College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

FIXR PRRS inac

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0342/001/DC
Name, strength and pharmaceutical form	FIXR PRRS inac, emulsion for injection for pigs
Applicant	Kernfarm B.V. De Corridor 14D 3621 ZB Breukelen The Netherlands
Active substance(s)	Inactivated PRRS virus, type 1, strain Bio-60 Inactivated PRRS virus, type 2, strain Bio-61
ATC Vetcode	QI09AA05
Target species	Pigs (gilts and sows)
Indication for use	Active immunization of gilts and sows to reduce reproductive disorders and viremia caused by porcine reproductive and respiratory syndrome virus strains of the European clade A and the American type lineage 1 (PRRSV-1 subtype 1 clade A and PRRSV-2 lineage 1, respectively). Onset of immunity: 3 weeks after primary vaccination. Duration of immunity: 6 months after primary vaccination.

MODULE 2

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this immunological veterinary medicinal product (IVMP) are available in the Union Product Database (UPD).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Not applicable.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Date of completion of the original decentralised procedure	16 December 2020
Concerned Member States for original procedure	BE
CMS for subsequent use procedure	DE, ES, FR, PT

I. SCIENTIFIC OVERVIEW

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.
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 of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains the following active substances: inactivated Porcine Reproductive and Respiratory Syndrome virus, type 1, strain Bio-60 and type 2, strain Bio-61. The product contains emulsigen (adjuvant), thiomersal, sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium hydrogen phosphate dodecahydrate, water for injection and sodium hydroxide.
The container/closure system consists of glass vials of hydrolytic Type I (10 ml) and Type II (50 or 100 ml) and HDPE vials (10, 50 or 100 ml) closed with chlorobutyl rubber penetrable stoppers and sealed with aluminium caps.

The choice of the adjuvant, vaccine strain, inactivating agent and presence of preservative are justified.

B. Method of Preparation of the Product

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

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

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 Ph. Eur. Guidelines; any deviation was adequately justified. For the substances where there is no such requirement the company has specified how quality is controlled. Starting materials of non-biological origin used in production comply with pharmacopoeia monographs (Ph. Eur.).
The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

D. Control tests during production

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

E. 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 tests include in particular appearance, extractable volume, sterility, potency, virus quantification and identity, safety, inactivation, pH, thiomersal content, viscosity, airtightness.

The demonstration of the batch to batch consistency is based on the results of 3 consecutive batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

F. Stability

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.
The in-use shelf-life of the broached vaccine is supported by the data provided.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated in two studies. In a study in gilts animals were vaccinated four times with 14-day intervals with a batch of vaccine containing maximum antigen titres. Animals were observed daily and temperatures were recorded. No systemic reactions were observed, temperature increases up to 38.9℃ and local reactions with a maximum diameter of 5 cm were found after vaccination. Local reactions persisted for a maximum of 10 days. The safety of an overdose was tested in pregnant sows that were vaccinated with a single overdose (4 ml) of a batch of vaccine containing maximum antigen titres, at day 6-0-70 of gestation. Animals were observed daily and rectal temperatures recorded. No systemic effects were observed and rectal temperatures remained within the normal range (38.0-39.5 ℃), injection site reactions were observed (max. 3 cm, max. 7 days duration). There was no difference in the average total number of piglets or the average

number of viable piglets between vaccinates and controls. The study provides evidence of safety when used in pregnant sows. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. An appropriate warning concerning local reactions is included in the SPC.

Effects on reproductive performance were examined in the overdose safety study in sows as described above: no evidence of reproductive effects was obtained, the product is considered to be safe for use during pregnancy.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.

The adjuvant and excipients used are Emulsigen, containing light mineral oil, sorbitan derived emulsifier, glyceride and glycerol derived emulsifier which are all permitted in food or feed. Thiomersal is included in the list of allowed pharamacologically active substances without an MRL. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

A clinical study was performed on three farms in the Czech Republic, on one farm in 2005-2007 and on two farms between 2010 and 2011. Three standard batches of the vaccine were used. In total 40 6-week old piglets and 30 gilts at the age of 4-8 months were vaccinated twice with a 14 day interval (basic vaccination). In total 28 1-4 year old sows were vaccinated twice with a 14 day interval, 20 sows served as non-vaccinated controls. One dose of vaccine was applied to 29 6-month old pregnant gilts, 17 gilt were included as unvaccinated controls. One dose of vaccine was also applied to 28 1-4 year old pregnant sows, 20 sows were included as non-vaccinated controls.
In all categories, animals were monitored for 14 days for local or systemic reactions. Rectal temperatures were recorded around vaccination (up to 4 days). Pregnant animals were monitored until parturition. No local or systemic reactions were observed. The maximum increase in rectal temperature was 0.3°C. no statistically significant difference was found between vaccinated and control groups (gilts or sows) for periparturient piglet mortality and total piglet mortality until weaning.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the vaccine has no undesirable effect on the environment and no special limitations are necessary to reduce the risk to the environment. No warnings are therefore required.

Residue Studies

The excipients used are considered as not falling within the scope of the MRL regulation. Based on this information, no withdrawal period is proposed.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the product has been demonstrated in 6 laboratory studies in accordance with the relevant requirements. The challenge viruses used were not identical to the vaccine strains but were found to be closely related following genetic analysis (same clade).

Two studies were performed in 6-month-old conventional gilts to determine onset of immunity. In both studies, a minimum titre batch was used to vaccinate 6 gilts twice with a three week interval, prior to mating. Animals were again vaccinated at day 60-70 of gestation. Another group of 6 gilts was vaccinated with a 50% minimum titre batch and third group of 2 gilts remained unvaccinated. At day 124 all animals were intravenously challenged: in one study with PRRS-EU strain virus, in the second study with PRRS-US strain virus. Clinical signs were not observed after challenge in either study. In both studies viremia and reproductive failure (as detected by piglet viraemia and death) were reduced in the vaccinated groups compared to the controls. Onset of immunity at 3 weeks after administration of the primary vaccination (3 doses) was supported by the data.

Two studies were performed in 5-month-old conventional gilts to determine duration of immunity. In both studies, a minimum titre batch was used to vaccinate 6 gilts twice with a three week interval, prior to mating. Another group of 2 gilts remained unvaccinated. At day 195 all animals were intravenously challenged: in one study with PRRS-EU strain virus, in the second study with PRRS-US strain virus. Clinical signs were not observed after challenge in either study. In both studies viremia and reproductive failure (as detected by piglet viraemia and death) were reduced in the vaccinated group compared to the controls. Duration of immunity at 6 months after administration of the first part of the primary vaccination (2 doses) was supported by the data. The vaccination schedule is considered to be a worst-case scenario and the data support the claimed duration of immunity after the full primary vaccination of 3 doses.

Two studies were performed in 3-4 month old conventional seronegative gilts. In each study, a group of 8 animals was vaccinated with a minimum titre batch twice with a three week interval and received a booster vaccination 6 months later at day 60-70 of gestation. Two gilts remained as non-vaccinated controls. All animals were challenged intravenously at 25 days after the last vaccination in one study with PRRS-EU strain virus, in the second study with PRRS-US strain virus. Clinical signs were not observed after challenge in either study. In both studies viremia and reproductive failure (as detected by piglet viraemia and death) were reduced in the vaccinated group compared to the controls. The efficacy of a booster vaccination at 6 months after administration of the first part of the primary vaccination (2 doses) was supported by the data. The vaccination schedule is considered to be a worst-case scenario and the data support the claimed single revaccination during the next pregnancy after the full primary vaccination of 3 doses.

Field Trials

The applicant has conducted a field trial on three farms in the Czech Republic, standard vaccine batches were used and the study was performed in one farm between 2005 and 2007 and in two farms between 2010 and 2011.
In total 30 gilts at the age of 4-8 months were vaccinated twice with a 14 day interval (basic vaccination). In total 28 1-4 year old sows were vaccinated twice with a 14 day interval. 20 sows served as non-vaccinated controls. One dose of vaccine was applied to 29 6-month old

pregnant gilts, 17 gilts were included as unvaccinated controls. One dose of vaccine was also applied to 28 1-4 year old pregnant sows, 20 sows were included as non-vaccinated controls. Reproductive indicators (Piglet mortality after the birth, piglet mortality before weaning) were not statistically different between vaccinated and control groups of gilts and sows.
The results of the field study provide no additional support for the claim for reduction of viraemia and reduction of reproductive disorders.

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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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/labelling/package leaflet is/are available in the Union Product Database (UPD).

This section contains information on significant changes agreed after the original procedure, which are important for the quality, safety or efficacy of the product.

None.