

CAO-DVMP

H-1107 Budapest, Szállás u. 8.

DECENTRALISED PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

PORCILIS M HYO ID ONCE

HU/V/0109/001/DC

MODULE 1

PRODUCT SUMMARY

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|-------------------------------|--|
| EU Procedure number | HU/V/0109/001/DC |
| Name, and pharmaceutical form | Porcilis M Hyo ID ONCE emulsion for injection for pigs IT: Porsilis M Hyo ID ONCE HU: Porcilis M Hyo ID ONCE vakcina A.U.V. |
| Applicant | Intervet International B.V. Wim de Körverstraat 35 5831 AN Boxmer The Netherlands |
| Active substance(s) | Inactivated whole cell concentrate of <i>Mycoplasma hyopneumoniae</i> strain 11 |
| ATC Vetcode | QI09AB13 |
| Target species | Pigs |
| Indication for use | For the active immunisation of finishing pigs to reduce pulmonary lesions and the decrease in daily weight gain during the finishing period due to infection caused by <i>Mycoplasma hyopneumoniae</i> . Onset of immunity: 3 weeks after vaccination. Duration of immunity: 22 weeks after vaccination. |

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

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|--|---|
| 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 decentralised procedure | 28 th September 2011 |
| Date product first authorised in the Reference Member State (MRP only) | Not applicable |
| Concerned Member States for original procedure | Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Germany, Denmark, Estonia, Greece, Spain, France, Ireland, Iceland, Italy, Lithuania, Luxembourg, Latvia, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Slovakia, United Kingdom |

I. SCIENTIFIC OVERVIEW

The enzootic pneumonia of pigs is caused by *Mycoplasma hyopneumoniae*. This pathogen occurs worldwide in the intensively reared herds inducing economically important loss in the swine production, because the poor environmental and hygienic conditions facilitate the spread of this pathogen. The lesions in the lung caused by *M. hyopneumoniae* provide a basis for the secondary infections reducing the [yield-growth performance](#) and elevating the mortality ratio during the [finishingattening](#) period. The vaccination can be an effective tool in the control of the herd infection beside of the antimicrobial drugs and the improvement of the management.

Porcilis M Hyo ID ONCE is an inactivated *Mycoplasma hyopneumoniae* vaccine developed for „one shot” intradermal immunisation providing [at least 22 weeks duration of long immunity after vaccination from 2 weeks of age](#). ~~Porcilis M Hyo was the ground for this product as an inactivated vaccine against *M. hyopneumoniae* adjuvanted with dl- α -tocopheryl acetate. The contents of these two products vary in the amount of the antigen and the adjuvant. The minimum vaccination age is 2 weeks.~~ Porcilis M Hyo ID ONCE contains a mixture of dl- α -tocopheryl acetate and light liquid paraffin [as adjuvant improving its efficacy](#). Furthermore injection without needle [is friendlier for the animal and the user, also helps to avoid bacterial contamination under farm conditions](#).

II. QUALITY ASPECTS

A. Composition

| Name of substance | Quantity per dose (0.2 ml) |
|--|--|
| Active substances: <i>Mycoplasma hyopneumoniae</i> antigen concentrate | 1.0 PCVU ¹ inducing $\geq 6.5 \log_2$ Ab titre ² |
| Adjuvant: dl- α -tocopheryl acetate Light liquid paraffin | 2.5 mg 34.6 mg |
| Excipients: Polysorbate 80 Simethicone NaH ₂ PO ₄ .2H ₂ O Na ₂ HPO ₄ .2H ₂ O | |
| Diluent: Water for injections to | 0.2 ml |

1 PCVU = packed cell volume units

2 Mean antibody titre (Ab) in mice.

The 10 and 20 ml glass vials used for Porcilis M Hyo ID ONCE are made of type I glass. The vials are closed with type I nitril rubber stopper and sealed with a coded aluminium cap. The particulars of the containers are conform to the regulation.

B. Method of Preparation of the Product

Porcilis ~~Porcilis~~ M Hyo ID ONCE ~~is the achievement of the improvement of two existing vaccines Intervet vaccines. The product~~ is manufactured in accordance with the principles of good manufacturing practice and with the European Pharmacopoeia.

Since the immunogenicity of *M. hyopneumoniae* strain 11 was proved ~~in case of for the company's *M. hyopneumoniae* product Porcilis M Hyo, this strain became also the basis of Porcilis M1-IDM Hyo ID ONCE, but in an increased amount. Ensuring the sufficient quantity of the antigen the manufacturer introduced a "campaign-like" fashion way in the production. Consequently some changes became necessary in the manufacturing process, which were approved in case of Porcilis M Hyo.~~

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

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C. Control of Starting Materials

Starting materials listed in Pharmacopoeia

The starting materials used for the production of Porcilis M ~~Hyo ID ONCE4-ID~~, which are in a pharmacopoeia (~~Light liquid paraffin, dl- α -tocopheryl acetate, Polysorbate 80, Simethicone, Na₂HPO₄·2H₂O, NaH₂PO₄·2H₂O, Na₂S₂O₃·5H₂O, Acetic Acid, NaOH, Purified water, Water for injection~~), meet the requirements of the specific monographs. The viscosity of light liquid paraffin used is lower, ~~than the viscosity~~ determined in Ph. Eur. ~~in order to avoid difficulties results in problems~~ with respect to the administration of the vaccine.

Starting materials not listed in Pharmacopoeia

Starting materials of biological origin

The vaccine strain of *Mycoplasma hyopneumoniae* strain 11 was isolated from swine in 1981. Bacteria are handled in a seed-lot system.

Medium components of animal origin are treated according to the requirements of the European Pharmacopoeia. The suitability of components derived from „TSE-relevant animal species“ is certified by EDQM.

Starting materials of non-biological origin

The starting material of non-biological origin used during production is the inactivating agent used for the inactivation of the vaccine strain.

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

The applicant provided a risk analysis according to the TSE guidelines of the potential transmission of TSE via the biological starting materials used for the production of Porcilis ~~M4-ID-M Hyo ID ONCE~~. It can be concluded that the risk of contamination of the product with TSE agents is ~~effectively zero minimal~~.

E. Control Tests during Production

The validated control tests are included into the crucial steps of the manufacturing process.

F. Control Tests on the Finished Product

The finished product controls test the relevant parameters of the vaccine. The tests (determination of pH, appearance, final inspection, potency test, determination of dl- α -tocopheryl acetate concentration, safety test, sterility test) and their limits are considered appropriate to control the quality of the product.

Satisfactory validation data of the methods have been provided.

G. Stability

The shelf-life of the finished product filled in glass vial is 24 months at 2-8°C. The results of the quality control tests on the batches ~~justified~~ showed that all of the studied parameters remained above the requirements during the 27 months long storage at 2-8°C.

The in-use stability tests data support that the shelf-life of the product after first opening the immediate packaging is 3 hours.

H. Genetically Modified Organisms

Not applicable.

III. SAFETY ASSESSMENT

Safety studies were conducted according to the following, relevant requirements:

Commission Directive 2001/82/EEC as amended by Commission Directive 2009/9/EC,

European Pharmacopoea General Texts and Monographs:

5.2.6: Evaluation of safety of veterinary vaccines and immunosera,

0062: Vaccines for veterinary use,

2448: Porcine enzootic pneumonia vaccine (inactivated),

Guidelines:

III/3181/91: "General requirements for the production and control of inactivated mammalian bacterial and viral vaccines"

III/3362/92: "Specific requirements for the production and control of pig live and inactivated viral and bacterial vaccines"

In order to evaluate the safety of Porcilis M Hyo ID ONCE the following studies were performed:

Laboratory safety studies

The safety of one dose, an overdose and a repeated dose was examined.

The duration of the local reactions after administration of a single dose and an overdose were studied.

Field safety studies

Combined safety and efficacy study was performed to investigate the safety of one dose. Also safety data were collected from field efficacy studies.

According to the safety test results the vaccine can be applied safely to pigs from the age of 2 week, using an intradermal device. Single vaccination is recommended.

All the adverse reactions (increase of temperature, local and systemic reactions) observed during the laboratory and field studies are mentioned in the relevant SCP points.

The vaccine is not intended for use in pregnant swine therefore the examination of reproductive performance was not tested.

Specific studies to evaluate a possible adverse influence on the immunological functions were not carried out because these were not deemed necessary considering the nature of adjuvant, excipients and active substances included in this product.

Concerning the composition of the vaccine there is no need to carry out studies for residues. The withdrawal period is zero day.

Porcilis M Hyo ID ONCE is not recommended to be mixed or concurrently temporarily administered with any other vaccine or pharmaceutical product. Therefore no specific study was conducted. No interaction is known.

The estimation of the risk to the environment is effectively zero, as all hazards identified have a negligible likelihood.

The vaccine does not containing any genetically modified organisms.

IV. CLINICAL ASSESSMENT (EFFICACY)

Clinical Studies

Efficacy studies were conducted according to the following, relevant requirements:

Commission Directive 2001/82/EEC as amended by Commission Directive 2009/9/EC, European Pharmacopoea General Texts and Monographs:

0062: Vaccines for veterinary use,

2448: Porcine enzootic pneumonia vaccine (inactivated),

Guidelines:

III/3181/91: "General requirements for the production and control of inactivated mammalian bacterial and viral vaccines"

III/3362/92: "Specific requirements for the production and control of pig live and inactivated viral and bacterial vaccines"

In order to evaluate the efficacy of Porcilis M Hyo ID ONCE the following studies were performed:

Laboratory efficacy studies

Laboratory vaccination-challenge studies ~~were performed, i.e; laboratory~~ dose-response studies, ~~laboratory vaccination challenge,~~ onset of immunity study, ~~and laboratory vaccination challenge,~~ duration of immunity studies ~~were performed.~~

Field ~~safety-efficacy~~ studies

Combined safety and efficacy study.

Field efficacy studies in which also safety data were collected.

The trials have been performed according to detailed trial protocols; trial results were presented in precise details. In case of field trials statements of Good Clinical Practice are included in the study reports.

The tested parameters were the presence and extent of the pulmonary lung lesions, the prevalence and extent of pleuritis lesions ~~caused by *M. hyopneumoniae* infection,~~ the daily weight gain, morbidity and mortality during the studies.

According to the efficacy test results the following claims of the SPC were proved:

1. For the active immunisation of finishing pigs to reduce pulmonary lesions and the decrease in daily weight gain during the finishing period due to infection caused by *Mycoplasma hyopneumoniae*.
2. Onset of immunity is 3 weeks after vaccination.
3. Duration of immunity is ~~at least~~ 22 weeks after vaccination.
4. ~~Porcilis M Hyo ID ONCE is efficacious in commercial pigs, in the presence of maternally derived antibodies (MDA).~~
~~Vaccination resulted in a significant reduction of mean LLS even in a 25 % antigenic dose.~~

V. OVERALL CONCLUSION AND BENEFIT- RISK ASSESSMENT

Based on the data presented by the Applicant the qualitative and quantitative composition of vaccine Porcilis ~~M1-IDM Hyo ID ONCE, it's manufacturing processes and its properties,~~ as well as the methods to control product quality have been substantiated.

The safety of the product is considered sufficiently proven.

The efficacy claims made by the Applicant are supported by results of specific trials contained in the dossiers.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

None