FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
14, rue Claude Bourgelat
Parc d'activités de la Grande Marche
CS 70611
35306 Fougères
FRANCE

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Suigen APP 2,9,11 emulsion for injection for pigs

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0465/001/DC
Name and pharmaceutical form	Suigen APP 2,9,11 Emulsion for injection
Applicant	VIRBAC
Active substance(s) and strength	Inactivated strains of: *Actinobacillus pleuropneumoniae* serovar 2 RP ≥ 1* *Actinobacillus pleuropneumoniae* serovars 9 and 11** RP ≥ 1* toxoid APX I RP ≥ 1* toxoid APX II RP ≥ 1* toxoid APX III RP ≥ 1* * RP = Relative potency (determined by ELISA method) in comparison with the reference serum obtained after vaccination of mice with a vaccine batch that has successfully passed the challenge test on the target species. ** The serovars 9 and 11 are determined together as one value because the potency test is not able to distinguish between these 2 antigen variants.
ATC Vetcode	QI09AB07
Target species	Pig
Indication for use	For active immunisation of pigs from 6 weeks of age onwards to reduce lung lesions and to reduce colonisation of the respiratory tract caused by pleuropneumonia due to *Actinobacillus pleuropneumoniae* serovars expressing the APX toxins I, II and III. Onset of immunity: 3 weeks after the second dose Duration of immunity: 20 weeks after the second dose

MODULE 2

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	Decentralised application in accordance with Article 8 of Regulation (EU) 2019/6
Date of completion of the original decentralised procedure	10/05/2023
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	DE

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

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 that may be observed are indicated in the SPC.
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. Composition

The vaccine contains inactivated whole-cell antigens of *Actinobacillus pleuropneumoniae* serovars 2, 9 and 11 and toxoids APX I, APX II and APX III, each at the relative potency ≥ 1 (determined by ELISA method in comparison with reference serum from mice vaccinated with batch which passed the challenge test on target species). The vaccine is adjuvanted with Montanide ISA 35 VG and contains excipients (thiomersal, saline solution containing sodium chloride and water for injections).

The container/closure system is made of glass vials or plastic bottles (HDPE) sealed with rubber stoppers and aluminium / flip-off caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choices of the adjuvant, vaccine strains, formulation, inactivating agent and presence of preservative are 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 practice from a licensed manufacturing site and 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 or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. monographs and European guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur. and other European guidelines; any deviation was adequately justified.

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

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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.

E. Control tests during production

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

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 tests include in particular:
- general characteristics of the finished product (appearance, volume filled, airtightness, pH and viscosity)
- identification of active substance and potency
- determination of residual content of the inactivation agent, formaldehyde, and content of the preservative thiomersal
- bacterial endotoxins
- residual toxicity
- sterility

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

G. Stability

Stability of the antigens is shown.
The shelf life of 2 years of the product is supported by data.
The in-use shelf-life of the broached vaccine, 10 hours, 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 (piglets aged 6 weeks) is demonstrated in a laboratory study.
Safety was assessed clinically, monitoring local and general reactions and rectal temperature in ten piglets. No control group was included.
The investigation was performed according to the recommendations in EU legislation and relevant guidelines were taken into account.
After vaccinations, no systemic reactions related to vaccination were observed in any of the laboratory safety studies. Local reactions in the form of a reddish lump (oedema) were observed in some animals and completely disappear 14 days after the vaccine administration.
The average temperature increase was in line with Ph. Eur. monograph 1360 (porcine actinobacillosis vaccine (inactivated)) requirements in all the laboratory safety studies (individual piglet range: 0 °C to 1.5°C; average increase range: 0.1°C to 0.4°C).

Overall, it was shown that the vaccine is well tolerated and adverse reactions that may occur, local reactions, are described in the SPC.

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

The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

The adjuvant and excipients used are Montanide ISA 35 VG, thiomersal and sodium chloride. Formaldehyde, used as inactivant, may be present as remnant. Whereas Montanide ISA 35 VG, formaldehyde and sodium chloride do not require MRL according to the Regulation EC 37/2010, thiomersal has a MRL set which is not exceeded in the final product.
Based on this information, no withdrawal period is proposed.

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

Field studies

A clinical trial was performed in three farms in Czech Republic including 90 piglets (60 vaccinated and 30 unvaccinated) 6 weeks old and vaccinated according to the vaccination schedule. The safety follow up shows that the vaccine complies with Ph. Eur. monograph 1360 safety requirements as no pig shows abnormal local or systemic reactions or dies from causes attributable to the vaccine, and as the average temperature increase for all pigs does not exceed 1.5 °C and no pig shows a rise greater than 2.0 °C.

The results confirm the observations made in the laboratory studies. The local and systemic reactions observed are described in the SPC and package leaflet as follows:

3.6 Adverse events

Very common (>1 animal / 10 animals treated):	*- Injection site induration*
Common (1 to 10 animals / 100 animals treated):	*- Injection site swelling** *- Injection site reddening* *- Elevated temperature***

* *with a diameter of 10 cm which spontaneously subsides within 3 to 14 days*
** *up to 0.8°C for 1 or 2 days after injection*

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative

or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No other adverse reactions were observed after an overdose administration (2 doses) of the veterinary medicinal product other than those described in section 3.6, except for a temporary elevation of body temperature up to 1.5 °C in some of the animals.

Ecotoxicity

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 no warnings are therefore required.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.B Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements including European Pharmacopoeia monograph 1360 “Porcine actinobacillosis vaccine”.
In laboratory conditions, efficacy of the vaccine was evaluated in three challenge studies (total of 98 piglets used). The efficacy against a challenge with *A. pleuropneumoniae* serovars 2 and 9, together expressing the three relevant APP toxins I, II and III was based on the follow up of lung lesions scores and

reisolation of *A. pleuropneumoniae* from the lungs, the tracheobronchial lymph nodes and the tonsils.
The vaccine complies with Ph. Eur. monograph 1360 requirements as the vaccinated pigs, when compared with controls, show lower incidence of typical lung lesions and re-isolation of *A. pleuropneumoniae* from the lungs, the tracheobronchial lymph nodes and the tonsils.
An onset of immunity of 3 weeks and a duration of immunity of 20 weeks have been demonstrated.
No impact of maternal antibodies on vaccination was shown.

Field Trials

A clinical trial was performed in three farms in Czech Republic including 90 piglets (60 vaccinated and 30 unvaccinated) 6 weeks old and vaccinated according to the vaccination schedule. In all farms, the average pulmonary score of the vaccinated group was significantly lower than the average pulmonary score of the control group. In two farms, significantly lower incidence of isolation of *A. pleuropneumoniae* from pulmonary tissue, tonsils and tracheobronchial lymph nodes was recorded in vaccinated animals compared with control groups of unvaccinated animals. In one farm, no significant difference was observed.

The following conclusions can be drawn from the results of the studies concerning onset of immunity, indications for use and immunisation scheme:

3.2 Indications for use for each target species

For active immunisation of pigs from 6 weeks of age onwards to reduce lung lesions and to reduce colonisation of the respiratory tract caused by pleuropneumonia due to Actinobacillus pleuropneumoniae serovars expressing the APX toxins I, II and III.

Onset of immunity: 3 weeks after the second dose
Duration of immunity: 20 weeks after the second dose

3.9 Administration routes and dosage

Before use, allow the vaccine to reach room temperature of 15 to 25 °C and shake well.
Administer intramuscularly (preferably to the paraauricular area) one dose (1ml) of the veterinary medicinal product according to the following regimen of vaccination.

From an age of 6 weeks, administer 2 doses at an interval of 3 weeks

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 is available on the veterinary Heads of Agencies website (HMAv).

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.