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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0350/001/DC
Name, strength and pharmaceutical form	INMEVA suspension for injection
Applicant	LABORATORIOS HIPRA, S.A.
Active substance(s)	Inactivated *Chlamydia abortus*, strain A22 Inactivated *Salmonella enterica* subsp. *enterica* serovar Abortusovis, strain Sao
ATC Vetcode	QI04AB
Target species	Sheep (ewe)
Indication for use	For active immunisation of animals to reduce clinical signs (abortions, stillbirth, early mortality and hyperthermia) caused by *Chlamydia abortus*, abortions caused by *Salmonella* Abortusovis and to reduce shedding of both pathogens from infected animals.

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MODULE 2

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

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MODULE 3

PUBLIC ASSESSMENT REPORT

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	04/2019
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Denmark, Germany, Greece, Hungary, Ireland, Italy, Luxemburg, The Netherlands, Poland, Portugal, Romania, Spain, Sweden, United Kingdom

I. SCIENTIFIC OVERVIEW

INMEVA is a bivalent inactivated vaccine for active immunisation of ewes to be used before gestation in order to reduce reproductive disorders caused by infection by *Chlamydia abortus* and *Salmonella* Abortusovis and to reduce shedding of both pathogens from infected animals. Vaccination before mating – 2 vaccine doses 3 weeks apart by SC route as basic vaccination and 1 dose for subsequent re-vaccination as described in the SPC - allows protection during the gestation period.

The vaccine was classified and assessed as MUMS (Minor Use Minor Species).

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.

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II. QUALITY ASPECTS

A. Composition

The product contains inactivated *Chlamydia abortus* strain A22 and inactivated *Salmonella* Abortusovis strain Sao [at least 1 relative potency as established using ELISA against a reference vaccine for each strain]. It is adjuvanted with aluminium hydroxide and DEAE dextran. The excipients are as follows: simethicone emulsion and PBS solution.

The container/closure system consists of polyethylene terephthalate vials, which are closed with rubber stoppers and sealed with anodised aluminium caps.

Cardboard box with 1 vial of 5 doses of vaccine.
Cardboard box with 1 vial of 25 doses of vaccine.
Cardboard box with 1 vial of 50 doses of vaccine.
Cardboard box with 1 vial of 125 doses of vaccine.

The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strains, formulation, inactivation processes and the absence of preservative are justified.

The inactivation processes 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.

C. Control of Starting Materials

The active substances are inactivated *Chlamydia abortus* and *Salmonella* Abortusovis. They comply with an in-house specification, adequate to control the quality of the material. 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.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of

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extraneous agents according to the Ph. Eur. and guidelines; any deviation was adequately justified. Starting materials of non-biological origin used in the production comply with the European Pharmacopoeia.

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

A variety of control tests are performed during production. They are described and the results of 2 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. The tests include those for appearance, pH, identification and potency of the vaccine strains, sterility, quantification of adjuvants, bacterial endotoxins.
The demonstration of the batch-to-batch consistency is based on the results of 2 batches produced according to the method described in the dossier.

G. Stability

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

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 10 hours.

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III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of an overdose and the repeated administration of one overdose in the target animal is demonstrated. It was concluded that the product had an acceptable safety profile. Transient hyperthermia and common local reactions at the injection site are observed that disappear spontaneously after 2 weeks. These reactions are described in the SPC.

14Pregnant ewes have been vaccinated during the gestation period (first dose during the 2nd third of gestation followed by a 2nd dose 2 weeks later). No adverse effect of the vaccination on gestation, parturition and progeny has been observed.

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.

The adjuvant and excipients used are either allowed substances included in table 1 of Commission regulation 37/2010 or are considered as not falling within the scope of Regulation 470/2009. 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.

Field studies

Field safety studies have not been performed with this vaccine. As safety laboratory studies show no safety risk, it has been considered – in accordance with MUMS guideline – that a study was not required.

Ecotoxicity

The applicant provided phase I environmental risk assessment in compliance with the relevant guideline, which showed that no further assessment is required. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

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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.

4 studies have been conducted to investigate efficacy of the vaccination.

Efficacy of the basic vaccination (2 administrations)

animals	vaccination	Experimental infection	RESULTS
Ewes from 5 months of age seronegative	Vaccination of 92 ewes receiving first vaccine dose 5 weeks prior to mating and 2nd dose 21 days later		
See above	17 vaccinated ewes + 20 controls ewes	*Salmonella* Abortusovis administered at the moment of maximum risk during the gestation	Significant reduction of abortion and bacteria excretion in vaccinated ewes
See above	19 vaccinated ewes + 21 control ewes	*Chlamydia abortus* administered at the moment of maximum risk during the gestation	Significant reduction of abortion, stillborn lambs or neonatal mortality and bacteria excretion in vaccinated ewes

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Efficacy of the single booster vaccination

28 Pregnant ewes from previous vaccination study (see above)	Single booster vaccination 1 year after basic vaccination		
See above	14 vaccinated ewes + 14 control ewes	*Salmonella* Abortusovis administered at the moment of maximum risk during the gestation	Significant reduction of abortion and bacteria excretion in vaccinated ewes
See above	13 vaccinated ewes + 13 control ewes	*Chlamydia abortus* administered at the moment of maximum risk during the gestation	Significant reduction of abortion, stillborn lambs or neonatal mortality and bacteria excretion in vaccinated ewes

Field Trials

Field efficacy studies have not been performed with this vaccine. As efficacy laboratory studies allow to establish efficacy of the vaccination, it has been considered – in accordance with MUMS guideline – that an additional study was not required.

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.

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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.

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