FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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France

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

14/11/2016

French agency for food, environnemental and occupational health safety– French Agency for Veterinary Medicinal Products
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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0158/001/
Name, strength and pharmaceutical form	Porcilis M Hyo Suspension for injection
Applicant	INTERVET INTERNATIONAL
Active substance(s)	*Mycoplasma hyopneumoniae* strain 11
ATC Vetcode	QI09AB13
Target species	Pigs
Indication for use	Active immunisation of finishing pigs from an age of 1 week onwards, to reduce the pulmonary lesions due to infection by *Mycoplasma hyopneumoniae*

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	New active substance, application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	21/12/2005
Date product first authorised in the Reference Member State (MRP only)	28/06/2004
Concerned Member States for original procedure	AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, HU, IE, IT, LT, LU, LV, MT, NL, NO, PL, PT, SE, SI, SK, UK

PRODUCT DETAILS	
Name of product	PORCILIS M HYO
Indication for use / target species	Inactivated vaccine indicated for the active immunisation of finishing pigs from an age of 1 week onwards, to reduce the pulmonary lesions due to infection by Mycoplasma hyopneumoniae
APPLICATION(S) DETAILS	
Type of application	Mutual recognition
Concerned member states	AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, HU, IE, IT, LT, LU, LV, MT, NL, NO, PL, PT, SE, SI, SK, UK
RMS DETAILS	
Member state responsible for preparing the assessment report	France
Date of preparation	02/01/06
Date product first authorised in the originating member state	28/06/2004
CONTACT WITH THE RMS	
Address	ANMV BP 90203 35302 Fougères CEDEX France

Analytical part

II.A. QUALITATIVE AND QUANTITATIVE PARTICULARS

The detailed composition is provided.
The particulars of the vials and controls performed are provided and conform to the regulation.
The choice of the adjuvant (dl-alpha-tocopheryl acetate), of the vaccine strain (*Mycoplasma hyopneumoniae* strain 11), of the formulation, of the inactivating agent, of the absence of preservative are justified. The inactivation process and the detection limit of the control of inactivation are correctly validated.

II.B. METHOD OF PREPARATION

The steps of the production process are detailed. The production is based on a seed lot system; the antigen is then inactivated and blended with the other ingredients (adjuvant and excipients) according to a straightforward process.
The production is performed in accordance with Good Manufacturing Practice (GMP).
Appropriate validation reports are provided to support the consistency of production and the quality of the control tests performed during production or on the final product. These reports focus mainly on the quantification of the antigen/active ingredient, adjuvant and inactivation process. Some minor modifications in terms of formulation and production site occurred during the development of the product; all were subjected to validation reports.

II.C. PRODUCTION AND CONTROL OF STARTING MATERIALS

All the starting materials used for the production of the vaccine are tested for quality and absence of extraneous agents (including TSE agents) according to the current regulation; any deviation was adequately justified.

II.D. CONTROL TESTS DURING PRODUCTION

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

II.E. CONTROL TESTS ON THE FINISHED PRODUCT

The tests performed on the final product conform to the prescriptions of the regulation; any deviation from these prescriptions is justified. The tests include in particular validated quantifications of the active ingredient and of the adjuvant.
The demonstration of the batch to batch consistency is based on the results of 4 batches produced according to the method described in the dossier. Other supportive data provided (results of 3 batches of the same formulation but containing also a preservative) confirm the consistency of the production process.

II.F. STABILITY TESTS

The stability of the finished product is demonstrated by a 39-month real time stability study, performed on 5 batches of vaccine. 1 batch was formulated using a 1-year old antigen and 4 batches were formulated using a recently produced antigen. All these batches were stored according to the specifications and tested at regular intervals until 39 months of storage (except 1 batch tested for 27 months) for potency, pH, adjuvant content and appearance; also the sterility was tested at the end of storage. The parameters recorded remain stable and conform to the release specifications.
These results justify a shelf-life of 36 months of the final product and 1 year for the antigen.

The claim of a 3-hour stability after broaching is based on the demonstration of the stability of the same parameters for a batch broached and stored 3 days at +30°C.

Safety

The vaccine is inactivated and formulated with a fixed amount of antigen, using a validated method of quantification; therefore, any batch of vaccine is suitable for the demonstration of the safety.

LABORATORY TRIALS

The safety of the administration of one dose, an overdose and the repeated administration of one dose is demonstrated in SPF piglets of the minimum age recommended for vaccination (1 week), 1 group of 10 piglets receiving 2 single doses at 3 three-week interval and 1 group of 10 piglets receiving a double dose of vaccine. The follow-up was performed according to the recommendations of the regulation (directive EC 2004/28 and guidelines volume 7A). The vaccine was well tolerated and the slight local and general reactions observed are reported in the SPC.

The examination of the reproductive performances was not performed because the vaccine is not intended for this category of animals.

There are no data suggesting a negative influence on the immune response of the vaccinated animal. Since generally no adverse effects of inactivated vaccines of this kind on the immune system are known and are not expected, no specific study was 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 in annex II of the MRL regulation. 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.

2009 update: additional clinical trials were performed to document the compatibility with Porcilis PRRS

FIELD STUDIES

One field safety study was performed, including 163 piglets vaccinated according to the recommended schedule and observed meticulously thereafter. No adverse reaction were recorded, except a statistically significant but low (0.1°C) rise in temperature in vaccinates compared to controls after the 1st injection.

The condemnation rate at the slaughter house was also assessed during an efficacy field study. The results confirm the safety of the vaccine, in particular at the injection site (none of the vaccinated pigs were condemned).

ECOTOXICITY

This is an inactivated vaccine, injected to the animal; unused vaccine is disposed according to national requirements. Therefore, the risk of possible ecological effects of the inactivated antigens, the adjuvant and the other substances present in the vaccine is considered as effectively zero.

CONCLUSIONS ON SAFETY

The laboratory and field studies provide a complete overview of the reactions to the vaccination, according to the recommendation for use:

- safety demonstrated at the youngest age recommended (1 week)
- safety demonstrated in SPF and conventional piglets of different breeds
- safety of the repeated injections
- local and general reactions carefully recorded

The vaccine is well tolerated, inducing no local reaction that would lead to condemnations or withdrawals, and no growth retardation. The mean rise in temperature after vaccination is very limited (+0.3°C in the laboratory study and +0.1°C in the field trial). The results are consistent from one trial to the other.
The vaccine is not a threat to the environment.
The overall safety is considered satisfactory.

Efficacy

The vaccine is inactivated and formulated with a fixed amount of antigen, using a validated method of quantification; therefore, any batch of vaccine is suitable for the demonstration of the efficacy.

A total of 11 trials (7 under laboratory conditions and 4 field studies) were performed to support the claims in term of efficacy.

2009 update: additional clinical trials were performed to document the compatibility with Porcilis PRRS

The efficacy was demonstrated :

- according to the recommended schedule (2 injections at a 3-week interval in all the trials)
- in the target species (finishing piglets in all the trials)
- at the minimum age recommended (all the trials except one)
- in SPF and in conventional piglets with Maternally Derived Antibodies (MDA)
- in laboratory studies and field trials

In terms of lung lesions, the results were consistent: a significant reduction of the lung lesion score was observed in all the trials except one (due to reduced lesions in controls), both under laboratory conditions and in field trials.
The onset of immunity was established by a controlled challenge 2 weeks after the 2nd injection of vaccine, both in SPF piglets and conventional piglets with MDA.
The duration of immunity was established by controlled challenges 19 and 20 weeks after the 2nd injection, both in SPF piglets and conventional piglets with MDA.
Detailed explanations and analysis of the difficulties encountered were provided (effect of MDA, analytical variations made on the vaccine, unexpected events during trials…); the initial (major) lacunae in the dossier were resolved by performing new trials. In particular, the results of the different trials were analysed leading to the conclusion that MDA have no impact on the efficacy of the vaccine.

Overall conclusion

The vaccine is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market.
The vaccine was demonstrated as safe using as recommended in the target species; the slight reactions observed are indicated in the SPC for the correct information of the user.
The efficacy of the vaccine was demonstrated according to the claims made in the SPC. The overall risk/benefit analysis is in favour of granting a marketing authorisation.

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 (http://mri.medagencies.org/veterinary/).

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: **Quality changes**

Summary of change	**Approval date**
additional site for secondary packaging	**2006**
change the manufacturing process of the active substance of Porcilis M Hyo	**2010**
Increase of the duration of storage of the active ingredient	2012

Safety / efficacy changes

Summary of change	**Approval date**
Compatibility with Porcilis PRRS IM	2010