum release titre. Piglets were inoculated with the master seed via intramuscular injection. Virus was recovered from blood / lung lavage fluid samples and four consecutive passages were performed in piglets intranasally. Piglets were observed for 14 days after each passage. The last passage collected was inoculated into seronegative pregnant sows (in a separate study) and clinical signs were observed and serology, viraemia, temperature and weight gain were noted.

The studies showed that there was no reversion to virulence of the vaccine strain under laboratory conditions. The recombination of the vaccine strain with field strains would not be expected to result in any worse consequence than that which may occur following natural recombination of field strains.

Study of residues

Ingelvac PRRSFLEX EU does not contain any adjuvant. All the other excipients present in the vaccine are either listed in Commission Regulation (EU) No. 37/2010 in Annex I (not being necessary for the protection of public health to establish MRLs), or are non-pharmacologically active substances for which no MRL is required. Consequently, there is no need to perform residue studies for the vaccine and no withdrawal period is required.

User Safety

The main risk concerning user safety is accidental self-injection. However, although the vaccine is live, PRRSV is not known to infect humans, and no other components are present in the vaccine that would present a risk to the user. It is accepted that use of the vaccine does not pose an unacceptable risk to the user. Advice is included in the SPC to seek medical advice in the event that an adverse reaction was to occur following accidental self-injection.

Interactions

The compatibility of Ingelvac PRRSFLEX EU for use with another veterinary medicinal product has not been established. Therefore, the standard warning when no information is available concerning the use of this product with any other veterinary medicinal product is included in the SPC.

Field studies

Two field studies were carried out in order to demonstrate the safety of the vaccine under field conditions, in farms with a previous history of PRRSV infection. Each of the studies was performed in a different European country, being representative of the current European pig husbandry practices. All the studies were carried out following the principles of Good Clinical Practice (GCP).

A sufficient number of piglets of the minimum required age were vaccinated with Ingelvac PRRSFLEX EU containing the maximum dose titre. In both studies, the safety profile of the vaccine in the vaccinated piglets was compared to a group of control piglets administered with a placebo.

The results obtained were in line with those observed in the laboratory safety studies (i.e. transient increases in body temperature and redness at the injection site) and confirmed the acceptable safety profile of the vaccine.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The assessment concluded that there is a very low risk to the environment associated with use of the vaccine. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV CLINICAL ASSESSMENT (EFFICACY)

The applicant justified that the vaccine strain included in Ingelvac PRRSFLEX EU is relevant to the current epidemiological situation in the EU. The challenge strain used in the laboratory efficacy trials as well as the field challenge strains detected in the field trials were confirmed as heterologous to the vaccine strain and are considered to represent a substantial genetic diversity across type 1 PRRSV in Europe.

Clinical Studies

Laboratory Trials

The claimed indications for Ingelvac PRRSFLEX EU are supported by seven laboratory efficacy (vaccination-challenge) studies. Most of the studies were carried out in seronegative piglets but the influence of maternally-derived antibodies on the efficacy of the vaccine was also evaluated. Piglets were vaccinated according to the recommended vaccination schedule and administration route with a dose of vaccine covering the minimum efficacious titre as specified by a $10^{4.4}$ $TCID_{50}$/dose. In all studies, parameters such as viraemia, clinical signs, serology and viral loads in lungs were monitored.

Challenge was carried out at different time points after vaccination using a heterologous PRRSv strain. In each study, a suitable number of negative control animals were also included.

The first study was a randomised, blinded study to evaluate the minimum immunising dose of PRRS vaccine in susceptible 2 week old piglets following challenge with a heterologous European isolate of PRRS. Piglets were divided into three groups, each group received a low dose, a medium dose or a high dose of the vaccine and negative controls were administered a placebo. Challenge was carried out five weeks after vaccination. The study demonstrated that vaccination at either dose resulted in a statistically significant reduction in coughing, lung lesions and viral loads in lungs and blood.

Two further studies evaluated the onset of immunity of the vaccine in susceptible piglets following challenge with a heterologous European isolate of PRRSV at two weeks and three weeks post-vaccination, respectively. Both were randomised, blinded studies. Piglets were divided into three groups: challenge group, vaccination group and negative control group. At the beginning of the studies, the vaccinate groups received a dose slightly below the minimum efficacious titre. The challenge and negative control groups received a placebo. Vaccination resulted in a statistically significant reduction in lung lesions, virus load in blood and lungs as early as 2 weeks post vaccination and a reduction of the negative effects of PRRSV infection on daily weight gain after challenge. In addition, a reduction in respiratory signs was observed in the study where piglets were challenged 3 weeks post vaccination. Therefore, an onset of immunity for this vaccine was established at 3 weeks post vaccination.

A randomised, blinded study was designed to evaluate the duration of immunity of the vaccine in susceptible two weeks old pigs following challenge with a heterologous European isolate of PRRSV at twenty weeks post-vaccination.

Seronegative piglets were divided into three groups: challenge, vaccinate and negative control groups. The vaccinate group received a vaccine dose covering the minimum efficacious titre at the start of the study and the challenge and negative control groups received a placebo. The study demonstrated that vaccination resulted in a statistically significant reduction in histological lung lesions, virus loads in blood and lung, and a reduction of the negative effects of PRRSV infection on daily weight gain after challenge.

Two further studies were carried out to assess the duration of immunity of the vaccine in susceptible two week old pigs following challenge with a heterologous European isolate of PRRSV at twenty-four and twenty-six weeks post vaccination, respectively. The studies were randomised and blinded. Seronegative piglets were divided into three groups, a challenge, vaccinate and negative control group. The vaccinate groups received a dose covering the minimum efficacious titre. Challenge and negative control groups received a placebo. The studies demonstrated that vaccination resulted in a statistically significant reduction in lung lesions, virus load in blood and lungs and in a reduction of the negative effects of PRRSV infection on daily weight gain after challenge.

The final study was a randomised, blinded study to evaluate the efficacy of Ingelvac PRRSFLEX EU in the presence of PRRSV maternally-derived antibodies. Seropositive piglets were derived from sows that had received a 10x overdose of the vaccine at approximately 60 days of gestation. Seropositive piglets were included in the challenge control group and in the seropositive vaccinated (minimum efficacious titre) challenged group. In addition, seronegative piglets were included in the non-treated control group and in the seronegative vaccinated (minimum efficacious titre) challenged group. Challenge was carried out approximately six weeks later with a heterologous PRRSV isolate. Maternally-derived antibodies were shown to interfere with vaccine efficacy. This has been reflected in the SPC where it is stated that in the presence of maternally-derived antibodies, timing of the initial vaccination of piglets should be planned accordingly.

The efficacy of the product has been demonstrated in the laboratory studies in accordance with the relevant requirements which show the efficacy of the vaccine with regard to the following claims:

For active immunisation of clinically healthy pigs at 17 days of age and older from farms affected with European (genotype 1) PRRSv:

Under experimental challenge conditions in which only seronegative animals were included:

- To reduce lung lesions, virus load in blood and lung tissues
- To reduce the negative effects of PRRSV infection on daily weight gain.
- To reduce respiratory clinical signs as demonstrated at the onset of immunity

Under field conditions:

- To reduce virus load in blood in seropositive animals.

The onset of immunity is 3 weeks and the duration of immunity is 26 weeks.

Field Trials

Three field studies were carried out in order to demonstrate the efficacy of the vaccine under field conditions, in farms with recent history of PRRSV outbreaks. Each of the studies was performed in a different European country covering a representative spectrum of the current European pig husbandry practices. In general, all the studies were carried out following the principles of Good Clinical Practice (GCP).

The efficacy of Ingelvac PRRSFLEX EU in vaccinated piglets was compared in all the cases to a negative control group (unvaccinated). Circulation of field PRRSV was detected in all the three studies confirming natural challenge. The respective field strains were characterised and confirmed to be heterologous to the vaccine strain.

Overall, and despite the limitations observed in some of the studies, an efficacy claim to reduce viraemia in seropositive animals was considered supported.

Study title	Field efficacy Study with PRRS vaccine in four week old piglets
Objectives	To study the efficacy of PRRS vaccine in four week old piglets
Test site(s)	Single-centre, EU country
Compliance with Regulatory guidelines	Good Clinical Practice (GCP)
Test Product	Ingelvac PRRSFLEX EU (below minimum efficacious titre)
Control product/placebo	Negative control
Animals	674 commercial piglets were vaccinated and 674 piglets were used as controls. Pigs were weaned and four weeks of age.
Randomisation	Randomised
Blinding	Blinded
Method	Piglets originated from PRRS vaccinated sows. Confirmed prior to study that herd had a recent and consistent history of field exposure to infection with EU PRRS. Virus was confirmed as circulating prior to the start of the study. Two groups included in the study, one group received 1 ml intramuscular injection of the test vaccine (minimum efficacious titre) at the start of the study and the second were the negative control group and received an injection of PBS. Three consecutive week groups were included in the study to

	allow sufficient numbers for statistical evaluation. Animals were individually weighed at four time-points and blood samples were collected. Additional blood samples were collected from pre-selected animals at approximate time points up to 17 weeks after vaccination. The efficacy of the vaccine was determined by average daily weight gain (ADWG), clinical observations, PRRS serology, viraemia and mortality.
Statistical method	Statistical analyses were performed using SAS 8.2 software. All tests on differences between groups were two-sided tests. Statistical significance was demonstrated at $p \leq 0.05$. Appropriate statistical analyses e.g. ANOVA, t-tests, Wilcoxon Mann-Whitney test and the Fischer exact test were performed for each treatment group.
RESULTS	Clinical observations for behaviour, respiration, coughing and other observations did not differ between the groups. A statistically significant difference in the analysis per treatment group revealed a higher bodyweight in the vaccinated group for the body weight at the beginning of fattening. Peak of viraemia was observed four weeks post vaccination. All animals in both the vaccinated and negative control group remained seropositive until the end of the study. For all time points, there were no statistically significant differences in seroconversion between groups or mortality rates.
Duration of follow-up	None
Adverse events	A number of adverse reactions were recorded during the study with similar numbers in the vaccination and control group. It was determined that none of the adverse events were in relation to the study medication.
DISCUSSION	Overall, and despite the limitations observed in some of the studies, an efficacy claim to reduce viraemia in seropositive animals was considered supported.

Study title	Field efficacy Study with PRRS vaccine in weaned piglets.
Objectives	To study the efficacy of PRRS vaccine in weaned piglets.
Test site(s)	Single-centre, EU country
Compliance with Regulatory guidelines	Good Clinical Practice (GCP)
Test Product	Ingelvac PRRSFLEX EU (minimum efficacious titre)
Control product/placebo	Negative control
Animals	Piglets were weaned and of 3 weeks of age. 663 piglets were included in the control group and 651 piglets in the vaccination group.
Randomisation	Randomised.
Blinding	Blinded.

Method	Piglets originated from PRRS vaccinated sows. Confirmed prior to study that herd had a recent and consistent history of field exposure to infection with EU PRRS. Virus was confirmed as circulating prior to the start of the study. Two groups included in the study, one group received 1 ml intramuscular injection of the test vaccine (minimum efficacious titre) at the start of the study and the second were the negative control group and received an injection of PBS. Six individual week groups were included in the study to allow sufficient numbers for statistical evaluation. Animals were individually weighed and blood samples were collected. Additional blood samples were collected from pre-selected animals. The efficacy of the vaccine was determined by average daily weight gain (ADWG), clinical observations, PRRS serology, viraemia and mortality.
Statistical method	Statistical analyses were performed using SAS 8.2 software. All tests on differences between groups were two-sided tests. Statistical significance was demonstrated at $p \leq 0.05$. Appropriate statistical analyses e.g. ANOVA, t-tests, Wilcoxon Mann-Whitney test and the Fischer exact test were performed per treatment group.
RESULTS	Clinical observations for behaviour, respiration, coughing and other observations did not differ between the groups. Results for mean body weight, weight gain and average daily weight gain (ADWG) did not reveal extensive significant differences. Peak viraemia (exposure to PRRSV field isolate) was observed on Day 70, during which a significant decrease in PRRS viraemia was observed in the vaccinated group compared to the control group. By the end of the fattening period, there was no statistically significant difference in seroconverson or mortality rates between the vaccination and control group.
Duration of follow-up	None
Adverse events	Adverse events were recorded during the study period. The same number of animals died in the vaccinated and control group during the study. The adverse events recorded during the study period were not considered to be related to the vaccine.
DISCUSSION	Overall, and despite the limitations observed in some of the studies, an efficacy claim to reduce viraemia in seropositive animals was considered supported.

Study title	Field efficacy Study with PRRS vaccine in 2, 3 and 4 week old piglets.
Objectives	To study the efficacy of PRRS vaccine in 2, 3 and 4 week old piglets.
Test site(s)	Single centre, EU country
Compliance with Regulatory guidelines	Good Clinical Practice (GCP)
Test Product	Ingelvac PRRSFLEX EU (minimum efficacious titre)
Control product/placebo	Negative control
Animals	763 piglets were used as controls and 792 piglets were vaccinated. Piglets were 2, 3 and 4 weeks old.
Randomisation	Randomised
Blinding	Blinded
Method	Piglets originated from PRRS vaccinated sows. Confirmed prior to study that herd has a recent and consistent history of field exposure to infection with EU PRRS. Presence of virus was confirmed prior to start of study. The negative control group received 1 ml of PBS at the start of the study and the vaccination group received the minimum efficacious titre of the vaccine intramuscularly. A two, three and four consecutive week groups were included in the study. Animals were weighed at beginning of study and at 6 and 14 weeks old. Blood sampling took place at beginning of study and weekly from 6 to 12 weeks of age. Mortality was recorded and clinical observations were carried out weekly.
Statistical method	Statistical analyses were performed using SAS 8.2 software. All tests on differences between groups were two-sided tests. Statistical significance was demonstrated at $p \leq 0.05$. Appropriate statistical analyses e.g. ANOVA, t-tests, Wilcoxon Mann-Whitney test and the Fischer exact test were performed per treatment group.
RESULTS	The PRRSV field challenge occurred at the same time among all three age groups (approximately 8 weeks after the start of the study). In the group of piglets treated at 2 weeks old, the vaccination group had significantly lower proportion of viraemic pigs compared to the control group. In the group of piglets treated at 3 weeks old, the vaccinated group has a significantly lower proportion of viraemic pigs compared to the control group. In the group of piglets treated at 4 weeks old, no significant difference was observed between groups. No difference was noted in mean body weights or ADWG in any of the groups. The vaccinated groups from the three age groups had significantly higher proportions of PRRS seropositive animals when compared to the control group. In the groups of piglets treated at 2 or 4 weeks of age, vaccinated piglets

	showed respectively less occurrences of diarrhoea and other clinical signs (non-respiratory signs). No differences were observed between vaccinated and control animals in the group of piglets treated at 3 weeks of age.
Duration of follow-up	None
Adverse events	No adverse events were reported in the study.
DISCUSSION	The field study was accepted as providing positive information on the efficacy of the product under typical EU field conditions. Overall, and despite the limitations observed in some of the studies, an efficacy claim to reduce viraemia in seropositive animals was considered to be supported by these study results.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit/risk profile of the product(s) is favourable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)