FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
14 rue Claude Bourgelat
Parc d'activités de la Grande Marche - Javené
BP 90203
35302 Fougères Cedex
France

" DECENTRALISED" PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0446/001/DC
Name and pharmaceutical form	Suigen Rota Coli Emulsion for injection
Applicant	VIRBAC
Active substance(s) and strength	*Rotavirus suis* inact. OSU 6 RP ≥ 1* *Escherichia coli* inact. O101:K99 (F5) RP ≥ 1* *Escherichia coli* inact. O147:K88ab and O149:K88ac (F4**) RP ≥ 1* *Escherichia coli* inact. K85:987P (F6) RP ≥ 1* *Escherichia coli* inact. O101:K99:F41 (F5, F41) RP ≥ 1* * Relative potency (determined by ELISA method) in comparison with reference serum obtained from mouse vaccinated with batch which satisfied in challenge test on target species. ** The fimbrial antigen variants F4ab and F4ac are determined together as one value because the potency test is not able to distinguish between these 2 antigen variants.
ATC Vetcode	QI09AL02
Target species	Pig (pregnant sow and gilt)
Indication for use	For the passive immunisation of newborn piglets by active immunisation of pregnant sows and gilts: - to reduce the clinical signs (neonatal diarrhoea) caused by enteropathogenic *Escherichia coli* expressing the fimbrial adhesins F4, F5, F6 and F41, - to reduce the clinical signs (vomitus, neonatal diarrhoea and anorexia) caused by porcine rotavirus and virus excretion in faeces. Onset of immunity: Passive immunity commences with suckling of piglets and is dependent on piglets receiving sufficient colostrum after birth.

	Duration of immunity: Protection is conferred during the first critical days of life to piglets that received colostrum from vaccinated dams.

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 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	20/05/2022
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 product contains inactivated *Rotavirus suis* strain OSU 6, *Escherichia coli* strains O101:K99 (F5), O147:K88ab and O149:K88ac (F4)[1], K85:987P (F6) and

[1] the potency test being not able to distinguish between these two fimbrial antigen variants F4ab and F4ac, they are determined together as one value

O101:K99:F41 (F5, F41), each at the relative potency ≥ 1 (determined by ELISA method in comparison with reference serum from mouse vaccinated with batch which satisfied in challenge test on target species). The vaccine is adjuvanted with Montanide ISA 25 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
- 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

Three batches of finished product, produced in 2001 according to the process described, are used for the safety laboratory trials.

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal (pregnant sows at the last month of pregnancy) and also in pigs with a weight of 25 – 30 kg is demonstrated in seven laboratory studies.
Safety was assessed clinically, monitoring local and general reactions and rectal temperature, in thirty pigs and thirty pregnant sows.
No control group was included.
The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines.
Overall, it was shown that the vaccine is well tolerated and adverse reaction that may occur, local reactions, are described in the SPC.

Effects on reproductive performance (recording the course of pregnancy, the delivery, the number of still births, live new born and health status of the live new born) were also examined in the same thirty pregnant sows. No comparison group was used. Results were showing no effect on the reproductive parameters. The vaccine is intended to be used in pregnant sows and gilts at the last stage of 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 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 25 VG, thiomersal and sodium chloride. Formaldehyde, used as inactivant, may be present as remnant. Whereas Montanide Isa 25 VG, formaldehyde and sodium chloride does 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 field study including 90 sows, 60 vaccinated and 30 unvaccinated was performed in three different breeds. Tested animals were vaccinated according to the vaccination scheme and followed for local and general reaction, rectal temperature and the pregnancy was monitored until delivery were the number and health status of the newborn piglets was evaluated.
The results confirmed the observations made in the laboratory studies.

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)

Four batches of finished product, produced in 2001 and two batches produced in 2006 according to the process described, are used for the efficacy laboratory trials.

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:
- Neonatal piglet colibacillosis vaccine inactivated monograph 0962.

The efficacy in the piglets was demonstrated by means of challenge trials and by serological investigation, too.

- Efficacy of the E.coli components:
The claims were supported in 4 studies performed between 2001 and 2006.

- one dose-finding study using twenty-five pigs which show the production of antibodies in twenty vaccinated animals (five were used as unvaccinated control).
- three laboratory studies with piglets from unvaccinated and vaccinated sows which were challenged with non-vaccinal E.coli strains after having suckled the colostrum.
A total of fifty-seven piglets from vaccinated mothers and thirty-nine piglets from unvaccinated mothers were used. After challenge, animals were followed for E.coli clinical signs. Results support the claims as indicated in the SPC and the vaccination and re-vaccination scheme.

- Efficacy of the rotavirus component :
The claims were supported in 3 studies performed between 1997 and 2006.

- one study using twenty-five piglets which show the production of antibodies twenty in vaccinated animals (five were used as unvaccinated control).
- two laboratory studies with piglets from unvaccinated and vaccinated sows which were challenged with a non-vaccinal rotavirus strain after having suckle the colostrum.
A total of 71 piglets from vaccinated mothers and 31 piglets from unvaccinated mothers were used. After challenge, animals were followed for rotavirus clinical signs and viral excretion in the faeces. Results support the claims as indicated in the SPC and the vaccination. Revaccination scheme was not supported.

Field Trials

A field study including 90 sows, 60 vaccinated and 30 unvaccinated was performed. Tested animals were vaccinated according to the vaccination scheme. Animals did not received a challenge. Serological analysis of blood samples showed a rise in antibodies levels after vaccination. The rise of the antibodies titres in the unvaccinated controls was insignificant.

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.