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"MUTUAL RECOGNITION DECENTRALISED" PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

INGELVAC MYCOFLEX

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0203/001/MR
Name, strength and pharmaceutical form	INGELVAC MYCOFLEX Suspension for injection for pigs
Applicant	BOEHRINGER INGELHEIM Vetmedica GmbH Binger Str. 173, D-55216 Ingelheim / Rhein Germany
Active substance(s)	Mycoplasma hyopneumoniae, J strain
ATC Vetcode	QI09AB13
Target species	Pigs (fattening pigs or future breeders until first reproductive service)
Indication for use	For active immunisation of pigs from 3 weeks of age to reduce lungs lesions following infection with *Mycoplasma hyopneumoniae* Onset of protection occurs by 2 weeks post vaccination and lasts for at least 26 weeks

MODULE 2

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

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (http://mri.medagencies.org/veterinary/) .

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual recognition application in accordance with Article 32 (2) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition decentralised procedure	25/03/2009
Date product first authorised in the Reference Member State (MRP only)	17/07/2008
Concerned Member States for original procedure	AT,BE,BG,CY,CZ,DE,DK,EE,EL,ES,HU,IE,IT,LT, LU,LV,NL,PL,PT,RO,SE,SI,SK,UK

I. SCIENTIFIC OVERVIEW

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 slight reactions 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 *Mycoplasma hyopneumoniae* J strain with a minimum quantity per dose of 1.00 RP and a maximal relative potency of 4.61 RP. RP represents a relative potency by ELISA test by comparison with a reference vaccine which has been demonstrated efficacious.
The product also contains the following adjuvants : carbomer.

The containers consist of 10, 50,100 and 250 doses high-density polyethylene bottles. The closure is a siliconised chlorobutyl rubber stopper, with a lacquered aluminium ring seal. The particulars of the containers and controls performed are provided and conform to the regulation.

The choices of :

- the adjuvant, aqueous non-virucidal adjuvant,
- the vaccine strain, already included in INGELVAC M HYO,
- and the formulation, which allows to guarantee safety of the vaccine (maximum dose of 4.61 RP) as well as efficacy of the vaccine (minimum dose of 1 RP)

are adequately 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.

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

C. Control of Starting Materials

The active substance(s) is an inactivated strain of *Mycoplasma hyopneumoniae*. The active substances are manufactured in accordance with the principles of good manufacturing practice.
The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

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 Ph. Eur. guidelines; any deviation was adequately justified.

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

Scientific data 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 visual appearance, pH, residual formaldehyde, potency, titration of adjuvant, safety test, sterility and control of inactivation.

The demonstration of the batch to batch consistency is based on the results of 8 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

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 of 24 months when stored under the approved conditions.

In-use stability data have been provided establishing that the product can be kept and used within 10 hours after broaching.

III. SAFETY ASSESSMENT

Details of the batches of INGELVAC MYCOFLEX used in laboratory safety studies were provided. These batches were formulated to contain the maximum target antigenic content.

Laboratory trials

The safety of the intramuscular administration of one dose, an overdose and the repeated administration of one dose in the target species was demonstrated.

The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. Laboratory studies to evaluate the safety of a single doe, a repeated dose and an overdose were performed in 3 weeks old pigs demonstrate safety of the vaccination. Transient swellings may be observed at the site of injection (up to 4 cm in diameter, associated with redness of the skin) up to 5 days and transient hyperthermia (mean of 0.8°C) may be observed up to 20 hours after vaccination. These reactions are described in the SPC.

Safety of the vaccination on reproductive performance has been examined. The vaccine is not intended for this category of animals during the reproduction service. This is underlined in the SPC.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny.
The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.
The adjuvant and excipients used are included in Annex II of the MRL regulation. Based on this information, no withdrawal period is proposed.

Data have been provided that demonstrate that the vaccine can be safely mixed with INGELVAC CIRCOFLEX before administration. No specific assessment of the interaction of this product with other medicinal product was made. Appropriate claims are presented in the SPC.

Field studies

3 field studies have been performed including more than 1000 vaccinated pigs from 2 weeks of age. These studies support safety of the vaccination with INGELVAC MYCOFLEX such as observed in laboratory conditions.

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 the risk of environment from the use of INGELVAC MYCOFLEX is negligible. No warnings in regards to environmental exposure from the use of the vaccine are therefore required.

Warnings and precautions as listed on 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)

IV.B Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements which show onset, duration of immunity and efficacy face to maternal derived antibodies in pigs of the minimal age receiving a vaccine formulated to contain the minimal antigenic dose.

Minimal protective dose has been validated through a dose-response study conducted in groups of seronegative pigs receiving vaccines with increasing amounts of antigen.
The onset of immunity was established after a challenge of seronegative pigs 2 weeks after vaccination, vaccinated and control animals were challenged with a virulent strain of *Mycoplasma hyopneumoniae.* Significant reduction of the lungs lesion score was noted after challenge. The same type of study was performed to establish the duration of immunity 26 weeks after vaccination. Interference of maternal derived antibodies was assessed in a study including seropositive animals vaccinated or not and seronegative animals vaccinated or not. Analysis of data confirm that maternal derived antibodies do not play major role in term of protection against *Mycoplasma hyopneumoniae* and do not interfere with vaccine take.
Compatibility of this vaccine with INGELVAC CIRCOFLEX has been satisfactorily addressed in safety and efficacy studies.

Field Trials

The applicant has conducted 5 field studies including about 1000 pigs vaccinated with INGELVAC MYCOFLEX such as recommended. Data confirm the efficacy of the vaccination in field conditions in reducing lungs lesions at slaughter in vaccinated pigs.

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 (http://www.hma.eu/vmriproductindex.html).

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**
change of the volume of the vials (in order to be able to mix INGELVAC MYCOFLEX and INGELVAC CIRCOFLEX in the vaccine vial)	2012
inclusion of in-use stability claim of 10 hours	2012
Extension of shelf-life from to 24 months	2016

Safety/efficacy changes

Summary of change	**Approval date**
inclusion of a compatibility statement with vaccine INGELVAC CIRCOFLEX (both vaccines can be mixed before administration).	2011