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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR AN IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT

Suigen Parvo L6, emulsion for injection for pigs

MODULE 1

PRODUCT SUMMARY

Procedure number	FR/V/0530/001/MR
Name and pharmaceutical form	Suigen Parvo L6, émulsion injectable
Applicant	VIRBAC 1 Avenue 2065 M L I D 06516 Carros cedex France
Active substances	Each dose of 2 ml vaccine contains inactivated strains: Porcine parvovirus Bio-37 min. titre 4 log2* *Leptospira interrogans* serogroup Pomona, serovar Pomona, strain MSLB 1037 min. 1:32** *Leptospira borgpetersenii* serogroup Sejroe, serovar Hardjo, strain MSLB 1039 min. 1:40** *Leptospira interrogans* serogroup Australis, serovar Bratislava, strain MSLB 1040 min. 1:40** *Leptospira kirschneri* serogroup Grippotyphosa, serovar Grippotyphosa, strain MSLB 1042 min. 1:51** *Leptospira interrogans* serogroup Icterohaemorrhagiae, serovar Icterohaemorrhagiae, strain MSLB 1041 min. 1:51** *Leptospira interrogans* serogroup Canicola, serovar Canicola, strain MSLB 1043 min. 1:51** * HI antibodies titre in guinea-pig serum after 1⁄4 of vaccination dose application. The antibodies in titre 16 and more must be proved in 4 from 5 guinea-pigs. ** Geometrical average of specific antibodies titres determined by agglutination-lytic reaction (ALR) after rabbits vaccination with batch with minimum antigens content.
ATC Vetcode	QI09AL
Target species	Pigs
Indication for use	For active immunisation of breeding pigs : -to reduce viral circulation, prevent transplacental infection and foetal death caused by porcine parvovirosis -to prevent transplacental infection and clinical signs caused by porcine leptospirosis.

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).

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 8 of Regulation (EU) 2019/6 as amended.
Date of completion of the original procedure	23 April 2024
Date product first authorised in the Reference Member State (MRP only)	23 April 2024
Concerned Member States for original procedure	AT

I. SCIENTIFIC OVERVIEW

Suigen Parvo L6 is an inactivated vaccine, which is indicated for the immunisation of breeding pigs against porcine parvovirus (PPV) infection and Leptospirosis. The vaccine contains Emulsigen (mineral oil emulsion in water) as adjuvant. Thiomersal is added as a preservative. The vaccine is presented as suspension for injection in multidose containers with a respective dose volume of 2 ml.
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 reactions observed are indicated in the SPC (Summary of Product Characteristics).
The product is safe for the user 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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

Each dose of 2 mL vaccine contains:

Porcine parvovirus inactivated, strain Bio-37 min. 4 $\log_2$ *
Leptospira interrogans serogroup Pomona, serovar Pomona, strain MSLB 1037, inactivated min. 1:32**

Leptospira borgpetersenii serogroup Sejroe, serovar Hardjo, strain MSLB 1039, inactivated min. 1:40**
Leptospira interrogans serogroup Australis, serovar Bratislava, strain MSLB 1040, inactivated min. 1:40 **
Leptospira kirschneri serogroup Grippotyphosa, serovar Grippotyphosa, strain MSLB 1042, inactivated min. 1:51 **
Leptospira interrogans serogroup Icterohaemorrhagiae, serovar Icterohaemorrhagiae, strain MSLB 1041, inactivated min. 1:51 **
Leptospira interrogans serogroup Canicola, serovar Canicola, strain MSLB 1043, inactivated min. 1:51 **

* HI antibodies titre in guinea-pig serum after ¼ of vaccination dose application. The antibodies in titre 16 and more must be proved in 4 from 5 guinea-pigs.
** Geometric average of specific antibodies titres determined by agglutination-lytic reaction (ALR) after rabbit vaccination

The suspension is filled in glass containers (type I or II), closed with chlorobutyl rubber stopper and sealed with an aluminium cap or flip-off-cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strains is justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

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

B. Method of Preparation of the Product

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

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

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with European pharmacopoeia monographs where these exist, or in-house specifications.

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 “Guideline on requirements for the production and control of immunological veterinary medicinal products” (EMA/CVMP/IWP/206555/2010-Rev2).

Seed lots have been produced as described in the relevant guideline.

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.

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 are in line with the relevant requirements; any deviation from these requirements is justified. The tests performed are as follows:

- Appearance
- Test on filling volume
- pH determination
- control of airtightness and viscosity
- Sterility: according to Ph. Eur. 2.6.1
- Potency and identity of porcine parvovirus and *Leptospira*
- Determination of formaldehyde and thiomersal concentration

The demonstration of the batch to batch consistency is based on the results of 3 batches of vaccine produced according to the method described in the dossier.

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 (2 years) when stored under the approved conditions (at 2-8° C).

The shelf life of the vaccine after broaching the immediate packaging is 10 hours. The claim of a 10 hours stability after broaching is based on the demonstration of stability for a batch broached and stored at 20-25 °C for 10 hours.

III. SAFETY ASSESSMENT

The studies were performed according to the recommendations of Regulation (EU) 2019/6 and the relevant guidelines.
All laboratory studies were completed according to the principles of Good Laboratory Practice. The methods used in the studies have been validated.

Laboratory trials

The trials have been performed in the target species (pigs). All animals used were seronegative to the individual antigens.

The safety of the intramuscular administration of one dose (12 seronegative gilts), a double dose (12 seronegative gilts), the repeated administration of one dose in gilts (43 seronegative gilts), sows (12 seronegative sows) and boars (19 seronegative boars) was demonstrated in laboratory trials. The pigs remained healthy after the vaccinations and no clinical/ systemic reactions in the vaccination groups were observed.
Injection site reactions were observed very commonly after each dose administration. The maximum size of a nodule seen was 10 cm, which could last 14 days. The associated pain disappears within 7 days post-vaccination.

Suigen Parvo L6 is an inactivated vaccine. There is no reason to suppose that it might adversely affect immunological functions of the vaccinated animal or its progeny. Therefore, specific tests on the impact of vaccination with Suigen Parvo L6 on immunological functions of the pigs were not performed.

Suigen Parvo L6 contains only inactivated antigens and thus the specific tests to be performed for live vaccines are not applicable.

No information is available on the safety of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

The adjuvant components (light mineral oil emulsion in water) and all excipients used are considered to be safe because they are mentioned in Table 1 of Commission regulation 37/2010 requiring no MRL insert status with reference to MRL regulations. Based on this information, no withdrawal period is proposed.

As the vaccine contains mineral oil, a warning to the user and to the physician is included in the SPC (Summary of Product Characteristics).
Overall, the vaccine proved to be well tolerated in the target species. The local reactions observed are described in the SPC and package leaflet under “adverse events”.

Field studies

A clinical trial was performed in three farms in Czech Republic including 90 seronegative gilts, 90 seronegative sows and 90 seronegative boars vaccinated according to the vaccination schedule. The safety follow up show that the vaccine complies with Ph. Eur. monograph 0965 Porcine parvovirosis vaccine section 2-3-1-2. Field studies as no pig shows abnormal body temperature or abnormal local reactions attributable to the vaccine.

The examination of the effects on reproductive performance shows that Suigen Parvo L6 can be safely used before insemination.
The results confirm the observations made in the laboratory studies.
The reactions observed are described in the SPC and package leaflet.

Ecotoxicity

The applicant provided an environmental risk assessment which showed that the risk for the environment and other animals and species posed by this vaccine can be considered as very low.

Warnings and precautions as listed in the product literature for its disposal are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

In laboratory conditions, efficacy of the vaccine against parvovirosis was evaluated in three challenge studies. The animals were vaccinated with two doses of vaccine 21 days apart.
The efficacy against a challenge with Parvovirus was based on the follow up of foetuses infection as demonstrated by birth of mummified foetuses and the presence of the virus detected by immunofluorescence.
In seronegative sows, the vaccine (containing minimum antigen content or 50% antigen content) complies with Ph. Eur. monograph 0965 requirements as more than 90 per cent of piglets from the control gilts (5 gilts) are infected and not fewer than 80 per cent of the total number of piglets from vaccinated gilts (14 gilts) are protected from infection after a challenge 62 days (40-50 days of pregnancy) after the second vaccination.

In seronegative boars (14 vaccinates and 5 controls) after a challenge 28 days after the second dose of vaccine, no virus was detected in vaccinates whereas all control boars were positive (mandibular, retropharyngeal lymph nodes and testicles).

In a third study, seronegative gilts (7 vaccinates and 7 controls) and boars (7 vaccinates and 7 controls) were vaccinated with two doses of vaccine 21 days apart and received a booster vaccination 150 days later for gilts and 112 days later for boars. The gilts were challenged with a parvovirus strain 63 days after the booster. No parvovirus was detected in the foetuses from vaccinated gilts whereas for the control animals parvovirus was detected in all foetuses.
A serological follow up showed that protective antibodies against parvovirus are present 140 days after the second vaccination.

In laboratory conditions, efficacy of the vaccine against leptospirosis was evaluated in two challenge studies.
Seronegative gilts were vaccinated 21 days apart and challenged 62 days (40-50 days of pregnancy) after the second vaccination with six different serovars of Leptospira (14 vaccinates and 7 controls per serovar). The efficacy against challenge with all Leptospira serovars was based on the follow up of clinical signs and of Leptospira infection as demonstrated by the presence of the Leptospira in blood, urine, liver and kidney samples of the piglets.
No clinical signs of leptospira infection were observed in vaccinates. Clinical signs occurred in the control groups for all *Leptospira* serovars. A statistically significant difference in the number of live and stillborn piglets, in the number of healthy and mummified/macerated piglets and in their birth weight was seen between the vaccinated groups and the control group. The protection against infection of piglets from the vaccinated mothers is 100% for all *L. interrogans* serovars. The vast majority of piglets from the unvaccinated mothers were infected with a respective serovar and leptospiras were detected in the urine, liver and kidneys (97 to 100% infection).

Seronegative boars were vaccinated 21 days apart and challenged 28 days after the second vaccination with six different serovars of Leptospira (14 vaccinates and 7 controls per serovar). The efficacy against challenge with all Leptospira serovars was based on the follow up of clinical signs and of Leptospira infection as demonstrated by the presence of the Leptospira in blood, urine, liver and kidney samples.
No clinical signs of leptospira infection were observed in vaccinates. Clinical signs occurred in the control groups for all *Leptospira* serovars.
No Leptospira (all serovars) was detected in the blood, urine, liver or kidneys of the vaccinated animals. Liver and kidney samples of all control animals were positive for the presence of respective serovars 28 days post-challenge. The control animals were positive for all Leptospira serovars in the blood from D2 to D11 after challenge. The duration of bacteremia was individual - it was observed in all subjects from D2 to D4 after challenge, on D11 after challenge it persisted only in some animals.
In urine Leptospira was detected in several individuals after challenge. The presence of leptospiras in urine was recorded between 14 and 28 days post challenge in almost all boars.

No study was performed to check the impact of maternal antibodies on the efficacy of the vaccine.

Field Trials

A clinical trial was performed in three farms in Czech Republic including 90 seronegative gilts and 90 seronegative sows vaccinated according to the vaccination schedule. A serological follow up of antibodies against Parvovirus and all Leptospira serovars was performed until 28 days after the second vaccination. Increase in antibodies against all antigens was observed after the first and the second vaccination.

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 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.

This section 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.